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ABSTRACT BOOK

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ORAL PRESENTATIONS

SESSION 1 Still's Disease, MAS, MIS-C

PReS25-ABS-1375

REAL-LIFE TREATMENT STRATEGIES FOR REFRACTORY STILL'S DISEASE: RESULTS FROM A WORLDWIDE SURVEY, THE METAPHOR PROJECT

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Introduction: The outcome of Still's disease (SD) has significantly improved in the past 15 years due to new therapeutic options[1], treatment strategies based on early biologic initiation (window of opportunity)[2,3] and a treat-to-target approach[4]. Nonetheless, a substantial proportion of patients still experiences a refractory course, severely impacting their quality of life. Recent reports have also highlighted an increasing occurrence of severe SD-associated lung disease (SDLD)[5]. Treatment strategies in these cases are not standardized and are affected by medication availability and clinician experience.

Objectives: To describe current treatment practices and major unmet needs, fostering a uniform approach to refractory SD.

Methods: As part of the METAPHOR project, a PReS/PRINTO initiative to optimize therapy in SD and Macrophage Activation Syndrome (MAS), a global survey on refractory SD treatment was developed, with the following proposed subtypes: 1) persistent arthritis, 2) recurrent/refractory MAS and 3) SD-LD. Topics were selected by 22 expert pediatric rheumatologists, including 1 patient representative and 1 adult rheumatologist. The survey covered demographic data, clinical practice insights and a patient-focused section on unmet needs. International physicians part of the PReS/PRINTO network together with adult rheumatologists involved in SD care were invited to complete the web-survey between 3/12/24 and 14/2/25.

Results: A total of 206 physicians completed the survey, predominantly pediatric rheumatologists (91%), from 56 countries. Methotrexate was the most common 1st-line choice for SD-refractory arthritis, followed by anti-TNF agents and intra-articular steroids. JAK inhibitors (JAK-i) were considered mainly as 2nd- or 3rd-line option. If systemic symptoms cooccurred, 62% of respondents would modify their strategy, favoring methylprednisolone (MPN) pulses, JAK-i and ciclosporin. In SD patients with recurrent/refractory MAS, ciclosporin, anakinra, and MPN pulses were the most frequently selected medications. Treatment decisions were mainly guided by clinical severity, inflammatory markers, history of ICU admission

and concomitant complications. Biomarkers played a minor role, partly due to limited access, reported by 22% of clinicians. For SD-LD, 41% would continue ongoing biologics, 30% withdraw and 29% decide case by case. Factors influencing withdrawal included persistent disease activity, history of adverse reactions and impending MAS. HLA genotyping was rarely considered relevant. The most used 1st-line agents for SD-LD included JAK-i, mycophenolate mofetil, and ciclosporin and only 8% would add Pneumocystis Jiroveci prophylaxis. Most respondents (82%) would consider Hematopoietic Stem-Cell Transplantation (HSCT) in difficult-to-treat SD patients, particularly for refractory MAS or SD-LD. **Conclusion:** Management for refractory SD is widely heterogeneous and varies by phenotype. JAK-i are the most commonly used agents alongside standard therapies and HSCT is increasingly considered a potential option, especially for refractory MAS and SD-LD. A consensus effort is essential to refine the definition and identify optimal treatment strategies for refractory cases.
References: 1. PMID 37923864; 2. PMID 24623686; 3. PMID 30848528; 4. PMID 39317417; PMID 31562126

PReS25-ABS-1481

THERAPEUTIC STRATEGIES IN NEWLY DIAGNOSED STILL'S DISEASE: REAL-LIFE CLINICIANS' CHOICES FROM THE METAPHOR PROJECT WORLDWIDE SURVEY

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Introduction: Despite continuous advances in care and the recent publication of updated international recommendations, relevant discrepancies in the management of Still's disease (SD) may still exist, mainly due to the heterogeneity of its clinical expression and the differences in access to medications worldwide.
Objectives: To assess current intial treatment strategies in SD worldwide, and to identify factors influencing clinical decision-making, particularly related to different settings and clinical scenarios.
Methods: As part of the METAPHOR project, a PReS/PRINTO initiative to optimize treatment in SD and macrophage activation syndrome, a global survey on SD treatment was developed based. Topics were selected by 22 experts, including 1 patient representative and 1 adult rheumatologist. The survey included demographic data, clinical practice insights, a patient-led section on unmet needs. International physicians part of the PReS/PRINTO network and adult rheumatologists involved in SD care were invited to complete the anonymous online survey (Dec 3, 2024–Feb 14, 2025).
Results: A total of 206 clinicians, mainly pediatric rheumatologists (91%), from 56 countries completed the survey. In newly diagnosed SD patients without MAS, 34% of respondents would initiate anti-IL1/IL6 biologic without glucocorticoids (GCs); the rest would use GCs alone (24%) or in combination with biologics (42%). Factors favoring GCs use included severe pericarditis (64%), severe arthritis (55%), and refractory disease risk factors (16%), as hyperferritinemia, lung involvement,

early onset and Trisomy 21. Anakinra was the most frequently used biologic in 1st line (59%), followed by Tocilizumab (25%). Only 1.5% reported unavailability of any anti-IL1/IL-6 therapy. Factors driving anakinra's choice were safety (72%),

cost (41%), and predominant systemic phenotype (73%), while Tocilizumab was chosen for compliance (56%) and arthritisdominant profile (80%). Difficult access to medication influenced decisions for Rilonacept (67%), Canakinumab (27%), Anakinra (17%); Tocilizumab was rarely unavailable (1.5%). In systemic-predominant SD, clinicians used NSAIDs (50%), GCs (46%), GCs pulses (42%), and Anakinra (45%) as first-line options. Second-line strategies included Tocilizumab (39%), GCs (31%), Anakinra (29%), GCs pulses (22%), and MTX (21%), while Tocilizumab (37%), JAK inhibitors (29%), and cyclosporin (24%) were the most selected options as third-line therapies. In SD patients with a prominent articular involvement at onset, half of the respondents would not change their therapeutic approach. Physician who modified thor strategy would use as a first line therapy GCs (47%), oral steroids (44%), Tocilizumab (39%), MTX (34%), and intra-articular steroids (31%) respectively. Second-line choices were mostly Tocilizumab and MTX (~40%).
Conclusion: Still's disease still represents a therapeutic challenge, mainly due to its heterogeneity in clinical expression. Our data reveals significant differences in treatment approaches, driven by clinical phenotype and drug availability. Future research is essential to optimize clustering of patients to foster tailored target treatments, while ensuring equitable access to effective therapies worldwide.

PReS25-ABS-1396

ANALYSIS OF CLINICAL PARAMETERS AND TRANSCRIPTIONAL BIOMARKERS FOR THE PREDICTION OF IL-1 INHIBITOR TREATMENT NON-RESPONSE IN THE CARRA FIRST-LINE OPTIONS FOR SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS TREATMENT (FROST) STUDY

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Introduction: Many patients with systemic juvenile idiopathic arthritis (sJIA) will experience incomplete response to firstline interleukin-1 (IL-1) inhibitors, however, the biologic mechanisms underlying treatment non-response are not well understood.
Objectives: We sought to characterize the clinical phenotype, inflammatory cytokines, and gene expression profile of responders and non-responders to IL-1 inhibitors in a real-world cohort of new-onset sJIA patients in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry.
Methods: We identified all patients in the FROST study who were started on IL-1 inhibitors. Responders were classified as those patients who fulfilled either the Wallace criteria of clinically inactive disease (CID), or criteria of low disease activity (LDA; cJADAS < 2.5 without fever or corticosteroid use) after 6 months. Children who did not fulfill these requirements were characterized as non-responders. In all patients with available serum or plasma, IL-18 and CXCL9 levels were measured using an Ella assay, and other cytokine and inflammatory protein levels were obtained using a custom Luminex panel. Candidate gene targets for a custom Nanostring panel were selected based on data from prior studies.
Results: Among the 61 patients who received IL-1 inhibitors, we identified 34 responders and 27 non-responders. A higher baseline physician global score was observed in non-responders (mean 7.2 vs 5.5; p = 0.006). Responders trended towards a higher neutrophil count at baseline, but this was not significant (mean 11,560 cells/µL vs 9,160; p= 0.09). There were no significant differences in the baseline joint count, arthritis joint count at one month, or in days to initiation of therapy between responders and non-responders. There were 30 total patients who received IL-1 inhibitors with existing baseline biosamples; of these, 17 were responders and 13 were non-responders. At baseline, median IL-18 levels were higher in

non-responders (46,823 pg/mL; range 4,612-157,713) vs responders (23,435; range 1,485- 150,479), but this difference was not significant (p=0.65). Luminex data revealed decreased baseline CCL25 (p=0.019) and MCP-1 (p=0.05) levels in nonresponders when compared to responders. Finally, we performed blood transcriptional profiling using Nanostring. A 29 gene score previously associated with response to canakinumab showed no significant difference between responders and non-responders. However, baseline gene expression levels of genes associated with canakinumab non-response – *STAB1*, *CD163*, and *VCAN* – were significantly higher in non-responders compared to responders. A composite geomean score of these three genes >545 yielded 78% sensitivity and 93% specificity for IL-1 inhibitor non-response.
Conclusion: In the FROST cohort, non-responders to IL-1 inhibitors by CID or LDA had higher baseline physician global scores and significantly decreased CCL25 and MCP-1 levels compared to responders. We also validated a previously described IL-1 non-response gene expression signature of *STAB1*, *CD163*, and *VCAN*. These findings support the hypothesis that subgroups of sJIA patients with different immunologic phenotypes exist, and that immune phenotyping could assist in predicting IL-1 inhibitor non-response.

PReS25-ABS-1247

FLIPPING THE SWITCH –CLASSICAL COMPLEMENT ACTIVATION CLOSELY LINKED TO IFN-SIGNALLING IN STILLS DISEASE

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Introduction: Stills disease (SD) is an autoinflammatory syndrome characterized by severe innate immune dysregulation. The complement system, an essential component of innate immunity, can drive inflammatory cascades through the classical, lectin or alternative pathway. Although complement activation has been implicated in various inflammatory disorders, its involvement in SD remains largely undefined. Elucidating the role of complement in SD may provide valuable insights into disease mechanisms and uncover novel therapeutic targets.
Objectives: To determine whether the complement pathway is activated in SD patients.
Methods: RNA was extracted from whole blood of SD (active n=27, inactive n=26) and active non-systemic juvenile idiopathic arthritis (JIA) patients (n=538). Gene expression of classical complement components C1QB, C1QC and IFNregulated genes (IFN-score) was quantified by NanoString. Additionally, RNA sequencing was conducted on sorted monocytes from SD patients (active n=7, inactive n=7). Inflammatory mediators (IL-18, CXCL9, CXCL10) and complement activation products (C1q, C3a, C5a) were quantified using Luminex and ELISA. Classical complement activity was evaluated in sera of SD (active n=32, inactive n=66) and non-systemic JIA patients (active n=12, inactive n=12). To explore potential mechanisms underlying complement activation, in vitro experiments were conducted to assess which inflammatory stimuli could induce C1q production in monocytes.
Results: RNA expression of classical complement protein C1q is upregulated in both whole blood and isolated CD14+ monocytes from active SD patients compared to those with inactive disease (NanoString: *C1QB* 43 vs. 11, p<0.01; *C1QC* 24 vs. 6, p<0.01; Monocytes: *C1QB* $\log_2$FC 3.6, p<0.01; *C1QC* $\log_2$FC 3.9, p<0.01) and to active non-systemic JIA patients (*C1QB* 43 vs 15, p<0.01; *C1QC* 24 vs 8, p<0.01). Moreover, whole blood C1QB and C1QC expression levels positively correlate with the IFN-score (r=0.34, p=0.01), plasma levels of IL18 (r=0.5, p<0.01) and IFN related chemokines CXCL9 (r=0.4, p<0.01) and CXCL10 (r=0.6, p<0.01) in SD. Protein analysis revealed elevated levels of C1q, C3a, and C5a, as well as enhanced classical complement activity in active SD compared to inactive SD (94% vs 74%, p<0.01) and active non-systemic JIA patients (94% vs 81%, p=0.02). Furthermore, in vitro stimulation of healthy control monocytes with IFNγ robustly and specifically induces

C1q mRNA expression. Flow cytometry analysis confirmed that IFNγ stimulation promotes the emergence of a distinct monocyte subset characterized by high C1q expression.
Conclusion: Our findings indicate activation of the classical complement pathway in SD, closely linked with IFN-signalling. Obtaining a better understanding of the role of the complement system, particularly the role of C1q-high monocytes, may open novel avenues for personalized therapeutic approaches in SD.

PReS25-ABS-1291

CLINICAL AND CELLULAR PHENOTYPE IN AN MTORC1-DRIVEN MOUSE MODEL OF STILL'S DISEASE–ASSOCIATED MACROPHAGE ACTIVATION SYNDROME

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Introduction: Macrophage activation syndrome (MAS) is a life-threatening hyperinflammatory syndrome occurring in 1030% of pediatric patients with Still's disease and is characterized by a high activation of mechanistic target of rapamycin complex 1 (mTORC1). Accordingly, overactivation of mTORC1 can induce experimental MAS in mice.
Objectives: To characterize the cellular phenotype of murine MAS by inducible deletion of tuberous sclerosis complex 2 (Tsc2), a negative regulator of mTORC1. With this leading to mTORC1 overactivation in hematopoietic cells, we aimed to assess the value of this model for studying human MAS.
Methods: Tsc2 deletion was induced in male and female Mx1-Cre^{+} Tsc2 fl/fl mice (C57BL/6, 4-11 weeks of age) by intraperitoneal injection of 250 µg poly(I:C) on days 0, 2, and 4. Tissues were collected and analyzed on day 25 by flow cytometry, complete blood count, histology and Olink-based cytokine profiling. In vivo MRI scans of the brain were conducted in seven males on days 0, 4 and 24 as an exploratory study after findings in brain histology.
Results: Mx1-Cre^{+} Tsc2 fl/fl mice of all age groups and both sexes developed hemophagocytosis in bone marrow and hepatosplenomegaly with disruption of normal lymphoid follicle formation in the spleen – phenotypes not apparent in poly(I:C)-treated Mx1-Cre^{-} littermate controls. While anemia was detected in the blood, leukocytopenia was observed only in the bone marrow. Weight loss and joint swelling were not observed. By flow cytometry, F4/80^{+} macrophages were highly increased in bone marrow and Ly6G^{+} neutrophils were increased in the spleen. Pro-inflammatory Ly6C^{hi} CX3CR1^{-} monocytes were increased, whereas Ly6C^{lo} CX3CR1^{+} monocytes were diminished in both marrow and spleen. Natural killer (NK) cell proportions were lower in both compartments. Cytokine analysis in serum from 24 mice revealed an upregulation of macrophage-associated inflammatory markers such as CCL4, CCL5 and CXCL1, while the anti-inflammatory cytokine CCL22 was decreased. Histology of brain tissue revealed a greater abundance of F4/80^{+} macrophages, particularly in the choroid plexus. However, hydrocephalus or other evidence of CNS-MAS was not observed by MRI.
Conclusion: mTORC1 overactivation induced by Tsc2 deletion replicates key cellular features of human MAS including hemophagocytosis in bone marrow and myeloid cell expansion. These findings support this model's relevance for investigating mTORC1-driven hyperinflammation in Still's disease and MAS.
References: 1. Huang, Z., et al., *mTORC1 links pathology in experimental models of Still's disease and macrophageactivation syndrome.* Nat Commun, 2022. **13**(1): p. 6915.

PReS25-ABS-1638

TRANSPOSABLE ELEMENT EXPRESSION AND CYTOKINE PROFILING IN MIS-C PATIENTS: INSIGHTS FROM TELOMERE-TOTELOMERE GENOME ALIGNMENT

B. Jenko Bizjan [1 2,*], L. Leko [1], A. Markez [1], M. Rob [1], T. Tesovnik [1 2], B. Vrhovsek [1], J. Kovac [1 2], N. Emersic [3], M. Z. Avramovic [2 3], T. Avcin [2 3]

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Introduction: Multisystem Inflammatory Syndrome in Children (MIS-C) is characterized by severe hyperinflammation following SARS-CoV-2 infection; however, underlying genomic and immune mechanisms remain incompletely understood.
Objectives: This study aimed to investigate differential expression of transposable elements (TEs) and cytokine profiles during MIS-C flare compared to remission phases, using comprehensive genomic alignments.
Methods: Bulk RNA sequencing was performed on blood samples from pediatric MIS-C patients (n=18) during flare and remission. Differential TE expression analysis was conducted using both hg38 and the comprehensive Telomere-

toTelomere (T2T) reference genome, facilitating identification of previously inaccessible repetitive genomic regions. Cytokine levels were measured using multiplex assays, and statistical significance was assessed using the Wilcoxon test with FDR adjustment.
Results: We identified significant upregulation (log2 fold change ≥1) of endogenous retroviruses (ERV1, ERVL, ERVK families), LTR retrotransposons, and LINE elements during MIS-C flares compared to remission. Notably, LTR161-ERV1 and LTR108e_Mam-ERVL were among the highest expressed elements (log2FC=2). T2T alignment exclusively uncovered additional TE transcripts, including unknown and poorly characterized elements (e.g., UCON61, UCON63), further emphasizing genomic regions traditionally underrepresented in reference genomes. Elevated TE expression coincided with significantly increased cytokine levels, including IL-6 (median flare: 484.81 vs remission: 2.40 pg/mL, adjusted p=0.019), IFN-γ (median flare: 2184.48 vs remission: 70.71 pg/mL), VEGF (median flare: 179.74 vs remission: 134.78 pg/mL, adjusted p=0.024), and CCL2 (median flare: 531.99 vs remission: 219.58 pg/mL, adjusted p=0.024). These cytokines are known to promote inflammatory responses and immune cell recruitment, potentially contributing to the transcriptional activation of TEs observed during MIS-C flares.
Conclusion: Comprehensive genomic analysis using the T2T reference genome revealed significant differential expression of transposable elements uniquely associated with MIS-C flares, strongly correlating with elevated cytokines such as IL-6, IFN-γ, VEGF, and CCL2. These findings highlight a potential interplay between cytokine-driven inflammation and epigenetic activation of TEs, suggesting novel mechanistic insights into MIS-C pathology and offering new avenues for diagnostic biomarker development and targeted therapies.
References: Grants This study was supported by grants from the Slovenian Research Agency (J3-50115, J3-50122), Interreg Concerto, and SLING.

SESSION 2 Non-systemic JIA

PReS25-ABS-1510

HOW TO CHOOSE SECOND-LINE BIOLOGICS IN JUVENILE IDIOPATHIC ARTHRITIS: INSIGHTS INTO TREATMENT EFFECTIVENESS FROM A REAL-LIFE EXPERIENCE

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Introduction: Currently, there are few and weak evidence supporting the choice of the second-line biological diseasemodifying anti-rheumatic drug (bDMARD) for non-systemic juvenile idiopathic arthritis (JIA).
Objectives: To describe prescription patterns of second-line bDMARDs in non-systemic JIA and to assess the effectiveness of TNFα inhibitors (TNFi) and non-TNFi as second-line bDMARDs.
Methods: This retrospective cohort study included non-systemic JIA patients treated with at least two bDMARDs and followed at two Rheumatology Pediatric tertiary centers. The presence of clinically inactive disease (CID) at both 6 and 12 months during the second course of bDMARD treatment was used as the dependent variable in a logistic regression analysis. Since repeated measurements were obtained from the same subjects at both time points, multivariate analyses were performed using logistic Generalized Estimating Equations (GEE) models with robust standard errors, specifying an exchangeable correlation structure. Propensity scores stratified into quintiles were included as an indicator variable in the regression models.
Results: A total of 127 patients were included. The main reason for switching to a second bDMARD was ineffectiveness, reported in 109 out of 127 patients (86%), with active uveitis accounting for 25 out of those 109 switches (23%). Adalimumab was the most frequently prescribed second-line TNFi (59%). In 25% of cases, a non-TNFi was chosen, with tocilizumab being the most common (66%). The choice of second-line bDMARD was influenced by the calendar year of prescription. Non-TNFi treatments had a median initiation year of 2021 [interquartile range (IQR) 2017–2023], compared to 2019 (IQR 2013–2022) for TNFi treatments (p = 0.03).

Time on the first TNFi did not significantly impact the likelihood of achieving CID during the second TNFi course [odd ratio (OR) 0.98, 95% confidence interval (CI) 0.79–1.21, p = 0.83]. Interestingly, the median duration of the second bDMARD (censored at discontinuation or last follow-up) was significantly longer in the TNFi group compared to the non-TNFi group [2.2 years (IQR 0.7–5.3) vs. 0.8 years (IQR 0.5–3.6); p = 0.02]. In the multivariate GEE model adjusted for propensity score quintiles, switching to a second TNFi rather than a non-TNFi was significantly associated with achieving CID (OR 5.42, 95% CI 1.91–15.40, p < 0.01). Additionally, in the same model, male sex (OR 3.37, 95% CI 1.08–10.49, p = 0.04) and switching due to an adverse event (OR 4.61, 95% CI 1.16–18.31, p = 0.03) were significantly associated with CID. Patients who switched due to active uveitis also showed a higher likelihood of achieving CID compared to those switching for active arthritis (OR 18.38, 95% CI 4.33–78.07, p < 0.01).

Conclusion: Our findings suggest that TNFi remains a viable and effective option as second-line bDMARDs in non-systemic JIA, regardless of the duration of prior TNFi exposure.

ARE CLINICAL DISEASE ACTIVITY MEASURES USED IN JUVENILE IDIOPATHIC ARTHRITIS (JIA) INTERCHANGEABLE WITH THE ADULT DISEASE ACTIVITY MEASURES? RESULTS FROM THE POPULATION-BASED NORDIC JIA COHORT

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Introduction: The choice of disease activity measures in juvenile idiopathic arthritis (JIA) is crucial, particularly during the transition from pediatric to adult rheumatology care. Since pediatric and adult rheumatology use different composite scores, it is essential to evaluate how they compare. However, data on the interchangeability of these measures remains limited.

Objectives: This study aims to evaluate whether the Juvenile Arthritis Disease Activity Score (JADAS) is interchangeable with the Disease Activity Score in 28 joints (DAS28), the Simplified Disease Activity Index (SDAI) and the Clinical Disease Activity Index (CDAI) in adults with JIA, and to identify factors contributing to discrepancies in disease activity states across these measures.

Methods: Patients who underwent a clinical examination nearly two decades after JIA onset, meeting the International League of Associations for Rheumatology (ILAR) criteria, were included. Spearman's rank correlation was used to assess relationships between outcome measures. Pediatric measures included cJADAS10, JADAS10 and JADAS27 while adult measures included DAS28, SDAI, and CDAI. Each measure has distinct cut-off values to define disease activity levels: inactive disease (ID)/remission, low/minimal (LDA), moderate (MDA), and high/severe (HDA). Reasons for discrepancies in disease activity classification were analyzed statistically, focusing on the patients classified to have remission with respect to adult scores yet HDA with respect to JADAS.

Results: A total of 329 patients (71% female) were examined at a median of 17.6 years after JIA onset, with a median age of 24 years (IQR 20–27). Disease activity measures showed strong correlations ($\rho > 0.70$), with the lowest between DAS28 and the JADAS versions, while SDAI, CDAI, and JADAS versions had higher correlations (0.92–0.98). Among patients in remission per DAS28, 32–37% were classified as having HDA by JADAS versions. For these, physician global assesment of disease activity (PhGA) and patient global assessment (PaGA) were significantly higher in the HDA subgroup defined using cJADAS10, JADAS10, or JADAS27 compared to patients with ID, LDA, and MDA ($p < 0.0001$). No patients in remission per SDAI or CDAI were classified as HDA by the JADAS versions. All patients with HDA according to DAS28, SDAI, and CDAI were correctly identified as HDA by the JADAS.

Conclusion: Pediatric and adult disease activity measures correlate strongly. However, DAS28 shows discrepancies in identifying HDA compared to JADAS. This discrepancy is related to the PhGA and PaGA. SDAI and CDAI correlate more strongly with the JADAS offering better interchangeability for JIA patients transitioning to adult care.

Trial registration identifying number: NA

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FROM PAEDIATRIC TO ADULT CARE: VALIDATING THE JADAS FOR JUVENILE IDIOPATHIC ARTHRITIS IN ADULTHOOD

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Introduction: Many children with Juvenile Idiopathic Arthritis (JIA) continue to experience active disease into adulthood, yet no validated disease activity measure exists for adult use. While the Juvenile Arthritis Disease Activity Score (JADAS) is established for children, its relevance and validation for adults remain unexplored.

Objectives: Validate the JADAS for JIA patients aged >18 years, focusing on criterion, convergent, construct, and discriminant validity.

Methods: Adults with JIA were selected if recruited to the EPOCA cross-sectional cohort or two prospective cohorts: Rheumatic Diseases Portuguese Registry (Reuma.pt), and Spanish national registry for adults with JIA (JUVENSER). Those selected were >18 years old, met ILAR criteria for JIA, and had available data for both pediatric and adult disease activity scores (JADAS, DAS28, SDAI, CDAI). Demographic details, disease characteristics, and clinical assessments were extracted from patient's most recent visits (range January 2001 to February 2024). Construct validity of JADAS and its components (joint counts, physician, and patient global assessment) were evaluated through Spearman's rank correlation and Cohen's weighted kappa with adult measures of disease activity (DAS28/SDAI/CDAI). Convergent validity of the JADAS with Health Assessment Questionnaire (HAQ) scores was tested using Spearman's rank correlation. Criterion and discriminant validity were assessed through the sensitivity and specificity of the JADAS at detecting clinically inactive disease between versus adult constructs, respectively. Differences in optimal JADAS cut-offs relating to i) the achievement/non-achievement of DAS28 EULAR response criteria and ii) clinically important differences in HAQ scores between two clinical visits were assessed via ROC curve analysis.

Results: A total of 1315 adult JIA patients, from Reuma.pt (N=545), JUVENSER (N=392), and EPOCA (N=378) across 39 nationalities were included. Median age at disease onset was 9 years for Reuma.pt (IQR 4-13) and JUVENSER (IQR 4-13) patients, and 11 years (IQR 7-14) for EPOCA patients. Reuma.pt patients were older (25 versus 19-21 years), with longer disease duration (18 versus 8-13 years). EPOCA patients had a median JADAS27 of 3.5 versus 2 (Reuma.pt) and 0 (JUVENSER).

High construct validity of the JADAS10 was demonstrated, particularly against the SDAI (correlation coefficient: 0.95; kappa: 0.72 (0.70-0.74) and CDAI (correlation coefficient: 0.96; kappa: 0.72 (0.70-0.74). Correlation between JADAS10 and DAS28 was lower (correlation coefficient: 0.69; kappa: 0.51 (95% CI 0.48-0.54). Similar correlations were seen for JADAS27 and JADAS71.

High convergent validity of the JADAS10 and HAQ was observed (correlation coefficient: 0.64), with clinical significant differences in JADAS 10 scores between those with low/mild disability (JADAS10 cut-off: < 2.95), moderate disability (JADAS10 cut-off: 2.95-4.85) and high disability (JADAS10 cut-off: >4.85).

High criterion validity of the JADAS10 was demonstrated, with sensitivities of detecting clinically inactive disease according to the CDAI at 88%, SDAI at 86%, and lower with the DAS28 at 64%. High discriminant ability was also demonstrated with specificities of excluding clinically inactive disease according to the CDAI at 97%, SDAI at 97% and DAS28 at 96%.

The JADAS10 had moderate to high classification ability at detecting DAS28 EULAR response between two-time points, with a change of 1.9 for moderate response and 4.3 for good response. The results were similar for all JADAS versions. AUC values were 0.73 for detecting moderate DAS28 EULAR response, and 0.74 for good response.

Conclusion: The JADAS is a valid tool for measuring disease activity in adults with JIA. Its strong performance in criterion, convergent, construct, and discriminant validity against existing adult tools supports its potential for broader use in clinical practice, helping to bridge the gap in transition care from pediatric to adult rheumatology. Of note, the DAS28, common

practice for use in adults with JIA, does not include relevant joint counts for JIA, and had poorer validity against the JADAS. Further studies are needed to explore the feasibility of implementing the JADAS in adult practice.

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COMPARATIVE PERFORMANCE OF DISEASE ACTIVITY INDICES IN JUVENILE IDIOPATHIC ARTHRITIS DURING TRANSITION OF CARE

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Introduction: Monitoring disease activity is a crucial aspect of the treat-to-target strategy in rheumatic diseases. However, no standardized protocols exist for monitoring disease activity in patients with Juvenile Idiopathic Arthritis (JIA) during the transition of care.

Objectives: The aim of this study is to compare different disease activity indices across JIA categories (excluding systemic JIA), and to assess their relative performance and clinical consistency in a real-life transition setting.

Methods: Young adult JIA patients eligible for transition of care underwent a prospective clinical evaluation by both paediatric and adult rheumatologists. Disease activity was assessed using validated clinical indices. All patients were evaluated with cJADAS, JADAS10, JADAS27, and JADAS71. Additional indices were applied according to JIA subtype: SDAI, CDAI, and DAS28 were used in persistent oligoarticular (oJIA-p), extended oligoarticular (oJIA-e), and RF-positive and RFnegative polyarticular JIA (polyJIA RF^-/RF^+); DAPSA was used for the psoriatic JIA (jPsA) category; and jSpADA, ASDAS-CRP, and BASDAI were used for enthesitis-related arthritis (ERA). Ultrasound data were collected as additional marker of articular inflammation when arthritis was clinically suspected or for disease monitoring, to detect active synovitis according to OMERACT ultrasound paediatric definitions. Spearman's correlation was used to assess associations between disease activity indices. ROC analyses were conducted to compare the relative performance of different clinical indices in relation to ultrasound-detected synovitis. Statistical analyses were performed using R software (version 4.5.0).

Results: A total of 124 JIA patients were included (median age 19 years, IQR 17–23). Disease activity was highest in jPsA compared to lower values in oJIA-e/polyJIA RF^-, and oJIA-p. Strong correlations were observed in oJIA-p, oJIA-e, and polyJIA RF^- among JADAS scores, CDAI, and SDAI ($\rho > 0.87$; $p < .001$), with slightly lower values for DAS28. Similar findings were confirmed in prospective analyses, with strong correlations between changes in JADAS, SDAI, and CDAI over time in both oJIA-e/polyJIA RF^- patients (ΔJADAS71 vs ΔSDAI: $\rho = 0.944$; $p < .001$) and oJIA-p ($\rho = 0.993$; $p < .001$). In jPsA, a moderate-to-strong correlation was observed between JADAS scores and DAPSA ($\rho \approx 0.87$, $p < .001$). In ERA, jSpADA correlated moderately with ASDAS-PCR ($\rho = 0.51$; $p = 0.161$), but not with BASDAI. Ultrasound was performed in 84.7% of patients, with a total of 1612 assessed joints. In oJIA-e and polyJIA RF^-, JADAS71-PCR and SDAI showed the highest AUCs (0.844–0.845) for ultrasound-detected synovitis; in prospective analyses, changes in these scores showed good discriminative ability for predicting new onset ultrasound-detected synovitis over time (AUC = 0.789 and 0.812, respectively). In oJIA-p, all indices performed well (AUCs ≥ 0.926). In jPsA, DAPSA showed the highest AUC (0.818) at baseline.

Conclusion: In this real-life transition cohort, both paediatric and adult-derived indices performed comparably across most JIA subtypes. In prospective evaluation, changes in JADAS71 and SDAI showed the strongest association with new-onset ultrasound-detected synovitis, particularly in oJIA-e and polyJIA RF^-. In jPsA, DAPSA demonstrated the highest baseline performance. In ERA, divergent correlations among available indices were observed. These findings highlight the need for a targeted approach to disease activity monitoring, tailored to the specific JIA subtype during the transition of care.

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DIGITAL HOME MONITORING IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS TO INCREASE INTERVALS OF HOSPITAL VISITS

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Introduction: Children with juvenile idiopathic arthritis (JIA) commonly visit their paediatric rheumatologist at regular standardized intervals, which is costly in time and money for patients, parents/guardians, hospital and other stakeholders.
Objectives: This non-inferior, single-centre study aims to test if JIA patients with inactive disease can safely increase a visit interval by home monitoring disease activity using the EuroQol five-dimensional youth questionnaire with five levels (EQ5D-Y-5L) and Juvenile Arthritis Multidimensional Assessment Report (JAMAR).
Methods: JIA patients with inactive arthritis from the Wilhelmina Children's Hospital in Utrecht, the Netherlands, skipped one three-monthly control visit and instead completed online EQ-5D-Y-5L and JAMAR questionnaires at home. Patients were included in 2022. Home monitoring questionnaires were evaluated by a research nurse to determine if a short-term control visit at the hospital was necessary. To test non-inferiority, rates of study-wide flares and flares after an actual prolonged visit interval were compared with a historical cohort flare rate and with matched JIA patients using relative risks (RR) with 95% confidence intervals (95% CI) and a non-inferiority margin of 15%. Secondary outcomes were the number of reminders sent for home monitoring, the number of patients that failed to complete questionnaires, rescheduled visits, and patient satisfaction with home monitoring.
Results: A total of 84 patients participated in the study. Seven participants had rescheduled visits before, and eleven after evaluation of the questionnaires. 63 participants completed the six-month visit without returning to the hospital earlier, of whom seven experienced a flare. The study-wide flare rate was 18.5%, compared to a historical flare rate of 18.4% (including non-inferiority margin) and the flare rate after an actual prolonged visit interval within the total study population was 8.6%. In comparison to matched controls, RRs were measured as 0.52 (95% CI: 0.25–1.06) for study-wide flares and 0.86 (95% CI: 0.29–2.54) for flares of patients with a prolonged visit interval. The RR for study-wide flares falls within the boundaries for non-inferiority, whereas the study was underpowered for the RR for flares after a prolonged visit interval. Two participants failed to complete home monitoring despite two reminders. 92% of participants who completed the patient satisfaction questionnaire indicated they would be willing to skip a hospital visit using home monitoring more often.
Conclusion: The findings indicate no clear evidence that replacing one hospital control visit with home monitoring poses a significant risk for JIA patients with inactive disease. There was a high questionnaire response, although reminders and rescheduled visits were necessary. Patient satisfaction with home monitoring was high.
Trial registration identifying number: The THUIS study is registered at ClinicalTrials.gov: NCT05603286

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PRG4 AS A REGULATOR OF JOINT HOMEOSTASIS

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Introduction: The lining layer of the synovial membrane is increasingly recognised as a key tissue niche determining joint health, producing synovial fluid components, including proteoglycan-4 (PRG4), to nourish and lubricate the joint(1-3). The rare monogeneic condition Camptodactyly-Arthropathy-Coxa Vara-Pericarditis (CACP) syndrome, caused by mutations in the *PRG4* gene, manifests with progressive arthropathy of the large joints arising in early childhood, demonstrating a critical for PRG4 in mediating normal joint homeostasis(4).

Objectives: We aim to investigate the role of PRG4 in maintaining joint homeostasis, particularly through its regulation of synovial lining layer macrophages, to better understand regulators of the lining layer niche and the pathophysiology of this rare condition.

Methods: Using synovial tissue biopsy samples from 6 individuals with CACP syndrome, as well as a Prg4 knockout mouse model that phenocopies the disease, we have undertaken histological, 2D/3D immunofluorescence (IF) imaging, flow cytometric, spatial and single cell transcriptomic analysis of synovial tissue to investigate the mechanisms underpinning synovial tissue pathology in the absence of PRG4.

Results: Single cell and spatial transcriptomic analyses of CACP syndrome synovium demonstrated an increased proportion of myofibroblasts and extracellular matrix deposition, which we validated at the protein level in human and mouse tissue using IF staining and flow cytometry, in accordance with the clinical manifestation of this condition. Interestingly, we observed multi-nucleated macrophages in the hyperplastic synovial lining layer in CACP syndrome, an uncommon feature of joint pathology. These lining layer macrophages displayed polarisation towards an *SPP1+* program, which is associated with fibrosis in the fibrotic liver and lung, and *in vitro* stimulation determined SPP1 expression to be directly regulated by PRG4. 3D imaging analysis of synovial lining macrophages in Prg4-knockout mice demonstrated altered morphology, suggesting impaired capacity to undergo immunoregulatory efferocytosis of synovial fluid debris.

Conclusion: We demonstrate that PRG4 suppresses the emergence of a pro-fibrotic *SPP1+* macrophage program in the synovial lining, which, in the absence of PRG4, promotes differentiation of myofibroblasts that drive synovial fibrosis, leading to restricted movement in the joints of individuals affected by CACP syndrome. Our further work aims to characterise defects in efferocytic capacity of lining macrophages in the absence of PRG4 and elucidate the role of efferocytosis in the healthy and inflamed synovium.

References: 1. Kemble S, Croft AP. Critical Role of Synovial Tissue–Resident Macrophage and Fibroblast Subsets in the Persistence of Joint Inflammation. Frontiers in Immunology. 2021 Sep 3;12.

2. Kurowska-Stolarska M, Alivernini S. Synovial tissue macrophages in joint homeostasis, rheumatoid arthritis and disease remission. Nature Reviews Rheumatology. 2022 Jun 7;18(7):384–97.
3. Jay GD, Waller KA. The biology of Lubricin: Near frictionless joint motion. Matrix Biology. 2014 Oct;39:17–24.
4. Maniscalco V, Pizzetti C, Marrani E, Perrone A, Maccora I, Pagnini I, et al. Pseudo-rheumatic manifestations of limping: Camptodactyly–arthropathy–coxa vara–pericarditis syndrome: Single case report and review of the literature. Frontiers in Pediatrics. 2022 Dec 5;10.

PReS25-ABS-1293

THE SOS PROJECT: TO SWITCH OR TO SWAP AFTER ADALIMUMAB FAILURE FOR THE MANAGEMENT OF CHILDHOOD NON-INFECTIOUS UVEITIS IN AN INTERNATIONAL COHORT

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Introduction: Childhood chronic non-infectious uveitis (cNIU) is a sight-threatening condition that can lead to blindness if not appropriately treated. cNIU is typically associated with Juvenile Idiopathic Arthritis or can occur in isolation when idiopathic. Adalimumab is the only approved treatment for cNIU and TNF inhibitors (TNFi) are the recommended first linebiologic treatment of cNIU. However, 25% of patients do not achieve disease remission. In these cases, there is no consensus whether switching to another TNFi or swapping drug class is more effective.

Objectives: We aim to evaluate the efficacy of the switch OR swap therapeutic approach to treating cNIU refractory to primary TNFi and the efficacy of the different drugs in these patients.

Methods: In a multicentre international retrospective study involving pediatric rheumatology centres in Florence, Boston, Cincinnati, Athens and Trieste, we enrolled children with a diagnosis of cNIU unresponsive to adalimumab and required the use of another biologic. Remission on treatment was determined according to the grading of ocular inflammation using the Standardization of Uveitis Nomenclature (SUN) criteria. Statistical analysis was performed using Spss 29 for windows. A p-value <0.05 was considered significant.

Results: We collected the data of 79 children with cNIU, of whom 57 had JIA-associated uveitis (JIA-U) and 17 had idiopathic uveitis (IU). Seventy-nine were treated with adalimumab as first-line TNFi. Forty-one children did not respond to treatment and were “switched” to a second TNFi (38 infliximab, 3 golimumab), and 38 “swapped” to a non-TNFi biologic (20 tocilizumab, 2 baricitinib, 2 tofacitinib, 11 abatacept, 1 canakinumab). We identified a significant difference in treatment approach, European swapped more frequently than American (χ^2 0.078 p 0.78). We did not find significant differences in remission between switching TNFi and swapping drug class (χ^2 0.078 p 0.78) or amongst the different drugs (χ^2 32.87p <0.001). On sub-analysis of the different sub-types of uveitis (JIA-U and Idiopathic), we did not find significant differences in remission of patients for either switching TNFi or swapping to non-TNFi ($\chi^2$0.021 p0.88 and χ^2 0.016 p 0.90 respectively) or for the different drugs regardless of switch/swap ($\chi^2$5.03 p0.754 and $\chi^2$2.57 p 0.463 respectively). There were no significant differences based on anatomical location- anterior NIU (switch vs swap $\chi^2$0.219 p0.64 and based on the drugs $\chi^2$4.97 p0.760) and non-anterior NIU ($\chi^2$0.117 p0.733 and $\chi^2$2.97 p0.395). Furthermore no significant differences were assessed considering the responder to the primary TNFi ($\chi^2$0.012 p0.912 and $\chi^2$3.35 p0.851) and non-responder ($\chi^2$0.024 p0.877 and $\chi^2$5.4 p0.24).

Conclusion: Management of childhood cNIU is challenging and evidence is scarce on treatment after failure of first-line TNFi. This is one of the largest multicentre international cohorts that showed that TNFi and non-TNFi biologics are reasonable next treatment and there is no preference for a specific class of biologics and all are reasonable therapeutic approach for the management of cNIU. The use of the European and US cohort allowed us to make a comparison between the two treatments approach. Further data are needed to make specific comparison among drugs. **Trial registration identifying number:** Not applicable

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INTERNATIONAL VALIDATION AND SIMPLIFICATION OF CLLDAS: FINDINGS FROM THE UK JSLE COHORT AND CARRA REGISTRY

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Introduction: Consensus-derived Childhood Lupus (cSLE) treat-to-target (T2T) endpoints have been endorsed by PReS including Childhood Lupus Low Disease Activity State (cLLDAS) (1). Validation with large international cohorts is needed to support their clinical implementation.

Objectives: Use a data-driven approach to evaluate whether the cLLDAS definition can be simplified, without compromising its ability to protect against subsequent high disease activity.

Methods: Data from UK JSLE Cohort Study and CARRA Registry patients, <18 years at diagnosis, with ≥4 ACR/SLICC criteria for SLE were included. Data were available from 1566 cSLE patients (11965 visits; UK JSLE: n=492, 5923 visits; CARRA: n=1074, 6042 visits). Criteria from the consensus-derived cLLDAS were either removed or transformed (18 variations in total). Prentice-Williams-Peterson (PWP) gap-time models assessed the impact of variations of cLLDAS, on episodes of high disease activity (SLEDAI-2K ≥10) over time. Hazard ratios (HRs) from the original and modified definitions were compared using Student's t-test. When variations of multiple target criteria showed comparable HRs to the original definition, they were evaluated in combination. Target attainability was also compared between original and modified cLLDAS definitions using Wilcoxon tests.

Results: Original cLLDAS attainment reduced the hazard of high disease activity by 72% (HR 0.28 [CI 0.21, 0.36]; p<0.001). Removing the PGA (HR 0.33 [CI 0.27, 0.41]), SLEDAI-2K (HR 0.30 [CI 0.23, 0.38]), or stable immunosuppression (HR 0.31 [CI 0.24, 0.39]) criteria statistically significantly diminished the protective effect of cLLDAS attainment. In contrast, (a) removing 'no new SLEDAI features,' (b) removing 'no major active organ involvement,' or (c) replacing the SLEDAI-2K criterion with the simpler clinical-SLEDAI ≤4 definition, did not significantly alter the hazard of subsequent high disease activity. A model evaluating a simplified cLLDAS definition combining modifications (a–c) yielded a statistically comparable hazard reduction (HR 0.32 vs. HR 0.28 for original cLLDAS). Additionally, the simplified version showed faster time to target attainment (12.9 vs. 16.3 months) and a greater proportion of follow-up time spent in target (54.5% vs. 46.6%) compared to the original cLLDAS definition.

Conclusion: These data suggest that refining the cLLDAS definition by applying the aforementioned changes, could serve to simplify targets for use in clinical and research settings, allowing real-time cLLDAS assessment during visits and removing the need to review past data or await serological results. Of note, the current analyses do not compare the consensus and modified cLLDAS definitions for the crucial prevention of cSLE-related damage.

References: 1. Smith E, et al. PReS-endorsed international childhood lupus T2T task force definition of childhood lupus low disease activity state (cLLDAS). Clinical Immunology. 2023;250:109296.

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CROSS-COHORT INTERNATIONAL VALIDATION OF TREAT-TO-TARGET ENDPOINTS IN CHILDHOOD LUPUS: DATA FROM THE UK JSLE COHORT AND CARRA REGISTRY

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Introduction: Consensus treat-to-target (T2T) endpoints for childhood-onset lupus, including the Childhood Lupus Low Disease Activity State (cLLDAS) (1), cSLE clinical remission on (cCR) and off-corticosteroids (cCR-0) (2), have been endorsed by the PReS. Validation in large international cohorts is needed to support their use in clinical care and research.

Objectives: To compare cSLE-specific T2T target attainment (cLLDAS, cCR, cCR-0) across UK and North American cohorts, identify predictors of sustained cLLDAS attainment, and assess the association between target attainment and future high disease activity.

Methods: Analysis included patients from the UK JSLE Cohort Study and CARRA Registry, diagnosed before age 18 and meeting ACR-1997 or SLICC-2012 classification criteria. Target attainment, time to target, and proportion of follow-up time in target were assessed; Wilcoxon signed-rank tests compared variables between cohorts. Further analysis was undertaken for the most easily attainable target, cLLDAS. Multivariable logistic regression identified independent predictors of spending above-median cumulative time in cLLDAS, reported as odds ratios (ORs). Risk of subsequent high disease activity (SLEDAI-2K ≥10) after cLLDAS attainment was assessed using Prentice-Williams-Peterson (PWP) models, adjusted for the cohort.

Results: Among 1,566 patients (11,965 visits [median disease duration 3.3 years]; UK JSLE: n=492, 5,923 visits [median 4.4 years]; CARRA: n=1,074, 6,042 visits [median 3.0 years]), 59% achieved cLLDAS (UK JSLE: 67% vs CARRA: 56%; p<0.001), 52% cCR (UK JSLE: 58% vs CARRA: 49%; p=0.003), and 43% cCR-0 (UK JSLE: 43% vs CARRA: 44%; p=0.756). Median time to cLLDAS was significantly shorter (13.1 vs 17.0 months; p<0.001) and cumulative time in cLLDAS was significantly greater (32% vs 23%; p<0.001) in CARRA compared to UK JSLE patients respectively. Multivariable logistic regression identified low complement C4 (OR 0.73 [CI 0.56, 0.96]; p=0.024), older diagnosis age (OR 0.87 [CI 0.84, 0.91]; p<0.001), and higher baseline SLEDAI-2K (OR 0.97 [CI 0.96, 0.99]; p=0.007) as independent predictors of reduced cumulative time in cLLDAS. In multivariable PWP models, longer disease duration (HR 0.26; p<0.001) and ever attaining any target (HR 0.35; p<0.001), were independently associated with a reduced risk of subsequent high disease activity. Black (HR 1.94; p<0.001) and Hispanic (HR 1.61; p=0.002) ethnicities were independently associated with a higher risk of high disease activity.

Conclusion: This is the first study to evaluate cSLE-specific T2T endpoints across international registries, identifying predictors of sustained target attainment and confirming the protective effect of target attainment against subsequent high disease activity, supporting the integration of T2T strategies into clinical care and research.

References: Smith E, et al. PReS-endorsed international childhood lupus T2T task force definition of childhood lupus low disease activity state (cLLDAS). Clinical Immunology. 2023;250:109296.

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EPIGENETIC PROFILING OF CHILDHOOD-ONSET LUPUS REVEALS DISTINCT EPIGENETIC CLUSTERS AND SUGGESTS EPIGENETIC DRIVERS OF DISEASE ACTIVITY

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Introduction: Childhood-onset lupus is generally associated with a more severe disease course than adult-onset lupus. DNA methylation alterations are known to play a key role in lupus pathogenesis. While we previously showed that childhood-onset lupus is linked to a higher genetic risk burden compared to adult-onset disease, the epigenetic landscape of childhood-onset lupus remains largely unexplored.

Objectives: This study aimed to characterize DNA methylation changes in childhood-onset lupus, and explore their potential association with clinical features and disease activity.

Methods: A total of 64 patients with childhood-onset lupus and 47 healthy controls were included in this study, along with an independent validation cohort of 38 additional patients. DNA was isolated from PBMCs in the study cohort and from whole blood in the validation cohort to assess DNA methylation using the Infinium MethylationEPIC v2.0 array (Illumina). Quality controls and statistical analyses were performed using *minfi* and *limma* R packages. Methylation differences among groups were tested through linear regression, adjusting for age, sex, medication use, and cell subset compositions. Differences in clinical manifestations were assessed using Fisher's exact tests. Gene ontology enrichment analyses were performed with Metascape and GREAT.

Results: Case-control differential DNA methylation analysis revealed significant hypomethylation in interferon-regulated genes in lupus, such as *DTX3L*, *PARP9*, *IFI44L*, and *MX1*. The enrichment analysis confirmed the presence of type I interferon signature-related biological processes, consistent with adult-onset lupus. Hypomethylation in genes related to B cell activation and cellular senescence was correlated with more active disease, as measured by SLEDAI scores. K-means clustering analysis of patients based on DNA methylation patterns identified 3 distinct lupus clusters. Cluster 1 was characterized by the enrichment of hypomethylated genes involved in cell adhesion and response to growth factor pathways; Cluster 2 exhibited hypomethylation in genes related to regulation of cell differentiation and cell fate determination; and Cluster 3 was enriched in response to oxidative stress and Rap1 signaling pathway in hypomethylated genes. Sex-based analysis revealed hypomethylation in males at sites enriched in immune response pathways, with over 80% of differentially methylated positions in male individuals with childhood-onset lupus validated in the replication cohort.

Conclusion: Childhood-onset lupus is marked by significant hypomethylation in interferon-regulated genes, with DNA methylation changes correlating with disease activity and revealing distinct epigenetic molecular subgroups. Sex-specific patterns further suggest epigenetic contributions to sex-based disease heterogeneity in lupus.

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NOVEL AUTOANTIBODIES PREDICTIVE OF ATHEROSCLEROSIS PROGRESSION AND STATIN RESPONSE IN JUVENILE-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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Introduction: Cardiovascular disease (CVD) is a leading cause of morbidity and mortality in juvenile-onset systemic lupus erythematosus (JSLE). There is an urgent need to identify biomarkers that can predict atherosclerosis progression and therapeutic responses, enabling personalised CVD-risk management in JSLE.

Objectives: This study aimed to investigate whether novel autoantibody signatures can predict atherosclerosis progression and atorvastatin response in young people with JSLE.

Methods: We conducted a biomarker discovery study using baseline serum samples from a sub-cohort of the APPLE (Atherosclerosis Prevention in Pediatric Lupus Erythematosus) trial, a large, multi-centre, randomised, double-blind, placebo-controlled trial of atorvastatin versus placebo (1:1) to prevent atherosclerosis progression in JSLE [1]. The trial was conducted across 21 sites in North America. Ninety-four JSLE patients (mean [SD] age 15.3 [2.4] years; 78% female), with matched baseline serum samples and complete longitudinal carotid intima-media thickness (CIMT) measurements over 36 months, were included (45 randomized to the placebo and 49 to the atorvastatin arm). Unsupervised cluster analysis based on CIMT progression over 36 months was used to identify groups with high and low atherosclerosis progression within each treatment arm. Differential autoantibody expression at baseline between these groups was assessed using Empirical Bayes moderated t-tests, and predictive performance was evaluated using logistic regression and receiver operating characteristic (ROC) analysis. Pathway enrichment analysis was performed using Metascape [2]. **Results:** A total of 579 autoantibodies were identified as true signals in the 94 baseline serum samples analysed. In the placebo arm, six autoantibodies (STK24, RAD23B, HDAC4, STAT4, SEPTIN9 and NFIA) were significantly associated with high versus low CIMT progression over 36 months, achieving a combined area under the curve (AUC) of 87% for distinguishing progression patterns. In the atorvastatin arm, a distinct autoantibody profile was identified that predicted response to statin treatment. Eight autoantibodies (ABI1, ATP5B, CSNK2A2, NRIP3, PRKAR1A, PDK4, BATF and NUDT2) were significantly associated with CIMT progression despite atorvastatin therapy, achieving an exceptional combined AUC of 96%. Enriched pathway analysis of the autoantibody profile in atorvastatin arm revealed lipid-independent mechanisms, potentially contributing to atherosclerosis progression in atorvastatin-treated patients. Based on the predictive models generated from these distinct autoantibody profiles, we can propose a two-step stratification strategy: first, identify JSLE patients at high risk using the placebo atherosclerosis progression signature, and second, stratify them for statin vs. other CVD-risk management strategies based on the statin response signature.

Conclusion: In this biomarker discovery cohort study, novel autoantibody signatures were identified as the first JSLEspecific biomarkers for atherosclerosis progression and prediction of statin response, suggesting possible autoimmune mechanisms underlying the increased CVD-risk associated with JSLE. These findings support the potential application of autoantibody profiling for precision medicine approaches for CVD-risk research and management in JSLE for ultimate patient benefit.

References: 1. Schanberg LE, Sandborg C, Barnhart HX, Ardoin SP, Yow E, Evans GW, et al. Use of atorvastatin in systemic lupus erythematosus in children and adolescents. Arthritis Rheum. 2012;64(1):285-96. 2. Zhou Y, Zhou B, Pache L, Chang M, Khodabakhshi AH, Tanaseichuk O, et al. Metascape provides a biologist-oriented resource for the analysis of systems-level datasets. Nature Communications. 2019;10(1):1523.

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COMPARATIVE IMMUNOMICS HIGHLIGHTS MECHANISTIC DIFFERENCES BETWEEN PEDIATRIC AND ADULT-ONSET LUPUS WITH THERAGNOSTIC IMPLICATIONS

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Introduction: Systemic Lupus Erythematosus (SLE) is a complex autoimmune disease affecting both children and adults. Childhood-onset SLE (cSLE) is often associated with more severe clinical features and increased steroid-related side effects. Treatments for cSLE are often adapted from adult studies due to the assumption of shared underlying mechanisms. However, the immunopathogenic complexity of SLE and limited understanding of age-related differences highlight the need for a comprehensive, comparative immunomics approach. This could uncover key mechanistic differences for more age-appropriate therapeutic strategies.

Objectives: To compare the childhood- and adult-onset SLE immunomes and test the hypothesis that distinct, age-related differences exist within the immunoregulatory and immune effector pathways.

Methods: Peripheral blood mononuclear cells (PBMCs) from 26 adult and 32 paediatric patients were analyzed using a 43marker mass cytometry panel. The adult SLE cohort (23 females) had a median age of 39.5 years [interquartile range (IQR): 28–53.5]. The cSLE cohort (26 females) had a median of 14.6 years (IQR 13.3–15). Data processing including quality control and visualization via t-distributed stochastic neighbor embedding (tSNE) plots was performed using our Extended Polydimensional Immunome Characterisation (EPIC) pipeline.[1] Cell frequencies were reported as percentages of total $CD45^+$ PBMCs and summarized using median and IQR. Statistical significance was defined as $p<0.05$ (Mann–Whitney U test).

Results: Widespread immune abnormalities were detected, with $CD4^+$ T cells showing the most pronounced alterations. Notably, we identified cSLE-specific immunologic alterations with increased frequencies of activated memory ($CD45RA^-$) $HLADR^+OX40^+CLA^+CD4^+$ T cells (cSLE vs. healthy: 0.26%[0.14–0.39] vs. 0.10%[0.05–0.17], $p<0.0001$), memory $IL\text{-}2^+IL21^+CD4^+$ T cells (0.41%[0.23–0.68] vs. 0.17%[0.13–0.29], $p=0.0002$) and memory $CD25^-FoxP3^+CTLA4^+TIGIT^+CLA^+CD4^+$ T cells (0.86%[0.68–1.24] vs. 0.35%[0.25–0.53], $p=0.0038$). These findings point to an immunopathogenic profile unique to cSLE.

In contrast, adult-onset SLE exhibited a distinct immunologic signature marked by significantly reduced CTLA4-expressing naïve ($CD45RA^+$) and memory effector $CD4^+$ T cells ($CD25^-FoxP3^-$) compared to healthy controls (naïve: 1.61%[0.85–2.62] vs. 4.65%[3.20–7.18], $p<0.0001$; memory: 0.54%[0.34–0.79] vs. 1.46%[1.00–2.06], $p<0.0001$), suggesting impaired negative immune regulation in adult-onset SLE.

Despite these differences, both childhood- and adult-onset SLE shared a common immunologic feature: expansion of memory T regulatory-like cells that lack CD25 but express $FoxP3^+CTLA4^+TIGIT^+PD1^{+/-}$.

Conclusion: SLE is characterized by multiple immune abnormalities consistent with its complex immunopathogenesis. Notably, in cSLE, there is an enrichment of memory T cells uniquely expressing OX40 (co-stimulatory receptor), IL-21 (cytokine produced by T follicular helper cells) and a subset of non-regulatory T cells ($CD25^-FoxP3^+$) expressing immune checkpoint markers CTLA4 and TIGIT. These cells also exhibit skin-homing potential due to CLA (cutaneous lymphocyteassociated antigen) expression. Conversely, adult SLE patients show reduced CTLA4 expression in both naïve and effector T cell populations. From a translational perspective, this underscores the importance of further investigating the mechanisms underlying CTLA4 downregulation in adult-onset SLE and exploring therapeutic strategies aimed at restoring CTLA4 expression to promote immune homeostasis.

References: 1. Yeo, J.G. et al., 2020. *Nat. Biotech., 38*(6), pp.679-684.

PReS25-ABS-1079

SEX-SPECIFIC MECHANISMS ASSOCIATED WITH FEMALE CHILDHOOD-ONSET SLE REVEALED BY TRANSCRIPTOMIC ANALYSIS OF TRANSGENDER ADOLESCENTS UNDERGOING GENDER-AFFIRMING SEX HORMONE THERAPY

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Introduction: Sex determinants may play a role in the immunological sexual dimorphism of childhood-onset systemic lupus erythematosus (cSLE).
Objectives: This study aimed to investigate the impact of sex determinants on immune transcriptomic changes and their association with cSLE.
Methods: We performed PBMC RNAseq analysis on post-pubertal cis-female adolescents with cSLE (n=74) and healthy controls (HCs, n=20), as well as transgender adolescents (trans-male, XX TM; trans-female, XY TF, n=32 samples) undergoing gender-affirming hormone therapy (GAHT) across 3 timepoints; pre-treatment, on gonadotrophin-releasing hormone agonist (GnRHa, puberty blocker) and on GAHT, TM on testosterone (T) and TF on oestradiol (E). Rstudio was used to identify the significantly differentially expressed genes (DEGs, DEseq2). Pathway enrichment analysis (PEA), clustering and normalised gene count analysis were conducted with compatible software.
Results: We identified 40 DEGs (fold change>1.5, P<0.05) in the cis-female cSLE cohort vs. HCs (defining a post-pubertal cSLE signature) that overlapped with the transgender cohort (on GAHT). Specifically, in the XY TF group (on E vs. GnRHa), there were 24 upregulated/1 downregulated DEGs, including *TLR2* (upregulated, p= 0.0077), and *IL1R2* (upregulated, p= 0.048 which overlapped with the cSLE signature. Similarly, in the XX TM group (on T vs. GnRHa), there were 6 upregulated/4 downregulated overlapping DEGs, including *IL15* (upregulated, p= 0.019). PEA revealed DEGs linked to the inflammatory response processes, cell migration/activation and lipid regulation.

Additionally, we discovered 63 X-linked DEGs (P <0.05) in the GAHT vs. GnRHa groups across both XX and XY backgrounds, however, these did not overlap with the cSLE signature, suggesting a lesser impact of sex hormones on X-linked transcripts related to cSLE susceptibility. However, the X-linked non-coding RNA X-inactive specific transcript (*XIST*) and the *XIST* antisense non-coding RNA *TSIX*, were both significantly increased in cSLE vs. HCs (p=0.018 and 0.0007). *XIST* correlated negatively with cSLE interferon scores (P=0.0010, r=-0.38) and X-linked *TLR7* expression (P=0.0004, r=-0.40), but *TSIX* did not, supporting a role for X chromosome inactivation in controlling the pathogenic mechanisms associated with cSLE in females.

Conclusion: This analysis demonstrated unique inflammatory transcriptomic changes (DEGs) induced by GAHT in transgender adolescents, which overlapped with cis-female cSLE adolescents, as well as sex hormone-independent associations between *XIST* expression and inflammatory cSLE pathogenic mechanisms. To our knowledge, this is the first exploration of the impact of sex hormones disaggregated from their corresponding sex chromosomal background in driving transcriptomic changes potentially relevant for understanding female cSLE pathogenesis.

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UNEXPLORED TYPE I INTERFERON SIGNALLING HETEROGENEITY IN CHILDHOOD-ONSET SLE REVEALS NOVEL CONSIDERATIONS FOR PERSONALISED THERAPY

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Introduction: Childhood-onset systemic lupus erythematosus (cSLE) is a severe autoimmune disease that causes significant morbidity in children and adolescents, with more aggressive clinical manifestations compared to adult-onset SLE. This is largely attributed to heightened type I interferon (IFN-I) signalling. In this study, we investigate the heterogeneity of IFN-I signalling in cSLE patients using a novel multi-omic approach, aiming to better understand disease mechanisms and identify therapeutic strategies.

Objectives: To explore the heterogeneity of IFN-I signalling in cSLE, assess its immunological impact, clinical relevance, and identify potential biomarkers for stratified therapy.

Methods: We performed RNA sequencing on peripheral blood mononuclear cells (PBMCs) from 74 female cSLE patients (mean age 19 years, disease duration 6.5 years) and 20 age/sex-matched healthy controls (HCs). Serum pan-IFNα levels were quantified using single-molecule array (SIMOA), and IFN-I activity was assessed using firefly luciferase reporter cells. We analysed IFN-I-sensitive BST2 expression by spectral flow cytometry, and serum proteins were quantified by Olink proteomics with selected proteins validated by ELISA. Clinical data informed disease endotyping.

Results: Gene expression analysis revealed 51 upregulated differentially expressed genes in cSLE. Sparse partial least squares discriminant analysis (sPLS-DA) revealed robust separation between cSLE and HC groups, with the strongest upregulation in IFN-I pathways ($p<0.0001$). Patients clustered into two groups: IFN-High (65%) and IFN-Low (35%), independent of disease activity, as validated by SLE IFN-stimulated gene (ISG) scores (AUC=1.00, $p<0.0001$). IFN-High patients had reduced lymphocyte counts ($p=0.0048$). Serum IFNα levels ($p=0.0014$) and reporter cell responses ($p<0.0001$) were significantly elevated in the IFN-High group and showed a greater reduction following anifrolumab treatment ($p=0.013$) compared to IFN-Low patients, supporting stratified therapy. These patterns were absent in HCs and systemic juvenile idiopathic arthritis (sJIA) disease controls, highlighting cSLE specificity. Proteomics identified LAMP3 as the most predictive biomarker for the IFN-High group (AUC=0.95, $p<0.0001$), validated by ELISA, with longitudinal stability regardless of disease activity across 82 data points. Cellular analysis showed increased BST2 expression in plasmacytoid dendritic cells, CD4+, and CD8+ T-cells, with functional consequences on activation, exhaustion, and abundance, indicating heightened IFN-I sensitivity in these subsets. Clustering multi-level IFN-I data revealed six patient endotypes with unique IFN-I activity and clinical phenotypes, including serum IFNα levels, ISG patterns, cell subset sensitivity to IFN-I, and profiles of disease activity, organ damage, anti-double-stranded DNA antibodies and lymphocyte counts. Thus, the impact of IFNI signalling exists on a heterogeneous spectrum in cSLE.

Conclusion: This study provides novel and detailed insights into the heterogeneity of IFN-I signalling in cSLE with clinically relevant subgroups identified. These findings support stratified use of IFN-I-targeted therapies in cSLE, with LAMP3 as a promising biomarker for monitoring IFN-I activity and guiding personalised treatment for patients.

SESSION 5 JDM & Scleroderma

PReS25-ABS-1132

TREATING JUVENILE DERMATOMYOSITIS TO TARGET: PRES/CARRA-ENDORSED RECOMMENDATIONS FROM AN INTERNATIONAL TASK FORCE

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Introduction: Despite the recent prognostic improvement, a sizeable proportion of patients with juvenile dermatomyositis (JDM) respond suboptimally to available therapies and experience chronic disease activity. The treat-to-target (T2T) strategy, which mandates the explicit definition of a therapeutic target and the adaptation of treatment interventions depending on whether the target is reached or not reached over time, has been recently proposed for juvenile idiopathic arthritis and childhood-onset systemic lupus erythematosus.

Objectives: To develop the recommendations for treating JDM to target.

Methods: A Steering Committee formulated a set of provisional recommendations based on evidence derived from a systematic literature review (SLR) and a retrospective chart review of patients followed in two tertiary care pediatric rheumatology centers. The provisional recommendations were shared with an international Task Force (TF) through an online consensus survey. The TF included 28 paediatric rheumatologists, two specialists in neuromuscular diseases, one dermatologist, one physical therapist, one research nurse, two patients with JDM and one parent of a patient with JDM. Based on the comments provided by the respondents, some recommendations were amended or reworded. The recommendations were, then, discussed, amended and voted by the TF members at a consensus conference convened in Genoa, Italy, on 7-8 October 2024.

Results: The TF reached consensus on 7 overarching principles and 12 recommendations. It was agreed that both patients/parents and treaters should share in setting treatment targets and therapeutic strategies, with inactive disease (ID) as the preferred target and minimal disease activity as an alternative target. ID is aimed to be achieved within 12 months after treatment start. Interim targets include minimal and moderate clinical improvement within 6 weeks and 3 months, respectively, and normalization of muscle strength within 6 months. High-dose glucocorticoids remain fundamental in the initial management, but progressive tapering and discontinuation within 12 months through optimisation of concomitant immunomodulatory therapy was advised. All items were agreed by more than 80% of TF members. A research agenda was formulated.

Conclusion: The TF developed recommendations for treating JDM to target, being aware that the evidence is not strong and needs to be expanded by future research. Implementation of the recommendations in clinical practice will help to reach optimal outcomes for JDM.

PReS25-ABS-1198

ELEVATED TRAJECTORIES OF BIOMARKERS GALECTIN-9 AND CXCL10 ARE ASSOCIATED WITH HIGH RISK OF FLARE IN JUVENILE DERMATOMYOSITIS – A MULTICOHORT STUDY

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Introduction: Juvenile dermatomyositis (JDM) has a heterogeneous and unpredictable disease course, with half of patients experiencing recurrent or persistent disease. Although there is a clear need for objective biomarkers to guide personalized treatment strategies, few novel candidates are successfully translated into clinical practice. Galectin-9 and CXCL10 have previously been validated as robust indicators of disease activity in JDM and may serve as reliable prognostic biomarkers.
Objectives: To validate Galectin-9 and CXCL10 as biomarkers for an impending flare.
Methods: We measured Galectin-9 and CXCL10 in >1,100 longitudinal serum or plasma samples from 158 JDM patients from four countries. Mean biomarker levels in the 2 years prior to flare were compared with levels in patients without flares. We applied joint latent class mixed models (jointLCMM) to jointly analyze biomarker trajectories and time to flare. For the jointLCMM, the total cohort was split in a training and validation cohort. Models with 1 to 5 classes were fitted and the optimal model was selected based on the lowest Bayesian Information Criterion (BIC). Mean posterior probabilities were used to assess classification quality (1 indicating perfect classification). The trained models for Galectin9 and CXCL10 were applied to predict class membership in the validation cohort. A flare was defined as the moment of treatment intensification due to worsening of disease.
Results: Galectin-9 and CXCL10 both started rising around 1 year prior to flare, while levels remained low in those without a flare. In contrast, conventional biomarker CK showed a slight increase only in the final 4 months, similar to the Physician's Global Assessment (PGA) score. For both Galectin-9 and CXCL10, two latent classes were identified; one class containing one-fifth of patients was characterized by elevated biomarker levels and a high flare risk, with flare rates of 91.3% (Galectin-9) and 77.8% (CXCL10). Median time-to-flare was 7.1 months from the first measurement. When comparing flares among the two classes, skin-only flares were relatively more common in the Galectin-9 class with low biomarker levels (50% vs 14% of flares, p = 0.03). In the validation cohort, 41 and 47% of patients were predicted to be in the class with high Galectin-9 and high CXCL10, respectively, with a mean posterior probability of 0.90 and a flare rate of 100%. The sole flare predicted to be in the low Galectin-9 class was limited to the skin.
Conclusion: In this comprehensive international cohort, patients with increased longitudinal measurements of Galectin-9 and CXCL10 had a high risk of flaring within a year. Skin-only flares were less likely to be preceded by increased levels of Galectin-9. Validation on an independent cohort confirmed the reproducibility of these findings. Our data indicate that Galectin-9 and CXCL10 could guide medication tapering decisions and timely treatment intensifications, reducing chronic inflammation and improving outcomes in children with JDM.

PReS25-ABS-1338

SPATIAL TRANSCRIPTOMIC ANALYSIS REVEALS MITOCHONDRIAL DYSFUNCTION IN TREATMENT-NAÏVE JUVENILE DERMATOMYOSITIS MUSCLE

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Introduction: Juvenile dermatomyositis (JDM) is a pediatric autoimmune disease characterized by chronic inflammation of muscle and skin tissues. While interferon (IFN)-driven inflammation is well-documented, the role of mitochondrial dysfunction in muscle pathology remains unclear. This study investigates spatial transcriptomic alterations in JDM muscle, focusing on mitochondrial pathways and their relationship to IFN signalling.
Objectives: To characterize the spatial transcriptomic landscape of muscle biopsies from treatment-naïve JDM patients, comparing mitochondrial and IFN-related gene expression with healthy controls.
Methods: Muscle biopsies from three JDM patients recruited from the JDCBS and three age-matched controls were analyzed using the Nanostring GeoMx Digital Spatial Profiler. Regions of interest (ROIs) included muscle fibres, immuneinfiltrated muscle, and CD68+ macrophage-enriched regions. Differential gene expression, pathway enrichment, and pathway clustering analyses were performed. Findings were validated in a bulk RNA-sequencing dataset (JDM n=4; controls n=5; PMID: 34997119) and a cohort of 19 JDM cases from the JDCBS using immunohistochemistry (IHC) for myxovirus-resistant-protein A (MxA, an IFN-driven protein marker) and histochemistry (HC) with COX-SDH staining (indicating mitochondrial deficiency).
Results: Spatial transcriptomics identified 448 differentially expressed genes (|LogFC|>1.5, FDR <0.05) between JDM and control muscle regions, with pathway analysis revealing concurrent IFN pathway activation and mitochondrial dysfunction. To quantify these patterns across ROI types, two gene expression scores were calculated: a 15-gene IFN score was elevated across all JDM regions (Kruskal-Wallis p=0.0034), while a 41-gene mitochondrial score showed significant suppression of genes associated with mitochondrial function (ANOVA p<0.0001), most marked in CD68+ macrophages. These mitochondrial abnormalities were confirmed in bulk RNA-sequencing from 5 additional JDM cases, demonstrating consistent suppression of oxidative phosphorylation pathways, linked to both nuclear-encoded and mitochondrialencoded gene transcription. Critically, IFN and mitochondrial signatures were clinically distinct: mitochondrial dysfunction was evident even in patients with minimal weakness or lower IFN activity. This was further validated in 19 JDM cases, where IHC demonstrated no association between MxA and COX-SDH scores (U-statistic permutation test, p=0.657), reinforcing that mitochondrial defects could occur independently of IFN-associated inflammation. Importantly, higher MxA expression was associated with more severe muscle symptoms, while mitochondrial deficiency showed no such association.
Conclusion: These data suggest that mitochondrial dysfunction is a consistent and IFN-independent feature of JDM muscle, involving genes encoded by both nuclear and mitochondrial genomes, and is detectable regardless of disease severity. These findings, validated across spatial transcriptomics, bulk RNA-sequencing, and IHC, highlight the potential for mitochondrial-targeted therapies alongside immunosuppressive treatment.

PReS25-ABS-1364

BIOLOGICS IN THE TREATMENT OF THERAPY RESISTANT CASES OF JUVENILE SCLERODERMA OF HEAD AND FACE ('EN COUP DE SABRE') AND PARRY-ROMBERG SYNDROME

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Introduction: Juvenile scleroderma of head and face ('en coup de sabre' and Parry-Romberg syndrome) (JSF) leads to deformation of the face with functional and aesthetic defects, neurological disorders, low quality of life and depression. Conventional initial therapy with glucocorticosteroids (GCS) and cytostatics is ineffective in about 30% of patient.

Objectives: To assess efficacy of biologics in the treatment of resistant cases of JSF.

Methods: The study included 49 children with (17 boys, 32 girls), average age 13,5±3,4yrs, average disease onset 6,3±3,1yrs, disease duration the before standard therapy 2,3±1,9yrs, average disease duration before biologics 5,3±2,9yrs. To assess efficacy of therapy, the activity score was used, it includes local skin activity, increase of lesion area, presence of uveitis, foci in the brain, neurological disorders equivalent to points. We assessed disease activity initialy, during conventional therapy and during biologics every 3 months. All the patients first received GCS 0,7- 1 mg\kilo for 8 weeks, then taped and withdrawn up to 12 months plus Methotrexate (MTX) and/or mycophenolate mofetil (MFM) in standard doses for 6-18 months, then due to low effectiveness biologics were started.

Results: Before initial standard therapy mean disease activity score was 9,4±2,8 points. By 12 month conventional therapy was effective in 22 patients (44%), average disease activity score decreased to 5,4±2,4(P = 0.0001). In 27 (56%) patients therapy was not effective- mean disease activity score was 9,4±2,7points. Biologics with combination with MTX or MFM was started in 27 patients (18 received Tocilizumab, 6- Rituximab, 3- Abatacept in standard doses). By 12 months therapy with biologics was effective in 24 patients, mean disease activity score decreased to 6,4±2,3points (P <0.0001), in 22 patients positive skin changes were noticed in 6 months. We did not notice a significant improvement in disease activity score in children on abatacept. Pneumocystis pneumonia was detected in 2 patients on rituximab, despite preventive treatment, in other 2 girls Rituximab was changed to Tocilizumab due to hypogammaglobuliemia or neutropenia. In 20 patients therapy with biologics lasted safely up to 24 months.

Conclusion: Combined therapy with biologics could signifficantly decrease desease activity in resistant cases of JSF. Tocilizumab is better tolerated than Rituximab. Further research should determine the timing of the initiation of biologics

Trial registration identifying number: Trial registration identifying number: The study was approved by the Local Ethical Committee of Sechenov University, Protocol N 01-25, dated 23.01.2025

PReS25-ABS-1696

THE ISSAID/PRES RECOMMENDATIONS FOR THE DIAGNOSIS, TREATMENT AND MONITORING OF PEDIATRIC BEHCET'S DISEASE AND MONOGENIC MIMICKERS.

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Introduction: Behçet's disease (BD) is a polygenic condition with a complex immunopathogenetic background and challenging diagnostic and therapeutic concepts. Despite the presence of classification criteria, the diagnosis of pediatric BD is still difficult due to multisystemic character of the disease, absence of definitive diagnostic biomarkers, and the incomplete manifestations in childhood cases. Due to the difficulties in diagnosing pediatric BD as well as the absence of randomized clinical trials, there is a lack of standardized treatment protocols for managing this condition.

Objectives: To establish evidence-based recommendations on diagnosis, treatment, and monitoring to standardize the management of patients with paediatric BD and identified monogenic mimics (TNFAIP3, RELA, Trisomy 8, NFKB1, ELF4).

Methods: A multinational, multidisciplinary task force consisting of physician experts including rheumatologists, neurologists, ophthalmologist, pharmacologist, geneticist, patient/caregivers, and allied health care professionals was established. Evidence synthesis including systematic literature review (EMBASE, Medline, PubMed, CINAHL, Cochrane, Clinical Trials.gov) and Delphi questionnaire via RedCap were conducted. Consensus meeting was convened in May 2025 in London, Ontario,Canada. Face to face consensus methodology (Round Robin Discussion) was utilized to formulate and vote on statements to guide optimal patient care.

Results: For pediatric BD, of 13043 references identified, 100 articles were selected for inclusion. For genetic mimickers, of 357 references identified, 96 studies were selected for inclusion. Delphi questionnaire consisted of 79 questions and was sent to 41 experts from 13 countries across Europe, United States, Canada, South America, and Asia.

The task force devised 33 statements including 4 overarching principles. Major themes endorse the importance of acknowledging that pediatric Behcet disease can be a challenging diagnosis, as symptoms emerge gradually over time. It's crucial to consider genetic or genomic conditions in the differential diagnosis, especially for patients with early-onset or family history of Behcet-like disease. In these cases, evaluation should include genetic testing using NGS-based

autoinflammatory gene panels or WES or WGS as well as screening (immune-phenotyping) for immune dysregulation, and disease-associated comorbidities. Monoclonal Anti TNFs should be used as a first-line biologic treatment for patients with severe major organ such as ocular, neuro, vascular and GI involvement. Close monitoring for disease progression and complications is essential as well as the access to specialized, multidisciplinary care at referral centers.
Conclusion: These recommendations represent state-of-the-art knowledge based on published data and expert opinion to guide diagnostic evaluation, treatment, and monitoring of patients with pediatric BD, and to standardize and improve care, quality of life and disease outcomes.

PReS25-ABS-1307

FUNCTIONAL CHARACTERIZATION OF NEMO-NDAS CAUSING VARIANTS IN PATIENTS' PBMCS AND IN WILDTYPE AND MUTANT U937 CELLS

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Introduction: NEMO-deleted exon 5 autoinflammatory syndrome (NEMO-NDAS) is an inflammatory disease caused by mosaic splice-site variants that lead to exon 5 skipping in *IKBKG*, encoding NEMO. Patients (pts) present with systemic inflammation, gdT-cells expansion, high serum IFNg, portal hypertension (PH) and porto-sinusoidal vascular disorders (PSVD).
Objectives: To characterize the effect of exon 5-skipped NEMO on NFkB signaling in U937 cells, and to assess intestinal barrier and gut microbiome dysregulation in the pathogenesis of PH and PSVD.
Methods: U937 cells with exon 5-skipped NEMO were created by CRISPR (MUT) and compared to wildtype U937 cells (WT). NFkB signaling, cell viability, p65 nuclear translocation, NEMO/IKKb colocalization, and mRNA transcription profiling were assessed in TNF-stimulated MUT and WT U937 cells. We assessed immune activation and target killing in pts' PBMCs cocultured with WT and/or MUT U937s and quantified live U937 cells by flow cytometry. To characterize the gut-liveraxis, we analyzed intestinal fatty-acid-binding protein (I-FABP) concentrations in serum, and the stool microbiome (including virome), in NEMO-NDAS pts, inflammatory controls, and healthy household controls (HCs).
Results: Following TNF stimulation, nuclear translocation of p65 was significantly attenuated in MUT U937 cells consistent with impaired NFkB signaling. Additionally, increased susceptibility to TNF-induced cell death of MUT U937 cells was associated with a lack of upregulation of the anti-apoptotic genes *BIRC3*/cIAP2 and *CFLAR*/c-FLIP.
To test the killing potential of expanded gd T cells in pts' PBMCs, we cocultured pts' PBMCs with WT or MUT U937 cells. While viability of WT U937 cells is not affected by the pts' PBMC, mutant U937 cells are killed. When mixed WT and MUT U937s were cocultured with PBMCs, both WT and MUT U937s had decreased survival compared to PBMC-free conditions. Exploration of contributing cell types and pathomechanisms is ongoing.
Liver-gut-axis evaluation suggested that NEMO-NDAS pts have increased IFABP serum levels compared to CANDLE pts and

HCs, suggestive of increased intestinal permeability and impaired gut barrier function. Microbiome studies showed increased abundance of Faecalibacterium phages and a decrease in metabolic protective markers, which is consistent with previously reported data in liver disease.
Conclusion: Exon 5-skipping in NEMO impairs NFkB signaling, sensitizes U937 cells to TNF-induced cell death, and leads to U937 cell death in cocultures with PBMCs from NEMO-NDAS pts. We hypothesize that exon 5-skipped NEMO impairs gut epithelial cell function and leads to dysbiosis and increased microbial translocation that contribute to PH and PSVD in NEMO-NDAS. Whether impaired gut barrier and dysbiosis contribute to activation and expansion of gd T cells in NEMONDAS is under investigation.

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DOMINANT NEGATIVE ADA2 MUTATIONS CAUSE ADA2 DEFICIENCY IN HETEROZYGOUS CARRIERS

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Introduction: Human ADA2 deficiency (DADA2) is an inborn error of immunity with a broad clinical phenotype encompassing vasculopathy including livedo racemosa and lacunar strokes as well as hemato-immunological manifestations. Combination of decreased serum ADA2 activity and the identification of biallelic deleterious alleles in the *ADA2* gene are used for diagnosis. DADA2 carriers harbor a single pathogenic variant in *ADA2* and are mostly considered healthy and asymptomatic. However, some DADA2 carriers present a phenotype compatible with DADA2 (1–4).
Objectives: We sought to investigate whether being heterozygote for specific variants in *ADA2* could explain the patients DADA2 phenotype.
Methods: A HEK293T cell overexpression system was used to evaluate impact of ADA2 variants on WT ADA2 protein expression/secretion and enzymatic activity. Finngen, UK biobank and the Bio*Me* Biobank were used to assess population genetics and evaluate correlation with DADA2 phenotypes. ADA2 enzyme activity was measured in a colorimetric assay adapted by Giusti et al (1974)
Results: In addition to diseased DADA2 carriers in literature (1–4), we report a cohort of 10 heterozygous carriers of pathogenic *ADA2* variants presenting with DADA2 clinical features. To study the potential effect of heterozygous pathogenic variants in ADA2 on WT ADA2 protein expression, secretion and enzymatic activity, we performed transient transfection of each *ADA2* variant together with WT *ADA2* to mimic carrier status. In vitro study of the *ADA2* variants identified in this patient cohort revealed that R169Q, H424N and Y453C affect secretion of WT ADA2 protein. Moreover, we demonstrate a dominant negative effect on the enzymatic activity of WT ADA2 by variants G47A, G47R, G47V, R169Q, E328K, H424N and Y453C both intracellularly and extracellularly. Data from PheWAS show that the heterozygous state for pLOF variants in *ADA2* is associated with phenotypes that align with DADA2. When studying the most frequent allele, R169Q, the enriched phenotypes are even more striking, despite the overall low number of cases.
Conclusion: Here, we describe how specific heterozygous variants cause ADA2 deficiency through distinct dominant negative effects on either ADA2 enzyme activity, dimerization and/or secretion. At the molecular level, heterozygosity for these variants mimics what is observed in DADA2. We conclude that humans with heterozygous dominant negative missense variants in *ADA2* are at risk of DADA2.
References: 1 Rama, M. *et al. European Journal of Human Genetics* 26, 960–971 (2018) 2. Moi, L. *et al. Journal of Clinical Immunology* 42, 959–961 (2022) 3. Nihira, H. *et al. Journal of Allergy and Clinical Immunology* 148, 550–562 (2021) 4. Izumo, H. *et al. Cureus* (2023)

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TRANSCRIPTOME ANALYSIS OF UNMEDICATED HETEROZYGOUS FAMILIAL MEDITERRANEAN FEVER PATIENTS REVEALS A TYPE I INTERFERON SIGNATURE DRIVING INCREASING PYRIN EXPRESSION

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Introduction: Familial Mediterranean Fever (FMF) is the most common monogenic autoinflammatory disorder, characterized by recurrent episodes of systemic inflammation. Although this largely is an autosomal recessive condition, a subset of heterozygous carriers of *MEFV* mutations exhibit a clinical phenotype consistent with FMF. The mechanisms underlying this phenomenon remain poorly understood.

Objectives: We aimed to identify differential molecular signatures and potential diagnostic pathways by comparing the transcriptomic profiles of patients with a single pathogenic mutation that display the classical FMF phenotype with those of healthy heterozygous carriers. We also assessed our results with FMF patients with two mutations and validated key results at the protein level.

Methods: Peripheral blood mononuclear cells (PBMCs) were isolated from 10 FMF patients (5 homozygous/compound heterozygous, 5 heterozygous exon 10 mutations) and 5 healthy heterozygous carriers (exon 10 mutations) recruited from tertiary centers. Patients met 2019 Eurofever/PRINTO criteria and were sampled during asymptomatic, treatment-naïve phases (prior to colchicine initiation) to avoid confounding effects.

For transcriptome profiling, total RNA from pooled groups (heterozygous FMF, homozygous FMF, healthy carriers) was extracted (Norgen Kit), followed by globin mRNA depletion (Qiaseq Fast Select) and library preparation (Qiaseq Stranded mRNA Kit). Libraries were sequenced on an Illumina NextSeq 500/550 (2×74 bp paired-end reads). Reads were aligned to hg19 (CLC Genomic Workbench), with differential expression analyzed via a negative binomial Generalized Linear Model (TMM-normalized; adjusted *p*<0.01, $|\log_2 FC|>1$). REACTOME pathways were assessed using ExpressAnalyst.

Protein studies utilized healthy donor-derived monocytes/PBMCs. Monocytes (isolated with Miltenyi Kit) and PBMCs were stimulated with IFN-α (1000 U/mL), and lysates were immunoblotted for IRF-3, ISG15, Pyrin, STAT1, AIM2, caspase-5, and β-actin. CXCL10 in supernatants was quantified via Luminex (Bio-Rad).

Results: We included 10 familial Mediterranean fever (FMF) patients (6 males/4 females; median age 9–11 years) and 5 healthy heterozygous carriers (1 male/4 females). All patients were treatment-naïve, with normal acute-phase reactants. Transcriptomic profiling of PBMCs identified 147 differentially expressed genes (DEGs; FDR ≤0.001, |Fold Change (fc)|≥2) between heterozygous FMF patients and healthy carriers (96 upregulated and 51 downregulated genes), including upregulated interferon-stimulated genes (*STAT1*, *STAT2*, *IRF7*, *ISG15*, *IFIT2*, *IFIT3*, *USP18*). Gene Ontology revealed enriched type I interferon responses, cytokine signaling, and inflammatory pathways (p-adj <0.01), with JAK-STAT signaling implicated. REACTOME analysis confirmed pronounced type I interferon activation (p-adj <0.01), particularly in IFN-α/β clusters. STRING network analysis highlighted interactions among innate immune genes (*STAT1*, *IRF7*, *ISG15*, *OAS1*). Inflammasome-associated genes (*CASP5*, *GBP1*, *NLRC4*) and *MEFV* (encoding Pyrin) were upregulated in heterozygous FMF (p-adj <0.05). Compared to homozygous patients, heterozygotes exhibited heightened cytokine signaling and persistent interferon-related gene expression. Kinetic analysis of IFN-α-stimulated monocytes/PBMCs from healthy donors demonstrated time-dependent increases in CXCL10 secretion and elevated expression of Pyrin, STAT1, ISG15, AIM2, and caspase-5, while IRF3 remained unchanged. These findings support a model wherein chronic type I interferon signaling

acts as a “second hit” in heterozygous *MEFV* carriers, driving mutant Pyrin overexpression and inflammasome activation, thereby precipitating the FMF phenotype.

Conclusion: These findings suggest that type I IFN signaling acts as a critical 'second hit,' amplifying Pyrin expression in heterozygous individuals and enabling disease manifestation despite a single *MEFV* mutation. This study offers an explanation for the much-debated issue of the carriers expressing disease phenotypes in diseases such as FMF, and presents novel insights for precision diagnosis and therapeutic intervention.

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VALIDATION OF HUMAN PHENOTYPE ONTOLOGY (HPO) TERMS AND DEVELOPMENT OF AN AI-BASED DIAGNOSTIC TOOL FOR SAIDS: THE ODINO PROJECT

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Introduction: An accurate classification of systemic autoinflammatory diseases (SAIDs) is crucial for an early diagnosis and therapy optimization. The Human Phenotype Ontology (HPO) project provides a standardized terminology for describing phenotypic features of genetic diseases. HPO help clinicians prioritize diagnosis by ranking diseases based on similarity scores between HPO terms and patient's symptoms. In 2022 the AutoInflammatory diseases section was revised, but the accuracy of the new terms has not yet been validated in real patients.

Objectives: i) to evaluate the diagnostic accuracy of HPO terms in a cohort of real patients, ii) to evaluate the accuracy of *Phenomizer* compared to different machine-learning algorithms based on a provided real-life patients' dataset. iii) to develop a novel diagnostic tool for SAIDs.

Methods: From the Eurofever Registry, 2,866 patients diagnosed with Familial Mediterranean Fever (FMF), CryopyrinAssociated Periodic Syndrome (CAPS), Mevalonate Kinase Deficiency (MKD), Periodic Fever, Aphthous Stomatitis, Pharyngitis, Adenitis (PFAPA), or Tumor Necrosis Factor Receptor-Associated Periodic Syndrome (TRAPS) were included. Eurofever clinical variables were codified with HPO terms, and missing terms were retained. The patients' dataset was split into training (n=2,005) and test sets (n=861). Four machine learning classifiers were evaluated: Elastic Net regression (EN), k-Nearest Neighbors (kNN), Random Forest (RF), and eXtreme Gradient Boosting (XGBoost), comparing their performance to *Phenomizer*.

Results: 224 Eurofever variables were codified into HPO terms. Of these, 195 had full HPO correspondence, 12 partial, and 17 no correspondence. XGBoost emerged as the best-performing algorithm in assigning the correct diagnosis to the analyzed patients, achieving an average accuracy of 0.80, and significantly outperforming *Phenomizer*, even when *Phenomizer* was trained on Eurofever HPO terms' frequencies. The addition of the terms "fever duration" and "ethnicity" (present in Eurofever but absent in HPO) improved the algorithm accuracy, highlighting the need for new HPO codes. Finally, based on the best-performing algorithm, a user-friendly web app where clinicians can input HPO terms to receive the probability of each SAID diagnosis (among those used in the training model) was developed.

Conclusion: Our results suggest that the HPO database should be updated including Eurofever patients' term frequencies. The developed web app correctly identifies the two most probable SAIDs in over 85% of cases, offering a valuable tool for early diagnosis. Further updates will refine the model as additional data from underrepresented diseases become available.

PReS25-ABS-1209

CONFIRMING THE VALIDITY OF THE NEW EULAR/ACR CLASSIFICATION CRITERIA FOR PEDIATRIC CHRONIC NONBACTERIAL OSTEOMYELITIS

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Introduction: Chronic nonbacterial osteomyelitis (CNO) is a noninfectious autoinflammatory bone disease which remains a diagnosis of exclusion, as existing diagnostic criteria are not widely accepted. Recently, the European Alliance of Associations for Rheumatology (EULAR) and the American College of Rheumatology (ACR) developed new classification criteria for CNO, demonstrating 82% sensitivity and 98% specificity in an initial study.

Objectives: We aimed to investigate sensitivity and specificity of the new EULAR/ACR classification criteria for pediatric CNO, in a distinct real-world clinical setting and compare it to the sensitivity and specificity of the existing Jansson and Bristol diagnostic criteria.

Methods: This was a single-center cross-sectional study including children ≤18 years, diagnosed with CNO, acute infectious osteomyelitis (AOM) and bone malignancy from June 1, 2018 to May 31, 2024. Patients with other mimicking conditions, immunodeficiency, sickle cell disease, or those previously included in the original development cohort were excluded. Patients were divided into two groups: a CNO group and a non-CNO group (AOM and bone malignancy), from the latter a representative, random, sample was selected (www.random.org). Demographic, clinical, laboratory, imaging and pathology data were collected at disease onset. EULAR/ACR criteria were retrospectively applied to the entire cohort, independently from the initial diagnosis. Patients with an aggregate score ≥ 55 points were classified as having CNO. A sensitivity analysis was also conducted where patients with criteria with missing data were excluded. Classification results using the new criteria were compared with the final clinical diagnosis based on physician assessment (criterion standard). The same analysis was applied to Jansson and Bristol criteria. From contingency tables, sensitivity and specificity were calculated.

Results: Of the 164 children included, 82 had CNO, 41 were randomly selected from 274 cases of AOM, and 41 from 849 cases of bone malignancy. The median age was 10 years (IQR 3–16), with 62% girls and 37% boys, 66% had a bone biopsy. Overall, 40% scored ≥ 55 and 60% did not, with 3 false positive and 19 false negative. The EULAR/ACR criteria demonstrated 77% sensitivity and 96% specificity, with a positive predictive value (PPV) of 95% and negative predictive value (NPV) of 80%. In our sensitivity analysis excluding patients with incomplete data, results remained consistent (sensitivity 79%, specificity 96%, PPV 95%, NPV 81%). In comparison, the Jansson criteria showed 78% sensitivity, 67% specificity, PPV of 70%, and NPV of 75%. The Bristol criteria yielded 89% sensitivity, 70% specificity, PPV of 86%, and NPV of 74%.

Conclusion: Based on its favorable sensitivity and specificity, especially in comparison to existing criteria, the new EULAR/ACR criteria appeared to be more effective in distinguishing CNO from AOM and bone malignancy at disease onset. These results were consistent with findings from the original validation cohort.

PReS25-ABS-1369

MOLECULAR MECHANISMS IN CHRONIC NONBACTERIAL OSTEOMYELITIS (CNO) AND THEIR THERAPEUTIC POTENTIAL

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Introduction: Chronic non-bacterial osteomyelitis (CNO) is an autoinflammatory bone disease mainly affecting children and adolescents. It can cause pain, hyperostosis and fractures, affecting patients' quality of life and psychomotor development. We recently identified rare *P2RX7* variants in a large proportion of CNO patients (32.4% versus 4.4% of controls) and demonstrated their functional impact. CNO-associated *P2RX7* variants are associated with impaired K^+ efflux, promoting NLRP3 inflammasome activation and pro-inflammatory cytokine release. Notably, *P2RX7* variants also associated with prolonged survival (reduced pyroptosis) of monocyte-derived macrophages.

Objectives: To understand how *P2XR7* variants contribute to prolonged cell survival, this project investigated effects of CNO-associated *P2RX7* variants on Ca^{2+} mobilisation, reactive oxygen species (ROS) production, mitochondrial integrity, and cytokine expression in THP-1 derived macrophages.

Methods: Genetically modified THP-1 monocytes were differentiated into macrophage-like cells, and used to investigate effects of CNO-associated *P2RX7* variants (c.349C>T, rare gain-of-function; c.920G>A rare loss-of-function; c.489C>T common gain-of-function). Activation of the NLRP3 inflammasome (ASC speck assay), K^+ (ELISA) and Ca^{2+} flux (flow cytometry), expression of pro- and anti-inflammatory cytokines (MSD and Luminex assays), ROS production (2',7'dichlorofluorescein diacetate/DCFDA and Lucigenin assays) and mitochondrial function (MitoTracker) were studied. Effects of small molecule P2X7 (A-804598) and NLRP3 (MCC950) inhibitors were interrogated.

Results: Compared to cells expressing wild-type P2X7, THP-1-derived macrophages expressing CNO-associated c.349C>T and c.489C>T variants associated with increased K^+ and sustained Ca^{2+} flux, enhanced inflammasome activation, increased IL-1β and IL-18 secretion, and reduced LDH release (approximating prolonged cell survival). Prolonged survival associated with reduced ROS content for all CNO-associated variants, reduced mitochondrial stress for the c.920G>A loss-of-function variant (superoxide production), and increased numbers of functional mitochondria for the c.349C>T and c.920G>A variants. Co-culture with the P2X7 inhibitor A-804598, across cell lines, resulted in reduced cellular K^+ and increased $Ca2^+$ content, reduced inflammasome assembly, ASC speck and cytokine release, and reduced mitochondrial damage. These P2X7 inhibitor mediated effects were greater when compared to co-culture with the NRLP3 inhibitor MCC950.

Conclusion: Imbalanced K^+ and Ca^{2+} mobilization in THP-1-derived macrophages expressing CNO-associated *P2RX7* variants associates with reduced mitochondrial stress and prolonged survival. Understanding the contribution of CNOassociated variation in *P2RX7* will promote the development of target-directed treatments.

References: Charras A, Hofmann SR, Cox A, Schulze F, Russ S, Northey S, Liu X, Fang Y, Haldenby S, Hartmann H, Bassuk AG, Carvalho A, Sposito F, Grinstein L, Rösen-Wolff A, Meyer-Bahlburg A, Beresford MW, Lainka E, Foell D, Wittkowski H, Girschick HJ, Morbach H, Uebe S, Hüffmeier U, Ferguson PJ, Hedrich CM. P2RX7 gene variants associate with altered inflammasome assembly and reduced pyroptosis in chronic nonbacterial osteomyelitis (CNO). J Autoimmun. 2024 Apr;144:103183. doi: 10.1016/j.jaut.2024.103183. Epub 2024 Feb 23. PMID: 38401466.

PReS25-ABS-1689

A COMPOSITE FITNESS PROFILE IN JUVENILE IDIOPATHIC ARTHRITIS AND FAMILIAL MEDITERRANEAN FEVER COMPARED TO HEALTHY PEERS: FAST AND FIT

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Introduction: Physical fitness (PF) is a key determinant of health outcomes, and its assessment in children and adolescents provides an effective means of estimating overall health status and functional ability (1).
Objectives: The aim of this study was to evaluate the PF profile of patients diagnosed with Juvenile Idiopathic Arthritis (JIA) and Familial Mediterranean Fever (FMF) and to compare the results with healthy peers.
Methods: A total of 343 children and adolescents aged 8–18 years participated in the study (JIA: 117, FMF: 61, Healthy: 166). PF was assessed using FitnessGram tests: Curl-Up Test (CT), Push-Up Test (PT), Trunk Lift Test (TLT), Back-Saver Sit and Reach Test (BSSRT), and the Progressive Aerobic Cardiovascular Endurance Run (PACER), along with estimated VO_2max. Functional capacity was evaluated using the 6-Minute Walk Test (6MWT), 30-Second Sit-to-Stand Test (30SST), and 10-Stair Climb Test (10SCT). Group comparisons were performed using ANOVA, post-hoc Tukey, and ROC analysis. A Composite Fitness Score (CFS) was calculated by averaging the z-scores of ten fitness and functional capacity tests. Each raw score was standardized and averaged to generate a single composite indicator of physical fitness.
Results: The mean ages of participants with JIA, FMF, and healthy controls were 13.19±1.34, 13.52±1.45, and 13.32±1.34 years, respectively. Patients with JIA and FMF had significantly lower PF and functional capacity compared to their healthy peers ($p<0.05$). The 30SST demonstrated the highest discriminative accuracy (AUC = 0.85), PT (AUC = 0.75) and CT (AUC = 0.72) also showed good discriminative value, whereas the 6MWT and BSSRT were less predictive (AUC = 0.67 each). The healthy group had a significantly higher CFS (+0.22) compared to JIA (−0.20) and FMF (−0.23) ($p<0.001$) however, no significant difference was observed between the JIA and FMF ($p>0.05$). According to the Random Forest regression analysis based on participants' CFS scores, PT, BSSRT, and PACER were identified as the most important predictors of PF.
Conclusion: The findings of this study demonstrate that PF and functional capacity outcomes are significantly lower in patients with JIA and FMF, particularly among those with JIA. The primary determinants of PF were identified as upper extremity muscular endurance and strength, flexibility, and aerobic performance. One of the key outcomes of the study is the identification of the 30SST as an excellent potential for rapid fitness screening in adolescents. Furthermore, the incorporation of the PT, BSSRT and PACER into the evaluation process has been shown to be valuable in identifying risk factors and planning of targeted exercise interventions.
This study was supported by Scientific and Technological Research Council of Turkey (TUBITAK) under the Grant Number 121E690.
References: Day et al. 2023. NYC FITNESSGRAM:population-level physical fitness surveillance for New York City youth. American Journal of Epidemiology

PReS25-ABS-1071

CUMULATIVE SOCIAL DISADVANTAGE MEDIATES THE IMPACT OF NEIGHBORHOOD DEPRIVATION ON JIA DISEASE ACTIVITY IN A U.S. POPULATION

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Introduction: Social determinants of health (SDOH) interact across individual, family, and community levels and are known contributors to health disparities. We previously demonstrated that cumulative social disadvantage, a score of individual and family-level SDOH, was associated with persistent disease activity among U.S. children with JIA in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry.
Objectives: To assess the role of community-level SDOH and its interaction with cumulative social disadvantage in relation to persistent disease activity in a cohort of U.S. youth with JIA.
Methods: This cohort study included children with JIA enrolled in the CARRA Registry (July 2015-January 2022). A cumulative social disadvantage score (range 0–3) was calculated using three binary indicators: family income <$50,000/year, guardian education <high school, and public or no insurance. Community-level SDOH was assessed using the U.S. Area Deprivation Index (ADI), a validated geocoded measure of neighborhood disadvantage. Demographic and clinical characteristics were summarized by ADI quartile. Mixed-effects logistic regression models evaluated the association between ADI and active disease by cJADAS-10 thresholds (>1.1 for oligoarticular JIA; >2.5 for others), adjusting for cumulative social disadvantage and covariates. Multiple imputation (50 cycles) addressed missing data: ADI (17%), income (25%), and education (16%). Causal mediation analysis assessed whether cumulative social disadvantage and its components mediated the ADI–disease activity relationship.
Results: Among 9,612 U.S. children with JIA, cumulative social disadvantage was more common in disadvantaged neighborhoods (ADI quartile 4: 64.9% with score >0 vs. quartile 1: 18.8%). Neighborhood disadvantage was independently associated with persistent disease activity (ADI Q4: OR 1.43, 95% CI: 1.15–1.76), but this was attenuated after adjusting for cumulative social disadvantage and covariates (quartile 4: aOR 1.06, 95% CI: 0.85–1.32). Causal mediation analysis identified cumulative social disadvantage as a significant mediator, accounting for 68% of the ADI-disease activity relationship. Low income (80%) and public/no insurance (75%) were significant mediators; guardian education was not (27%).
Conclusion: Neighborhood disadvantage (ADI) was associated with persistent JIA disease activity, but this relationship was largely mediated by individual and family-level SDOH. These findings highlight the need to address modifiable social risk factors, especially financial insecurity and insurance access, when developing strategies to reduce JIA health disparities. Interventions such as social work support or patient navigation may help mitigate these inequities. This conceptual framework should be studied in European settings, where socioeconomic disparities exist but healthcare systems differ from the U.S. and may require alternative intervention.

E-POSTER PRESENTATIONS

ePoster short communications-1 Autoinflammatory Diseases-I

PReS25-ABS-1210

EVALUATING CONSENSUS TREATMENT PLANS FOR CHRONIC NONBACTERIAL OSTEOMYELITIS USING REAL-WORLD DATA

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Introduction: Chronic nonbacterial osteomyelitis (CNO) is a rare autoinflammatory bone disease of childhood. Due to the lack of standardized assessment tools in the diagnosis and treatment process, the Childhood Arthritis and Rheumatology Research Alliance (CARRA) developed three consensus treatment plans (CTPs) for CNO. The Clinical Disease Activity Score (CDAS) for CNO was created to assess disease activity in the absence of imaging findings.
Objectives: To evaluate the applicability and effectiveness of the CNO CTPs in real-world settings using the CNO CDAS, and to assess the diagnostic and therapeutic processes as well as the outcomes at final visit to determine the practical success of current treatment approaches.
Methods: This retrospective study included 171 patients diagnosed with CNO across 18 centers. Disease activity was assessed at diagnosis, treatment modification, and final visit using the CNO CDAS, which is based on the number of clinically active lesions, patient pain assessment, and global disease activity. Responses to the CTPs—comprising DMARDs, biologics (anti-TNF agents), and pamidronate—were analyzed.
Results: Of 171 patients, 68 (39.8%) were female and 103 (60.2%) male. Median age at symptom onset was 10 years (IQR: 4), at diagnosis 11 (IQR: 4.8), and at final visit 14 (IQR: 4); median follow-up was 30 months (IQR: 5). Bone pain (95.3%), functional limitation (67.8%), and fatigue (35.1%) were the most common presenting symptoms. Regional MRI was performed in 139 patients (81.3%) and whole-body MRI in 71 (42.1%), revealing a median of 6 lesions (IQR: 9). Frequently involved sites included the lower extremities (66%), pelvis (33.9%), and spine (15.7%). NSAIDs were used in 156 patients (91.2%), methotrexate in 146 (85.4%), anti-TNF agents in 93 (54.4%), and corticosteroids in 90 (52.6%). Remission was

achieved in 69 patients (40.3%) with anti-TNF therapy, 52 (30.4%) with methotrexate, 9 (5.3%) with sulfasalazine, and 5 (2.9%) with pamidronate. Among 89 patients requiring treatment modifications, 83 switched from DMARDs to anti-TNF agents. At final follow-up, 106 patients (62%) achieved medicated remission, 50 (29.2%) were in drug-free remission, and 15 (8.8%) had persistent active disease. Median CDAS scores declined from 15 (IQR: 5) at diagnosis to 15 (IQR: 5) after treatment modification and 0 (IQR: 5) at final visit ($p < 0.05$), indicating a significant improvement over time.

Conclusion: This study demonstrates the real-life applicability of the CNO CTPs. Anti-TNF therapy was associated with the highest remission rate (40.3%). Significant reductions in CDAS scores were observed following treatment modifications, supporting the clinical utility of these strategies in CNO management.

References: 1. Zhao Y, Wu EY, Oliver MS, Cooper AM, Basiaga ML, Vora SS, et al. Consensus Treatment Plans for Chronic Nonbacterial Osteomyelitis Refractory to Nonsteroidal Antiinflammatory Drugs and/or With Active Spinal Lesions. Arthritis Care Res (Hoboken). 2018 Aug 1;70(8):1228–37

2. Wu EY, Oliver M, Scheck J, Lapidus S, Akca UK, Yasin S, et al. Feasibility of Conducting Comparative Effectiveness Research and Validation of a Clinical Disease Activity Score for Chronic Nonbacterial Osteomyelitis [Internet]. 2022. Available from: http://medrxiv.org/lookup/doi/10.1101/2022.10.03.22280351

Disclosure of Interest: None Declared

PReS25-ABS-1093

GENOME-WIDE DNA METHYLATION ANALYSIS IN FAMILIAL MEDITERRANEAN FEVER

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Introduction: Familial Mediterranean fever (FMF) is an autoinflammatory disease most commonly associated with biallelic mutations in the *MEFV* gene. Patients carrying the same pathogenic variant in *MEFV* can exhibit a broad spectrum of clinical phenotypes. Identifying factors contributing to this clinical variability is essential for understanding disease mechanisms. DNA methylation has been proposed as a potential modifier of *MEFV* mutations and clinical presentation. However, prior studies exploring this hypothesis included heterogeneous cohorts, lacked genome-wide methylation analyses, and yielded inconsistent findings.
Objectives: We aimed to investigate the role of DNA methylation in FMF using a genome-wide DNA methylation approach.
Methods: We conducted a cross-sectional, genome-wide DNA methylation analysis using whole blood samples from 32 pediatric FMF patients and 16 age- and ethnicity-matched healthy controls (2:1 ratio), all recruited from Istanbul University Medical School. To minimize confounding, we included only patients homozygous for the M694V mutation and from the same geographical region. DNA methylation profiling was performed using the Illumina Infinium MethylationEPIC v2.0 BeadChip array, covering over 930,000 CpG sites. Data analysis was conducted in R (v4.4.0), adjusting for age, sex, and cell composition.
Results: We identified 22 differentially methylated CpG sites in FMF patients compared with healthy controls. Of these, 18 were hypomethylated—including a CpG site within the *MEFV* gene—and four were hypermethylated. Notably, several differentially methylated CpGs were located in genes encoding zinc finger proteins, a family of transcriptional regulators. Of the 22 CpGs, 13 were found on chromosome 16, where *MEFV* is located. Three hypomethylated CpGs were within 1.1 kb of the *MEFV* transcription start site, two of which overlapped with enhancer regions, suggesting a potential regulatory role. Cell-type–specific analysis revealed significant differential methylation in NK cells, $CD8^+$ T cells, and $CD4^+$ T cells in FMF patients compared with controls.
Conclusion: Our findings suggest that DNA methylation changes may contribute to the pathogenesis of FMF. The enrichment of differentially methylated sites near *MEFV* on chromosome 16 and in immune cell subsets supports a role for epigenetic regulation in disease expression. These results highlight DNA methylation as a potential modifier of FMF and a promising target for future biomarker development and personalized therapeutic strategies.
Disclosure of Interest: None Declared

PReS25-ABS-1602

ULTRASONOGRAPHIC EVALUATION OF EXERTIONAL LEG PAIN IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER: A SILENT COMPONENT OF THE DISEASE?

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Introduction: Exertional leg pain (ELP) is a common finding in patients with Familial Mediterranean Fever (FMF). Although its pathophysiology has not been fully elucidated, the most widely accepted hypothesis is that it represents a silent enthesopathy.
Objectives: The aim of this study is to investigate the radiological manifestations and clinical significance of ELP in patients with FMF through ultrasonographic evaluation of lower extremity joints and tendons

Methods: Patients diagnosed with FMF and followed in our clinic between June and September 2024, who were found to carry homozygous or compound heterozygous pathogenic variants in the MEFV gene, were included in the study. Patients with comorbid musculoskeletal diseases, active professional athletes, and those with a follow-up period of less than one year were excluded. All included patients underwent bilateral ultrasonographic (USG) examination of the hip, knee, and ankle joints, as well as assessment and thickness measurements of the patellar tendon, Achilles tendon, and plantar fascia. USG images were obtained by a single blinded investigator and evaluated according to the OMERACT pediatric USG guidelines.

Results: A total of 50 patients were included in the study, comprising 25 FMF patients with ELP and 25 without. No significant differences were observed in demographic characteristics, MEFV variants, disease activity, or treatment regimens between groups. Joint USG revealed grade 1 synovial effusion in nine patients—seven of whom were in the ELP group—synovial hypertrophy in three patients, and loss of the normal fibrillar tendon structure in one patient. Among those with synovial effusion, 6 patients (67%) had elevated acute phase reactants and active disease. The Achilles tendon was found to be significantly thicker in the ELP group compared to those without ELP (right and left median values: 0.50 and 0.42 cm vs. 0.39 and 0.36 cm, p=0.003 and p=0.009, respectively). This difference remained significant even after adjusting for factors known to affect tendon thickness, such as age and sex, using a multivariate linear regression model (B= 0.065, p=0.007). No differences were observed between the groups in other tendon or plantar fascia thickness measurements.

Conclusion: Although the pathophysiology of ELP in FMF remains unclear, this study suggests that it may be associated with increased Achilles tendon thickness. This finding may indicate subclinical enthesopathy and highlight the potential need for further investigation and treatment modification. Moreover, synovial effusion may be present in FMF patients even in the absence of symptoms or physical examination findings and is generally associated with increased disease activity.

References: 1) Bruyn GA, Iagnocco A, Naredo E, Balint PV, Gutierrez M, Hammer HB, et al. OMERACT definitions for ultrasonographic pathologies and elementary lesions of rheumatic disorders 15 years on. The Journal of rheumatology 2019;46(10):1388-93.

2) Eshed I, Rosman Y, Livneh A, Kedem R, Langevitz P, Ben-Zvi I, et al. Exertional leg pain in familial Mediterranean fever: a manifestation of an underlying enthesopathy and a marker of more severe disease. Arthritis & rheumatology 2014;66(11):3221-6.

3) Kushnir T, Eshed I, Heled Y, Livneh A, Langevitz P, Zvi IB, et al. Exertional muscle pain in familial Mediterranean fever patients evaluated by MRI and 31P magnetic resonance spectroscopy. Clinical Radiology 2013;68(4):371-5.

Disclosure of Interest: None Declared

PReS25-ABS-1648

CUTANEOUS MANIFESTATIONS OF AUTOINFLAMMATORY BONE DISEASES: A RETROSPECTIVE MULTICENTER STUDY

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Introduction: Autoinflammatory bone diseases are a group of disorders characterized by sterile osteomyelitis, caused by impaired regulation of the innate immune system [1]. Cutaneous manifestations may include palmoplantar pustulosis, generalized pustulosis, pyoderma gangrenosum, and acne. In addition to cutaneous manifestations, CNO may be coexistent with psoriasis and palmar plantar pustulosis [2]. Cutaneous manifestations are considered to be secondary to increased inflammation. The treatment for cutaneous manifestations is not clear. The management of the disease and local therapies are effective in the treatment of cutaneous manifestations [3].

Objectives: The aim of this study was to describe the cutaneous manifestations of patients with autoinflammatory bone diseases and to evaluate the relationship between cutaneous manifestations, bone involvement, and systemic inflammation in Turkish children.

Methods: This retrospective multicenter study was conducted in 9 pediatric rheumatology centers between the years 2013 and 2023 in patients with a diagnosis of autoinflammatory bone disease with cutaneous manifestations. Demographic data, laboratory findings, cutaneous manifestations, bone involvement, and treatments were recorded.

Results: Two hundred and sixty-nine autoinflammatory bone disease patients were evaluated. Fifty-one patients with cutaneous manifestations [46 CNO and 5 Majeed syndrome] were included in this study. Cutaneous manifestations preceded bone symptoms in 21 (41.2%) patients. The mean diagnostic delay was 16.1 ± 11.7 months in those with cutaneous manifestations and 25.3 ± 9.9 months in those with bone involvement (p=0.02). The most common skin lesions were acne (n=26), pustules (n=23), and papules (n=10). In a comparison of patients with and without acne, patients with acne had more frequent male sex and higher ESR, CRP levels (p=0.01,p=0.03, and p=0.04, respectively). In a comparison of patients with and without pustules, patients with pustules had younger age at symptom onset and age at diagnosis and higher ESR and CRP levels (p=0.04,p=0.04,p=0.04,p=0.02,p=0.03, respectively). In patients with CNO, the mean time to remission was 2.1 ± 0.7 years for cutaneous manifestation and 2.9 ± 1.4 years for bone involvement (p=0.04).

Conclusion: Skin lesions may appear before bone lesions in autoinflammatory bone diseases, serving as an important early warning sign for diagnosis, lesions such as acne and pustules are more common in these conditions and may contribute to the severity of inflammation in autoinflammatory bone diseases.

References: Masters SL, Simon A, Aksentijevich I, Kastner DL. Horror autoinflammaticus: the molecular pathophysiology of autoinflammatory disease (*). Annu Rev Immunol 2009;27:621–68.

Giovannelli E, Iacono A, Sprocati M. Osteomielite cronica non-batterica: descrizione di tre casi pediatrici [Chronic nonbacterial osteomyelitis: description of three pediatric cases.]. Recenti progressi in medicina 2021;112(7), 532–7.

Koker O, AktayAyaz N. Autoimmune and autoinflammatory diseases with mucocutaneous manifestations: A pediatric rheumatology perspective. International journal of dermatology 2023;62(6),723–36.

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THE IMPACT OF GENOTYPE ON NUTRITIONAL STATUS IN PEDIATRIC FMF PATIENTS: LINKING ANTHROPOMETRICS TO MUTATIONS AND DIETARY INTERVENTIONS IN COLCHICINE-RESISTANT CASES

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Introduction: Familial Mediterranean Fever (FMF) is an autoinflammatory disorder caused by mutations in the *MEFV* gene, characterized by recurrent fever, abdominal pain, and serositis attacks. Chronic inflammation may lead to metabolic disturbances, increasing the risk of growth retardation and malnutrition.

Objectives: This study aims to evaluate the impact of *MEFV* genotypes on malnutrition in pediatric FMF patients by comparing nutritional status and anthropometric measurements across different genotypes. Furthermore, we aim to investigate the relationship between genotype and malnutrition to identify high-risk populations. To date, only a limited number of studies have examined the relationship between genotype and malnutrition in this specific population.

Methods: This study was designed as a cross-sectional, single-center investigation. Patients aged ≤18 years with a diagnosis of familial Mediterranean fever (FMF), who had been followed for at least two years, were included. Demographic data (age, sex, age at diagnosis, disease duration) were recorded from medical files and socioeconomic status was assessed based on family income. Malnutrition was evaluated using weight and height percentiles, nutritional status, mid-upper arm circumference, height-for-age, and body mass index (BMI) z-scores. The Pediatric Yorkhill Malnutrition Score (PYMS) and Tool for Risk On Nutritional status and Growth in Kids (STRONGkids) scores were compared. Laboratory parameters, including C-reactive protein (CRP) and serum amyloid A (SAA) levels during attack-free periods, were analyzed. Comorbidities, chronic diseases, and known food allergies were documented. Statistical analyses were performed using IBM SPSS version 27.0, with a significance threshold of $p < 0.05$.

Results: A total of 224 patients were enrolled in the study. Female patients accounted for 56.7% (n = 129) of the study cohort.The mean age was 11.9 (7.6–15.0) years; age at diagnosis was 7.0 (4.0–10.0) years; disease duration was 3.0 (2.0–6.0) years; and colchicine treatment duration was 24.0 (12.0–48.0) months. It was determined that 17% (n=38) of the patients had at least one comorbid condition, while 67.4% (n=151) had a families with intermediate socioeconomic status. Among the patients, 46% (n=104) carried at least one M694V mutation in the MEFV gene, and 12.5% (n=28) were diagnosed with colchine resistant FMF. Patients with at least one M694V mutation in exon 10 exhibited significantly higher rates of mild and moderate malnutrition (59.7% and 18.8%, respectively) compared to those without the mutation (16.0% and 5.3%, p<0.001). Additionally, patients with homozygous M694V mutations in exon 10 demonstrated significantly lower mid-upper arm circumference z-scores and height-for-age z-scores (median [IQR]: 2 [2–2] and -1.86 [-2.96–-0.72], respectively) compared to non-carriers (3 [3–3] and -0.72 [-1.24–-0.12], p=0.002 and p=0.004, respectively).The PYMS and STRONGkids total scores were significantly higher in patients with colchine resistant FMF (1.03 ± 0.74 and 0.96 ± 0.42, respectively) than in those without (0.37 ± 0.62 and 0.35 ± 0.49, p<0.001 for both). Furthermore, a statistically significant positive correlation was observed between SAA levels and both PYMS and STRONGkids scores (r=0.204, p=0.002 and r=0.229, p=0.001, respectively).

Conclusion: Children with homozygous M694V mutations exhibit anthropometric measurements significantly associated with malnutrition, suggesting that this genotype may adversely affect growth parameters. These findings underscore the importance of close monitoring and targeted nutritional interventions in this patient population.

References: 1.Kişla Ekinci RM, Balci S, Akay E, Doğruel D, Altintaş DU, Yilmaz M. Disease Severity and Genotype Affect Physical Growth in Children With Familial Mediterranean Fever. Arch Rheumatol. 2019;34(3):288-293.

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PReS25-ABS-1640

SUBCLINICAL INFLAMMATION IN PEDIATRIC FAMILIAL MEDITERRANEAN FEVER: PREDICTORS AND FOLLOW-UP RESULTS

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Introduction: Familial Mediterranean fever (FMF) is the most common monogenic autoinflammatory disease of childhood. Subclinical inflammation, characterised by persistently elevated acute phase reactants in the absence of clinical episodes, is an increasingly recognised risk factor for long-term complications. Undetected inflammation can lead to severe outcomes such as amyloidosis, organ damage such as renal failure, and growth retardation. Despite the significant clinical relevance of the issue, there is a paucity of research on the predictors and outcomes of subclinical inflammation in paediatric FMF patients.

Objectives: The aim of this study was to determine the frequency and clinical predictors of subclinical inflammation in pediatric FMF patients and to evaluate the response to treatment adjustments for subclinical inflammation.

Methods: The medical records of FMF patients followed up at our clinic between December 2011 and February 2024 were retrospectively reviewed. Patients were grouped according to the presence or absence of subclinical inflammation, defined as elevated CRP levels during attack-free periods at more than 75% of follow-up visits. The clinical and genetic results of the two groups were compared.

Results: 572 FMF patients were included in the study, 288 (50.3%) of whom were female. Mean age was 168 ± 60 months. Subclinical inflammation was found in 15.6% of patients (n=89). Patients with subclinical inflammation had a significantly earlier age at diagnosis (p=0.038), longer duration of disease (p<0.001), more frequent attacks of fever (p=0.004) and arthritis (p<0.001), higher frequency of comorbid inflammatory diseases (p=0.027), and more frequent attacks per year (p<0.001). Independent predictors of subclinical inflammation included longer disease duration (OR=1.09, p=0.023), biallelic exon 10 mutations (OR=3.90, p=0.020), colchicine resistance (OR=2.60, p=0.048), arthritis (OR=7.06, p<0.001), and higher disease severity scores (ISSF) (OR=5.67, p<0.001). Maximum tolerated dose escalation of colchicine controlled inflammation in 45% of cases (n=40), while 55% (n=49) required biologics. Of those treated with biologics, 87.7% (n=43) achieved normalisation of inflammatory markers.

Conclusion: In paediatric FMF patients, subclinical inflammation can be seen with appropriate treatment doses of colchicine. Earlier age at diagnosis, carrying a biallelic exon 10 mutation, presence of arthritis, and higher ISSF scores seem to be related with subclinical inflammation. Increasing colchicine to the maximum tolerated dose is effective in almost half of these cases. Anti-IL-1 treatments are effective in those who are resistant to colchicine.

Disclosure of Interest: None Declared

PReS25-ABS-1055

ASSOCIATIONS OF MYOSITIS-SPECIFIC AUTOANTIBODIES WITH SPECIFIC CLINICAL FEATURES IN JUVENILE DERMATOMYOSITIS IN A LARGE REAL-WORLD MULTI-SITE REGISTRY

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Introduction: Myositis-specific autoantibodies (MSAs) are associated with distinct clinical features in juvenile dermatomyositis (JDM) and are increasingly being used to tailor treatment. However, there is a paucity of data on sensitivity and positive likelihood ratios (LR) of MSAs for specific clinical manifestations in a real-world multi-site JDM cohort.

Objectives: To determine the sensitivity and LR of MSAs with specific baseline and chronic clinical features of JDM in a large multi-site registry.

Methods: Patients with JDM enrolled between January 2019 and June 2024 in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) North America-based Registry with MSA testing were included. Sensitivity and LR of MSAs for clinical features were calculated for those with more than 2 observations per MSA group. MSA groups with more than 5 patients were analyzed.

Results: There were 395 patients diagnosed with JDM per enrolling providers. 303 were tested for at least 1 MSA, and 141 were positive for 1 MSA. 16 who were positive for more than 1 MSA were excluded. MSA testing was most commonly performed at Oklahoma Medical Research Foundation (n=49, 35%) and Associated Regional and University Pathologists, Inc., (n=35, 25%), both in the USA. The most common MSA was anti-TIF1 (n=46, 33%) then anti-NXP2 (n=41, 29%), anti-Mi2 (n=24, 17%), and anti-MDA5 (n=24, 17%). Overall, the MSAs were poorly sensitive (5-70%) for specific clinical features. Significant associations for anti-TIF1 included LR for baseline V-sign (2.23, 95% CI 1.19-4.18) and baseline malar/facial erythema (2.10, 95% CI 1.06-4.14). For anti-MDA5, LR for interstitial lung disease (7.78, 95% CI 4.23-14.30), baseline arthritis (6.21, 95% CI 2.56-15.06), and baseline skin ulcer (3.88, 95% CI 1.75-8.60) were significant. Of note, LR for lipodystrophy in anti-TIF1 (1.19, 95% CI 0.43-3.30) and for calcinosis in anti-NXP2 (0.95, 95% CI 0.33-2.74) were not significant.

Conclusion: MSAs had low sensitivity for specific disease features. Anti-TIF1 and anti-MDA5 had significant LR for a few known associated disease manifestations. Strengths of this study include large sample size and multi-site data source. Limitations include missing data in setting of retrospective study design and variable MSA assays with potential for antibody status misclassification. More studies are needed to better understand the sensitivity and predictive value of MSAs for clinical manifestations in JDM.

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Health/Technical Resources International., Consultant with: Cabaletta Bio (scientific advisory board, paid consulting), Childhood Arthritis & Rheumatology Research Alliance (Vice Chair JDM Committee paid consultant position), Paid Instructor with: Rheumatology Research Foundation Pediatric Visiting Professorship travel reimbursement and honorarium 2024-2025, American College of Rheumatology travel reimbursement for invited speaker 2024, SingHealth - honorarium (paid to my institution, not directly to me) for grant pre-review program, S. Kim: None Declared, S. Tarvin: None Declared, H. Kim Grant / Research Support with: Intramural Research Program of the National Institutes of Health, National Institute of Arthritis and Musculoskeletal and Skin diseases (NIAMS) (AR041215). , Consultant with: Juvenile myositis expert panel member for Cabaletta Bio (unpaid), part of NIAMS CRADA with provision of drug (deucravacitinib) with Bristol Myers Squibb, previous part of NIAMS CRADA with study support and drug (baricitinib) with Eli Lilly and Company., B. Feldman: None Declare

PReS25-ABS-1366

RECONSTITUTION OF THE B CELL COMPARTMENT FOLLOWING ANTI-CD19 CAR-T CELL THERAPY IN REFRACTORY PATIENTS WITH JUVENILE DERMATOMYOSITIS (JDM)

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Introduction: CD19 CAR T-cell therapy is an innovative strategy to induce profound B cell depletion in patients with refractory idiopathic inflammatory myopathies (IIM). However, its effects on B cell phenotypes in pediatric patients remain largely unknown.
Objectives: To characterize the reconstitution profile of B cell subsets in three patients with juvenile dermatomyositis (JDM) treated with anti-CD19 CAR T-cell therapy.
Methods: Three patients with refractory JDM received a single infusion of autologous, second-generation anti-CD19 CAR T cells (1×10^6 CAR T cells/kg; lentiviral vector), manufactured on the CliniMACS Prodigy system. Lymphodepletion was achieved using cyclophosphamide (1000 mg/m² over 2 days) and fludarabine (90 mg/m² over 3 days). B cell immunophenotyping was performed according to standard operating procedures (SOPs) before and after CAR T-cell infusion. A comparator group of five JDM patients treated with rituximab (RTX) was included.
Results: B cell reconstitution occurred at a median of 8 weeks (IQR: 8.0-12.0) post-CAR T therapy, with an immature transitional B cell phenotype. B cell subsets distribution was assessed at a median of 27.3 weeks (IQR: 22.5–40.2) after treatment, when all B cell subsets were present for each patient, and compared to pre-treatment profiles. In the RTX group, B cell phenotyping was performed at a median of 47 weeks (IQR: 33.4–50.7) post-treatment. The proportion of $CD19^+$ B cells among lymphocytes was similar before and after CAR T-cell treatment (pre: 32% [IQR: 23–40], post: 21% [IQR: 20–24]). B cell subset analysis showed comparable levels of transitional, naïve and plasmablast populations pre- and post-treatment. However, there was a notable reduction in total memory B cells (MBCs) post-treatment (pre: 6.4% [IQR: 6.3–9.1], post: 3.9% [IQR: 3.1–4.0]), particularly in the switched MBC subset. Interestingly, JDM patients treated with RTX showed higher frequencies of switched MBCs during B cell reconstitution compared to those treated with CAR T cells: CAR T treated-patients 16.0 % [IQR: 8.5-18.0], RTX group 52.0% [IQR: 28.0, 60.0].
Conclusion: These data show that following CAR T cell treatment, the memory B cell compartment presents a lower frequency of switched MBCs when compared to pre-treatment levels and to patients treated with RTX, suggesting a specific effect of CAR T cell treatment in regulating the memory B cell compartment in JDM patients.
Disclosure of Interest: None Declared

PReS25-ABS-1279

JUVENILE AND ADULT-ONSET DERMATOMYOSITIS: A COMPARATIVE STUDY IN A COHORT FROM A TERTIARY CENTER

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Introduction: Dermatomyositis (DM) is a rare inflammatory myopathy with distinct clinical features in juvenile (JDM) and adult (ADM) forms. Both present with symmetrical proximal muscle weakness and characteristic skin lesions; notable differences exist in organ involvement, disease course, and malignancy risk (1). Identifying these differences is crucial for the development of age-specific diagnostic, therapeutic, and follow-up strategies.

Objectives: To define the differences and similarities between JDM and ADM in terms of clinical presentations, diagnostic procedures, autoantibody profiles, treatment options, and disease outcomes.

Methods: We retrospectively reviewed medical records of DM patients diagnosed per 2017 EULAR/ACR criteria (2) at the pediatric and adult rheumatology clinics of Istanbul University-Cerrahpasa from January to April 2025. Patients were classified as JDM if diagnosed under 16 years and ADM if 16 years or older.

Data were analyzed using SPSS (v.27). Non-normally distributed variables were assessed with the Mann-Whitney U test, while categorical data were compared using the Chi-square or Fisher's exact tests. Statistical significance was set at $p<0.05$.

Results: A total of 164 patients were included: 84 with JDM (63.1% female) and 80 with ADM (67.7% female). Age at diagnosis showed a bimodal distribution, peaking at 6.9 and 44.2 years.

Joint involvement was more prevalent in JDM ($p=0.019$), whereas cardiac involvement was more common in ADM ($p=0.038$). Calcinosis occurred in 33.3% of JDM cases but only in one ADM case ($p<0.001$). Among the myositis-specific and myositis-associated antibodies, Anti-NXP2 and Anti-TIF1g were more prevalent in JDM, whereas Anti-Mi2, Anti-Jo1 and Anti-SSa were more common in ADM.

Acute phase reactants were higher in ADM at both diagnosis and last visit ($p<0.005$ for all). While MRI was more frequently utilized to demonstrate myositis in JDM cases, biopsy, EMG and PET/CT were more commonly employed in ADM ($p<0.001$ for all)

Glucocorticoids were initiated in nearly all patients (>98%) in both groups. At follow-up, most ADM patients remained on treatment, while only 11.6% of JDM patients were still receiving steroids ($p<0.001$). Malignancy was observed in 26.2% of ADM cases, whereas no such association was found in JDM ($p<0.001$). The hospitalization and mortality rates were higher in the ADM group ($p<0.001$ for both).

Conclusion: JDM and ADM have distinct clinical features: ADM is characterized by more severe organ involvement, particularly cardiac and respiratory, higher acute phase reactants, prolonged steroid rates, and poorer outcomes, including higher rates of malignancies, hospitalization, and mortality. In contrast, JDM is associated with more frequent calcinosis and joint involvement, along with a relatively better prognosis. These differences emphasize that JDM should not be approached merely as the pediatric form of ADM, but as a distinct clinical entity requiring tailored management strategies.

References: 1. Robinson AB, Reed AM. Clinical features, pathogenesis and treatment of juvenile and adult dermatomyositis. Vol. 7, Nature Reviews Rheumatology. 2011. p. 664–75.

2. Lundberg IE, Tjärnlund A, Bottai M, Werth VP, Pilkington C, de Visser M, et al. 2017 European League Against Rheumatism/American College of Rheumatology Classification Criteria for Adult and Juvenile Idiopathic Inflammatory Myopathies and Their Major Subgroups. Arthritis and Rheumatology. 2017 Dec 1;69(12):2271–82.

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PReS25-ABS-1435

AFRICAN CHILDREN WITH JDM PRESENT WITH SEVERE DISEASE AND HAVE WORSE OUTCOMES OVER TIME COMPARED TO NORTH AMERICAN CHILDREN

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Introduction: There is limited data on pediatric rheumatic diseases (PRD), including juvenile dermatomyositis (JDM), in low and middle-income countries (LMIC). Existing data suggests higher prevalence of severe manifestations and worse outcomes.

Objectives: Our study aims to compare severity of JDM – as measured by severity of weakness and prevalence of calcinosis, interstitial lung disease (ILD), and damage – in a cohort of sub-Saharan African children with North American children in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry.

Methods: Children diagnosed with JDM before age 19 were included. North American children were from the CARRA Registry and African children were from 1 center in Nairobi, Kenya and 2 centers in Cape Town, South Africa. Socio-demographic characteristics, clinical information, and treatment were collected prospectively in the CARRA Registry and retrospectively in the African cohort via manual chart review. Descriptive statistics were used to summarize each variable. Bivariate analysis was performed using t-test or Chi-squared test, or their non-parametric equivalents (Mann Whitney and Fisher's exact tests). Logistic regression was performed for the main outcomes of interest (weakness severity, calcinosis, and presence of damage) at two time points: baseline and 12 months of follow-up. There was insufficient power to perform multivariable analysis for ILD.

Results: A total of 379 children were included in the study: 349 North American and 30 African (23 South African and 7 Kenyan) children. At baseline, African children were more likely to experience delays of greater than 12 months both in diagnosis (30% vs 12%; p=0.04) and in being seen by a pediatric rheumatologist (37% vs 12%; p=0.001). They were more likely to have moderate/severe weakness (79% vs 39%; p=0.02), though this was no longer seen in multivariable analysis. At baseline, African children were more likely to have ILD (20% vs 2%; p<0.001). African children were also more likely to have calcinosis at baseline both in univariate (23% vs 4%; p=0.001) and multivariable analysis (odds ratio [OR]=6.59, p=0.002). However, at baseline, African children trended towards having less damage, which was supported in multivariable analysis (OR=0.36; p=0.09) (Tables 1, 2). At 12-months, African children had higher prevalence of damage (50% vs 23%; p=0.047) and were 4.81 times more likely to accrue damage than North American children when adjusting for other variables (p=0.008) (Table 3). Overall mortality was 7% in the African cohort by the 12-month visit; there were no deaths among North American children.

Conclusion: This is the first multicenter study of JDM in Africa and the first comparison of JDM between North American and African children. Our study suggests that African children may present with severe disease and delays in care, accrue more damage, and have higher mortality rates than what is reported in studies of high-income countries. Future studies with a larger sample size from an even more diverse patient population over a longer follow-up period will be critical to improve the power to detect important differences and to understand reasons for these differences in clinical manifestations and outcomes over time.

Disclosure of Interest: None Declared

PReS25-ABS-1501

MONOCYTE SIGLEC-1 AS AN IFN-INDUCIBLE BIOMARKER IN JUVENILE DERMATOMYOSITIS: CORRELATION WITH DISEASE ACTIVITY AND TREATMENT RESPONSE

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Introduction: Juvenile dermatomyositis (JDMS) is the most common inflammatory myositis in children, characterized by proximal muscle weakness and distinctive skin features. Its pathogenesis involves a vasculopathy with an exaggerated type 1 interferon (IFN) response, driving immune cell activation and muscle inflammation (1). Siglec-1, an IFN-inducible marker, is elevated in JDMS and other autoimmune diseases, correlating with disease activity. Studies by Lerkvaleekul et al. (2) and Graf et al. (3) highlight Siglec-1 as a promising biomarker for JDMS, aiding in disease assessment and treatment response evaluation.
Objectives: To estimate Siglec-1 (CD169) expression in monocytes of children with JDMS and healthy controls, and to prospectively assess Siglec-1 levels after immunosuppressive treatment, and correlate Siglec-1 expression with disease activity in JDMS patients.
Methods: Siglec-1 was assessed by flow cytometry on circulating monocytes of 14 newly diagnosed JDMS patients and 6 relapsed cases. 16 of them were also assessed at 2 months and 13 of them at 6 months. 26 patients in remission and 8 patients with persistent skin disease activity on treatment were also assessed cross sectionally. Siglec-1 was assessed on CD14+ monocytes using [CD14 Alexa flour 700, CD169 FITC]. Gating was performed using (FlowJo), with isotype controls for background subtraction. Siglec-1% is the percentage of Siglec-1+ monocytes and ΔMFI is the change in mean fluorescence intensity.
Results: Monocyte Siglec-1 expression, measured by flow cytometry was significantly elevated at disease onset in children with juvenile dermatomyositis JDMS (n=14) compared to controls (n=20): Siglec-1% AUC=0.986 (95% CI: 0.957–1, p<0.001); Siglec-1 ΔMFI AUC=1.0 (95% CI: 1–1, p<0.001). Expression levels substantially reduced with treatment in newly diagnosed patients-Siglec-1%: Friedman $\chi^2(2)=13.55$, $p=0.001$; Siglec-1 ΔMFI: Friedman $\chi^2(2)=18.00$, $p<0.001$-and in relapsed cases-Siglec-1 ΔMFI: Friedman $\chi^2(2)=6.50$, $p=0.039$. Monocyte Siglec-1 expression also remained significantly higher in patients in remission (n=27) compared to controls (Siglec-1 ΔMFI: AUC=0.681, 95% CI: 0.528–0.835, $p=0.035$). Isolated skin disease activity had an independent effect on monocyte Siglec-1 levels (Siglec-1%: $U=61.0$, $p<0.05$; Siglec-1 ΔMFI: $U=77.0$, $p<0.05$), whereas calcinosis did not (Siglec-1%: $U=32.5$, $p=0.372$; Siglec-1 ΔMFI: $U=37.0$, $p=0.576$). Clinical markers of muscle disease activity such as CMAS, MMT8, and MDAS, showed moderate correlations with Siglec-1 expression (r=0.4–0.52, $p<0.05$), while skin disease activity exhibited only weak correlations (r=0.2–0.3, $p<0.05$).
Conclusion: Siglec-1 on monocytes is a newly identified IFN-inducible biomarker in JDMS that correlates with clinical disease activity and reduces with treatment.
References: 1. Papadopoulou C, Chew C, Wilkinson MGL, McCann L, Wedderburn LR. Juvenile idiopathic inflammatory myositis: an update on pathophysiology and clinical care. Nat Rev Rheumatol. 2023 Jun;19(6):343–62.
2. Lerkvaleekul B, Veldkamp SR, van der Wal MM, Schatorjé EJH, Kamphuis SSM, van den Berg JM, et al. Siglec-1 expression on monocytes is associated with the interferon signature in juvenile dermatomyositis and can predict treatment response. Rheumatol Oxf Engl. 2022 May 5;61(5):2144–55.
3. Graf M, von Stuckrad SL, Uruha A, Klotsche J, Zorn-Pauly L, Unterwalder N, et al. SIGLEC1 enables straightforward assessment of type I interferon activity in idiopathic inflammatory myopathies. RMD Open. 2022 Feb;8(1):e001934.
Disclosure of Interest: None Declared

PReS25-ABS-1184

DEEP IMMUNOPHENOTYPING IN PATIENTS WITH JUVENILE LOCALIZED SCLERODERMA REVEALS TWO DISTINCT IMMUNOLOGICAL ENDOPHENOTYPES

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Introduction: Juvenile localized scleroderma (JLS) is a rare autoimmune disorder causing skin inflammation and fibrosis in children under the age of 16 years. Disease hallmarks include dermal sclerosis and inflammatory infiltration, linking inflammation and fibroblast activation with excess extracellular matrix production (1). Current clinical tools may struggle to distinguish active from inactive lesions, highlighting the need for reliable biomarkers to assess activity and predict response to therapy.
Objectives: The aim of this project is to perform immunophenotyping of JLS patients and healthy controls to assess dysregulated immunological pathways in JLS, and to identify biomarkers able to predict clinical features.
Methods: We included in this study pediatric patients diagnosed with linear and mixed JLS. PBMC and plasma samples at diagnosis and before the initiation of treatment were analyzed. Levels of 50 cytokines were measured in the plasma by protein array. Lymphocyte and monocyte subsets were analysed with a 26-colour flow cytometry panel and acquired on a FACSymphony.
Results: We identified samples at baseline from 11 patients with JLS and 10 controls. Cytokine array identified 15 cytokines that were significantly elevated in JLS patients compared to controls. Using Principal Component Analysis (PCA), we observed a distinct distribution between patients and controls, with approximately 50% of patients clustering away from controls, and the remaining 50% aligning closely with them. Patients clustering near controls exhibited the lowest cytokine levels and were designated as non-inflammatory JLS (no_inf JLS), whereas those clustering away had the highest cytokine levels and were classified as inflammatory JLS (inf_JLS). Flow cytometry analysis identified 81 subpopulations of interest; PCA analysis highlighted significant differences in the distribution of lympho-monocytic subsets between patients and controls. We observed a reduction in monocyte populations, including classical ($CD14^+CD16^-$) and atypical monocytes ($CD14^+CD16^+$), and an expansion of dendritic cells compared to controls. Within lymphocyte subsets, significant differences were observed in the frequency of $CD4^+$ T cells, particularly of activated $CD4^+$ T cells ($CD38^+$ $HLA\text{-}DR^+$). Patients stratified into inf_JLS and no_inf JLS groups based on cytokine levels showed minimal differences in cellular subpopulations upon PCA. However, two subpopulations demonstrated significant variability: activated $CD4^+$ T cells ($CD38^+$ $HLA\text{-}DR^+$) and terminally differentiated effector memory $CD4^+$ T cells (TEMRA) expressing PD1, were significantly expanded in patients with inf_JLS.
Conclusion: This study identified two distinct groups of patients with JLS: a non-inflammatory group, characterized by normal levels of circulating proinflammatory cytokines, and an inflammatory group, marked by elevated levels of circulating cytokines and increased levels of activated $CD4^+$ T cells. Our findings highlight the central role of activated T cells in JLS pathogenesis, particularly in patients within the inflammatory group. Furthermore, these results pave the way for novel therapeutic approaches for JLS, including the potential use of treatments targeting T cells.
References: 1. Walker D, J Am Acad Dermatol. 2017

PReS25-ABS-1433

FREQUENCY OF TISSUE-SPECIFIC ACTIVATED CD8+ T CELLS IS CORRELATED TO DISEASE SEVERITY IN JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Juvenile Idiopathic Arthritis (JIA) is characterized by joint pain and inflammation. Persistent oligoarticular JIA(oligoJIA) is defined by the involvement of up to 4 joints throughout disease course. OligoJIA can progress to an extended form of arthritis (extended-oligoJIA), involving 5 or more joints after the first 6 months of disease. Polyarticular JIA is defined as affecting 5 or more joints in the first 6 months of disease. Over 30% of children with extended-oligoJIA experience uncontrolled disease requiring the use of several immunosuppressive medications even after 8-year follow-up. Moreover, even with current treatment options, 50-60% of children with extended-oligoJIA continue to experience pain, functional disability, disease activity, and impaired quality of life extending into adulthood. There is limited understanding of the cellular composition of inflammatory tissues in JIA, particularly in the affected synovium, which is a major barrier for the identification of disease biomarkers, diagnosis, and therapeutic targeting.
Objectives: The purpose of this study was to identify cell subsets associated with disease progression and severity in the synovium of children with JIA.
Methods: Fourteen synovial tissue biopsies of children with oligoJIA or polyarticular JIA, were collected by ultrasound guided biopsy. Cryopreserved synovial tissue was thawed and enzymatically digested in Liberase and DNAse I, prior to staining with a comprehensive antibody panel encompassing all major immune and non-immune cell types. Matching PBMC samples were also stained for flow analysis from 5 of the individuals. Synovial fluid biomarkers were measured by Luminex.
Results: Flow cytometry analysis revealed significant differences in the cellular composition of B cells, fibroblasts, and T-cell subtypes between PBMC and synovium samples from patients with JIA. Interestingly, we note a significant difference in tissue-specific HLA-DR+ CD8+ activated T cells in polyarticular JIA when compared to oligoJIA. Extending this analysis, we discovered significant correlations of activated and regulatory CD8+ T cell states with Juvenile Arthritis Disease Activity Scores (JADAS). Synovial fluid biomarkers such as IL-18, CD25, IL-6, and IL-23 were similarly correlated to disease activity and the frequency of tissue-specific activated T cells (PD-1+ CD-8+), T peripheral helper cells (HLA-DR+ CD4+), and HLA-DR+ fibroblasts.
Conclusion: With comprehensive flow cytometry analysis, we characterized the heterogenous cellular composition of JIA in both PBMC and disaggregated synovium. We observed increased frequencies of activated T cells specifically within the synovium correlated to disease severity and synovial fluid biomarkers.
Disclosure of Interest: None Declared

PReS25-ABS-1056

PATIENT, PARENT AND PHYSICIAN GLOBAL ASSESSMENT DISCORDANCE RELATED TO PAIN COPING STRATEGIES IN JUVENILE ARTHRITIS

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Introduction: It has previously been shown that there can be a discordance between patient and physician global assessment in patients with juvenile idiopathic arthritis (JIA). Only a few studies on the factors influencing the discordance have been done in children [1-3].

Objectives: We aim to investigate the factors underlying the discordance in physicians', patients', and caregivers' perceptions of disease state in patients with newly diagnosed or suspected JIA.

Methods: We invited all children in eight centres in Finland from November 2021 to March 2024 presenting with newly confirmed or suspected diagnoses of JIA and the accompanying parents to participate. Children over 8.0 years and all the parents filled in the patient's and parent's proxy pain and global assessment at 0 and 3 months and the pain coping scale for both children and their parents [4] at 3 months after diagnosis. The discordance between patient or parent global assessment and physician global assessment was determined by subtracting the physician global assessment from the patient or parent global assessment. The factors explaining discordance between the global assessments were evaluated by a multivariable linear model.

Results: In total, 186 families participated in the study. Children and caregivers used effective pain coping strategies more often than catastrophizing. Discordance between the patient or parent and physician global assessment of less than +/-10 mm was seen in 51% of the children and 52% of the parents. When a discordance of more than +/-10 mm was seen, it was mainly positive, i.e. the patients' and parents' perception of the disease state was higher than the physician's. A global assessment discordance of +/- 30 mm or greater was seen in 17% of the children and 11% of the parents. In the patients, the lower the active joint count (AJC) ($p=0.006$) and the higher the pain assessment ($p<0.001$), the greater the discordance between patient and physician global assessment. In parents, the lower the AJC ($p<0.001$) and the higher the parent proxy pain assessment ($p<0.001$) and catastrophizing score ($p=0.005$), the greater the discordance between parent and physician global assessment.

Conclusion: The discordance between the parent and physician global assessment is greater among parents who use catastrophizing as a pain coping strategy. The lower the AJC and the higher the pain assessment score, the greater the discordance between the patient or parent and physician global assessment. Children and caregivers used effective pain coping strategies more often than catastrophizing.

References: 1.Sztajnbok F, Coronel-Martinez D L, Diaz-Maldonado A et.al. Discordance between physician's and parent's global assessments in juvenile idiopathic arthritis. Rheumatology 2007;46:141–5.

2. Consolaro A, Vitale R, Pistorio A et al. Physicians' and parents' ratings of inactive disease are frequently discordant in juvenile idiopathic arthritis. J Rheumatol 2007;34:1773-6.
3. Trachtman R, Issa R, Pan S et al. The value of the patient global health assessment in polyarticular juvenile idiopathic arthritis: a nested cohort study. *J Patient Rep Outcomes* 2021;5:50.
4. Backström M, Vuorimaa H, Tarkiainen M, et al. Pain-coping scale for children and their parents: a cross-sectional study in children with musculoskeletal pain. Pediatr Rheumatol Online J. 2023;21(1):9.

Disclosure of Interest: None Declared

PReS25-ABS-1089

IS JUVENILE ARTHRITIS ASSOCIATED WITH LOWER PHYSICAL ACTIVITY LEVELS AMONG U.S. CHILDREN? A CROSS-SECTIONAL ANALYSIS OF THE NATIONAL SURVEY OF CHILDREN'S HEALTH (2016–2021)

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Introduction: Juvenile arthritis (JA) is characterized by joint pain, stiffness, and decreased mobility, potentially affecting participation in physical activity (PA)[1]. The CDC and WHO recommend that children engage in at least 60 minutes of PA daily. While research in PA level and JIA has been conducted in European countries like Germany and the Netherlands, limited data exists in the U.S. [2,3.] It remains unclear whether children with arthritis in the U.S. meet PA guidelines or how achieving these recommendations impacts their overall health outcomes.
Objectives: To assess whether a current diagnosis of arthritis is associated with lower PA levels among a nationally representative sample of U.S. children and adolescents.
Methods: This cross-sectional study assessed adherence to daily PA recommendations among U.S. children with JA compared to peers without JA, using 2016–2021 National Survey of Children's Health (NSCH) data, a nationally representative survey that investigates health of pediatric population in the U.S. Univariable and multivariable logistic regression models examined the association between JA and meeting daily PA recommendations. A sensitivity analysis using ordinal logistic regression assessed PA frequency ("0 days," "1–3," "4–6," "daily"). Models were adjusted for potential confounders.
Results: Children with JA were less likely to meet daily PA recommendations than peers without arthritis (13.5% vs. 17.0%; $p = 0.05$), and had higher rates of obesity (23.3% vs. 13.9%; $p < 0.001$), physical limitations, pain (69.9% vs. 10.3%; $p < 0.001$), and comorbidities (55.2% vs. 30.6%; $p < 0.001$). However, in adjusted analyses, arthritis was not significantly associated with meeting PA guidelines (aOR = 1.34; 95% CI: 0.78–2.32; $p = 0.29$). Similarly, arthritis was not significantly associated with PA level in ordinal logistic regression (aOR = 1.17; 95% CI: 0.81–1.69; $p = 0.41$). Female sex, older age, presence of mental health conditions, and obesity (aOR for ≥95th percentile = 0.64; 95% CI: 0.52–0.78), were negatively associated with PA. Sports participation was strongly associated with meeting guidelines for PA (aOR = 1.58; 95% CI: 1.44–1.74; $p < 0.001$).
Conclusion: Children and adolescents with and without arthritis demonstrated low adherence to the CDC and WHO-recommended PA levels. Overall, arthritis was not found to be a statistically significant predictor of PA levels in unadjusted or adjusted analyses. These findings might suggest that while arthritis poses challenges, it may not be a key independent barrier to PA. Efforts to increase PA should address modifiable barriers like obesity and mental health, and promote sports participation, especially among older children with JA.
References: 1. Klepper SE. Exercise and fitness in children with arthritis: evidence of benefits for exercise and physical activity. Arthritis Rheum. 2003;49(3):435-43. doi:10.1002/art.11055

2. Milatz F, Hansmann S, Klotsche J, et al. Level and correlates of physical activity among children and adolescents with juvenile idiopathic arthritis compared to controls: results from a German nationwide prospective observational cohort study. Pediatr Rheumatol. 2024;22:39. doi:10.1186/s12969-024-00976-2.

3. Bos GJ, Lelieveld OT, Armbrust W, Sauer PJ, Geertzen JH, Dijkstra PU. Physical activity in children with Juvenile Idiopathic Arthritis compared to controls. Pediatr Rheumatol. 2016;14(1):42. doi:10.1186/s12969-016-0102-8
Disclosure of Interest: None Declared

PReS25-ABS-1356

CHARACTERIZATION OF MIR22HG EXPRESSION AND ROLE IN OLIGOARTICULAR JUVENILE IDIOPATHIC ARTHRITIS PATIENTS AT DISEASE ONSET

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Introduction: Oligoarticular Juvenile Idiopathic Arthritis (OJIA), the most common form of pediatric rheumatic disease, is characterized by joint immune cell infiltration and synoviocyte proliferation, causing inflammation and cartilage erosion. While most patients achieve remission, others experience a severe, treatment-refractory course with joint damage and functional impairment. Understanding the molecular mechanisms underlying OJIA development and progression may provide early biomarkers and therapeutic targets. Recent studies suggest that the long non-coding RNA, MIR22HG**,** plays a role in adult arthritis, showing potential as a biomarker and therapeutic target. However, its expression and function in OJIA remain unexplored.
Objectives: This study investigates MIR22HG expression in peripheral blood (PB)- and synovial fluid (SF)-derived cells from new-onset OJIA patients, its correlation with patient clinical parameters at 1 year of follow up and functional role.
Methods: PB and SF mononuclear cells (PBMC, SFMC) from 30 OJIA patients were collected at onset, and CD14+ monocyte (Mn) and CD14- lymphocyte subsets were isolated. PBMCs from 25 age/gender-mached controls were analyzed in parallel. Fibroblast-like synoviocytes (FLS) were isolated from SF of 6 patients Cells were phenotypically characterized, and MIR22HG expression analyzed by RT-qPCR.
Results: MIR22HG expression was significantly higher in CD14+ than in CD14- cells from patient PBMCs and SFMCs and control PBMCs. However, OJIA patients showed lower MIR22HG levels than controls in PBMC subsets with good discriminatory power and expression correlation with clinical course at follow up. FLS exhibited an inflammatory synovial sublining phenotype and expressed MIR22HG. To asses MIR22HG function, siRNA-mediated silencing was performed in THP-1 human monocytic and FLS cell lines. Silencing increased apoptosis, IL-6 and IL-1β secretion in THP-1 cells, and IL-6 and IL-8 in FLS.
Conclusion: These findings suggest that MIR22HG has a protective role on inflammation by modulating Mn and FLS viability and activities. Its downregulation in OJIA represents a molecular mechanism promoting inflammatory processes, thus highlighting MIR22HG potential as an early biomarker of disease progression and therapeutic target.
Disclosure of Interest: None Declared

PReS25-ABS-1383

DISCORDANCE BETWEEN PHYSICIAN RATINGS IN JUVENILE IDIOPATHIC ARTHRITIS PATIENTS WITH INACTIVE DISEASE: COMPARISON OF MULTICENTER VERSUS SINGLE-CENTER COHORTS

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Introduction: Concern was raised by the recent observation of a wide variability in physician global assessment (PhGA) scores across pediatric rheumatologists. Some studies have highlighted the tendency of some clinicians not to mark their PhGA at zero when no active joints are detected, and even when all the other inactive disease (ID) criteria are met. However, it is still unclear whether training improves the concordance between clinicians in rating the PhGA in juvenile idiopathic arthritis (JIA) patients with ID.
Objectives: To compare the frequency of visits in which the physician provided a PhGA > 0 despite the absence of joints with active arthritis between two multicenter patient samples and one cohort of patients assessed in a single pediatric rheumatology center with a long tradition in clinimetric assessments.
Methods: Data were extracted from three cross-sectional datasets: the first included 9081 patients enrolled in a multinational study of the epidemiology, treatment and outcome of JIA (EPOCA dataset); the second comprised 563 patients with systemic JIA who were part of a multicenter study aimed to develop and validate the systemic JADAS (sJADAS) and its cutoffs; the third was a single-center dataset composed of 394 patients followed at the Gaslini Institute (Gaslini dataset). For the purposes of the study, only patients with an active joint count = 0 were evaluated in each dataset. The state of ID was established using the 2004 or 2011 Wallace criteria. UpSet plots were generated to visualize combinations of ID criteria.
Results: A PhGA > 0 and the elevation of acute phase reactants (APR) were the most frequent reasons for not meeting the ID definition in patients with no active joints. The proportion of patients who had a PhGA > 0 with all the other ID criteria met was lower in the Gaslini dataset (5.1%) than in the EPOCA and sJADAS datasets (14.8% and 13.7%, respectively). As compared with the two multicenter cohorts, the Gaslini cohort also had a lower frequency of patients with a PhGA > 0 plus one or more of the other ID criteria not met, and with a PhGA > 0 plus the other ID criteria met or not met. The percentage of patients who did not meet ID criteria because of isolated elevation of APR was lower in the EPOCA dataset (10.8%) than in the sJADAS and Gaslini datasets (19% and 18.8%, respectively). The frequency of patients who had a PhGA > 0 plus elevated APR, but all other ID criteria met was higher in the sJADAS dataset (19.6%) than in the EPOCA and Gaslini datasets (5.5% and 2.7%, respectively).
Conclusion: Our study confirms the previous observation that a sizeable proportion of physicians provide a PhGA > 0 in patients who are found not to have clinical evidence of inflammation in any joint. However, this disparity was less pronounced in patients evaluated in a single center with tradition and expertise in making clinimetric assessments. This observation suggests that regular application and training may increase the consistency of the PhGA. An important finding of our study is that a sizeable proportion of patients did not meet the ID definition due the isolated increase of APR.
References: Alongi A, et al; Pediatric Rheumatology International Trials Organization (PRINTO). Drivers of non-zero physician global scores during periods of inactive disease in juvenile idiopathic arthritis. RMD Open. 2022 Mar;8(1):e002042.
Disclosure of Interest: None Declared

PReS25-ABS-1363

ENHANCING JUVENILE IDIOPATHIC ARTHRITIS MANAGEMENT THROUGH CO-DESIGNED DEVICES: INSIGHTS FROM A FEASIBILITY STUDY

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Introduction: Juvenile Idiopathic Arthritis (JIA) is the most common childhood rheumatic disease, causing pain, joint inflammation and stiffness requiring daily self-management[1]. Existing studies highlight significant impacts across emotional, physical, social, psychological, and educational wellbeing. Despite this, JIA remains largely invisible in the technology space, with available products often designed for adults or perceived by children and young people (CYP) as stigmatising or failing to respond to their unique needs[2-5].

This feasibility study builds on prior co-design work and a successful proof-of-concept study[6], trialling a suite of three co-designed technologies, collectively called 'JIA Toolbox', developed in response to needs identified by CYP, parents,

healthcare professionals and teachers.

Objectives: To assess the effectiveness of the improved 'JIA Toolbox' in supporting CYP's self-management, particularly regarding independence and functional ability.
To obtain real-world feedback to guide future development.
To gather contemporary insights into daily experiences of managing JIA.
Methods: 'JIA Toolbox' comprises three co-designed prototype devices: P1: A wearable pain management device, P2: A motivational physiotherapy tool and P3: A school-based communication aid.
25 CYP (aged 7–16) with JIA, their parents and teachers used 'JIA Toolbox' over a 16-week period in a self-directed manner. Initial training was provided. Data collection included baseline, intervention, and post-intervention self-reported diaries, interviews, and prototype usage data.
Results: Preliminary analysis indicates 85–95% of participants found one or more tools beneficial. Reported improvements included better pain management, enhanced adherence to physiotherapy, improved classroom communication, and greater independence. Usage varied by individual need, reflecting the fluctuating nature of JIA. P1 was the most widely used, described as helpful for "aching and stiffness" due to its soothing effects. One participant noted regret at not bringing it to school during a flare. P2 supported physiotherapy adherence, with one participant progressing from non-adherence to regular stretching, reportedly leading to functional improvements. The gamification element was positively received. P3's impact was influenced by classroom confidence and school support. Where used, CYP "did not feel embarrassed asking for help", improving communication with teachers, enabling stronger relationships and understanding of the condition. Battery life emerged as a consistent area for improvement across devices.
Conclusion: This feasibility study suggests the 'JIA Toolbox' is a suite of beneficial tools to support self-management for CYP with JIA. It also underscores the value of addressing the less visible aspects of the condition, such as disbelief in schools or physiotherapy motivation. These findings suggest potential applicability beyond JIA as these needs are not specific to JIA. Next steps include further device development based on this study data, and applying for a larger funding grant to carry out a multi-site pilot study.
Disclosure of Interest: None Declared

PReS25-ABS-1175

IMPACT OF METHOTREXATE-ASSOCIATED ADVERSE EVENTS ON ONE-YEAR OUTCOMES IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Methotrexate (MTX) is a first-line treatment for juvenile idiopathic arthritis (JIA), aimed at reducing disease activity and improving function. However, MTX-associated adverse events (AEs), particularly gastrointestinal symptoms, may affect treatment experiences and patient-reported outcomes. The potential longer-term impact of AEs on wellbeing and disease activity remains unclear.
Objectives: To explore the impact of MTX-associated AEs experienced during the first year of treatment on six core JIA outcomes at one year in children and young people (CYP) with JIA.
Methods: This analysis used data from the UK JIA Biologics Register, a national prospective observational treatment cohort. CYP starting MTX between January 2003 and December 2018 with at least 12 months of follow-up were included. MTX-associated AEs were recorded by the treating physician and reported to the register at 6 and 12 months. Six JIA core outcomes were assessed at one year: patient/parent global assessment of wellbeing, physician global assessment of disease activity, active joint count, limited joint count, Childhood Health Assessment Questionnaire (CHAQ) for functional ability, and erythrocyte sedimentation rate (ESR).

Linear regression models were used to compare core outcome variables between those with and those without AEs at baseline, one year, as well as change in outcomes from baseline to one year. Multivariable linear regression models adjusted for age, gender and baseline outcome values were used to assess associations between experiencing an AE and one-year outcomes. Baseline and 1 year core outcomes were imputed to account for missing data.

Results: A total of 774 CYP starting MTX were included, of whom 234 (30%) reported at least one AE during the first year. At one year, those who experienced AEs had significantly worse global wellbeing scores (median 1.7 cm vs 0.8 cm, $p = 0.014$) and worse physician global assessment scores (median 0.7 cm vs 0.1 cm, $p = 0.045$). In the adjusted multivariable regression model, AE exposure remained significantly associated with poorer wellbeing ($\beta = 0.45$, 95% CI: 0.05–0.86). No significant differences were observed in joint counts or ESR

Conclusion: CYP who experienced MTX-associated AEs during the first year of treatment reported poorer wellbeing at one year. These findings highlight the longer-term impact of MTX-associated AEs on patient-reported outcomes.

Disclosure of Interest: None Declared

PReS25-ABS-1087

PREDICTING FLARE AFTER LOW DISEASE ACTIVITY: AN ASIAN CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS COHORT EXPERIENCE

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Introduction: Sustaining childhood lupus low disease activity state (cLLDAS) is an important treatment goal in childhood-onset systemic lupus erythematosus (cSLE) therapy, but recurrent flares remain a clinically significant challenge.
Objectives: To evaluate the frequency and predictors of recurrent flares following episodes of cLLDAS in an Asian cSLE cohort.
Methods: Prospective longitudinal data from a cSLE cohort at KK Women's and Children's Hospital, Singapore, were included. Patients were recruited from inception in 2009 to 2025 with at least 6 months of follow-up. Demographic data, disease manifestations, treatment and disease activity outcomes were collected. Patients who achieved at least one cLLDAS episode (clinical SLEDAI-2K ≤ 4 without major organ activity, prednisolone ≤0.15mg/day or ≤7.5mg/day, whichever lower, no new lupus activity, Physician Global Assessment ≤1/3, and stable immunosuppressants) were included. Multiple cLLDAS and flare episodes were recorded per patient. Kaplan-Meier survival analysis, Cox and Poisson regressions were used where appropriate.
Results: Among 148 patients (83% female, median age at diagnosis 13.1 years [IQR 10.9–14.6], median follow-up duration 6.1 years [IQR 3.2 - 8.6]), 135 (91%) achieved at least one cLLDAS episode. Of these, 67 (49.6%) experienced 91 flare episodes, with 20 (29.9%) having more than one flare. Median duration of initial cLLDAS before first flare was 17.2 months (IQR 7.2-30.0), while median duration of subsequent cLLDAS remained similar before flares (14.4 months, IQR 10.3–18.5, p=0.958).

Kaplan-Meier analysis demonstrated significantly shorter flare-free intervals among patients with neuropsychiatric involvement (log-rank p=0.003), discoid rash (p = 0.040) and photosensitivity (p=0.005). Cox regression identified neuropsychiatric involvement (hazard ratio [HR] 2.51, 95% confidence interval [CI] 1.35–4.69, p=0.004) and photosensitivity (HR 2.13, 95% CI 1.21–3.73, p=0.008) as independent predictors of time to flare. The duration in first cLLDAS did not correlate with duration of first flare (p=0.683) nor flare severity (p=0.942).

Poisson regression showed shorter duration in first cLLDAS (Incidence Rate Ratio [IRR] 1.05 per decreasing month, 95% CI 1.03-1.06, p<0.001) and older age at diagnosis (IRR 1.53 per increasing year, 95% CI 1.29-1.80, p<0.001) were associated with higher flare rate when accounting for follow-up duration.

Conclusion: Despite achieving cLLDAS, half of our cSLE patients experienced flares. Neuropsychiatric involvement and photosensitivity predicted shorter time to flare. One-third of patients will experience recurrent flares, with lower flare rates in younger patients. Time in first cLLDAS also functions as a protective buffer, hence maintaining disease control is critical. These findings highlight the need for tailored maintenance strategies following cLLDAS in cSLE.

PReS25-ABS-1665

EVALUATION OF MICROCIRCULATION IN PATIENTS WITH CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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Introduction: Microcirculatory involvement is an underrecognized yet critical aspect of childhood-onset systemic lupus erythematosus (cSLE), potentially contributing to irreversible organ damage. Two techniques can be used to evaluate microcirculation in cSLE. These are nailfold (video) capillaroscopy (NFC) reflecting peripheral microvascular anatomy and Incident Dark Field (IDF) imaging reflecting central microvascular anatomy. While NFC studies in cSLE are scarce, to our knowledge this is the first study to explore central microvascular anatomy in cSLE.
Objectives: We aimed to evaluate peripheral and central microvascular alterations in patients with cSLE using NFC and IDF imaging and to assess the concordance between these two imaging modalities.
Methods: In this prospective cross-sectional single-center observational pilot study, 29 cSLE patients fulfilling the SLICC classification criteria were evaluated at the Erasmus University Medical Center, Rotterdam, Netherlands. NFC was performed in all patients, while 10 patients underwent IDF imaging. Capillary morphology, density, apical diameter, and presence of hemorrhages were assessed in NFC. IDF imaging analysis included total vessel density (TVD), functional capillary density (FCD), proportion of perfused vessels (PPV), red blood cell velocity (RBCv), capillary hematocrit (cHct), and total red blood cell perfusion (tRBCp). Microangiopathy pattern was defined as abnormal capillary pattern (with abnormal capillary morphology and/or capillary hemorrhages and without criteria for a scleroderma pattern). All results are reported as mean ± SD.
Results: NFC revealed a mean capillary density of 7.5 ± 1.5/mm and a mean apical diameter of 18.4 ± 4.9 µm. Five patients exhibited dilated capillaries (range 20–50 µm), seven showed abnormal morphology, and four had hemorrhages. No scleroderma pattern was observed; seven patients displayed a microangiopathy pattern. IDF imaging in 10 patients showed TVD of 19.39 ± 3.94 mm/mm², FCD of 18.83 ± 3.91 mm/mm², and PPV of 0.97 ± 0.02. Mean RBCv was 321.2 ± 42.7 µm/s, with cHct 0.07 ± 0.01 and tRBCp 43.51 ± 11.98. All these results were within the normal range. Interestingly, two patients with microangiopathy on NFC did not exhibit pathological findings in IDF imaging.
Conclusion: This study provides the first combined data of NFC and IDF imaging in cSLE. These findings support the need for further studies exploring multimodal vascular monitoring in pediatric autoimmune diseases to better understand central and peripheral microvascular involvement.
Funding: This study was supported by The Scientific and Technological Research Council of Türkiye (TÜBİTAK) under the 2219 International Postdoctoral Research Fellowship Programme.

PReS25-ABS-1061
THE FIRST CASE OF OBINUTUZUMAB USE TO TREAT A CHILD WITH LIFE THREATENING JSLE IN THE UK.

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Introduction: B-cell targeted therapies such as Rituximab and Belimumab work well for treating juvenile lupus (1-3), however, there is a medical dilemma when a patient either reacts to one of the commonly used agents or is refractory to their use.
Objectives: To postulate the use of obinutuzumab in juvenile lupus as a potential alternative to other B-cell targeted therapies.
Methods: Case presentation:

A 9 years old girl fulfilled 8 SLICC criteria for lupus diagnosis (acute autoimmune haemolytic anaemia, leukopenia, proteinuria, acute cutaneous rash, low complement, positive ANA, anti-Sm and antiphospholipid).
The patient was initially managed with steroids, hydroxychloroquine and rituximab. Unfortunately, patient had severe reaction to rituximab in the form of widely spread hives. MMF was decided before the patient developed rapid respiratory deterioration and was admitted to PICU with Macrophage Activation Syndrome. CT chest showed an ARDS like picture. IV

anakinra was instituted and was then escalated to continuous infusion as patient was clinically unstable with recalcitrant fever, rashes and rising ferritin levels. A more aggressive treatment including IVIG, IV Ciclosporin and IV cyclophosphamide were consecutively decided. Despite initial stabilization, patient was persistently pyrexial and lung infiltrates did not change. Following extensive multidisciplinary discussions, plasmapheresis was decided. Due to inadequate response and previous rituximab reaction, obinutuzumab was administered after multidisciplinary consensus and informed parental consent. Dosing followed the NOBILITY trial protocol with paediatric adjustments: 1000 mg/1.73m^2 IV on Days 1 and 15. No serious infections or infusion reactions occurred.

Results: Patient was stabilised clinically. Ventilatory support was gradually weaned with consequent extubation. Cardiac function and CXR returned back to normal. Anakinra was weaned and eventually stopped together with ciclosporine. Six cyclophosphamide doses were completed according to Eurolupus protocol. MMF was started as a maintenance therapy. Folowing multidisciplinary discussions, no further Obinutuzumab doses were advised.

Conclusion: Obinutuzumab may offer a promising therapeutic alternative in JSLE patients with refractory disease, particularly where conventional therapies, including rituximab, have failed or induced severe allergic reactions. This report aligns with findings from adult trials such as NOBILITY and supports the exploration of obinutuzumab in paediatric lupus patients. Larger paediatric studies and longer follow-up are warranted.

References: 1. Brunner HI, Abud-Mendoza C, Mori M, Pilkington CA, Syed R, Takei S, et al. Efficacy and safety of belimumab in paediatric and adult patients with systemic lupus erythematosus: an across-study comparison. RMD open. 2021 Sep;7(3).

2. Watson L, Beresford MW, Maynes C, Pilkington C, Marks SD, Glackin Y, et al. The indications, efficacy and adverse events of rituximab in a large cohort of patients with juvenile-onset SLE. Lupus. 2015 Jan;24(1):10–7.

3. Peterknecht E, Keasey MP, Beresford MW. The effectiveness and safety of biological therapeutics in juvenile-onset systemic lupus erythematosus (JSLE): a systematic review. Lupus. 2018 Nov;27(13):2135–45.

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PReS25-ABS-1670

ASSESSMENT OF RETINAL AND PERIPHERAL MICROVASCULAR CHANGES IN JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS: A COMPARATIVE STUDY USING OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY AND NAILFOLD VIDEOCAPILLAROSCOPY

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Introduction: Microvascular dysfunction plays a central role in the pathogenesis of Juvenile systemic lupus erythematosus (jSLE), and its early detection may help predict disease activity and prevent long-term organ damage. Optical coherence tomography angiography (OCTA) is a noninvasive imaging technique that provides high-resolution, real-time imaging of the retinal microvasculature. Since the retina is considered a window to the systemic microcirculation, OCTA is a potential tool for assessing subclinical vascular involvement. Nailfold videocapillaroscopy (NVC) is another noninvasive method used to assess peripheral microcirculation.

Objectives: The aim of this study was to investigate the relationship between retinal microvascular changes detected by OCTA and NVC findings in patients with jSLE. In addition, the study aimed to investigate the relationship of these imaging findings with clinical disease activity and relevant laboratory markers.

Methods: In this prospective observational study, 29 patients diagnosed with jSLE based on the SLICC criteria and without any ocular involvement, along with 11 age-and sex-matched healthy controls (HC) were enrolled and evaluated. Disease activity was evaluated using the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K). All participants underwent a comprehensive ophthalmologic evaluation, including measurements of axial length (AL), central corneal thickness (CCT), and spherical equivalent refraction. Retinal imaging included assessment of retinal nerve fiber layer

thickness (RNFL), central macular thickness (CMT), and retinal microvasculature using OCTA. All patients with JSLE underwent standardized, simultaneous NVC. Capillary density, morphology, and the presence of microvascular abnormalities including microhemorrhages and neoangiogenesis were evaluated and compared with OCTA parameters.
Results: In the 29 patients with jSLE, the median age at diagnosis was 12.2 years (IQR: 9.1–13.8), and the median age at assessment was 16.2 years (IQR: 12.5–17.7). NVC evaluation revealed a normal pattern in 11 patients and a nonspecific pattern in 18 patients. The median vessel density of the deep capillary plexus was lower in JSLE [53 (IQR 51.95–52.35)] compared to controls [53.6 (IQR 52.87–54.12)] ($p = 0.041$). Similarly, the median vessel density of the superficial capillary plexus was also reduced in the patient group [48.35 (IQR 47.6–49.1)] relative to controls [50.1 (IQR 49.12–50.62)] ($p = 0.05$). However, no significant differences were observed between JSLE patients and HC in SE, AL, CCT, or CMT with p-values of 0.10, 0.47, 0.12, and 0.54, respectively. When patients were stratified by disease activity based on SLEDAI scores (<4 vs. ≥4), both deep and superficial capillary plexus vessel densities remained comparable ($p = 0.19$ and $p = 0.09$, respectively). Comparison of OCTA parameters with NVC findings revealed that the superficial capillary plexus vessel density was significantly lower in patients who exhibited dilated capillaries on NVC (median: 48.05, IQR: 47.0–48.8) compared to those without capillary dilatation (median: 48.95, IQR: 48.58–49.26; $p = 0.02$).
Conclusion: This study suggests that retinal microvascular changes detected by OCTA may be present in jSLE patients without clinical ocular involvement. The observed association between increased superficial capillary plexus vessel density and dilated capillaries on NVC indicates a possible link between retinal and peripheral microvascular alterations. These findings may indicate that OCTA and NVC could be useful noninvasive tools for detecting subclinical vascular involvement in jSLE; however, larger studies are needed to confirm their clinical significance.
Disclosure of Interest: None Declared

PReS25-ABS-1631

CLINICAL PRESENTATION OF CHILDREN WITH LUPUS NEPHRITIS FROM A LOW AND MIDDLE INCOME COUNTRY (LMIC): AN INITIAL REPORT FROM INDIAN PSLE NEPHRITIS REGISTRY

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Introduction: Systemic Lupus Erythematosus (SLE) is a systemic multisystem autoimmune disease with usual age predominance between 15-44 years.Childhood onset SLE occurs in up to 20% of cases with a prevalence of 3.3-8.8 per 100000 pediatric population .Lupus nephritis (LN), is a major determinant of morbidity and mortality in patients with SLE. Incidence of LN is more common amongst children (50-82%) as compared to adults (20-40%) and with greater disease severity and earlier accrual of disease damage than in adults.Although the 5-year survival rate of pediatric LN (pLN) has improved markedly, the mortality rate seen in pLN still higher. There is of very limited data from Low -Middle Income Countries (LMICs) on renal outcomes in these children.
Objectives: It is a collaborative effort of pediatric nephrologists and rheumatologists from centers across India with the aim to study the epidemiology, clinic-pathologic characteristics, treatment patterns, and kidney outcomes of Indian children with LN, and to assess the factors affecting kidney outcomes. The current data aims to describes the initial presentation of children with LN at the time of enrollment in the registry.

Methods: The Indian Pediatric Lupus Nephritis registry was initiated in 2020 across multiple centers in India. Children (≤ 18 years) diagnosed with Lupus (as per 2012 SLICC criteria), presenting with nephritis, and confirmed by kidney biopsy are beingprospectively enrolled. Clinical data, laboratory investigations, kidney biopsy results, and treatment responses are being documented prospectively. The current report documents their initial presentation.

Results: 154 children (75% female) biopsy-proven LN children were enrolled by July 2024 with the median age being 12 years (IQR: 10-14 years). 9 children (6%) were <7 years. Nearly two-thirds had LN at SLE diagnosis and the rest developed within maximum of 5 years of initial presentation. Common manifestations at presentation included edema (75%), hypertension (54%), and proteinuria (98%), of which 68% presented with nephrotic-range proteinuria. Acute Kidney Injury (AKI) was observed in 43%, with 20% in stage 3. 94% of our cohort had low complements (C3, C4 or both) and 96% was ANA positive. Class IV LN was most common (45%). Muco-cutaneous manifestation was the most common extra-renal manifestation (59%) followed by hematological involvement (28%) then neuropsychiatric manifestation (10%). 3% had significant infection at the time of diagnosis of LN.

Conclusion: This initial analysis from the prospective multicentre registry from India, we have demonstrated that pLN often manifests with significant renal involvement at or near the time of SLE diagnosis, It highlighs the need for routine kidney screening in SLE patients. 10% of patients presented with subclinical nephritis hence lies the importance of thorough renal evaluation. Children enrolled in the registry are being followed up to assess the renal responses, and associated treatment toxicities, which will help optimize the management of pLN in LMICs.

Disclosure of Interest: None Declared

PReS25-ABS-1548

DAMAGE ACCRUAL AND TRANSITION FROM PEDIATRIC TO ADULT CARE IN PATIENTS WITH CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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Introduction: Childhood-onset SLE (cSLE) is associated with significant morbidity and early organ damage, and transitioning these patients to adult care presents notable challenges.

Objectives: We aimed to analyze damage accrual in a retrospective cohort of cSLE patients who transitioned from tertiary pediatric to tertiary adult rheumatology care within our institution.

Methods: We retrospectively analyzed cSLE patients diagnosed before age 18, followed at our Pediatric Rheumatology Department and transitioned to Adult Rheumatology between 2005 and 2020. All patients met the 1997 ACR or 2019 ACR/EULAR classification criteria. We analyzed demographics, cumulative fulfillment of 1997 ACR criteria, disease activity (SLEDAI-2k), damage accrual (SDI), and immunosuppressive treatment. Kaplan-Meier analysis assessed damage-free survival (DFS). Chi-square or Fisher's exact test were used for categorical variables, and T-test or Mann-Whitney U-test for continuous variables.

Results: A cohort of 33 patients was analyzed (7 males, 21%), with 3 having a family history of SLE. The mean age at diagnosis was 13.8 years (SD 2.7), with a mean follow-up of 14.4 years (SD 5.0). Median transition was 4 months (IQR 2-10). Transition occurred over several joint visits with both pediatric and adult rheumatologists. A psychologist was regularly included in the transition. Cumulatively, the most frequent clinical classification criteria were malar rash (24/33), arthritis (21/33) and photosensitivity (15/33). Lupus nephritis was biopsy-proven in 11 patients (class III: 3; IV: 6; V: 2). Frequent laboratory criteria included anti-dsDNA antibodies (28/33) and cytopenia (26/33), mostly leukopenia (23/33). Hemolytic anemia was seen in 9 patients, mostly autoimmune, and one microangiopathic due TTP. Secondary APS was diagnosed in one patient. Damage (SDI ≥1) occurred in 15/33 patients, with SDI ≥2 in 6: Most frequent damage types included cataract (4/15); deforming arthritis (3/15); osteoporosis with fracture, muscle atrophy, nephrotic-range proteinuria (2/15 each). In 10/15 patients, damage was observed at pediatric age (<18 years). Damage-free survival (DFS) was 71% at 5 years and 59% at 10 years, much lower in those with lupus nephritis. Renal disorder and photosensitivity

were more frequent in the damage group (p=0.026 and p=0.016). No differences were observed in disease activity (at diagnosis or one year after) or most treatments, except cyclophosphamide, which was more common in the damage group (10/15 vs. 1/18, p=0.026).

Conclusion: Our analysis highlights the long-term burden of disease in cSLE, with lupus nephritis emerging as a key contributor to damage accrual in these patients. Despite regular physician visits and a well coordinated transition team, damage accrual increased, emphasizing the need for more effective strategies to support patients during the transition to adult care.

PReS25-ABS-1667

PREDICTING THE RECURRENCE RISK OF IMMUNOGLOBULIN A VASCULITIS DUE TO CLINICAL AND LABORATORY FEATURES IN CHILDREN

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Introduction: Immunoglobulin A vasculitis (IgAV) is the most common vasculitis in childhood, characterized by affecting the small vessels of the skin, gastrointestinal tract, and kidneys. Although IgAV is a benign and self-limited disorder, relapses may occur during follow-up.
Objectives: The aim of this study is to evaluate the frequency and predictors of IgAV relapses according to clinical and laboratory features in children.
Methods: We retrospectively reviewed the medical records of 546 pediatric IgAV patients between 2005 and 2025. IgAV-related recurrence was accepted as a recurrence of skin lesions and/or any systemic organ involvement after an asymptomatic period of at least 6 months. Patients were divided into two subgroups: Group 1, which consisted of IgAV patients who had at least one recurrence related to IgAV, and Group 2, which consisted of IgAV patients who had no recurrence.
Results: There were 546 IgAV patients with a male dominance. A total of 40 (7.3%) patients had a relapse related to IgAV after an asymptomatic period of at least 6 months (Group 1). Patients' characteristics and laboratory features were presented in Table 1. Male predominance, diarrhoea, bloody stool, bloody vomiting, gastrointestinal involvement, testicular involvement, WBC, creatinine, and pediatric vasculitis assessment scale (PVAS) at first visit were significantly higher, while mean age at diagnosis of IgAV was significantly lower in Group 1 than Group 2 (p=0.033, p=0.015, p=0.013, p=0.045, p=0.047, p=0.003, p=0.012, p=0.012, p=0.000, and p=0.015, respectively). The most recurrent clinical finding was purpuric skin eruption (65%) (Table 2). Recurrence free survival of Group 1 was illustrated in Fig1. Logistic regression analysis for the prediction of recurrence of IgAV was shown in Table 3. Male sex, diarrhoea, testicular involvement, Hb value, and PVAS were found as independent risk factors for the prediction of IgAV recurrence in the long-term follow-up (p=0.033, p=0.015, p=0.003, p=0.025, and p=0.005, respectively).
Conclusion: In this study, we have shown that male sex, diarrhoea, testicular involvement, higher Hb value, and higher PVAS at first visit were found as independent risk factors for the prediction of IgAV recurrence in the long-term follow-up. Close follow-up is important especially in the presence of male gender, testicular involvement in boys, presence of diarrhoea and high PVAS at first visit, considering that the disease may recur in the long term.
Disclosure of Interest: None Declared

PReS25-ABS-1672

EVALUATION OF ENZYME ACTIVITY AND GENOTYPES IN PATIENTS SUSPECTED OF ADENOSINE DEAMINASE 2 (ADA2) DEFICIENCY IN PEDIATRIC RHEUMATOLOGY CLINICS ACROSS TÜRKIYE: A FUNCTIONAL ANALYSIS STUDY

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Introduction: Deficiency of adenosine deaminase 2 (DADA2) is an autosomal recessive monogenic vasculitis syndrome.It typically presents in early childhood with clinical features such as vasculitis, stroke, hematological abnormalities, and immune dysregulation.Diagnosis of DADA2 is based on the presence of pathogenic variants in the *ADA2* gene and low serum ADA2 enzyme activity.However, due to the high cost and time-consuming nature of genetic testing, enzymatic activity measurement is increasingly important, particularly for screening and differential diagnosis in symptomatic patients.

Objectives: To evaluate the association between serum ADA2 enzyme levels and genetic variants in patients suspected of DADA2 across pediatric rheumatology clinics in Türkiye, and to assess the diagnostic sensitivity and specificity of ADA2 enzyme activity measurement

Methods: This multicenter, cross-sectional observational study was conducted across 16 pediatric rheumatology centers and included a total of 97 pediatric patients, comprising 83 symptomatic, 14 asymptomatic cases.ADA2 enzyme activity was measured using a kinetic enzymatic assay developed with BioSystems GLDH reagent.To ensure the specificity of ADA2 measurement, ADA1 activity was selectively inhibited using EHNA (erythro-9-(2-hydroxy-3-nonyl) adenine).Patients were classified into three groups based on ADA2 gene status determined by Sanger sequencing: biallelic, monoallelic, or no variants.

Results: Among 83 symptomatic patients, ADA2 enzyme levels varied significantly based on genetic findings. Patients with biallelic ADA2 variants (n=26) had a median enzyme level of 6.6 U/L (range: 2.8–16.4; IQR: 4.5–8.8), while monoallelic variants (n=10) had a higher median 9 U/L (range: 5.8–27.4; IQR: 6.5–12.3). Patients without any detected pathogenic variants detected (n=47) showed the highest median ADA2 levels at a median 13.1 U/L (range: 3–30.2; IQR: 8.9–17.7). The difference among these three groups was statistically significant ($p < 0.001$). Comparison between symptomatic (n=10) and asymptomatic (n=10): monoallelic carriers revealed no significant difference in enzyme levels (median 9 U/L vs. 11.2 U/L, p=0.65). In evaluating the diagnostic performance of ADA2 enzyme activity, a threshold of <8 U/L predicted the presence of biallelic mutation with a sensitivity of 79% and a specificity of 69.2%.

Conclusion: This study demonstrated that ADA2 enzyme levels are significantly lower in patients with biallelic pathogenic variants, and that a cut-off value of <8 U/L has meaningful diagnostic utility for identifying such mutations. The EHNA-inhibition-based kinetic enzymatic assay is a rapid and reliable tool for the screening of DADA2. When supported by genetic testing, this approach may facilitate early identification of affected individuals, particularly among symptomatic pediatric patients.

References: Escherich C, Bötticher B, Harmsen S, et al. The Growing Spectrum of DADA2 Manifestations-Diagnostic and Therapeutic Challenges Revisited. *Front Pediatr*. 2022;10:885893. Published 2022 Jun 14.

Lee PY, Kellner ES, Huang Y, et al. Genotype and functional correlates of disease phenotype in deficiency of adenosine deaminase 2 (DADA2). *J Allergy Clin Immunol*. 2020;145(6):1664-1672.e10.

Gibson KM, Morishita KA, Dancey P, et al. Identification of Novel Adenosine Deaminase 2 Gene Variants and Varied Clinical Phenotype in Pediatric Vasculitis. *Arthritis Rheumatol*. 2019;71(10):1747-1755.

Disclosure of Interest: None Declared

PReS25-ABS-1284

PERFORMANCE OF KOBAYASHI AND KAWANET SCORES IN PREDICTING IVIG RESISTENCE: DATA FROMTHE KIWI STUDY

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Introduction: Between 10% and 20% of patients with Kawasaki disease (KD) exhibit resistance to intravenous immunoglobulin (IVIg) therapy. The Kobayashi scoring system demonstrated a good sensitivity (77–86%) and specificity (67–86%) for predicting IVIg resistance in Japanese KD cohorts. However, its predictive accuracy has not been confirmed in European, American, or other Asian populations. The Kawanet group proposed a new scoring model that showed promising sensitivity (77%) and acceptable specificity (60%) in non-Asian KD populations
Objectives: To evaluate the performance of the Kobayashi and Kawanet scores in a multicenter cohort of European, Asian and Indian KD children. To identify demographic, clinical, and biological factors associated with IVIg resistance.
Methods: Retrospective-prospective, observational, international multicenter study, supported by the 2020 PRINTO/PReS grant. KD patients, diagnosed according to the AHA criteria were enrolled from April 2022 to January 2024. Retrospective data were also collected for patients diagnosed from January 1st, 2015.
Results: 723 KD patients were included across 19 paediatric rheumatology units. 62.0% (448) were male, with a median age of 2.40 years (IQR 1.19–4.30). The cohort comprised 57.9% (418) Caucasian, 20.5% (148) Indian, 14.2% (102) Asian, 5.3% (38) African, and 2.4% (17) Hispanic patients. Complete KD was diagnosed in 396 patients (54.8%), incomplete KD in 296 (41.0%), and atypical features were noted in 18 (2.5%). KD shock syndrome was observed in 12 patients (1.7%). Coronary ectasia was observed in 87 cases (12%), and coronary aneurysms in 181 (25.1%). IVIg resistance rate was 19.8% (143). No significant differences in ethnicity or age were observed between IVIg responders and non-responders. However, extremity desquamation (p=0.017), musculoskeletal signs (p=0.006), cardiac involvement (p < 0.001), longer fever duration (p<0.001) and long-term sequelae (p<0.001) were significantly more common in the IVIg-resistant group. Higher ESR (p = 0.002), neutrophil count (p=0.021), ALT (p=0.001), and AST (p<0.001) values were more commonly observed in IVIg-resistant patients. The Kobayashi score demonstrated a balanced accuracy of 55.3% with sensitivity and specificity of 71.3% and 39.2%, respectively. The Kawanet score showed a balanced accuracy of 53.3% with a sensitivity and specificity of 16.1% and 90.4%, respectively. When analysed across the three main ethnic subgroups—Caucasian, Indian, and Asian—the performance of both scores remained consistent with that observed in the overall cohort.
Conclusion: In our multicenter, multiethnic cohort, the Kobayashi score retained a sensitivity comparable to that reported in the original Japanese population but demonstrated a lower specificity. In contrast, the Kawanet score proved to be

poorly sensitive but highly specific in predicting IVIg resistance. Both scores maintained similar performance across different ethnic subgroups.

Trial registration identifying number: Trial registration identifying number: NCT06305611

References: Kobayashi T, et al. Prediction of intravenous immunoglobulin unresponsiveness in patients with Kawasaki disease. Circulation 2006.

Piram M, et al. Defining the risk of first intravenous immunoglobulin unresponsiveness in non-Asian patients with Kawasaki disease. Sci Rep. 2020

Disclosure of Interest: None Declared

PReS25-ABS-1068

FIRST-LINE INTENSIFICATION THERAPY WITH ANAKINRA IN HIGH-RISK KAWASAKI DISEASE PATIENTS

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Introduction: Kawasaki Disease (KD) patients with a high-risk profile, defined by age (under 6 months) and/or the presence of coronary artery involvement (Z score ≥ 2.5 at diagnosis), may benefit from a more aggressive first-line anti-inflammatory approach[1].

Objectives: Given the central role of interleukin (IL)-1 in the pathogenesis of KD[2,3], this study aims to contribute to the evidence supporting the safety and effectiveness of IL-1 blockade with intravenous Anakinra, administered as first-line treatment alongside intravenous immunoglobulins (IVIg), in high-risk KD infants.

Methods: We retrospectively selected 2 cases of KD treated at Meyer Children's Hospital, who satisfied the following criteria: (a) diagnosis of KD according to the American Heart Association guidelines[1]; (b) age under 6 months and/or presence of coronary artery aneurysms (CAA) at diagnosis; (c) first-line treatment with Anakinra along with the first infusion of IVIg.

Results: Patient 1, a 3-month-old male, was diagnosed with a complete form of KD, complicated by CAA: common arterial trunk measuring 3 mm (Z score 4.6), right coronary artery (RCA) measuring 2 mm (Z score 2.19) and left anterior descending artery (LAD) measuring 2 mm (Z score 2.79). Patient 2, a 4-month-old male, was diagnosed with an incomplete form of KD, complicated by CAA: common arterial trunk measuring 2.5 mm (Z score 2.91), RCA measuring 2.2 mm (Z score 2.66) and LAD measuring 2 mm (Z score 2.66). Both patients were treated simultaneously with one infusion of IVIg and intravenous administration of Anakinra at 10 mg/kg/day, achieving fever resolution the day after. Anakinra was progressively tapered down and then shifted to daily subcutaneous administration. Periodic echocardiogram controls showed normalization of the previous coronary artery lesions, respectively, on day 18 and day 19 since fever onset. Anakinra was discontinued after about 8 weeks of therapy. In both patients, the last echocardiogram control at 12 weeks confirmed the complete resolution of the coronary complications.

Conclusion: Intravenous administration of Anakinra in KD represents an off-label use both for route of administration and for patient population. However, in refractory KD patients, it has already been shown to be effective as second-line therapy on fever, systemic inflammation and coronary artery dilatations in the open-label phase IIA clinical trial KAWAKINRA[2]. These 2 cases represent high-risk patients, both for age (≤ 6 months) and for coronary artery involvement; to the best of our knowledge, they represent the first infants with KD and CAA successfully treated with intravenous Anakinra as first-line intensification therapy. Therefore, combined first-line treatment with IVIg and anti-IL1 blockade may be considered in high-risk KD patients.

References: 1. Jone PN, et al. Update on Diagnosis and Management of Kawasaki Disease: A Scientific Statement From the American Heart Association. *Circulation*. 2024.

2. Koné-Paut I, et al. Phase II Open Label Study of Anakinra in Intravenous Immunoglobulin–Resistant Kawasaki Disease. *Arthritis and Rheumatology*. 2021;73(1):151-161.

3. Koné-Paut I, et al. The use of interleukin 1 receptor antagonist (anakinra) in Kawasaki disease: A retrospective cases series. *Autoimmun Rev*. 2018;17(8):768-774.

Disclosure of Interest: None Declared

PReS25-ABS-1690

TOWARDS STANDARDIZED DATA COLLECTION IN PEDIATRIC ANTIPHOSPHOLIPID SYNDROME: A CONSENSUS-BASED CORE DATASET

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Introduction: Pediatric antiphospholipid syndrome (APS) is a rare, thrombo-inflammatory autoimmune disease characterized by thrombosis and nonthrombotic manifestations in patients with persistent positive antiphospholipid antibodies, with clinical features that differ from adult APS. Current APS classification criteria are derived from adult data, and pediatric APS data collection is fragmented and inconsistent between institutions and regions.
Objectives: This project aims to develop an international consensus that defines critical data fields to facilitate international registry-based pediatric APS research.
Methods: Data fields were compared from existing International Ped-APS Registry and CARRA Registry, which identifies patients with APS within the lupus cohort. The 2023 ACR/EULAR APS classification criteria were reviewed and systematic literature review of pediatric APS between 2003-2024 was conducted to identify potential data elements for future registries (Figure 1). Delphi surveys were completed by physicians with APS experience, which included pediatric rheumatologists, med/peds rheumatologists, adult rheumatologists, and pediatric hematologists representing 12 countries and two caregiver representatives. Items were scored from 1 (not important) to 9 (very critical). Consensus “in” was reached for core items scored > 7 by > 70% of experts, as well as all items included in the adult 2023 APS Classification Criteria. Consensus “out” was reached for items with average score < 5. The remaining items were labeled “equivocal” for voting at a hybrid consensus meeting. During the meeting, items with ≥80% agreement were included in the final dataset (either Core or Expanded), and items failing to meet consensus were either excluded or revised and re-evaluated when appropriate. Items scoring ≥6 were eligible for either Core or Expanded datasets. Items scoring ≥ 5 but < 6 were only voted upon for the Expanded dataset.
Results: A total of 32 experts completed the first-round Delphi survey, and 26 participated in the second round. Two caregiver representatives completed a modified version of the survey. Of 316 total candidate items, 72 reached consensus “in,” 87 were rated “out,” and 157 were classified as “equivocal.” These equivocal items were reviewed and voted upon by 19 experts during a hybrid consensus meeting. Based on >80% agreement thresholds, additional items were included. Ultimately, a final dataset comprising **60 core** and **22 expanded data elements** was established. These were categorized under **18 thematic domains**, including demographics, thrombotic and non-thrombotic features, laboratory parameters, comorbidities, therapies, and outcomes. The resulting dataset reflects both expert consensus and parent perspectives and is intended to support consistent international data collection in future pediatric APS research initiatives.
Conclusion: Through systematic evaluation of existing registries, literature review, and Delphi process, we have identified several critical variables to inform future pediatric APS registries. By leveraging international expertise and integrating it with patient patient perspectives, we are laying a solid foundation for the development of a harmonized dataset to advance pediatric APS research efforts globally.

PReS25-ABS-1453

RISK ASSESSMENT FOR PEDIATRIC RHEUMATIC DISEASES IN CHILDREN WITH A HISTORY OF KAWASAKI DISEASE: A LONG-TERM RETROSPECTIVE COMPARATIVE BIG DATA COHORT STUDY

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Introduction: Kawasaki disease (KD) is an acute systemic vasculitis predominantly affecting children under 5 years old. Although primarily known for its cardiac complications, the long-term immune-related outcomes remain poorly understood. Recent evidence suggests a potential link between KD and subsequent development of autoimmune conditions, possibly due to immune dysregulation and Th1/Th2 cytokine imbalance.
Objectives: To assess the long-term risk of pediatric rheumatic diseases in children with a history of KD compared to the general pediatric population.
Methods: This comprehensive 20-year retrospective cohort cohort study analyzed Clalit Health Services data in Israel between 2002-2022. KD patients (N=2126) were compared with matched controls (N=10630) with follow-up assessments conducted at multiple intervals (2, 5, 10, 15, and 20 years). Primary outcomes included juvenile idiopathic arthritis (JIA), systemic lupus erythematosus (SLE), and Henoch-Schönlein purpura (HSP) development.
Results: Children with KD demonstrated a significantly higher risk of developing pediatric rheumatic diseases compared to controls. JIA incidence was markedly elevated at 2 years (117.83 vs. 9.41 per 100,000 person-years; HR 12.51, 95% CI: 2.43-64.50, P=0.003), with this significance persisting throughout the 20-year follow-up (HR 4.38, 95% CI: 1.59-12.09, P=0.004). SLE showed consistently significantly higher incidence from early follow-up (HR 15.01, 95% CI: 1.56-144.30, P=0.019) at 2 years, through 15 years (HR 5.01, 95% CI: 1.01-24.80, P=0.049), though not at 20-years. HSP risk was elevated at 2 years (HR 5.01, 95% CI: 1.45-17.30, P=0.011), with an approximately two-fold increased risk thereafter, without statistical significance.
Conclusion: Our findings reveal a crucial message for clinicians caring for children with KD: the battle doesn't end when the fever subsides. These children face significantly higher risks of developing pediatric rheumatic diseases, with JIA risk up to 12.5 times higher at 2 years post-diagnosis and consistently elevated through 20 years of follow-up. SLE risk was significantly higher up to 15 times at early follow-up and 5 at 15 years. Additionally, we observed a significant initial five-fold increased risk of HSP at 2 years, with a persistent approximately two-fold elevated risk thereafter. Our findings support a paradigm shift in post-KD care that extends beyond traditional cardiac monitoring to include systematic screening for pediatric rheumatic diseases in susceptible children, particularly during the first decade following diagnosis.
Disclosure of Interest: None Declared

PReS25-ABS-1405

RETROSPECTIVE ANALYSIS OF CLINICAL MANIFESTATIONS, GENETIC FINDINGS AND TREATMENT STRATEGIES IN PATIENTS WITH BEHÇET-LIKE SYMPTOMS: ALMOST TWO DECADES OF EXPERIENCE FROM A TERTIARY RHEUMATOLOGY CENTRE

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Introduction: Behçet's disease (BD) is a chronic, complex inflammatory disorder with unclear multifactorial pathogenesis.[1] Recently, monogenic disorders mimicking BD have emerged, whose identification may improve understanding of pathogenesis and allow tailored therapies.[2,3]
Objectives: To describe the demographic, clinical, genetic features, and treatment approaches in a pediatric cohort with BD-like symptoms.
Methods: A retrospective study of patients with BD-related symptoms (e.g., mucosal ulceration, erythema nodosum) and systemic inflammation, referred to a tertiary center (Jan 2007 - Apr 2025), who underwent genetic testing for monogenic BD-mimics. Data included demographics, clinical details, genetic results (Sanger, panel, WES), laboratory findings (monocyte SIGLEC-1, Interferonic Signature), and treatments. The cohort was grouped by genetics: A (pathogenic variant), B (VUS), C (benign variant or negative). Descriptive statistics were used.
Results: 47 patients (71% female, median age at onset: 4.5 years) underwent genetic analysis. 14 (29.8%) had a pathogenic variant (TNFAIP3, DNASE1L3, PTPN22); 19 (40.5%) had one or more VUS (MRTF-A, IFIH1, SOCS1, RIPK1, MEFV, NLRP3, NCF4, ELF4); 14 (25.5% negative, 4.2% likely benign) formed the rest. Interferon inflammation markers (SIGLEC-

1/Interferonic score) were raised in 20% A, 14% B, 17% C. Most common manifestations: oral ulcers (100% A and C, 89% B), genital ulcers (14% A, 0% B, 64% C), arthralgia (14% A, 37% B, 50% C). Ocular involvement in 7% A and C, 5.2% B. Vascular complications only in C (14.2%). Recurrent fever in 14% A, 47% B, 42.8% C; recurrent abdominal pain in 21.4% A, 29.4% B, 35.7% C. Neurological involvement in 7.1% A, 10.5% B, 14.2% C. HLA-B51 positive in 14.2% tested in A, 5.3% B, 28.5% C. Pathergy test negative. Colchicine was the most used treatment. Group A: 85.7% colchicine, 57% conventional immunosuppressant, 42.8% thalidomide, 42.8% biological, 28.6% corticosteroids, 14.2% apremilast. Group B: 87.5% colchicine, 62.5% corticosteroids. Group C: 70% corticosteroids, 50% colchicine, 40% biological, 30% conventional immunosuppressant, 20% apremilast, 10% thalidomide.

Conclusion: Patients with BD-like symptoms and systemic inflammation show a spectrum based on genetic results. Group A (pathogenic variant) often presents only oral ulcers and systemic inflammation. Group C (negative/benign) is more similar to classical BD (more HLA-B51, genital, vascular, ocular, neurological lesions). Group B (VUS) showed intermediate traits. While colchicine was the most used treatment in all groups, classical symptoms correlated with more corticosteroids/thalidomide use, and defined variants with targeted biological therapies.

References: 1. Saadoun D, Bodaghi B, Cacoub P. Behçet's Syndrome. N Engl J Med. 2024 Feb 15;390(7):640-651.

2. Perazzio SF, Allenspach EJ, Eklund KK, et al. Behçet disease (BD) and BD-like clinical phenotypes: NF-κB pathway in mucosal ulcerating diseases. *Scand J Immunol*. 2020; 92:e12973.

3. Burleigh A, Omoyinmi E, Papadopoulou C, Al-Abadi E, Hong Y, Price-Kuehne F, Moraitis E, Titheradge H, Montesi F, Xu D, Eleftheriou D, Brogan P. Genetic testing of Behçet's disease using next-generation sequencing to identify monogenic mimics and HLA-B*51. Rheumatology (Oxford). 2024 Dec 1;63(12):3457-3470.

Disclosure of Interest: None Declared

ePoster short communications-6 Basic/ Translational Science

PReS25-ABS-1246

THE SYNOVIAL FLUID OF JIA PATIENTS IS ENRICHED IN CYTOTOXIC IMMUNE CELLS AND GRANZYME A AND B

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Introduction: Juvenile idiopathic arthritis is the most common rheumatic disease in childhood and adolescence. Previous studies have shown an immunological imbalance leading to chronic inflammation of affected joints. Granzymes are secreted by cytotoxic immune cells, in particular CX3CR1 expressing CD8+ T cells, and are capable of extracellular matrix degradation and remodeling[1, 2]. Whether granzymes are involved in JIA pathogenesis is not yet understood.
Objectives: We aim to deliver a better understanding of the implication of cytotoxic immune cells and granzymes in the pathogenesis of JIA.
Methods: We collected peripheral blood mononuclear cells (PBMC), plasma, synovial fluid cells (SFC) and synovial fluid (SF) from 27 patients with JIA. Samples were frozen at -80 °C until the time of analysis. We performed flow cytometry based immunephenotyping of PBMC (n=45) and SFC (n=31) and Legendplex™ multiplex cytokine analysis in plasma and SF.
Results: The immune composition in the blood of patients differed significantly from the immune composition in the synovial fluid. In particular, we observed a marked increase in the level of cytotoxic immune cells such as NK bright cells and CD8+ T cells in the SF compared to PBMCs. In addition, we show that CX3CR1 is expressed on synovial fluid CD8+ T cells. Granzyme A, granzyme B and granulysin, all of which are secreted by cytotoxic immune cells are significantly enriched in the synovial fluid compared to plasma samples of JIA patients.
Conclusion: Our study delivers a comprehensive overview of the immune signature (cellular composition and major cytokines) of JIA patients during active disease. The observed high levels of granzyme A, granzyme B and granulysin in the synovial fluid of JIA patients indicate an increased presence of cytotoxic immune cells. These findings are in line with an increased infiltration of NK bright and CD8+ T cells in the synovial fluid compared to PBMCs of JIA patients. Delineating the contribution of cytotoxic immune cells to inflammatory dysregulation in the affected joints of JIA patients could help to identify novel treatment targets.
References: 1 Obasanmi G, Uppal M, Cui JZ, Xi J, Ju MJ, Song J, To E, Li S, Khan W, Cheng D, Zhu J, Irani L, Samad I, Zhu J, Yoo HS, Aubert A, Stoddard J, Neuringer M, Granville DJ, Matsubara JA. Granzyme B degrades extracellular matrix and promotes inflammation and choroidal neovascularization. Angiogenesis. 2024 Aug;27(3):351-373.
2 Böttcher, J., Beyer, M., Meissner, F. et al. Functional classification of memory CD8+ T cells by CX3CR1 expression. Nat Commun 6, 8306 (2015).
Disclosure of Interest: None Declared

PReS25-ABS-1460

MONOCYTES UPREGULATE M1 AND M2 MARKERS UPON MIGRATION TO THE SYNOVIAL FLUID IN OLIGO- AND POLYARTICULAR JIA

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Introduction: Juvenile idiopathic arthritis is the most common rheumatic disease in children. Upon inflammation circulating monocytes infiltrate the synovia and the synovial fluid. In vivo, recruited monocytes are capable of

perpetuating inflammation e.g. by secretion of chemoattractants leading to immune cell infiltration into the joint. On the other hand monocytes can aid in resolving an inflammation by expression and secretion of CD163, Arginase-1 or cytokines such as IL- 1 RA [1, 2]. Previous studies have highlighted the role of monocytes in rheumatoid arthritis but their role in JIA is much less understood.
Objectives: We aim to characterize synovial fluid monocyte polarization patterns and cytokine profiles to deliver a better understanding of JIA pathogenesis.
Methods: We collected peripheral blood mononuclear cells (PBMC), plasma, synovial fluid cells (SFC) and synovial fluid (SF) from 27 patients with JIA (persistent and extended oligoarthritis, RF + and RF - polyarthritis). Samples were frozen at
-80 °C until the time of analysis. We performed flow cytometry based immunephenotyping of PBMC (n=29) and SFC (n=24) and Legendplex™ multiplex cytokine analysis in plasma and SF.
Results: Monocytes from PBMC and SFC of JIA patients showed a significantly different surface marker profile. Classical and intermediate monocytes from the SF showed an upregulation of CD64, CD68 indicating a mature and macrophage like differentiation. M1 polarization markers CD86 and HLA-DR were increased on classical and intermediate monocytes in the SF compared to PBMCs. Non-classical monocytes did not aquire an M1 polarization upon migration to the joint cavity. Interestingly, non-classical, intermediate and classical monocytes displayed an upregulation of CD163 and CD206, indicative of an M2 phenotype. In line with this mixed phenotype, legendplex cytokine profiling revealed an upregulation of CXCL10, IL-6 and IL-1 RA in the SF compared to plasma, as described before. Additionally, we saw a strong upregulation of Arginase activity in SF.
Conclusion: Synovial fluid monocytes display a mixed activation profile with both, M1 and M2 polarization markers upregulated upon migration into the SF. This is reflected by the cytokine profile of SF showing upregulated pro-inflammatory factors (IL-6, CXCL10) as well as an upregulation of immunoregulatory factors (Arginase, IL-1 RA). Since Arginase-1 expression has been reported on monocytes in SF of JIA patients, we hypothesize that monocytes might employ an Arginase dependant pathway for immunemetabolic regulation in the inflamed joint. Nonetheless, despite upregulation of M2-like markers and immunoregulatory agents JIA patients show chronic synovial inflammation, substantiating the notion of immune dysregulation is a key component in JIA disease pathogenesis.
References: [1] Schmidt, T., Berthold, E., Arve-Butler, S. *et al.* Children with oligoarticular juvenile idiopathic arthritis have skewed synovial monocyte polarization pattern with functional impairment—a distinct inflammatory pattern for oligoarticular juvenile arthritis. *Arthritis Res Ther* **22**, 186 (2020).
[2] Giacalone, V.D., Cammarata-Mouchtouris, A., Moncada-Giraldo, D. *et al.* Immunometabolic Analysis of Synovial Fluid from Juvenile Idiopathic Arthritis Patients. *Immunohorizons* 1 November 2022; 6 (11): 768–778.
Disclosure of Interest: None Declared

PReS25-ABS-1047

A METHOD FOR ASSESSING PLASMACYTOID DENDRITIC CELL PHENOTYPE AND TLR7 AND 9 INDUCED TYPE 1 INTERFERON PRODUCTION IN WHOLE BLOOD.

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Introduction: Plasmacytoid dendritic cells (pDCs) are the main cell type producing type I interferons, cytokines which are crucial in many rheumatic diseases, including SLE and JDM. These unique traits make pDCs potential therapeutic targets, necessitating further investigation into their activation and function in disease settings. However, most studies on pDCs rely on isolating peripheral blood mononuclear cells (PBMCs), which is an expensive and time intensive assay, and does not fully replicate the physiological environment. Here, we propose the use of whole blood (WB) as a more accessible and physiologically relevant alternative. WB retains all blood cell types and host serum factors, thereby providing a more natural milieu for immune interactions.
Objectives: Develop a protocol for the flow cytometric assessment of pDC in whole blood including
Optimising a protocol to assess the phenotype of pDC in whole blood, including the expression of TLR7/9 and HLADR
Optimising a protocol to stimulate pDC in whole blood with TLR7 and 9 agonists and measure pDC IFNα
Methods: Blood from healthy volunteers was stimulated with TLR 7 agonist, Imiquimod (R837) or TLR9 agonist, CpG ODN 2006, or left unstimulated, for either 5 hours or 24 hours at 37°C. Brefeldin-A (Bref-A) was added at the

time of stimulation or 2 hours post-stimulation for 5-hour incubations. For 24-hour incubations, Bref-A was added at 20 hours post- stimulation. Following incubation, red blood cells were lysed, and remaining cells were either cryopreserved for later use or immediately analyzed. Cells were stained for intracellular and extracellular markers and analyzed using flow cytometry. **Results:** We found that pDCs in WB were readily detectable via flow cytometry and expressed intracellular TLR7, TLR9, and surface HLA-DR, with no differences between stimulated and unstimulated conditions. pDC IFNα production was detectable after stimulation with R837 and CpG. R837 stimulation induced rapid IFNα production within 5 hours, whereas CpG-induced IFNα production was only observed after 24 hours. Additionally, adding Bref-A 2-hours post-stimulation for a 5-hour incubation resulted in a higher frequency of IFNα+ cells compared to adding Bref-A at the start of stimulation. **Conclusion:** Here we demonstrate a novel protocol to measure pDC phenotype and function in whole blood via flow cytometry. This optimized protocol provides a more physiologically relevant method for studying pDC activation and function in immune responses. This protocol is also readily available and accessible to laboratories in less resourced settings that may not have the capacity to separate PBMC, allowing for a more representative sample.
Disclosure of Interest: None Declared

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HUMAN BETA 2 DEFENSIN LEVELS IN PATIENTS WITH IMMUNOGLOBULIN A VASCULITIS

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Introduction: Immunoglobulin A vasculitis (IgAV), is the commonest form of systemic vasculitis in children. It may affect various systems but oftenly presents with palpable purpura in addition to gastrointestinal system, musculoskeletal system or genitourinary system (1). Human Beta Defensin-2 (hBD-2) is the first inducible anti-microbial peptide (2) which is primarily synthesized in the gastrointestinal tract (3) elevated through inflammation both in acute infection and other diseases such as cystic fibrosis (4).
Objectives: Our primary objective is to determine whether hBD-2 levels differ between children with IgAV and healthy controls. Our secondary aim was to compare hBD-2 levels in children with IgAV with gastrointestinal (GI) and/or genitourinary (GU) involvement and those with skin and joint involvement only.
Methods: The study included 45 children diagnosed with IgAV who presented to our pediatric rheumatology clinic and 35 healthy controls. Blood samples for hBD-2 measurement were collected from patients prior to steroid administration, if used. Healthy controls had no infections and had not used antibiotics or steroids in the week prior to sampling. Patients with IgAV were divided into two groups according to steroid use and baseline laboratory parameters and hBD-2 levels were compared. Patients were also grouped by age (<10 and ≥10 years) to compare hBD-2 levels. Human Beta Defensin- 2 ELISA kits were provided by E-Lab Science™. We used SPSS v28 for statistical analysis.
Results: IgAV onset was spontaneous in 8 patients (18.2%), while potential triggers included upper respiratory infections (URTI) (23, 52.3%), gastroenteritis (5, 11.4%), lymphadenitis or trauma (3 each, 6.8%), and skin infection or preseptal cellulitis (1 each, 2.3%). The hBD-2 levels of patients with IgAV (median:10410 pg/dl);min-max: 6410-55614 pg/dl) were higher than in healthy controls (median:8662 pg/dl; min-max: 5438-18303 pg/dl) (p=0.005). Among IgAV patients, hBD-2 levels were higher in patients who were 10 years or older (p=0.008). Additionally, hBD-2 levels were higher in patients with a history of URTI prior to the onset of the disease compared to those with spontaneous IgAV (p=0.015).
Conclusion: Patients with IgAV had higher blood hBD-2 levels than healthy controls. Furthermore hBD-2 levels in IgAV patients who are older than 10 years were higher. That age difference was not observed in the healthy control group. Despite the control group had a higher median age and patients who are older had higher hBD-2 levels, it's outstanding that we have found hBD-2 levels higher in IgAV group than the healthy control group. Additionally, patients who suffered from URTI had higher hBD-2 levels than the spontaneous group. Despite URTI is the most common predisposing factor in our study group, it only covered half of the cases. These results indicate that elevation of hBD-2 levels in IgAV patients doesn't necessarily correlate with age or infection alone, and it may serve as a marker for the disease.

References: 1-Oni L, Sampath S. Childhood IgA Vasculitis (Henoch Schonlein Purpura)-Advances and Knowledge Gaps. Front Pediatr. 2019 Jun 27;7:257.doi:10.3389/fped.2019.00257.

2- Harder J. et al. A peptide antibiotic from human skin. Nature 1997;387:861.

3- O'Neil DA. Regulation of expression of beta-defensins: endogenous enteric peptide antibiotics. Mol Immunol. 2003 Nov;40(7):445-50. doi: 10.1016/s0161-5890(03)00161-

4- Dalcin D et al. the Role of Human Beta-Defensin-2 in Pseudomonas aeruginosa Pulmonary Infection in Cystic Fibrosis Patients. Infect Dis Ther.
2013 Dec;2(2):159-66. doi: 10.1007/s40121-013-0015-5.

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PReS25-ABS-1220

ANALYSIS OF ENVIRONMENTAL EXPOSURES IN PEDIATRIC CHRONIC NON-INFECTIOUS UVEITIS: A CASE-CONTROL STUDY

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Introduction: Chronic uveitis in pediatric rheumatology practice have due to diagnostic difficulties, latent course and treatment-resistant conditions. The most common non-infectious cause of chronic uveitis in children is juvenile idiopathic arthritis (JIA), but idiopathic uveitis is also seen quite frequently. The importance of environmental factors in the development of rheumatological diseases is increasing day by day.
Objectives: The aim of this study was to investigate the effects of air pollution and some other environmental factors on the development of non-infectious uveitis.
Methods: The study was planned as a case-control study. The data of 102 patients (<18 years of age) who were followed up in tertiary center between January 2015 and January 2023 were reviewed using electronic medical records. Patients were divided into 3 groups as JIA, idiopathic uveitis and uveitis associated with JIA (JIA-U), 34 patients from each group. Then, pairwise comparison was made between these three groups. Demographic and clinical characteristics of the patients, recurrence frequency, treatments, various familial and environmental factors (smoking exposure during pregnancy, breast milk use), and Mediterranean diet compliance were assessed with KIDMED questionnaires[1] during outpatient clinic visits. Air quality indexes and air pollutants data were recorded for the place of residence one year before the last uveitis attack, and for the place of residence of those without remission of the attack and those with a diagnosis of JIA.
Results: 102 patients (66 female, 64.7%) were included in the study. In total (101 eyes for sixty-eight patients) were 38 (55.9%) were bilateral and 25 eyes (36.8 %) were unilateral.The median disease durations for JIA, JIA-U, and idiopathic uveitis were 9.9, 7, and 3 years, respectively.
There were no significant differences between the groups in demographic factors such as parental consanguinity, parental age and number of siblings, except for maternal smoking during pregnancy ($p<0.001$). However, caesarean section rates were significantly higher in the idiopathic uveitis groups compared with JIA and JIA-U ($p=0.007$). The Mediterranean diet quality scores were evaluated between patient groups, the median KIDMED score differed significantly between JIA-U and idiopathic uveitis ($p=0.007$).
Environmental factors including air pollutants (PM10, PM2.5, SO2) and weather parameters (precipitation, daily maximum temperature, daily diurnal temperature difference, average relative humidity) were found to influence disease severity and frequency. In particular, air pollutants (PM10, PM2.5, SO2) above defined thresholds were associated with an increased risk of disease, while SO2 showed a potentially protective effect. Statistical analysis of total precipitation, daily maximum temperature, and daily diurnal temperature difference across the three groups revealed significant differences, with the most pronounced variations observed in the uveitis group, evident throughout the year and in the last 3 months. **Conclusion:** Our study found that environmental factors, especially PM10 air pollution and climate parameters, were significantly different between JIA and JIA-U. In contrast, familial effects, smoking exposure during pregnancy and caesarean section delivery were more influential in differentiating idiopathic uveitis from JIA-U. In particular, maternal exposure to cigarette smoke during pregnancy emerged as a significant cause of uveitis. These findings highlight the importance of environmental factors in the

management of JIA, JIA-U and idiopathic uveitis.
References: [1] Sahingoz SA, Sanlier N. Compliance with Mediterranean Diet Quality Index (KIDMED) and nutrition knowledge levels in adolescents. A case study from Turkey. Appetite. 2011;57(1):272-7.
Disclosure of Interest: None Declared

PReS25-ABS-1464

NOVEL HEMIZYGOUS TLR8 GAIN-OF-FUNCTION VARIANTS: A GENETIC CAUSE OF POLYARTERITIS NODOSA AND POLYCHONDRITIS IN MALE CHILDREN

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Introduction: Germline TLR8 gain-of-function is a recently described inborn error of immunity (1–3).
Objectives: We aimed to assess the pathogenicity of an undescribed NM_138636.5: c.1027G>C (p.D343H) variant of *TLR8* in two kindreds and describe its clinical presentation.
Methods: We performed *in silico* analyses of the c.1027G>C variant, reported the genetic and clinical familial segregation and explored the impact of the variant on the NF-κB pathway using a luciferase reporter assay.
Results: Familial segregation revealed an X-linked transmission of the disease, and genetic assessment found a c.1027G>C variant of *TLR8*. This variant was predicted pathogenic by CADD score and AlphaMissense. This mutation was not disclosed in healthy genetic database, but another variant at the same position was recorded in a healthy female, carrying c.1028A>T, p.D343V variant. As both variants were located on the same residue, we explored the impact on the protein function using a NF-κB reporter luciferase assay. After TLR stimulation, both variants presented an increased NF-κB activity compared to wild type TLR8 and were activated at lower concentration. Interestingly, p. D343H variant exhibits a marked loss of ligand specificity and unexpectedly responds to R837, a specific agonist of TLR7. Location of the mutation was shown to be in the site of interaction with degraded RNA, which likely explains TLR8 overactivation (4).
From a clinical perspective, female carriers were mainly asymptomatic, as previously described (2,3). Several symptoms presented by the patients were evocative of ADA2 deficiency and were reported as polyarteritis nodosa diagnoses with thrombotic vasculitis, *livedo* or *erythema nodosum*, and infectious manifestations that could be fatal. Moreover, vasculitis, uveitis, neutrophilic dermatitis and polychondritis were as many manifestations compatible with *UBA1* somatic mutation and could be evocative of another somatic disease, the VEXAS syndrome. These manifestations, associated with the effect of TLR8 variants on hematopoietic stem cells, provide promising clues to understand how NF-κB overactivation in myeloid cells contributes to these phenotypes (1,3).**Conclusion:** We characterized two novel gain-of-function variants of TLR8 and highlighted the proximity of the clinical manifestations with two genetic diseases: ADA2 deficiency and VEXAS syndrome. Due to the clinical overlap, common explorations of these diseases will enable us to better understand their pathophysiology.
References: 1. Aluri J et al. Immunodeficiency and bone marrow failure with mosaic and germline TLR8 gain of function. Blood. 2021 May 6;137(18):2450–62.
2. Fejtkova M et al. TLR8/TLR7 dysregulation due to a novel TLR8 mutation causes severe autoimmune hemolytic anemia and autoinflammation in identical twins. Am J Hematol. 2022 Mar 1;97(3):338–51.
3. Liang J et al. Erythroid-intrinsic activation of TLR8 impairs erythropoiesis in inherited anemia. Nat Commun. 2024 Jul 6;15(1):5678.
4. Tanji H et al. Toll-like receptor 8 senses degradation products of single-stranded RNA. Nat Struct Mol Biol. 2015 Feb;22(2):109–15.

PReS25-ABS-1263

GENOME-WIDE ASSOCIATION STUDY AND XQTL ANALYSIS IN SYNDROME OF UNDIFFERENTIATED RECURRENT FEVER (SURF): A MULTI-OMICS APPROACH FOR IDENTIFYING NOVEL CANDIDATE BIOMARKERS AND MOLECULAR PATHOPHYSIOLOGICAL MECHANISMS

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Introduction: The Syndrome of Undifferentiated Recurrent Fever (SURF) is characterized by recurrent fever episodes and systemic inflammation whose etiology is currently unknown, being probably multifactorial.
Objectives: This study aimed to identify genetic variants underlying SURF and characterize their functional impact through comprehensive multi-omics analysis.
Methods: We collected Whole-Genome Sequencing (WGS) data from 79 SURF patients and 321 healthy controls. Genome- wide association study (GWAS) and sequence kernel association test optimal (SKAT-O) were performed to identify common and rare genetic variants associated with the disease. Candidate variants were further investigated through quantitative trait loci (xQTL) analysis using machine learning (ML) methods to evaluate their impact on multiple omics profiles: immunomics, lipidomics, metabolomics, transcriptomics, proteomics, and epigenomics. Pathway enrichment analysis was performed on candidate biomarkers to identify biological processes involved in the disease pathogenesis.
Results: We identified several candidate SNPs and rare variants-enriched genomic regions associated with the disease, mostly localized in non-coding areas. Subsequent xQTL analyses revealed novel expression quantitative trait loci (eQTLs), methylation QTLs (meQTLs), protein QTLs (pQTLs), and metabolite QTLs (mQTLs), suggesting a functional impact across multiple omics layers. A systematic comparison across different ML algorithms demonstrated that integrating multiple omics layers yields a more comprehensive and reliable set of putative QTL associations. We prioritized our findings based on evidence from publicly available datasets and manually-curated lists of autoinflammatory diseases-related genes, generating a focused set of high-confidence candidate variants/genes for future functional validation.
Conclusion: To the best of our knowledge, this is the first genome-wide study on SURF. We identified several significant genetic associations that need to be validated on an independent dataset. Functional characterization suggests that many identified variants may influence clinical phenotype through regulatory QTL mechanisms. Our multi-omics approach reveals candidate biomarkers potentially underlying SURF pathogenesis, while demonstrating how ML effectively links genomic findings with their functional impacts across multiple molecular layers, enhancing our understanding of this complex condition.

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Disclosure of Interest: None Declared

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RE-EVALUATION OF MEFV CARRIERS PREVIOUSLY DIAGNOSED WITH FMF: A COLCHICINE DISCONTINUATION STUDY

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Introduction: Familial Mediterranean Fever (FMF) is an autoinflammatory disease associated with mutations in the MEFV gene. While typically inherited in an autosomal recessive pattern, heterozygous individuals may also exhibit FMF symptoms, often with a milder disease course. The long-term management of colchicine therapy in heterozygous patients, particularly decisions regarding its discontinuation, remains a clinical challenge.
Objectives: Our objective was to evaluate heterozygous patients under follow-up to identify those in whom colchicine could be successfully discontinued, in order to assess predictive factors for treatment cessation and, consequently, the need to reconsider treatment decisions.
Methods: This retrospective cohort study evaluated pediatric patients with a heterozygous pathogenic MEFV mutation who were followed at a single tertiary center between September 2024 and March 2025. Patients who successfully discontinued colchicine therapy and those who could not were analyzed. Included patients were those with only one pathogenic mutation who were regularly monitored with acute-phase reactants, including SAA, both before and for at least two years after colchicine cessation, who experienced no clinical attacks and no elevated CRP during the last two years, and who had undergone full sequencing of the MEFV gene Clinical characteristics, attack features, inflammatory markers, and treatment outcomes were assessed. Multivariate logistic regression and ROC curve analyses were performed to identify predictors of successful colchicine discontinuation.
Results: A total of 136 patients were included. Of the 84 patients who attempted colchicine discontinuation, 72 (85.7%) remained off therapy, while 12 (14.3%) resumed treatment. The mean age at which colchicine was discontinued was 10.06 ± 2.65 years. The attack-free duration before colchicine stop was as follows: Of the patients, 32.2% had two years, 26.2% had three years, 28.5% had four years, 10.7% had five years, and 2.4% had six years or more of follow-up. The mean follow-up duration after treatment discontinuation in patients who did not resume colchicine was 3.46 ± 1.98 years. The mean duration before colchicine was resumed was 1.9 ± 1.1 years.
In the univariate analysis, fever ($p = .008$), myalgia ($p = .014$), chest pain ($p < .001$), arthritis ($p = .001$), attack reduction percentage ($p < .001$), and younger age at symptom onset ($p = .012$) were significantly associated with colchicine discontinuation. No significant differences were observed between groups in terms of median attack frequency ($p = .774$) or duration ($p = .772$).
Multivariate logistic regression analysis included variables that were significant in the univariate analysis. Reduction in attack frequency was the strongest predictor of colchicine discontinuation ($p < .001$), while the presence of arthritis significantly reduced the likelihood of discontinuation. Chest pain showed a borderline association ($p = .049$). ROC analysis was performed to further evaluate the predictive value of attack frequency reduction during the first 6 months of treatment. The analysis demonstrated high discriminative ability (AUC = 0.883, 95% CI: 0.823–0.943, $p < .001$), with an optimal cut-off of 70.8% yielding a sensitivity of 90.3% and specificity of 76.6%.
Conclusion: Our findings suggest that colchicine therapy can be safely discontinued in selected heterozygous individuals who show early absence of attacks, indicating that these children may not have had FMF at treatment initiation. However, it is important to closely monitor these children after treatment cessation, and decisions should be guided by careful follow-up and regular reassessment.
Disclosure of Interest: None Declared

PReS25-ABS-1604

JAK-INHIBITORS SAFETY AND EFFICACY IN A GROUP OF PATIENTS WITH AUTOINFLAMMATORY DISEASES (AIDS): SINGLE CENTER EXPERIENCE

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Introduction: AIDs are a group of diseases caused by genetic or multifactorial defects of the innate immune response mechanisms and characterized by systemic inflammation and a plethora of manifestations, that represent a significant therapeutic challenge
Objectives: To analyze response to treatment with JAK-inhibitors (JAKinibs) in a group of patients with AIDs
Methods: We retrospectively analyzed data of 48 patients (24- females) treated with JAKinibs at our Center in 2014-2025.
The forms of AIDs included: type I Interferonopathies - 14, genetically undefined AIDs -13, adenosine deaminase 2 deficiency (DADA2) – 5, PSTPIP1-associated syndrome (PAID) - 4, SAMD9 deficiency - 2, SOCS1 haploinsufficiency – 2, SAMD9L deficiency - 1, A20 haploinsufficiency (HA20) - 1, proteasome-associated autoinflammatory syndrome (PRAAS) – 1, IL-18–mediated PAP and recurrent MAS -1, NLRP1- associated autoinflammation with arthritis and dyskeratosis (NAIAD) – 1, RELA haploinsufficiency -1, NEMO-NDAS – 1, C1q deficiency – 1.
JAKinibs were used as monotherapy in 19 cases, and in combination with other immunosuppressive therapy (steroids, anti-IL1, anti-TNFα and others) - in 29. Before initiation of JAKinibs therapy, 27 patients received therapy with other immunosuppressive drugs which was not effective
Results: Median age of onset of any disease symptoms was 0.1 years (range 0; 16). Median age at diagnosis was 3 years (range 0; 17), with the mean diagnostic delay of 3.7 years.
24 patients had autoinflammatory, 22 – autoinflammatory and hematological and 2 - hematological manifestations.
Tofacitinib was used in 32/48 cases, and ruxolitinib - in 16/48. Average initial dose was 0.9±0.2 mg/kg. Median duration of therapy – 3.0 years (0.3; 10.0). Median age of initiation of therapy – 5.0 years (0.5; 17.0).
JAKinibs therapy led to a complete remission in 23/48 cases, partial remission in 20/48, and had no effect in 5/48.
Side effects that were attributed to JAKinibs were noted in 8/48 patients and included infections in 5, lymphopenia in 2, hepatotoxicity in 1, none of them were severe and led to discontinuation of treatment.
Conclusion: Based on our experience JAKinibs are effective and safe in a variety of AIDs
Disclosure of Interest: None Declared

PReS25-ABS-1495

NERIDRONATE VS PAMIDRONATE IN CHRONIC NONBACTERIAL OSTEOMYELITIS (CNO): A COMPARATIVE EFFECTIVENESS AND SAFETY STUDY

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Introduction: Chronic Nonbacterial Osteomyelitis (CNO) is a rare autoinflammatory bone disorder. Whole-body MRI (WB-MRI) is the gold standard for diagnosis and monitoring, although bone biopsy is necessary in doubtful cases. Currently, there is no consensus on treatment which may include anti-inflammatory drugs, corticosteroids, bisphosphonates and anti-TNF agents. Pamidronate has the strongest evidence of efficacy but alternative therapies

are being explored.

Objectives: To compare the efficacy and safety of Neridronate (NER) with Pamidronate (PAM) in the treatment of pediatric CNO.

Methods: A retrospective study was conducted in patients under 18 years diagnosed with CNO (according to Bristol criteria) and treated with PAM or NER at the Pediatric Rheumatology Unit in Padua. Clinical, laboratory, imaging and therapeutic data were collected at baseline (T0) and after 6 and 12 months (T6, T12). Radiological involvement was measured (T0, T12) using a Whole Body Imaging Score (WBI score), based on WB-MRI or bone scintigraphy. Disease activity was assessed using two scoring systems by three independent evaluators: the standard Physician Global Assessment (PGA; T0, T6, T12), based on clinical findings, and a redefined PGA (r-PGA; T0, T12), which incorporated clinical and radiological scores. Clinical outcomes were defined at T12 as remission off therapy (CR), remission on medication (CRM) or active disease (AD).

Results: Twenty-nine patients (59% female) were included: 9 NER, 20 PAM. Mean age at diagnosis: 10.9 years. At T0, 97% had bone pain, 93% had multifocal disease. At T0, PGA scores were significantly higher in the NER group [6.6 ± 1.4 vs 5.2 ± 1.3, p = 0.02], along with higher ESR and fever prevalence. At T6 and T12, PGA scores decrease significantly in both groups, with more marked reduction in the PAM cohort in the first 6 months. No major adverse events were reported. A slight WBI score reduction was noticed in both groups at T12. At baseline mean rPGA score were lower than PGA in the NER group and higher in the PAM group. At T12 mean rPGA scores were higher than PGA in both groups. Final clinical outcomes: NER- 44% CR, 33% CRM, 22% AD; PAM-35% CR, 25% CRM, 40% AD.

Conclusion: This is the first study comparing the use of NER and PAM for the treatment of pediatric CNO. Clinical and radiological responses were comparable, although NER showed slightly better final outcome. Clinical improvement appeared to precede radiological response at T12, underscoring the need for standardized timing in radiological follow-up. Overall, NER appears to be a valid and safe therapeutic alternative to PAM.

Disclosure of Interest: None Declared

PReS25-ABS-1232

PREDICTIVE FACTORS FOR THERAPEUTIC RESPONSE AND CLUSTER ANALYSIS IN SYNDROME OF UNDIFFERENTIATED RECURRENT FEVER (SURF)

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Introduction: Syndrome of Undifferentiated Recurrent Fever (SURF) defines a group of patients with recurrent fevers lacking a clear monogenic cause. Despite clinical similarities to Familial Mediterranean Fever (FMF) and frequent colchicine responsiveness, no causative mutations are found, even with next-generation sequencing. (1) Recent studies suggest SURF may represent a distinct autoinflammatory entity, with unique inflammatory features and altered pyrin inflammasome activation. (2, 3, 4) However, its clinical spectrum, therapeutic response predictors, and optimal management remain poorly defined.

Objectives: To study a homogeneous cohort of SURF patients longitudinally, differentiate their phenotype from other recurrent fevers, evaluate their response to colchicine, identify factors linked to colchicine resistance, and assess the efficacy of interleukin-1 (IL-1) inhibitors.

Methods: A longitudinal study was conducted on 101 SURF patients, excluding those with Periodic Fever, Aphthous Stomatitis, Pharyngitis, and Cervical adenitis (PFAPA), Familial Mediterranean Fever (FMF), and other known

monogenic systemic autoinflammatory diseases (SAIDs). Demographic, clinical, and therapeutic data were analyzed to identify predictors of colchicine response and define subgroups using cluster analysis.
Results: The predominantly European cohort had a median diagnostic delay of 2.6 years. Less than 20% had a family history of recurrent fever. Common symptoms included arthralgia, abdominal pain, and myalgia, while PFAPA-like features (lymphadenopathy, tonsillitis, oral aphthae) were observed in one-third of cases, sporadically. Colchicine was effective in nearly half of the patients, but resistance was linked to PFAPA-like symptoms and prolonged fever. Tonsillectomy was ineffective. Multivariate analysis identified aphthous stomatitis as a predictor of colchicine inefficacy. IL-1 blockade showed benefits in refractory cases, with anakinra having a better response than canakinumab. Cluster analysis revealed three distinct subgroups with varying symptoms and colchicine responses.
Conclusion: These findings offer new insights into SURF, highlighting predictors of colchicine resistance and supporting IL-1 blockade efficacy. Cluster analysis suggests heterogeneity within SURF, emphasizing the need for refined diagnostic criteria and personalized treatment strategies.
References: 1) Papa R, Penco F, Volpi S, Sutera D, Caorsi R, Gattorno M. Syndrome of Undifferentiated Recurrent Fever (SURF): An Emerging Group of Autoinflammatory Recurrent Fevers. J Clin Med. 2021 May 3;10(9):1963. 2) Luu I, Nation J, Page N, Carvalho D, Magit A, Jiang W, et al. Undifferentiated recurrent fevers in pediatrics are clinically distinct from PFAPA syndrome but retain an IL-1 signature. Clin Immunol. 2021 May;226:108697.
3) Macaraeg M, Baker E, Handorf E, Matt M, Baker EK, Brunner H, et al. Clinical, Immunologic, and Genetic Characteristics in Patients With Syndrome of Undifferentiated Recurrent Fevers. Arthritis Rheumatol.
4) Palmeri S, Penco F, Bertoni A, Bustaffa M, Matucci-Cerinic C, Papa R, et al. Pyrin Inflammasome Activation Defines Colchicine-Responsive SURF Patients from FMF and Other Recurrent Fevers. J Clin Immunol. 2024 Jan 17;44(2):49.
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PREDICTING FMF50 RESPONSE IN PEDIATRIC FMF: EVALUATING DISEASE ACTIVITY SCORES AND COLCHICINE RESISTANCE RISK

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Introduction: Familial Mediterranean Fever (FMF), the most common monogenic autoinflammatory disease characterised by recurrent episodes of fever, polyserositis, and arthritis, is assessed using various tools: the Auto-Inflammatory Diseases Activity Index (AIDAI), Pras, Mor scores, and the International Severity Score for FMF (ISSF) are utilised to measure disease activity; the FMF50 score measures treatment response; and the TURPAID score is used to predict the risk of colchicine resistance at diagnosis.
Objectives: The aim of this study was to determine whether these scores and acute-phase reactants can predict the FMF50 response earlier.
Methods: Children diagnosed with FMF according to the Eurofever/PRINTO criteria and treated with colchicine for ≥6 months were included. Patients with poor adherence or those without exon 10 mutations were excluded. Disease activity was assessed using AIDAI, Pras, Mor, and ISSF, while FMF50 criteria evaluated treatment response. TURPAID score was used to assess risk of colchicine resistance at diagnosis. Concordance between scores was analysed using Cohen’s kappa and Fleiss' Kappa. The patients were classified as FMF50 responders or non-responders. Predictors of

non-response were identified via logistic regression. The association between TURPAID score categories (≥2 vs. <2) and FMF50 response was analyzed with chi-square test.

Results: Among 117 patients (44.4% female), 73 (62.4%) and 84 (71.8%) achieved FMF50 response at 3 and 6 months, respectively. The ISSF, AIDAI, and Pras scores were significantly higher in non-responders (p<0.001). Elevated CRP (OR 1.035, 95% CI 1.002–1.070, p=0.038), ISSF (OR 1.703, 95% CI 1.135–2.557, p=0.010), and AIDAI (OR 1.253, 95% CI 1.053–1.491, p=0.011) at three months were significantly associated with FMF50 non-response at sixth month. Multivariate analysis identified high ISSF (OR 1.745, 95%CI 1.129–2.698, p=0.012) and AIDAI (OR 1.265, 95%CI 1.056–1.514, p=0.011) as independent predictors. Although the TURPAID score was not significantly associated with the FMF50 response, patients with higher TURPAID scores tended to have lower FMF50 achievement rates. APRs were significantly correlated with ISSF, Pras, and AIDAI. Kappa coefficients revealed poor agreement among the activity scores (Kappa values = 0.157 to –0.048).

Conclusion: The ISSF and AIDAI scores may predict the FMF50 response as early as the third month. While the TURPAID score was not a statistically significant predictor, its potential role in early risk stratification warrants further exploration in clinical settings.

References:

1. Batu ED, Şener S, Arslanoğlu Aydın E, Aliyev E, Bağrul İ, Türkmen Ş, et al. A score for predicting colchicine resistance at the time of diagnosis in familial Mediterranean fever: Data from the TURPAID registry. Rheumatology. 2024;63(3):791–797.

2. Eroglu Kara F, Beşbaş N, Topaloglu R, and Ozen S. Treatment of colchicine-resistant Familial Mediterranean fever in children and adolescents, Rheumatol Int, 2015;35(10):1733-37.

3. Ozen S, Demirkaya E, Duzova A, Erdogan O, Erken E, Gul A, Kasapcopur O et al. FMF50: a score for assessing outcome in familial Mediterranean fever. Ann Rheum Dis, 2014;73:897–901.

Disclosure of Interest: None Declared

PReS25-ABS-1413

RATES OF INFECTIONS IN CHILDREN AND ADOLESCENTS WITH RHEUMATIC DISEASES AND ASSOCIATION WITH THERAPIES: ANALYSIS OF GERMAN NATIONWIDE HEALTH INSURANCE DATA

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Introduction: Infections might be more frequent in children and adolescents with rheumatic diseases compared to the general population due to disease-inherent immune dysregulation or required medication, but studies upon this topic are scarce and show conflicting results.

Objectives: Compare rates of selected infections, antibiotic therapies and hospitalization because of infection among children and adolescents with different rheumatic diseases and matched controls using nationwide health insurance data.

Methods: Nationwide data from the statutory BARMER health insurance company for 2018-2023 were analyzed. The study included individuals aged 0-18 years with an ICD-10-GM diagnosis of juvenile idiopathic arthritis (JIA), juvenile systemic lupus erythematosus (jSLE), juvenile dermatomyositis (jDM) or chronic non-bacterial osteomyelitis (CNBO) in at least two quarters. Rates of selected infections, identified by ICD-10-GM codes (all infectious and parasitic diseases, 41 individual infections), hospitalization for infection, and annual antibiotic prescription rates (identified by Anatomical Therapeutical Chemical [ATC] code) were assessed and compared to sex- and age-matched controls. Incidence rates of infections, antimicrobial therapies and hospitalizations were calculated. Poisson regression models were used in order

to assess the association of infections with rheumatic diseases as well as treatments.

Results: In the study period 2018-2023, 7796 observation years of patients with JIA, 124 of patients with jSLE, 91 of patients with jDM and 38 of patients with CNBO were recorded. Rates of several infections as well as antimicrobial therapies and hospitalization due to infections were higher in patients with JIA, jSLE and jDM compared to their matched controls. The most common infections were infections of the upper respiratory tract like tonsillopharyngitis (8.8/100 JIA patient years (py) vs. 6.4/100py in matched controls) or acute bronchitis (7.0/100py vs. 5.6/100py). Risk ratio was also increased for some bacterial infections such as pyelonephritis (RR 3,1 [1,7-5,7]) or opportunistic infections like herpes zoster (RR 3,4 [2,1-5,5]). Rates of hospitalization due to infection were 1.7/100py in JIA, 3.2/100py in SLE, 2.2/100py in jDM, and 0/100py in CNBO. Frequency of antibiotic therapies were 15/100py, 19/100py, 25/100py and 13/100py CNBO. In JIA patients, risk of antimicrobial therapy and hospitalization was already increased in patients without treatment (RR 1.2 [1.1-1.3] and RR 2.6 [1.9-3.3]) and was further increased by therapy with glucocorticoids (RR 1.5 [1.2-1.7] and RR 2.4 [1.6-3.8]), while therapy with c- and/or bDMARDs had no effect on hospitalization rates.

Conclusion: Patients with JIA, jSLE and JDM seek medical attention for infections more frequently, are more often hospitalized and receive more antibiotics than age-matched controls. In JIA, this was the case even for patients without GC or DMARDS, however, rates of hospitalized infections were overall low. Particularly GC treatment increases the risk for several infections including antimicrobial treatment and hospitalization significantly.

Disclosure of Interest: None Declared

ePoster Short Communications -8: Juvenile Dermatomyositis and Scleroderma-II

PReS25-ABS-1090

SERUM IL-18 AND CXCL-9 AS BIOMARKERS OF INTERSTITIAL LUNG DISEASE ASSOCIATED WITH JUVENILE IDIOPATHIC INFLAMMATORY MYOPATHIES

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Introduction: Interstitial lung disease (ILD) is a potentially life-threatening complication and a major cause of mortality in patients with juvenile idiopathic inflammatory myopathies (JIIM). However, studies evaluating biomarkers associated with ILD are limited, and their findings remain inconsistent.
Objectives: This study aimed to investigate role of serum IL-18 and CXCL-9 as biomarkers of ILD in JIIM patients.
Methods: This study is part of the Juvenile Dermatomyositis Cohort Biomarker Study and Repository (UK and Ireland). We included 26 patients with ILD, 41 without ILD, all with available serum samples at diagnosis and/or follow-up. Serum samples at diagnosis were available from 15 ILD patients and 39 non-ILD patients. Additionally, samples from 25 healthy controls were included. Serum IL-18 and CXCL-9 levels were measured using U-PLEX Human Assays (Meso Scale Discovery, Maryland, US). Clinical data, muscle weakness scores, laboratory findings, and ILD-related information were comprehensively reviewed.
Results: Patients with ILD were significantly older at presentation than those without ILD (median age 11.1 [IQR 9.8–14.3] vs 8.3 [IQR 4.9–12.6] years; p = 0.003). While most patients in both groups were diagnosed with juvenile dermatomyositis, overlap syndromes were more common in the ILD group (30.8% vs 4.9%; p = 0.018). The ILD group had a higher prevalence of anti-MDA5 antibodies (30.8% vs 2.4%; p = 0.005) and higher serum IgG levels (16.4±4.5 vs 11.7±4.8 g/dL; p = 0.002). At diagnosis, serum IL-18 levels were significantly higher in the ILD group (median 20,583.6 [IQR 15,461.2–29,648.2] pg/mL) compared to the non-ILD group (7,832.2 [IQR 5,392.3–12,441.2] pg/mL; $p < 0.001$) and healthy controls (722.3 [IQR 419.5–863.4] pg/mL; $p < 0.001$). Serum CXCL9 levels were also significantly higher in the ILD group compared to healthy controls (1,999.5 [IQR 791.8–8,915.0] vs 926.1 [IQR 454.6–1,515.9] pg/mL; p = 0.032) and trended higher than the non-ILD group (972.2 [IQR 585.5–2,480.4] pg/mL; p = 0.137). At 1-year follow-up, both serum IL-18 (4,158.0 [IQR 2,932.0–6,839.0] pg/mL; p = 0.005) and CXCL9 (634.8 [IQR 432.9–760.7] pg/mL; p = 0.016) significantly decreased from baseline. Serum IL-18 levels at diagnosis showed significant positive correlations with ferritin (r = 0.58), lactate dehydrogenase (r = 0.33), IgG levels (r = 0.45), IgA (r = 0.47), and significant negative correlations with FEV_1 % predicted (r = –0.51), FVC % predicted (r = –0.46), DLCO % predicted (r = –0.53), and KCO z-score (r = –0.88), all with $p < 0.05$.
Conclusion: Serum IL-18 and CXCL-9 may serve as potential biomarkers in juvenile idiopathic inflammatory myositis (JIIM) for both identifying the presence of ILD and monitoring treatment response.
Disclosure of Interest: None Declared

PReS25-ABS-1199

REDUCED CD4+ IFNG+ T CELL RESPONSE IS ASSOCIATED WITH MORE SEVERE CLINICAL DISEASE IN JUVENILE DERMATOMYOSITIS

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Introduction: Juvenile Dermatomyositis (JDM) is a rare, systemic autoimmune disorder, resulting in skin and muscle inflammation. JDM aetiology is not well understood, meaning treatment is not targeted to specific pathways in disease pathology, highlighting the need for further research. Dysregulation of Type I and Type II interferon (IFN) has been observed in JDM in blood and muscle and has previously been shown to be associated with more severe clinical disease in JDM and other autoimmune rheumatic conditions.
Objectives: The aim of this project is to investigate whether CD4+IFNγ+ T cell dysregulation can be identified in blood from JDM patients compared to age-matched healthy controls, and if so, whether this is associated with clinical disease activity.
Methods: Expression of IFNγ, IL-17 and IL-2 in CD4+ T cells in peripheral blood mononuclear cells (PBMC) of JDM patients, obtained from treatment-naïve (JDM Pre, n=15), and on-treatment (JDM On, n=29) patients and from age-matched healthy controls (HC, n=36) was assessed by flow cytometry, following stimulation with PMA/Ionomycin/Brefeldin A (P/I/B) for 4 hours. Clinical disease activity measures including Physician's global assessment of disease activity (PGA), determined using the physician Visual Analogue Scale, were obtained from the JDCBS database. Clinically inactive disease or active disease were defined using the Almeida et al amended PRINTO criteria (2015).
Results: Intracellular cytokine staining following P/I/B stimulation showed a significant decrease in the proportion of CD4+ IFNγ+ T cells in JDM Pre ($p<0.0001$) and JDM On ($p=0.0036$) patients compared to HC. JDM Pre patients had a trend to decreased proportion of CD4+IL-17+ T cells compared to HC. No significant differences between JDM and HC were observed in CD4+IL-2+ T cells. An abnormal Th17/Th1 ratio was observed between JDM patients and controls ($p=0.0001$). A significant recovery of CD4+IFNγ+ T cell frequency was seen in JDM patients on treatment in remission ($p=0.0069$), compared to JDM treatment-naive patients with active disease. Significant negative ($p=0.0314$) correlation was observed between PGA and CD4+IFNγ+ T cell frequency in JDM patients, suggesting that deficit of CD4+IFNγ+ Th1 cells is associated with more severe clinical disease.
Conclusion: Our findings show a lack of CD4+IFNγ+ T cell response in JDM patients compared to controls. Clinical data indicated that lack of CD4+IFNγ+ T cell response is associated with more severe clinical disease in JDM patients, and recovery of this population is seen in remission of clinical disease.
Disclosure of Interest: N. Evans: None Declared, L. Marshall: None Declared, E. Rosser: None Declared, C. Deakin: None Declared, A. Syntakas: None Declared, Q. Wu: None Declared, D. Cancemi: None Declared, M. Wilkinson: None Declared, L. Wedderburn Grant / Research Support with: Pfizer , Consultant with: Pfizer, Cabaletta

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CLINICAL PROFILE OF JUVENILE DERMATOMYOSITIS PATIENTS WITH INTERSTITIAL LUNG DISEASE FROM A TERTIARY CARE CENTER IN INDIA

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Introduction: Idiopathic inflammatory myopathies (IIMs) are a group of rare and heterogeneous rheumatological

diseases with systemic involvement. Juvenile dermatomyositis (JDMS) forms the most common subtype among IIMs. Interstitial Lung Disease (ILD) associated with anti-MDA5 positivity is the most common cause of mortality among IIMs.
Objectives: To describe the clinical profile of JDMS patients with ILD from a tertiary care center in North-West India.
Methods: We did a retrospective review of the medical records of pediatric patients diagnosed with JDMS and being followed up at a tertiary care center in North-West India. Prevalence of ILD and the risks associated were studied.
Results: A total of 172 patients diagnosed with JDMS were included. ILD was present in 21 (12.2%) patients in our cohort. Of these, 38.1% were males and 61.9% were female. Age of onset of symptoms was 9.8 years (IQR-4.4) with a delay in diagnosis of 7 months (IQR-14). Most of the patients were diagnosed with ILD at the time of diagnosis of JDMS. Fever and cutaneous symptoms like Gottron's papules were noted at onset in most patients (61.9%, 81% respectively). 16 out of 21 patients with ILD complained of proximal muscle weakness. Nail fold capillaroscopy showed abnormal findings in 42.9% patients with ILD. Most of the patients (16/21) had elevated liver enzymes. Autoantibodies associated with interstitial lung disease include anti-MDA5, anti-PmScl, and anti-Ku. 75% patients received pulse dose of corticosteroids followed by methotrexate injection (13/21) and additional Cyclophosphamide (45.5%) was administered in 8 patients (44.4%). 3 out of 21 children with ILD died with cause of death being attributed to Rapidly Progressive ILD (RP-ILD).
Conclusion: ILD is a major contributor to extramuscular morbidity and mortality in these patients. Risk factors for ILD include presence of fever and anti-MDA5 positivity. Early diagnosis and interventions such as intensive immunosuppression are imperative in the management of ILD.
Disclosure of Interest: None Declared

PReS25-ABS-1635

TYPE I INTERFERON SIGNATURE IS ASSOCIATED WITH DISEASE ACTIVITY AND MUSCLE OUTCOMES IN JUVENILE DERMATOMYOSITIS

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Introduction: Type I interferons play a key role in the pathogenesis of juvenile dermatomyositis (JDM). Type I IFN-related gene signatures (IGS) have emerged as potential biomarkers of disease activity, but their association with clinical outcomes in JDM remains to be fully defined.
Objectives: To evaluate associations between IGS and clinical parameters, disease activity states, and remission status in JDM.
Methods: All available IGS measurements made in JDM patients followed at the Gaslini Institute (Genoa, Italy) between 2019 and 2025 were retrieved (N=101). After excluding repeated samples, 43 patients were included, of whom only the first available sample was analyzed. IGS was determined as previously described[1]. Correlations of IGS with Juvenile DermatoMyositis Activity Index (JDMAI) 1 and 22, physician global assessment (PhGA), MMT8, hybrid MMT/CMAS (hMC)3, muscle and skin component of DAS, and 0-10 skin visual analog scale (VAS) were tested using Spearman's rank correlation. IGS were compared across JDMAI1- and JDMAI2-defined disease activity states4, using the Kruskal-Wallis test and post-hoc comparisons. Mann-Whitney U test was used to compare IGS by the presence or absence of muscle and skin remission and complete clinical response, and by muscle enzyme status (normal vs elevated).
Results: IGS showed a moderate correlation with JDMAI1 (R=0.64, p<0.001), JDMAI2 (R=0.65, p<0.001), PhGA (r=0.61,

p<0.001), MMT8 (R=-0.56, p<0.001) and hMC (R=-0.42, p=0.008), whilst no significant correlations were observed with skin VAS and skin DAS. IGS levels were significantly higher in patients classified as being in the state of high disease activity (HDA) than in those with inactive disease (ID) (median JDMAI1 3.5 vs 0.31, p=0.018; median JDMAI2 3.3 vs 0.3, p=0.0009) and low disease activity (LDA) (median JDMAI1 3.5 vs 0.3, p=0.017). IGS distinguished well patients with muscle remission vs those with active muscle disease (p=0.007), with complete clinical response vs no response (p=0.056), and with normal vs elevated muscle enzymes (p=0.020).

Conclusion: IGS levels were associated with higher global and muscle disease activity scores, but not with skin disease activity measures. IGS levels discriminated strongly between HDA and ID/LDA states, as well as between patients who experienced or did not experience muscle remission, complete clinical response, or had or did not have normal muscle enzymes. These observations support the potential role of IGS measurement as a biomarker for disease monitoring and for defining treatment targets in the treat-to-target strategy for JDM.

References:

Tesser A et al. Type I interferon signature: a quantitative standardized method for clinical application. Clin Exp Immuno. 2025

Rosina S et al. Development and validation of a composite disease activity score for measurement of muscle and skin involvement in juvenile dermatomyositis. Rheumatology (Oxford) 2019.

Varnier GC et al. Development and testing of a hybrid measure of muscle strength in juvenile dermatomyositis for use in routine care. Arthritis Care Res (Hoboken) 2018.

Rosina S et al. Defining criteria for disease activity states in juvenile dermatomyositis based on the Juvenile Dermatomyositis Activity Index. RMD Open 2024

Disclosure of Interest: None Declared

PReS25-ABS-1480

TYPE-1 INTERFERON SIGNATURE AND B CELL SUBSETS IN JUVENILE DERMATOMYOSITIS: ASSOCIATIONS WITH DISEASE ACTIVITY

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Introduction: Juvenile Dermatomyositis (JDM) is a rare pediatric autoimmune disease characterized by muscle weakness and distinct dermatological features. The pathogenesis of JDM involves an elevated type-1 interferon (IFN) signature and dysregulation of the humoral immune response, leading to the production of pathogenic myositis-specific autoantibodies (MSAs). Despite its relevance, studies on B-cell subsets in JDM are limited, and the correlation between immunological abnormalities, disease activity scores, and MSA subtypes remains poorly understood

Objectives: To assess peripheral B cell subsets and type I interferon signatures in juvenile dermatomyositis patients, comparing disease activity states and controls, and correlate immune profiles with clinical severity and treatment response.

Methods: Blood samples were collected from 45 individuals, including 30 juvenile dermatomyositis (JDM) patients (15 in remission and 15 undergoing treatment) and 15 healthy controls. Flow cytometry was used to analyze peripheral B cell subsets, including $CD19^+$ B cells, transitional B cells, class-switched ($CD19^+IgD^-CD27^+$) and non-switched memory B cells ($CD19^+IgD^+CD27^+$), as well as Bm1–Bm5 subsets defined by IgD and CD38 expression. Participants were categorized into high and normal B cell groups, and comparisons were made using the Mann–Whitney U test. Type I interferon-stimulated gene expression was measured via RT-qPCR, and an IFN score was calculated to assess interferon activity and its correlation with disease parameters.

Results: We examined 30 juvenile dermatomyositis (JDM) patients—20 with active disease (ADG) and 10 with inactive disease (IDG)—along with 15 healthy controls. The average age was 10.71 ± 4.28 years, with a male-to-female ratio of

3:4. CD19⁺ B cells were slightly increased in ADG compared to IDG and controls (p = 0.02). Both switched (CD19⁺IgD⁻CD27⁺) and non-switched memory B cells (CD19⁺IgD⁺CD27⁺) were significantly elevated in ADG (p = 0.04 and p < 0.01, respectively), as were transitional B cells (p = 0.01). Among the Bm1–Bm5 subsets, Bm2' cells were significantly higher in JDM patients (p = 0.01) and showed a positive correlation with Disease Activity Score (DAS) and a negative correlation with Childhood Myositis Assessment Score (CMAS). Switched memory B cells were inversely related to DAS and CMAS. Type I IFN scores were significantly higher in JDM patients, negatively correlated with CMAS, and were highest in the anti-MDA5 autoantibody subgroup

Conclusion: Active juvenile dermatomyositis patients showed elevated CD19⁺ B cells, naive and unswitched B cells, and higher type-1 interferon scores, correlating with CMAS and DAS, indicating their potential as disease activity biomarkers.

Disclosure of Interest: None Declared

PReS25-ABS-1560

THE ROLE OF NAILFOLD CAPILLAROSCOPY IN THE ASSESSMENT OF JUVENILE RHEUMATIC DISEASES

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Introduction: Nailfold videocapillaroscopy (NVC) represents a reliable, non-invasive tool for the diagnosis of several adult rheumatic diseases, and the assessment of peripheral microvascular abnormalities may serve as a potential biomarker of disease severity in these patients1. However, data on NVC findings and their clinical significance in pediatric patients are limited.

Objectives: To evaluate nailfold videocapillaroscopy (NVC) findings in children with primary Raynaud's phenomenon (PRP) and connective tissue diseases (CTDs). In juvenile CTDs, we aimed to assess potential associations between NVC features and clinical or organ involvement.

Methods: NVC was performed in patients followed at the Paediatric Rheumatology Unit of our hospital for PRP or a definite diagnosis of CTD. For each child, 32 images were acquired, and microvascular alterations were analysed and classified as either non-specific or scleroderma patterns (early, active, and late) by two independent observers. A semi-quantitative rating scale from 0 to 3 was adopted to score six capillary abnormalities2 (enlarged capillaries, giant capillaries, microhaemorrhages, loss of capillaries, microvascular disarray, and capillary ramifications) and calculate an average score. The capillary density score was identified as "avascular score".

Results: A total of 800 NVC images from 50 subjects (30 females; mean age 16.4±4.0 years) were evaluated. Scleroderma pattern was significantly more frequent in juvenile systemic sclerosis (jSSc) compared to both juvenile dermatomyositis and PRP (p=0.003 and p<0.001, respectively). In terms of capillaroscopic alterations, differences were observed only in PRP vs. jSSc for reduction of capillary density (p<0.001) and presence of giants (p=0.01). Scleroderma pattern was associated with skin sclerosis (21/25 vs. 0/9; p<0.001), digital ulcers (8/25 vs. 0/9; p=0.07) and gastrointestinal involvement (17/25 vs. 1/9; p=0.006). Avascular score was higher in children with interstitial lung disease (ILD) than in those without (p<0.05). Patients with severe reduction of capillary density (≤4/mm) were more likely to have ILD (5/10 vs. 4/13; p=0.02). Multivariate logistic regression analysis showed that the association between severe reduction of capillary density and ILD was independently of the presence of scleroderma pattern (OR 3.2; 95%CI 0.9-11.6) and skin fibrosis (OR 2.7; 95%CI 0.8-9.3).

Conclusion: As in the adult population, NVC may help differentiate primary from secondary RP, supporting the early diagnosis of CTDs. In these patients, NVC may have a role in risk stratification for organ involvement, particularly ILD.

References: Smith V, Decuman S, Sulli A, Bonroy C, et al. Do worsening scleroderma capillaroscopic patterns predict future severe organ incolvement? A pilot study. Ann Rheum Dis 2012; 71:1636–9.

Sulli A, Secchi ME, Pizzorni C, Cutolo M. Scoring the nailfold microvascular changes during the capillaroscopic analysis in systemic sclerosis patients. Ann Rheum Dis 2008; 67:885–7.
Disclosure of Interest: None Declared

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PARENTS AND PHYSICIANS DO NOT ALWAYS AGREE IN IDENTIFYING JOINTS WITH ACTIVE ARTHRITIS. DATA FROM A LARGE MULTINATIONAL STUDY.

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Introduction: Patient's self-assessment (or parent's proxy assessment) has gained increasing importance in chronic diseases in recent years. This is due both to the widespread use of telemedicine and to the evidence that including patient's perception in the evaluation of the disease course may improve the outcome of the disease. The count of joints with active arthritis is an essential outcome measure in Juvenile Idiopathic Arthritis (JIA), used alone or as part of composite scores and criteria for inactive disease (ID) to summarize providers' appraisal of disease activity. Patient's self-assessment or parents' proxy evaluation of joints with active arthritis might be an important outcome measure of JIA disease course for both telemonitoring and routine assessment.

Objectives: To measure the agreement between parents and physicians in identifying joints with active arthritis and to assess factors affecting the agreement variability.

Methods: Patients' data were obtained from a large multinational dataset of subjects enrolled in the Epidemiology Treatment and Outcome of Childhood Arthritis (EPOCA) study (1). Briefly, the EPOCA study is a survey conducted by the Paediatric Rheumatology International Trials Organisation (PRINTO) between 2011 and 2016, involving 9081 JIA patients from 130 paediatric rheumatology centres in 49 countries, grouped into eight geographical areas. Parent/child reported outcomes were collected with the juvenile arthritis multidimensional assessment report (JAMAR). The proxy- and self-assessment of joint inflammatory signs was obtained by asking the parent or the patient to rate the presence of pain or swelling in the following joints or joint groups: shoulders, elbows, wrists, small hand joints, hips, knees, ankles, and small foot joints. The agreement between parents and physicians was calculated by Cohen's Kappa analysis in each joint, by adapting the rheumatological exam to the joints or joint groups listed in the JAMAR. The mean Kappa coefficient of the joints was then compared among eight geographic areas, three levels of socioeconomic status (low, average, and high), and three levels of education (elementary, high school, and degree) of the parent filling the JAMAR. Kappa results were interpreted as follows: values ≤ 0 as indicating no agreement and 0.01–0.20 as none to slight, 0.21–0.40 as fair, 0.41– 0.60 as moderate, 0.61–0.80 as substantial, and 0.81–1.00 as almost perfect agreement.

Results: A total of 9,081 visits had all the evaluations available for the tested tools in the EPOCA dataset. Kappa coefficient was in the fair range for the shoulder (lowest Kappa at 0.22), hip, and toes and in the moderate range in elbow, wrist, fingers (highest Kappa at 0.50), knees and ankles. Highest mean Kappa was observed in Eastern Europe (0.46) and lowest in North America (0.25) (Figure). Mean Kappa coefficients were similar in the different levels of parent's education, ranging from 0.40 (elementary) to 0.42 (degree); mean Kappa coefficients was higher in patients with high socioeconomic status 0.46 and lower in in patients with average socioeconomic status (0.38)

Conclusion: Agreement between parents and physicians in identifying active joints was fair to moderate, with important variability among different joints. The agreement remained stable among different levels of parents' education, but it showed remarkable variability after grouping by geographic areas.

References: 1. Consolaro A. Lancet Child Adolesc Health. 2019

Disclosure of Interest: None Declared

PReS25-ABS-1553

HOW DO WE DEFINE FLARE IN JUVENILE IDIOPATHIC ARTHRITIS?

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Introduction: Assessing disease activity in juvenile idiopathic arthritis (JIA) is essential for both clinical practice and research. While cutoffs to define disease activity states in oligoarticular and RF-negative polyarticular JIA were published in 2021 and later validated for other subtypes, a standardized definition according to the International League of Associations for Rheumatology (ILAR) classification of disease flare remains lacking. This limits comparability across studies and may influence treatment decisions. A preliminary flare based on the six core response variables (CRVs) was proposed by Brunner et al. in 2002, but it was only preliminary validated and it was not adopted in all trials. This highlights the urgent need for a wildly accepted flare definition.

Objectives: To describe the definitions of disease flare used in JIA clinical trials and highlight the heterogeneity across studies.

Methods: A literature search of ClinicalTrials.gov and PubMed was conducted to identify JIA trials reporting a definition of flare. Trials initiated between May 1997 and January 2025 were considered. Trials without a clearly stated flare definition were excluded. A descriptive analysis was performed to assess the frequency and characteristics of definitions used.

Results: 38 JIA trials were identified; 10 were excluded due to the absence of a flare definition. Among the 28 included studies, the most adopted definition (16/28, 57%) was the PRINTO/PRCSG criteria developed by Brunner et al., defining flare as a ≥30% worsening in at least three of the six core set variables (CRVs), without ≥30% improvement in any CRV, and requiring at least two active joints, with the reference point being the end of phase 1. Five trials (18%) defined flare as the reappearance of active disease after a previously inactive joint count. Four studies (14%) adopted a definition of flare based on the juvenile arthritis disease activity score (JADAS): a patient previously in inactive disease was considered to experience a flare if he/she had a JADAS above the thresholds for minimal disease activity (2 studies) or for moderate disease activity (2 studies). Other definitions included worsening of CHAQ, ESR, and AJC, or the need to intensify treatment.

Conclusion: The analysis confirms significant heterogeneity in how flare is defined across JIA trials. While the PRINTO/PRCSG definition is most common, it has notable limitations, including its validation in a small population and the discontinuation of follow-up once flare criteria were met. Additionally, the reference visit for comparison is not consistently defined. While JADAS-based definitions offer a simplified tool, optimal cutoffs for flare detection remain undefined. The results of this survey highlight the need for an evidence-based definition of flare in JIA.

Disclosure of Interest: None Declared

PReS25-ABS-1245

LONG-TERM OUTCOMES AND PREDICTION OF JUVENILE IDIOPATHIC ARTHRITIS-RELATED DENTOFACIAL DEFORMITY: A 17-YEAR FOLLOW-UP STUDY IN THE NORDIC JIA COHORT

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Introduction: Temporomandibular joint (TMJ) involvement in juvenile idiopathic arthritis (JIA) can lead to dentofacial deformities. Early and timely diagnosis remains both urgent and challenging, and predictive markers have not been identified.

Objectives: We aimed to identify predictors of dentofacial deformity in JIA that could inform early intervention and improve long-term outcomes.

Methods: Participants were included from the population-based, Nordic JIA cohort with baseline visits (1997–2000) and 17 years of follow-up. All met the ILAR criteria for JIA. Of the original cohort, 420 were eligible for clinical orofacial and radiographic evaluation. Full-face cone-beam computed tomography (CBCT) scans were used to assess dentofacial morphology. The validated dentofacial deformity index was applied to CBCT scan data to classify dentofacial deformities into four grades: Normal, minor deformity, severe deformity, and very severe deformity. Ordinal regression and cluster analysis (recursive partitioning) were conducted using baseline variables such as gender, age at onset, JIA categories, CRP, height-for-age standard deviation score (height SDS), and weight-for-age standard deviation score (weight SDS) to explore associations with deformity grade.

Results: Of the 420 eligible participants, 245 (58%) underwent full-face CBCT and were included in the present study. The deformity grades were distributed as follows: Normal = 74 (30.2%), minor deformity = 104 (42.9%), severe = 50 (20.4%), and very severe = 16 (6.5%). Cluster analysis showed limited predictive value and failed to classify deformity severity accurately. However, baseline CRP (threshold value = 29 mg/ml), height SDS (threshold value 0.56 SD), and weight SDS (threshold value -0.38 SD) were the most relevant predictors in the cluster analysis. In the ordinal regression, a high height

SDS (OR = 0.74, 95% CI [0.59, 0.92], p = 0.009) and high weight SDS (OR = 0.74, 95% CI [0.60, 0.92], p = 0.006) were protective of developing severe deformity. Baseline CRP as a continuous variable (OR = 1.00, 95% CI [0.99; 1.01], p = 0.788) was not significantly associated with deformity grade in the ordinal regression. Dentofacial deformities were found in all JIA categories.

Conclusion: In the Nordic JIA cohort, 27% of patients exhibited severe or very severe dentofacial deformity 17 years after disease onset. Our findings suggest a potential association between baseline height and weight SDS, and the

severity of dentofacial deformity, which has not been previously described. Given the limited predictive utility of the cluster analysis applied, our findings emphasize the importance of regular orofacial assessments for all JIA patients, regardless of their JIA categories, to enable early detection and intervention.
Disclosure of Interest: None Declared

PReS25-ABS-1200
LONG TERM COMORBIDITY PATTERNS IN JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Patients with Juvenile idiopathic arthritis (JIA) suffer considerable morbidity due to articular and extra-articular manifestations, including ocular, non-articular musculoskeletal, endocrine, cutaneous sequelae, and secondary amyloidosis, which can lead to serious impairment of their physical function and health-related quality of life [1]. To date, little is known about the prevalence and incidence rate of comorbidities in long term JIA.
Objectives: To assess the prevalence and incidence rates of key comorbidities in JIA patients reaching adulthood and its possible association with specific demographic and clinical characteristics.
Methods: This is a national multicentric retrospective observational cohort study. Data on sociodemographic, clinical features and comorbidities were collected from patients with JIA according to the 2001 revised International League of Associations for Rheumatology (ILAR) criteria, registered in the Rheumatic Diseases Portuguese Register (Reuma.pt), who were at least 18 years old at the time of data extraction. Comorbidities included cardiovascular disease, arterial hypertension, dyslipidaemia, diabetes, thyroid disease, amyloidosis, inflammatory bowel disease, allergy and asthma, osteoporosis, psychiatric disease, and autoimmune disease.
Due to small frequencies of some comorbidities these were clustered into wider groups, namely cardiovascular disease, which included ischemic heart disease, cardiac failure, arrhythmia, pericarditis, peripheral arterial disease, ischemic stroke, and valvular disease; as well as autoimmune disease, which included type 1 diabetes mellitus, Graves and Hashimoto's thyroiditis, vitiligo, myasthenia gravis, multiple sclerosis, coeliac disease, and autoimmune hepatitis. We did not consider extra-articular manifestations of JIA, such as psoriasis or uveitis.
Incidence rates of comorbidities were calculated as the number of new events per 1,000 person-years with 95% CI and

prevalence was defined using frequencies.
Results: This study included 924 patients, of which 557 (60.3%) were female with a median [IQR] age of 29.7 [21.2] years. Median age at disease onset was 11.5 [7.8] years, median disease duration was 20.6 [19.7] years and median diagnostic delay was 1.0 [4.7] year. The most frequent category of JIA was undifferentiated JIA (n=293, 31.7%), followed by rheumatoid factor-negative polyarticular JIA (n=191, 20.7%). Most patients were prescribed conventional synthetic DMARDs (csDMARDs; 668, 72.2%) and biologic DMARDs (bDMARDs; 504, 54.7%).
The comorbidities with the highest incidence rate were autoimmune diseases (6.3/1,000 person-years), followed by arterial hypertension (6.1/1,000 person-years) and dyslipidaemia (4.6/1,000 person-years). The incidence of malignancy was 0.6/1000 person-years.
The most prevalent comorbidities were hypertension (n=95, 10%), psychiatric disease (n=60, 6%) and osteoporosis (n=54, 5.6%).
Biologic DMARD therapy in these patients was associated with a decreased risk of developing cardiovascular disease (OR 0.48, p=0.03), arterial hypertension (OR 0.39, p<0.001), dyslipidaemia (OR 0.49, p=0.01), thyroid disease (OR 0.16, p=0.01), amyloidosis (OR 0.12, p=0.049), anaemia (OR 0.21, p=0.02), inflammatory bowel disease (OR 0.31, p<0.001), autoimmune diseases (OR 0.13, p<0.001, osteoporosis (OR 0.39, p=0.003), psychiatric disease (OR 0.3, p<0.001), asthma and allergy (OR 0.19, p<0.001).
No significant association between therapy with bDMARDs and development of malignancy or infections was found.
Conclusion: JIA patients commonly experience comorbidities in the long term, with hypertension being the most frequent. Biologic DMARD treatment seems to be associated with a decreased risk of developing comorbidities. These findings underscore the importance of careful management and monitoring of comorbidities in JIA patients.
References: 1. Ramos FO, Rodrigues A, Martins FM, Melo AT, Aguiar F, Brites L, et al. Health-related quality of life and disability in adults with juvenile
Disclosure of Interest: None Declared

PReS25-ABS-1531

RADIOGRAPHIC ASSESSMENT OF MEASURABLE OSTEOARTICULAR DAMAGE IN JUVENILE IDIOPATHIC ARTHRITIS (JIA) PATIENTS TRANSITIONING TO ADULT CARE

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Introduction: Juvenile idiopathic arthritis (JIA) is the most common pediatric rheumatic disease, causing chronic joint inflammation and potential damage. While conventional radiography is the gold standard for detecting structural damage, interpreting scans in children is challenging due to skeletal immaturity. Routine radiographic monitoring is less common in JIA than in adult rheumatoid arthritis, partly based on the belief that damage is infrequent. However, recent studies indicate significant damage rates, particularly in certain JIA subtypes. Evidence suggests anti-TNFα agents may better prevent damage than methotrexate (MTX) in polyarticular cases. Critically, joint outcomes in JIA patients transitioning to adult rheumatology care have not been quantified.
Objectives: This study's primary aim was to quantify radiographic damage in a cohort of JIA patients after physeal closure and assess associations with childhood treatments. The secondary aim was to explore correlations between radiographic damage and clinical/laboratory variables.
Methods: This cross-sectional study, conducted from January to October 2023, included 30 patients with JIA (83.3% female) transitioning to adult care. Hands/wrists, knees, and pelvis radiographs were assessed using Larsen and modified Sharp/Van der Heijde scores. Clinical, laboratory, and treatment data were collected retrospectively. The

Juvenile Arthritis Damage Index (JADI) was also applied. Fisher's test and Pearson correlation in R explored potential associations.

Results: No significant clinical differences were found between patients with and without radiographic damage, except for higher clinical hip involvement in the damaged group. Osteophytosis (71.4%) was the most common radiographic finding, followed by joint space narrowing (28.6%) and erosions/juxta-articular osteoporosis (14.3%). Of 14 patients with radiographic damage, 6 had positive scores on Larsen or Sharp/Van der Heijde scores. The hips were the most frequently affected joints on radiographs (9 patients), followed by the carpus (6) and knees (3). No substantial link was found between radiographic damage and MTX therapy duration, treatment with biologics, previous arthrocentesis, or cumulative months of active illness, but there was a mild inverse correlation with the JADI-A score.

Conclusion: This study found that up to 50% of patients with JIA exhibit radiographic damage after physeal closure. Notably, many presented only with osteophytosis, often missed by standard damage scores like Larsen and Sharp/Van der Heijde. Furthermore, the observed inverse correlation between JADI-A and the measures of radiographic damage underscores the poor agreement between different assessment tools. This highlights the limitations of current scoring methods and the need for revised approaches, although the clinical significance of osteophytosis, potentially reflecting mechanical stress rather than inflammation, warrants further study.

Disclosure of Interest: None Declared

PReS25-ABS-1124

COMBINATION THERAPY WITH BIOLOGICAL DMARDS AND JAK INHIBITORS IN CASES OF REFRACTORY JIA

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Introduction: Despite biological disease-modifying anti-rheumatic drugs (bDMARDs), 25% of JIA patients enter adulthood with active disease[i]. Janus kinase inhibitors (JAKis) may only achieve inactive disease in about half of JIA patients. bDMARD/JAKi combination therapy has been used predominantly in refractory inflammatory bowel disease, but also in rheumatoid arthritis, ankylosing spondylitis, and Still’s disease in adults.

To our knowledge, there are no published case reports of combination bDMARD/JAKi therapy in JIA. We present a UK multicentre case series of bDMARD/JAKi combination therapy in refractory JIA.

Objectives: To describe current UK experience of bDMARD/JAKi combination therapy in refractory JIA.

Methods: Cases of refractory JIA managed by bDMARD/JAKi combination therapy were identified across 7 tertiary centres. Written consent was obtained, and data collected on patient characteristics, treatment history, adverse effects, and outcomes.

Results: 10 patients were identified (6 Systemic; 1 Psoriatic; 2 Polyarticular, 1 Extended oligoarticular), with median age of 3.5 years at diagnosis. A median 5 DMARDs (all types, range: 3-8) were used before combination therapy, over a median 6.5 years (range: 3-15). The indication in all cases was failure of disease control, with one case of HLH.

bDMARDs combined with tofacitinib included: tocilizumab (n=5), anakinra (n=2), infliximab (n=2), or adalimumab (n=1), whereas baricitinib was combined with tocilizumab (n=1), anakinra + emapalumab (n=1), or rituximab (n=1). 9/10 remain on combination therapy (median 11 months). 3 switched combinations, and 1 reverted to bDMARD monotherapy due to non-adherence.

Full data were available for 7 patients. Historical joint damage was seen in 4/7. In the 12 months before combination

therapy, all received IV methylprednisolone (median cumulative dose 110mg/kg), with 5/7 also receiving oral prednisolone (median duration 108 days ≥0.3mg/kg). Steroid adverse effects were seen in 6/7 including growth concerns (n=4), adrenal suppression (n=3), cataracts (n=1), and vertebral compression (n=1). Following combination therapy, all 7 reported steroid reduction, with no systemic glucocorticoid use since initiation in the 4/7 on combination ≥12 months. At
last follow-up (median 14 months), 3/7 were in clinical remission on medication and 4/7 had active disease managed by: steroid joint injection only (n=2), low-dose oral steroids (n=2), and changing JAKi (n=1).
There was an incidental case of CMV on screening, and another of mild VZV in a previously immune child. No serious side effects including bacterial infections or venous thromboembolism were reported.
Conclusion: Following individual risk-benefit assessment and multi-disciplinary discussion with the family and child, bDMARD/JAKi combination therapy may enable reduction of steroid burden and improved control in refractory JIA. Clinical trials are required to investigate long-term safety and efficacy.
References: [i] Glerup M et al. Long-Term Outcomes in Juvenile Idiopathic Arthritis: Eighteen Years of Follow-Up in the Population-Based Nordic Juvenile Idiopathic Arthritis Cohort. Arthritis Care Res (Hoboken). 2020 Apr;72(4):507–16.
Disclosure of Interest: None Declared

PReS25-ABS-1416

PERSONALISING ADALIMUMAB THERAPY IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS: DEFINITION OF CUT-OFF CONCENTRATION FOR THERAPEUTIC DRUG MONITORING AND IMPACT OF THE FCGR3A RS396991 GENETIC VARIANT

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Introduction: Adalimumab (ADM) is an effective therapeutic choice in juvenile idiopathic arthritis (JIA). However, many patients do not respond to therapy or lose response over time due to a pharmacokinetic (PK) failure. Knowing a cut-off of adalimumab levels for therapeutic drug monitoring (TDM) and genetic variants that impact the PK of adalimumab can reduce the rate of therapeutic failures (1,2).
Objectives: To confirm the association between serum adalimumab levels and anti-adalimumab antibodies (AAA) appearance with clinical remission and disease activity in JIA patients, to calculate a cut-off for TDM and to evaluate the effect of the *FCGR3A* rs396991 on adalimumab levels, ADA appearance, clinical remission and disease activity.
Methods: JIA patients (age < 16y at diagnosis) treated with adalimumab for more than 2 months (6 months for correlations with remission) were considered. Clinical remission was evaluated according to Wallace criteria (3). Disease activity was assessed using JADAS27 clinical score. adalimumab was quantified in serum using a lateral flow assay while an ELISA kit was used to detect AAA. Genetic analyses were conducted using TaqMan assay. Statistical analyses were performed using software R. The association between continuous-categorical, continuous-continuous and categorical-categorical variables was assessed respectively by the Kruskal-Wallis, Spearman's and Chi-squared test. ROC curve was constructed for adalimumab levels to determine the optimal therapeutic cut-off.
Results: Fourty-seven patients, for a total of 134 samples (median age 11.96 years, 33 female, median therapy duration 21.3 months) were enrolled. adalimumab levels were higher in patients in clinical remission (p=0.033, median 6.8 mg/L (IQR: 12.7) vs 13.5 mg/L (IQR: 12)) and inversely correlated with JADAS27 (p=0.015, r=-0.21). The cut-off for adalimumab levels associated with remission is 6.9 mg/L (ROC AUC=61.6%, specificity=53.1%, sensitivity=75.0%).

Regarding pharmacogenetics, adalimumab levels tended to be lower in patients carrying the *FCGR3A* rs396991 variant, in both the additive, recessive and dominant models (p=0.080, 0.058 and 0.081 respectively).

Conclusion: Adalimumab levels are correlated with clinical remission and JADAS27, with a cut-off of 6.9 mg/L that could be considered for dose adjustment. Furthermore, the *FCGR3A* rs396991 presented a trend with reduced adalimumab levels. After validation by further studies, adalimumab levels and the *FCGR3A* rs396991 could be proposed as pharmacological determinants useful to personalize adalimumab therapy in patients with JIA.

References:

1. Dehoorne JL, Groth H, Carlé E, De Schrijver I, Sys C, Delbeke P, et al. Defining a therapeutic range for adalimumab serum concentrations in the management of pediatric noninfectious uveitis, a step towards personalized treatment. Pediatr Rheumatol. 2023 Dec 20;21(1):148.

2. Tutuncu Z, Kavanaugh A, Zvaifler N, Corr M, Deutsch R, Boyle D. Fcγ receptor type IIIA polymorphisms influence treatment outcomes in patients with inflammatory arthritis treated with tumor necrosis factor α–blocking agents. Arthritis & Rheumatism. 2005 Sep;52(9):2693–6.

3. Wallace CA, Ruperto N, Giannini E, Childhood Arthritis and Rheumatology Research Alliance, Pediatric Rheumatology International Trials Organization, Pediatric Rheumatology Collaborative Study Group. Preliminary criteria for clinical remission for select categories of juvenile idiopathic arthritis. J Rheumatol. 2004 Nov;31(11):2290–4.

Disclosure of Interest: None Declared

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PERSISTENT SEROLOGICAL ACTIVITY PREDICTS RISK OF FLARE AFTER T2T GOAL ATTAINMENT IN CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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Introduction: Childhood-onset systemic lupus erythematosus (cSLE) is a multisystem autoimmune disease. Disease flares contribute significantly to organ damage, morbidity, and mortality. The utility of ongoing biomarker monitoring, including anti-dsDNA antibodies, complement levels (C3, C4), and erythrocyte sedimentation rate (ESR) in predicting flares after achieving treat-to-target (T2T) goals remains unclear.

Objectives: To evaluate the association between biomarker levels and flare occurrence in patients with cSLE who had attained T2T goals.

Methods: Patients from the UK JSLE Cohort Study (<18 years at diagnosis, ≥4 ACR/SLICC criteria) were included. Flares were defined using the BILAG-2004 flare index. Longitudinal biomarker data (anti-dsDNA, C3, C4, ESR) were analysed using Prentice–Williams–Peterson (PWP) gap-time models for recurrent flares, adjusted for T2T attainment: Childhood Lupus Low Disease Activity State (cLLDAS), clinical remission on-treatment (cCR), and off-treatment (cCR-0), and for covariates found to be significant ($p < 0.01$) with each T2T state. As cLLDAS includes dsDNA, C3, and C4 in its definition, only ESR was evaluated for additional prognostic value within that model. Hazard ratios (HRs) with 95% confidence intervals (CIs) were reported, representing the change in flare risk per 1-unit change in the corresponding biomarker.

Results: 401 patients from the UK JSLE Cohort Study were included, contributing 4,602 visits. In univariable PWP analyses of patients who had attained either cCR and cCR-0, each unit change in both anti-dsDNA (cCR model HR 1.0004, 95% CI 1.0001–1.0007, p=0.0035, cCR-0 model HR 1.0004, 95% CI 1.0001–1.0007, p=0.0048) and ESR levels (cCR model HR 1.0046, 95% CI 1.0028–1.0063, p<0.0001, cCR-0 model HR 1.0050, 95% CI 1.0032–1.0070, p<0.0001) was associated with significantly increased risk of subsequent flare. In contrast, C3 and C4 levels were not statistically significantly associated with flare risk (p>0.05). In the multivariable model, both anti-dsDNA and ESR remained independently associated with risk of subsequent flare in the cCR (anti-dsDNA: HR 1.0005, 95% CI 1.0001–1.0008, p=0.0078; ESR: HR 1.0041, 95% CI 1.0020–1.0063, p=0.0002) and cCR-0 (anti-dsDNA: HR 1.0004, 95% CI 1.0000–1.0008, p=0.0188; ESR: HR 1.0045, 95% CI 1.0023–1.0067, p<0.0001) models. In the univariable model of patients in cLLDAS, ESR was also significantly associated with subsequent risk of flare (HR 1.0047, 95% CI 1.0029–1.0065, p<0.0001).

Conclusion: Despite attainment of T2T goals, elevated anti-dsDNA and ESR levels independently predicted flare risk in cSLE. These findings support continued biomarker monitoring even in clinically stable patients to guide long-term disease management. Further studies with larger international cohorts are needed to confirm these associations.

Disclosure of Interest: None Declared

PReS25-ABS-1083

GENETIC INSIGHTS INTO EARLY-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS IN INDIA: FINDINGS FROM A COHORT OF 365 PEDIATRIC PATIENTS

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Introduction: Early-onset systemic lupus erythematosus (EOSLE) is a rare autoimmune disorder with significant morbidity in children. Monogenic lupus, caused by single-gene mutations, often presents with early-onset and severe phenotypes, requiring specialized diagnostic approaches. This study explores the genetic basis of EOSLE in the largest cohort of patients with pediatric SLE (pSLE) from India.
Objectives: Unraveling the Genetic Landscape of Early-Onset Systemic Lupus Erythematosus in India: Insights from a Large Cohort Study of 365 Patients
Methods: This prospective observational study investigated monogenic causes in 97 of 365 pSLE patients. Inclusion criteria for study comprised patients with EOSLE (age ≤8 years) and/or those with a clinical suspicion of monogenic lupus. Monogenic cause was suspected in 97 patients. Genetic screening was performed using targeted next-generation sequencing on the Ion S5 system in 55 of 97 patients [complement defect gene panel in 28 and type 1 interferonopathy gene Interferon (IFN) panel in 27]. Remaining 42 patients underwent whole exome sequencing (WES).
Results: Among 97 patients who underwent genetic sequencing, 22 (22.68%; 11 boys and 11 girls) were found to carry pathogenic or likely pathogenic variants. Median age of symptom onset in patients with monogenic lupus was 2 years (range: 2 months - 9 years). Consanguinity was reported in 7/22 (31.8%) patients. Variants were detected in *C1QA (n=7), C1QC (n=2), C1R (n=1), C1QB (n=1), C3 (n=2), ACP5 (n=2), TMEM173 (n=1), DNASE2 (n=1), ADAR (n=1), TREX1 (n=1), DNASE1L3 (n=1), PEPD (n=1), SLC7A7 (1)* genes. Functional complement deficiencies and elevated Type 1 interferon signatures were consistent with genetic findings.
Conclusion: This study highlights the genetic heterogeneity of EOSLE in India, with monogenic causes identified in 22.68% of cases, with C1q deficiency caused by genetic defects in *C1QA*, *C1QC*, and C1QB being the most common defect. Overall, C1QA was the most common single gene defect detected in 7/97 (7.2%) patients screened. Our findings support the need to evaluate underlying genetic causes in childhood lupus.
References: Belot A, Rice GI, Omarjee SO, Rouchon Q, Smith EMD, Moreews M, et al. Contribution of rare and predicted pathogenic gene variants to childhood-onset lupus: a large, genetic panel analysis of British and French cohorts. Lancet Rheumatol. 2020 Feb 1;2(2):e99–109.
Batu ED, Koşukcu C, Taşkıran E, Sahin S, Akman S, Sözeri B, et al. Whole Exome Sequencing in Early-onset Systemic Lupus Erythematosus. J Rheumatol. 2018 Dec;45(12):1671–9
Tirosh I, Spielman S, Barel O, Ram R, Stauber T, Paret G, et al. Whole exome sequencing in childhood-onset lupus frequently detects single gene etiologies. Pediatr Rheumatol Online J. 2019 Jul 30;17(1):52.
Disclosure of Interest: None Declared

PReS25-ABS-1276

COMMON TOLL-LIKE RECEPTOR 7 VARIANTS DEFINE DISEASE RISK AND PHENOTYPES IN JUVENILE-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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Introduction: While the pathophysiology of juvenile-onset systemic lupus erythematosus (jSLE) is incompletely understood, genetic variation significantly contributes to increased type 1 interferon (IFN) expression.
Objectives: This study investigated genetic variability of *TLR7* and associations with disease outcomes in 319 jSLE patients enrolled in the UK JSLE Cohort Study.
Methods: Sequence capture enrichment (NimbleGen/Roche), followed by next-generation sequencing (MiSeq2500/Illumina) was performed. Allele frequencies were extracted from Allele Frequency Aggregator, 1000 genomes, and the Genome Aggregation Database. Haplotype analyses and linkage disequilibrium parameters were investigated using SNPstats, and associations with organ domain involvement (pBILAG-2004) were analysed. Functional impacts of *TLR7* variants were studied in HEK293T cells following transfection with reporter plasmids including the *TLR7* promoter and plasmids carrying the *TLR7* cDNA sequence. Transcription factor recruitment was evaluated through chromatin immunoprecipitation (ChIP). Messenger RNA (mRNA) stability was investigated through the transcriptional inhibitor 5,6-Dichloro-1-β-D-ribofuranosylbenzimidazole (DRB).
Results: Three jSLE-associated variants with a minor allele frequency ≥5% and an *in silico* predicted impact on gene function were retrieved: rs2302267/n.-20T>G (promoter); rs179008/c.32A>T/p.Gln11Leu (loss-of-function); and rs3853839/c.*881C>G (3' untranslated region/UTR). Among girls carrying rs3853839 GC/GG, JSLE risk was increased in African/Caribbean girls (OR: 1.8; 95% CI: 1.2-2.9) and reduced in those of European ancestry (OR: 0.5; 95% CI: 0.4-0.7). The SLE-associated rs2302267 minor G allele associated with reduced leukopenia. The non-random rs79008/rs3853839 T-C/TT-CC haplotype associated with increased overall disease activity, and activity in the constitutional and musculoskeletal domains. Two SNPs lacked functional data in the literature: rs2302267/n.-20T>G and rs3853839/c.*881C>G. To study rs2302267, cells were transfected with reporter plasmids and promoter luciferase activity was reduced for the minor G allele when compared to the major T allele. Recruitment of the negative transcriptional regulator transcription factor 7-like 1 (TCF7L1) was higher for the G allele, suggesting reduced *TLR7* expression and a protective effect against leukopenia. Cells transfected with *TLR7* expression plasmids carrying the rs3853839 minor G allele showed increased *TLR7* and IFN expression. As 3'UTRs are involved in fine-tuning gene expression through microRNAs, mRNA stability was investigated and found to be elevated in transcripts carrying the rs3853839 G variant.
Conclusion: Common *TLR7* variants may influence jSLE risk and organ involvement in an ancestry-specific manner, supporting the rationale for genetic risk stratification and future consideration of TLR7-targeted treatments.
Disclosure of Interest: None Declared

PReS25-ABS-1378

COMPARING CHILDHOOD-ONSET AND ADULT-ONSET SJOGREN'S DISEASE: RESULTS OF A NATIONAL MULTICENTRE STUDY

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Introduction: Sjögren's disease (SjD) is an autoimmune disorder affecting exocrine glands. No studies to date have directly compared the childhood-onset SjD (coSjD) with adult-onset SjD (aoSjD), representing a critical knowledge gap in Sjögren's disease research.

Objectives: In our study, we aimed to highlight the differences between coSjD and aoSjD by comparing the clinical features, immunological profiles, activity/damage patterns, and long-term disease outcomes of SjD.

Methods: Data were evaluated for 115 patients diagnosed with coSjD across 22 pediatric rheumatology centers and for 82 patients followed at a single center with aoSjD. The EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) and the Sjögren's Syndrome Damage Index (SSDI) were used to assess activity and damage.

Results: In this nationwide study, 84.3% of childhood-onset patients and 94% of adult-onset patients were female. The mean age at diagnosis was 12.6 years for coSjD and 49.7 years for aoSjD. The fulfillment of the EULAR/ACR criteria at diagnosis was statistically significantly lower among those with coSjD(73.0% vs. 98.7%). Dry eye (60.0% vs. 82.9%) and dry mouth (55.6% vs. 84.1%) were the most common clinical symptoms in both groups; however, they were significantly more prevalent in the adult group. Constitutional symptoms (49.5% vs. 24.3%), lymphadenopathy (46.4% vs. 17.0%), recurrent parotitis (43.4% vs. 8.5%), and Raynaud's phenomenon (15.6% vs. 2.4%) were significantly more common in coSjD, whereas hematologic involvement (15.6% vs. 39%), pulmonary involvement (5.2% vs. 12.1%), and anti-SSA positivity (63.4% vs. 84.1%) were found to be more frequent in aoSjD. Salivary gland biopsy positivity was the most common

diagnostic parameter, with a rate exceeding 90% in both groups. Schirmer test positivity (53.1% vs. 76.1%) was statistically significantly more prevalent in aoSjD. The median ESSDAI score at diagnosis was 8 (5-12) in the childhood-onset group and 3 (2-8.5) in the adult-onset group, with the score being statistically significantly higher in coSjD. The ESSDAI score at the last visit showed similar results, with a median score of 2 (0-5) for both groups. A damage score greater than 0 (36.5% vs. 59.8%) was found to be significantly higher in the adult-onset group at the last visit SSDI.

Conclusion: Childhood-onset Sjögren's disease might exhibit a different clinical course compared to adults. Our study emphasizes the necessity for updated criteria in this age group.

References: 1) Randell RL, Stern SM, Van Mater H, Schanberg LE, Lieberman SM, Basiaga ML. Pediatric rheumatologists' perspectives on diagnosis, treatment, and outcomes of Sjögren disease in children and adolescents. Pediatr Rheumatol Online J 2022; 20(1): 79. 2022/09/06. doi: 10.1186/s12969-022-00740-4.

2) Wright TB. Updates in childhood Sjogren's syndrome. Curr Opin Pediatr 2022; 34(2): 217-22. 2021/12/09. doi: 10.1097/mop.0000000000001093.

3) Ramos-Casals M, Acar-Denizli N, Vissink A, et al. Childhood-onset of primary Sjögren's syndrome: phenotypic characterization at diagnosis of 158 children. Rheumatology (Oxford) 2021; 60(10): 4558-67. 2021/01/26. doi:

10.1093/rheumatology/keab032.
Disclosure of Interest: None Declared

PReS25-ABS-1179

THE CONTRIBUTION OF SALIVARY GLAND ULTRASONOGRAPHY TO THE CLASSIFICATION CRITERIA IN JUVENILE SJÖGREN DISEASE: DIAGNOSTIC VALUE AND PREDICTIVE PERFORMANCE OF A WEIGHTED SCORING MODEL

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Introduction: Juvenile Sjögren's disease (jSjD) is a rare and diagnostically challenging autoimmune condition that lacks pediatric-specific classification criteria.
Objectives: This study evaluated the diagnostic utility of salivary gland ultrasonography (US)—not currently included in the 2016 ACR/EULAR criteria—in jSjD, and assessed its performance within a weighted scoring model (WS) incorporating conventional parameters.
Methods: Seventeen patients diagnosed with jSjD between 2017 and 2024 were retrospectively analyzed. All underwent B-mode parotid US scored using the OMERACT system. Diagnostic parameters included anti-SSA (Ro) positivity, Schirmer test (≤5 mm/5 min), labial salivary gland biopsy with focus score ≥1, and salivary gland US score ≥1. The WS (range 0–8) was calculated as:
WS = (anti-SSA positivity × 3) + (labial salivary gland biopsy positivity × 3) + (Schirmer test positivity × 1) + (parotid gland ultrasound positivity × 1)
ROC analyses evaluated the WS's ability to predict patients exceeding the ACR/EULAR threshold (>4 points), and the predictive value of US alone in identifying patients with ≥2 conventional criteria (Composite Score ≥2). WS and the classic model (excluding US) were compared by AUC and diagnostic metrics.
Results: Among 17 patients (94.1% female, n=16), salivary gland US score ≥1 was present in 64.7% (n=11), Schirmer test was positive in 41.2% (n=7), anti-SSA was positive in 35.3% (n=6), and biopsy was positive in 88.2% (n=15). The median US score was 1.0 (IQR: 0.0–2.0), median biopsy focus score was 2.0 (IQR: 1.0–2.0), and median WS was 4.0 (IQR: 4.0–5.0). The WS yielded an AUC of 0.72 for predicting ACR/EULAR positivity, indicating an acceptable level of discriminative performance. US alone showed strong alignment with classification components (AUC: 0.84 for Composite Score ≥2). ROC comparison revealed similar overall performance between WS and the classic model (AUC: 0.85 vs. 0.87; p = 0.76). However, WS had superior specificity (92% vs. 77%) and PPV (86% vs. 73%), enhancing its diagnostic value in borderline cases.
Conclusion: Although adding US to the classification model did not significantly increase overall AUC, it improved specificity and PPV. Its strong concordance with core criteria, noninvasive nature, and feasibility in pediatric settings support salivary gland US as a promising adjunct to jSjD classification—potentially substituting more impractical tests such as unstimulated salivary flow rate and ocular staining score. However, prospective validation in larger, multicenter pediatric cohorts is essential before its integration into formal classification systems. **Keywords:** Classification criteria, Juvenile Sjögren, salivary gland ultrasonography
Disclosure of Interest: None Declared

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IMPLEMENTING TREAT-TO-TARGET IN CHILDHOOD LUPUS: EARLY OUTCOMES AND LESSONS FROM A UK PAEDIATRIC CENTRE

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Introduction: International experts recommend a Treat-to-Target (T2T) approach to optimise the management of childhood-onset systemic lupus erythematosus (cSLE), with the aim of reducing flares and long-term damage1. T2T is an approach in which treatment is escalated or adjusted until predefined goals, such as childhood lupus low disease activity (cLLDAS), cSLE clinical remission on steroids (cCR) and cSLE clinical remission off steroids (cCR-0), are reached2,3.

Objectives: To implement a T2T approach at a tertiary UK hospital, and assess its feasibility and initial impact on clinical outcomes and treatment, including SLEDAI score, physician global assessment (PGA), and corticosteroid dosing.

Methods: A dedicated T2T clinic was established. Appointments were standardised to collect relevant clinical and laboratory data for target calculation. A preliminary treatment plan was made in clinic and finalised post-clinic, after target review. T2T fidelity was assessed using a devised T2T implementation score based on documentation of: target specified, target calculated, corticosteroid dose recorded, treatment plan aligned with target, and appropriate follow-up (4–6 weeks if target not met; 3 months if achieved).

Results: Between July-2023 and March-2025, 15 cSLE patients attended 74 T2T appointments (median 4 per person, range: 2-9). Eleven (73%) achieved a T2T target (cLLDAS, cCR or cCR-0) during this period. The cSLE patients not achieving or maintaining targets were either non-adherent to treatment or had <6 months' follow-up. Overall, median SLEDAI-2K scores decreased from 5 (IQR 3, 8) at baseline to 4 (IQR 2.5,7) at last visit. When comparing patients based on adherence, non-adherent patients had an increase in SLEDAI-2K score from 7 (IQR 5.5, 9.5) at baseline to 9 (IQR 7.5, 11.5) at last visit. Median PGA scores reduced from 1 (IQR 0.5, 1.5) to 0.75 (IQR 0.375,1), with PGA higher in non-adherent patients, 1.25 (IQR 0.875, 1.625) at baseline to 1 (IQR 0.875, 1.375) at last visit. All patients on corticosteroids at T2T initiation had undergone subsequent dose reductions (mean 83% reduction); 11/15 discontinued corticosteroids entirely by the last visit. Assessment of the T2T implementation score indicated that 89.5% of key T2T components were documented and followed, with delayed follow-up being the most common barrier, affecting 54% of visits.

Conclusion: These findings demonstrate that T2T implementation is feasible in a single tertiary centre with establishment of a bespoke T2T clinic. This has been associated with initial improvements in disease activity and corticosteroid reduction. Non-adherence remains a barrier to target attainment. Further work should expand T2T to diverse settings and explore perspectives of patients, families, and clinicians through qualitative research.

References: 1. Smith EMD, et al. cSLE T2T International Task Force. Towards development of treat to target (T2T) in childhood-onset systemic lupus erythematosus: PReS-endorsed overarching principles and points-to-consider from an international task force. Ann Rheum Dis. 2023. 2. Smith EMD, et al. PReS-endorsed international childhood lupus T2T task force definition of childhood lupus low disease activity state (cLLDAS). Clin Immunol. 2023. 3. Smith EMD, et al. Defining remission in childhood-onset lupus: PReS-endorsed consensus definitions by an international task force. Clin Immunol. 2024.

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PReS25-ABS-1154

MONITORING IL-18 IN PEDIATRIC STILL'S DISEASE: DIAGNOSTIC AND PROGNOSTIC VALUE

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Introduction: Systemic juvenile idiopathic arthritis (sJIA), also known as Still's disease in children, is a rare autoinflammatory disorder of unknown etiology. Interleukin-18 (IL-18) has emerged as a key cytokine implicated in the pathogenesis of Still's disease in both children and adults. Its role in diagnosis and disease monitoring remains an active area of investigation.
Objectives: This study aimed to assess the diagnostic value of IL-18 levels in pediatric Still's disease by comparing them with those observed in other pediatric rheumatic conditions. Moreover, the study evaluated the potential of IL-18 as a biomarker for monitoring disease activity and therapeutic response over time.
Methods: Data were collected from pediatric rheumatology departments at multiple French hospitals including Lyon's Hôpital Femme Mère Enfant, Necker-Enfants Malades, Kremlin-Bicêtre, Valence Hospital, Villefranche Hospital, and Lille Hospital. Patients included in the study had IL-18 measurements performed either at Henri Mondor Hospital (Paris) or the Immunology Laboratory at Lyon Sud, both of which used the same testing protocols. Over 170 patients including 100 patients with Still disease and more than 500 IL-18 measurements were analyzed. Among them, 30 patients had IL-18 levels measured at the time of diagnosis prior to treatment initiation, and longitudinal data were available for 60 patients.
Results: IL-18 levels were significantly higher in patients diagnosed with Still's disease compared to those with other rheumatic conditions. Elevated IL-18 concentrations were particularly associated with active disease states. Patients experiencing macrophage activation syndrome (MAS) exhibited especially high IL-18 levels, which remained elevated even in the absence of acute flares. Longitudinal follow-up revealed that IL-18 levels correlated with disease activity over time, suggesting its potential utility in predicting disease progression and treatment response.
Conclusion: In line with previous findings, this study reinforces the diagnostic relevance of IL-18 in identifying pediatric Still's disease. In addition, persistently high IL-18 levels appear to be associated with severe disease phenotypes, including chronic MAS and pulmonary involvement. These findings support the integration of IL-18 monitoring into routine clinical practice to aid in diagnosis, risk stratification, and longitudinal disease management in pediatric patients with Still's disease.
References: Quartier-dit-Maire P, Belot A, Protocole National de DIagnostic et de Soins. Arthrites Juvéniles Idiopathiques. 2023. Sur LM, Sur G, Investigations of cellular immunity in juvenile idiopathic arthritis. Cent Eur J Immunol. 2019
Fautrel B, Mitrovic S, De Matteis A, Bindoli S, Antón J, Belot A, et al. EULAR/PReS recommendations for the diagnosis and management of Still's disease, comprising systemic juvenile idiopathic arthritis and adult-onset Still's disease. Annals of the Rheumatic Diseases. déc 2024;83(12):1614
Mitrovic S, Fautrel B. New Markers for Adult-Onset Still's Disease. Joint Bone Spine. mai 2018;85(3):285
Disclosure of Interest: None Declared

PReS25-ABS-1222

PROGNOSTIC VALUE OF INTERLEUKIN-18 IN STILL'S DISEASE: ASSOCIATIONS WITH DISEASE ACTIVITY, COURSE, AND MAS DEVELOPMENT

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Introduction: Still's disease (SD) is a systemic inflammatory disorder characterized by nonspecific clinical and laboratory features, which pose diagnostic challenges at onset (e.g. Kawasaki disease, leukemia). Although IL-1 inhibitors (IL-1i) are standard treatment, reliable biomarkers to predict disease activity, clinical course, and complications such as macrophage activation syndrome (MAS) are lacking. Interleukin-18 (IL-18) has been proposed as a potential biomarker, but its predictive value remains unclear.
Objectives: To assess the association between IL-18 levels at disease onset and subsequent disease activity and course. A secondary aim was to evaluate whether IL-18 levels could predict the risk of MAS.
Methods: We retrospectively analyzed 64 pediatric patients with newly diagnosed SD, all treated with IL-1i for at least 12 months. Demographic, clinical and laboratory data, including IL-18 levels, were collected at onset (T0), before treatment initiation and at 3 (T3), 6 (T6) and 12 (T12) months of therapy. Disease activity was defined according to EULAR/PReS 2024 criteria; disease course was classified as monocyclic, polycyclic, or chronic-persistent. Statistical adjustments were made for potential confounders, including MAS and concomitant treatments.
Results: The median IL-18 level at onset was 59.215 pg/ml (IQR 14.261–630.037). MAS was present in 23 (35%) patients at disease onset. Sixty-one patients were treated with anakinra and 3 with canakinumab. IL-18 levels significantly decreased during treatment (median pg/ml: T0 59.215; T3 1.984; T6 1.100; T12 788). However, patients with active disease (AD) had consistently higher IL-18 levels than those in clinical inactive disease (CID) at all time points. Patients with AD at 12 months had significantly higher IL-18 levels at baseline compared to those who achieved CID. IL-18 levels >45.000 pg/ml at onset predicted AD at 12 months with an area under the curve (AUC) of 78% (Se 91%, Sp 53%, p=0,001). Regarding disease course, 54% patients had a monocyclic, 26% a polycyclic, and 20% a chronic-persistent course. After treatment initiation, IL-18 levels significantly decreased in mono-/poly-cyclic course patients, but remained stable over-time in those with a chronic-persistent course. IL-18 levels >45.000 pg/ml at disease onset predicted a chronic-persistent course (AUC 72%, p=0,01, Se 91% Sp 56%). Furthermore, IL-18 levels >15,000 pg/ml at three months (T3) more accurately predicted a persistent course, yielding an AUC of 91% (p<0.0001; se 90%, sp89%). Additionally, elevated IL-18 levels at baseline were strongly associated with MAS development (AUC 81%, p=0.004, Se 100%, Sp 77%).
Conclusion: Baseline IL-18 levels are predictive of disease activity, clinical course, and MAS risk in Still's disease. IL-18 may serve as a valuable biomarker, offering a valuable tool for tailoring treatment strategies and improving patient outcomes.
References: 1. Fautrel B et al. EULAR/PReS recommendations for the diagnosis and management of Still's disease, comprising systemic juvenile idiopathic arthritis and adult-onset Still's disease. *Ann Rheum Dis*. 2024
2. Yasin S et al. IL-18 as a biomarker linking systemic juvenile idiopathic arthritis and macrophage activation syndrome. *Rheumatol*. 2020.
3. Mizuta M et al. Clinical significance of interleukin-18 for the diagnosis and prediction of disease course in systemic juvenile idiopathic arthritis. *Rheumatol*. 2021.
Disclosure of Interest: None Declared

PReS25-ABS-1529

DIFFERENT PERSPECTIVES BETWEEN PHYSICIANS AND PATIENTS ON TREATMENT PRIORITIES AND CHALLENGES IN STILL'S DISEASE

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Introduction: Despite therapeutic advances, major concerns and disparities persist in the care of Still's Disease (SD). Capturing both patient/caregiver and physician perspectives is essential to optimize patient-centered care.
Objectives: This real-life study aims to assess and compare the perspective of physicians and patients/caregivers regarding treatment goals, challenges, and unmet needs related to the treatment of SD.
Methods: As part of the METAPHOR project, a PReS/PRINTO initiative to optimize SD and Macrophage Activation Syndrome (MAS) management, 2 surveys, 1 addressed to physicians and 1 to patients/caregivers, were developed by a core team, involving physicians and patients representatives. The physician survey was forwarded through the PReS/PRINTO network, while the patient survey via the Systemic JIA Foundation to all their members. Responses were analyzed using chi-square tests to assess group differences.
Results: 197 physicians and 139 patients/caregivers participated. Most patient respondents were parents or legal guardians (94%), primarily from the United States (64%) and Europe (19%). Physicians were mainly pediatric rheumatologists (90%), from 56 countries worldwide. Regarding treatment goals, both groups prioritized complete symptom control (84% vs 79%, p=0.28) and achieving a quality of life similar to peers (63% vs 73%, p=0.44). However, patients considered pain control a key objective more often than physicians (43% vs 13%, p< 0.001), whereas physicians placed greater emphasis on glucocorticoid reduction (79% vs 54%, p< 0.001). In terms of glucocorticoid-related concerns, mood changes were predominantly reported by patients (65% vs 14%, p<0.001), whereas physicians were more concerned about osteoporosis (66% vs 32%, p< 0.001), glucose intolerance (52% vs 27%, p< 0.001), and hypertension (51% vs 37%, p=0.02). Both groups highlighted growth delay and infection risk as shared concerns. Regarding fears at treatment initiation, both groups were concerned about treatment failure (82% patients vs 66% physicians, p=0.001) and adverse events (77% vs 72%, p=0.27). However, physicians were more worried about treatment duration (57% vs 21%, p< 0.001), while patients emphasized infection risk (52% vs 27%, p< 0.001) and lack of clear information about the treatment (34% vs 23%, p=0.03). As for future challenges, both groups stressed the need to reduce the burden of glucocorticoid use (68% patients vs 59% physicians, p=0.10). Physicians more frequently cited the inability to prevent MAS (52% vs 40%, p=0.03), while patients highlighted limited physician expertise (57% vs 15%, p< 0.001) and lack of access to psychological support (33% vs 10%, p< 0.001) as major unmet needs.
Conclusion: Besides shared perspectives, patients and physicians show relevant differences in prioritizing treatment outcomes and concerns in SD. Including patient priorities early in the disease course is essential to advancing truly patient-centered care.
Disclosure of Interest: G. B. Beretta: None Declared, L. Pereira: None Declared, G. Rogani: None Declared, F. Baldo: None Declared, C. Bracaglia: None Declared, D. Foell: None Declared, M. Gattorno Grant / Research Support with: Novartis, Consultant with: SOBI, Novartis, Speaker Bureau with: Fresenius-Kabi, SOBI, Novartis, M. Jelusic: None Declared, S. Vastert Grant / Research Support with: SOBI, Consultant with: SOBI, Novartis, Speaker Bureau with: SOBI, Novartis, R. Sinha: None Declared, F. Minoia: None Declared

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PREDICTORS OF OUTCOME IN MACROPHAGE ACTIVATION SYNDROME: A RETROSPECTIVE STUDY FROM A TERTIARY CARE HOSPITAL IN INDIA

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Introduction: Macrophage Activation Syndrome (MAS) is a severe, life-threatening hyperinflammatory condition associated with various rheumatic diseases. Identifying predictors of adverse outcomes is crucial for early risk stratification and timely intervention.
Objectives: This study aims to determine the clinical and laboratory factors associated with mortality in children diagnosed with MAS at a tertiary care hospital in India.
Methods: This retrospective study included children diagnosed with MAS based on PRINTO 2016 criteria, admitted between 2018 and 2024. Patient data were extracted from medical records. The primary outcome was survival at discharge. Predictor variables included demographics like age, gender, underlying illness, duration of symptoms, organ involvement (CNS, myocarditis, ARDS, AKI, shock), laboratory parameters (hemogram, liver enzymes, ferritin, fibrinogen, triglycerides), treatment modality (IVIG/methylprednisolone pulse) and time to initiation. Univariate and multivariate analyses were performed to compare the outcome and predictor variables. Firth's penalized logistic regression was used for multivariate analysis to address small sample size, using the variables gender, duration of illness, clinical foci of infection, ARDS, CNS involvement, platelet count at admission, AST and ALT peak. ROC curve analysis assessed the performance of regression model.
Results: A total of 41 children with 46 episodes of MAS having a median age (IQR) of 11.5 (7,13) years at presentation were included in the study. The most common underlying conditions were systemic-onset JIA (56.1%) and SLE (36.5%). Mortality was 28% in our cohort (n=13). Forty-seven percent of our cohort had a clinical focus of infection simultaneously. Univariate analysis showed presence of shock, AKI, ARDS, myocarditis, longer duration of symptoms and lower levels of AST and ALT enzyme levels were associated with increased risk of mortality with p- value <0.05. Multivariate analysis identified acute respiratory distress syndrome (ARDS) as the strongest predictor of mortality (OR = 3.375, 95% CI : 1.103, 10.33, p = 0.03) while other laboratory markers failed to show any association with mortality. The model couldn't fit other multi organ involvement as they were perfect predictors of mortality. Firth's logistic regression improved model stability, and ROC analysis (AUC = 0.9059) demonstrated excellent predictive capability.
Conclusion: MAS remains a critical pediatric emergency with a high mortality risk. Early recognition and aggressive treatment remains the key for survival. Presence of ARDS and multi organ failure were associated with increased odds of mortality. Early identification of these might improve the outcome. No reliable laboratory markers for early detection of an impending stormy clinical course could be identified from our cohort. Further prospective studies are warranted to validate these findings and identification of potential biomarkers to optimize risk stratification in pediatric MAS.
References: 1. Ravelli A, Minoia F, Davì S, Horne A, Bovis F, Pistorio A, et al. 2016 Classification Criteria for Macrophage Activation Syndrome Complicating Systemic Juvenile Idiopathic Arthritis: A European League Against Rheumatism/American College of Rheumatology/Pediatric Rheumatology International Trials Organisation Collaborative Initiative. Ann Rheum Dis. 2016 Mar;75(3):481–9.
Disclosure of Interest: None Declared

PReS25-ABS-1630

DIVERGING PATHS WITHIN JUVENILE SPONDYLOARTHROPATHIES: AXIAL INVOLVEMENT IN ENTHESITIS-RELATED ARTHRITIS AND JUVENILE PSORIATIC ARTHRITIS IN A LARGE NATIONAL COHORT STUDY

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Introduction: Enthesitis-related arthritis (ERA) and juvenile psoriatic arthritis (JPsA) are considered within the broader

context of juvenile spondyloarthropathies (JSpA). However, emerging evidence highlights distinct differences in pathophysiology, clinical presentation, and treatment response, particularly in relation to axial disease manifestations.
Objectives: This study aimed to evaluate and compare axial involvement in patients with ERA and JPsA, identifying shared features, overlapping characteristics, and key differences in disease expression and treatment response.
Methods: We utilized data from PERA research group, a large, real-world national cohort. Eligible patients were those with axial involvement of either JPsA or ERA who had at least 6 months of follow-up and imaging to assess axial disease. Data collected included age, sex, disease duration, joint and skin findings, laboratory parameters, HLA-B27 status, and disease activity scores.
Results: Overall, 314 ERA (65%, male) and 58 JPsA (72%, female) patients were included. The median age at disease onset was 11.4 years (IQR:8.7–13.2) in the JPsA group and 12.1 years (IQR:9.5–14.3) in the ERA group. In terms of clinical features, peripheral arthritis was universal in both groups at onset, but dactylitis was more commonly observed in JPsA (48.7% vs. 10.6%, $p < 0.001$), while enthesitis was significantly more prevalent in ERA (85.1% vs. 28.2%, $p < 0.001$). Uveitis occurred in 10.3% of ERA and none of JPsA patients, predominantly anterior and non-granulomatous. HLA-B27 positivity was significantly more frequent in ERA (72.4%) compared to JPsA (28.6%, $p < 0.01$). Axial involvement as defined by imaging (MRI evidence of sacroiliitis and/or spinal inflammation) was present in 61.7% of ERA patients and 35.9% of JPsA patients ($p = 0.03$). The pattern of axial disease also differed: symmetric sacroiliitis was more frequent in JPsA, whereas ERA patients more commonly exhibited unilateral or asymmetric sacroiliac inflammation. Disease activity score (JSpADA) was higher in ERA patients with axial disease compared to their JPsA counterparts, although treatment response at 12 months was comparable between groups following anti-TNF therapy initiation. ERA patients demonstrated more frequent bone marrow edema of the sacroiliac joints and spine, while JPsA patients occasionally showed coexisting joint arthritis and diffuse enthesopathy. Ultrasound confirmed active enthesitis in 18.6% of ERA patients and 4% of JPsA patients with axial disease.
Conclusion: The higher prevalence of HLA-B27 and enthesitis in ERA supports its closer resemblance to adult-onset axial spondyloarthritis. In contrast, the occurrence of axial disease in JPsA patients-often HLA-B27 negative and more frequently female- suggests that axial involvement in JPsA may represent a distinct clinical entity, potentially reflecting a psoriatic spondyloarthritis phenotype.
References: 1. Srinivasalu H, Sikora KA, Colbert RA. Recent Updates in Juvenile Spondyloarthritis. Rheum Dis Clin North Am. 2021 Nov;47(4):565-583. 2. Demir S, Ergen FB, Taydaş O, Sağ E, Bilginer Y, Aydıngöz Ü, Özen S. Spinal involvement in juvenile idiopathic arthritis: what do we miss without imaging? Rheumatol Int. 2022 Mar;42(3):519-527.
Disclosure of Interest: None Declared

PReS25-ABS-1318

JUVENILE ONSET SPONDYLOARTHRITIS IS ASSOCIATED WITH PERIPHERAL, SKIN INVOLVEMENT AND INCREASED FREQUENCY OF RARE VARIANTS IN SYSTEMIC AUTO-INFLAMMATORY DISEASES GENES

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Introduction: Spondyloarthritis (SpA) is a heterogeneous chronic inflammatory disorder, of unknown origin, frequently beginning in late childhood. Compared to adult-onset SpA (ao-SpA), juvenile-onset SpA (jo-SpA) is associated with increased peripheral involvement and less strength of HLA-B27 association, suggesting the potential involvement of other genetic risk factors.
Objectives: We aimed to compare jo-SpA *vs.* ao-SpA at the phenotypic and immunogenetic level in a cohort of SpA patients.

Methods: We reviewed our retrospective cohort of unrelated adult SpA patients and compared the disease phenotype of those with jo-SpA (before 16yo) *vs*. ao-SpA (after 16yo), adjusting for disease duration. In a subset of this cohort, we calculated the polygenic risk score (PRS) for axial SpA in patients of European descent, using an algorithm kindly provided by MA Brown. Additionally, the occurrence of rare variants (minor allele frequency <0.01 in European population) in genes associated with systemic auto-inflammatory diseases (SAID, *Infevers* panel) was compared between jo- and ao-SpA patients, using whole genome sequencing data from 351 familial SpA cases belonging to 68 families.

Results: Among 1,211 unrelated adults with SpA, disease began before 16yo in 160 (13%) and after 16yo in 1051 (87%) patients. As expected, disease duration was longer in jo-SpA group (25.1±15.1 *vs.* 17.7±12.1 years, $p<0.0001$). The jo-SpA patients' phenotype was characterized by an increased frequency of peripheral arthritis (n=77 [48%] *vs.* 345 [33%], $p=0.0002$) and psoriasis (n=58 [36%] *vs.* 298 [28%], $p=0.04$). HLA-B27 prevalence (n=117 [73%] *vs.* 744 [71%], $p=0.5$) and the SpA PRS, a measure of common risk variants (0.4±0.2 [n=18] *vs.* 0.3±0.3 [n=115], $p=0.9$), were comparable between both groups. However, SpA family history was more common in jo-SpA patients (n=72/158 [46%] *vs.* 380/1022 [37%], *p=0.04), suggesting the potential role of rare variants in earlier disease onset. Given that SpA is at least partly considered* related to innate immune response dysregulation, we examined the presence of rare variants in SAID-related genes. We found a higher frequency of carriers of at least one such variants in jo- compared to ao-SpA patients (n=31/68 [46%] *vs.* 64/283 [23%], $p=0.001$). These variants were found in genes involved in NFκB (*CARD14*, *RELA*, *SH3BP2*) and IL-1 (*MVK*, *MEFV*) pathways. Overall, carrying such variants was significantly associated with a twice-fold increased frequency of psoriasis (29% *vs.* 16% $p=0.03$).

Conclusion: Juvenile onset of SpA is associated with more frequent peripheral involvement and psoriasis. It is also characterized by a higher frequency of familial history of SpA, that might be related to increased frequency of rare variants, especially involved in NFκB and/or IL-1 pathways. These results need external and functional validation, and might offer a better understanding of SpA pathogeny and heterogeneity.

References: *Comparison of juvenile-onset versus adult-onset ankylosing spondylitis*. DOI:10.1136/ard.2008.092304 ; *Polygenic Risk Scores have high diagnostic capacity in ankylosing spondylitis.* DOI:10.1136/annrheumdis-2020-219446 ; *Ankylosing spondylitis: an autoimmune or autoinflammatory disease?* DOI:10.1038/s41584-021-00625-y

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A COMPARATIVE ANALYSIS OF PEDIATRIC-ONSET AND ADULT-ONSET SPONDYLOARTHROPATHY

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Introduction: The term spondyloarthropathy (SpA) encompasses a group of heterogeneous HLA-B27-related inflammatory diseases characterized by the involvement of axial skeletal and peripheral joints. In addition to joint involvement, enthesitis, nail changes, dactylitis, psoriasis, uveitis, and inflammatory bowel diseases may also be SpA-related findings (1). SpA can occur in a wide age range, but the highest incidence is in late adolescence and early adulthood (2).

Objectives: Although they share similar pathologic mechanisms and clinical features, adult-onset and juvenile-onset spondyloarthropathies differ significantly in terms of associated features, patterns of involvement, presenting symptoms, and treatment modalities. We aimed to reveal the differences between these two onset stages and identify the distinguishing features.

Methods: The medical records of 163 pediatric and 165 adult patients from our clinics were retrospectively reviewed.

Data on demographic characteristics, medical history, presenting symptoms, family history, test results, joint involvement during follow-up, and treatment regimens were collected and analyzed.

Results: The study included 163 pediatric (67.5% male) and 165 adult (59.4% male) patients (p=0.128). The median age at diagnosis was 13(10-15) years in children and 32(25-40) years in adults. Follow-up was significantly longer in adult patients than in pediatric patients (37 and 49 months, respectively)(p=0.000).

Presentation with peripheral arthritis was 57.7% (94/163) in children versus 17% (28/165) in adults (p=0.000). The rate of sacroiliitis at presentation was 98.8% (163/165) in adults compared to 61.3% (100/163) in children (p=0.000).

Acute phase reactant positivity was similar at initial evaluation. HLA-B27 positivity was significantly higher in adults than in pediatric patients (58.7% vs. 46.3% p=0.036).

AAA was more common in pediatric patients (12.9% vs. 1.2% p=0.000), while uveitis was more common in adults (18.2% vs. 3.6% p=0.000). The most common musculoskeletal system involvements in pediatric patients were sacroiliitis (69.3%), enthesitis (42.3%), and ankle involvement (36.8%). In adults, sacroiliitis (98.8%) was most common, followed by hip (44.2%) and enthesitis (28.5%).

In terms of initial treatment, systemic steroid (p=0.000) and cDMARD (p=0.000) use were significantly more frequent in pediatric patients. In adults, the use of NSAIDs as initial treatment was more frequent (p=0.000). bDMARDs were added to the treatment earlier in pediatric patients (p=0.000).

Conclusion: Children presented more frequently with peripheral arthritis and enthesitis, whereas adults had predominantly axial involvement. While HLA-B27 positivity was higher in adults, AAA was significantly more common in pediatric patients. However, uveitis was more common in adults. Treatment options differed significantly between groups, with pediatric patients more commonly receiving steroids, cDMARDs, and bDMARDs started earlier in the disease.

References:

1.Yıldız M, Haşlak F, Adroviç A, Şahin S, Barut K, Kasapçopur Ö. Juvenile spondyloartropathies. Eur J Rheumatol. 2021;9(1):42-49.

2.Colbert RA. Classification of juvenile spondyloarthritis: Enthesitis-related arthritis and beyond. Nat Rev Rheumatol. 2010;6(8):477-85.

Disclosure of Interest: None Declared

PReS25-ABS-1361

PREDICTORS OF RENAL INVOLVEMENT AND PERSISTENT NEPHRITIS IN PEDIATRIC IGA VASCULITIS: A MULTICENTER COHORT

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Introduction: Renal involvement occurs in about one-third of pediatric patients with IgA vasculitis (IgAV), even so, factors associated to the development and persistence of nephritis (IgAVN) remain unclear, especially in ethnically diverse populations.
Objectives: To determine associated factors with IgAVN and persistent IgAVN in a large multicenter cohort study in a mixed-ethnic country in Latin-America.
Methods: A multicenter study in four academic referral centers of Pediatric Rheumatology in Brazil assessed 687 pediatric patients who met the EULAR/PRINTO/PRES classification criteria for pediatric IgAV1. Demographic, clinical, laboratory and treatment data were retrospectively collected from medical records. Clinical and laboratory data at presentation as well as recurrent and persistent symptoms were compared between IgAVN and non-IgAVN patients. Those with IgAVN were further categorized into self-limited (≤3 months) or persistent (>3 months) nephritis. Ethics approval was obtained from all centers.
Results: Of the 687 patients, 253 (36.8%) developed nephritis. Among them, 17 (6.7%) had nephrotic syndrome, 109 (43%) had persistent nephritis and 46 (18.0%) underwent renal biopsy. Regarding therapy, 177 patients (70%) received steroids, 27% antiproteinurics, 11% azathioprine, 2% mycophenolate, 1% cyclosporine, and 0.4% IV cyclophosphamide. Only one patient underwent renal replacement therapy. Patients with IgAVN were older (median 76 vs 68 months; p=0.004) and more frequently presented with persistent purpura (14% vs 6%; p=0.001), recurrent purpura (28% vs 20%; p=0.02), hypertension (12% vs 4%; p=0.001), and abdominal pain (69% vs 56%; p=0.001). Persistent (6% vs 1%; p=0.01), recurrent (68% vs 12%; p=0.001), and moderate/severe abdominal pain (57% vs 42%; p=0.004) were also more common in these patients. Orchitis (22% vs 11%; p=0.01) and painful subcutaneous edema (36% vs 30%; p=0.05) were more frequent in IgAVN patients, whereas arthritis was more common in non IgAVN patients (78% vs 84%; p=0.03). Laboratory findings were mostly similar, except for elevated CRP, more frequent in IgAVN patients (61% vs 40%; p=0.001).
Patients with persistent nephritis were older at diagnosis (median 78 vs 71 months; p=0.02), and more frequently presented proteinuria and nephrotic syndrome compared to those with self-limiting nephritis (77% vs 45%, p=0.01 and 19% vs 2%, p=0.01, respectively). Interestingly, previous tonsillitis at IgAV diagnosis was more commonly detected in patients with self-limited nephritis (63% vs 33%, p=0.02). No laboratory markers were discriminative between the two groups.
Conclusion: In this large multicenter cohort in a mixed-ethnic country in Latin American, older age as well other clinical features were associated with nephritis and persistence of nephritis in pediatric IgAV. These findings may aid in the earlier identification of patients at high risk for renal involvement and enable more personalized management strategies.

References: 1. Ozen S, Pistorio A, Iusan SM et al. EULAR/PRINTO/PRES criteria for Henoch–Schönlein purpura, childhood polyarteritis nodosa, childhood Wegener granulomatosis and childhood Takayasu's arteritis: Ankara 2008. Part II: final classification criteria. Ann Rheum Dis 2010;69: 798–806.
Disclosure of Interest: None Declared

PReS25-ABS-1687

CLINICAL SPECTRUM AND OUTCOMES IN PEDIATRIC AND ADULT IGA VASCULITIS

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Introduction: IgA vasculitis (IgAV), formerly known as Henoch-Schönlein purpura (HSP), is a type of small vessel vasculitis characterized by purpura, abdominal pain, arthritis, and renal involvement, predominantly seen in childhood. In contrast, it can rarely manifest in adults and demonstrate a more severe form especially in terms of renal involvement.
Objectives: The aim of this study is to analyze the differences in clinical and pathological manifestations, treatment patterns and response between pediatric and adult patients with IgAV, aiming to determine whether pediatric patients present differently from adult patients.
Methods: This retrospective study analyzed patients diagnosed with IgA vasculitis (IgAV) who presented to the pediatric and adult rheumatology clinics at Eskişehir Osmangazi University Hospital. Patients fulfilling the 1990 ACR and the Ankara 2008 EULAR/PRINTO/PRES classification criteria for Henoch-Schönlein purpura were included in this study. The cohort was divided into two groups based on the age of disease onset: childhood-onset (<18 years) and adult-onset (>18 years). Comparative analyses were conducted to evaluate demographic, clinical, laboratory, and histopathological features among the two groups.
Results: A total of 142 patients with childhood-onset IgAV (cIgAV) and 69 with adult-onset IgAV (aIgAV) were included in the study. The female-to-male ratio was 0.56 in the cIgAV group and 0.63 in the aIgAV group. The mean follow-up duration was significantly longer in adults compared to children (51 ± 68 vs. 11 ± 13 months; $p < 0.001$). While seasonal distribution was similar between groups, predisposing factors—particularly drug exposure and surgical history—were more frequently observed in adults (63.8% vs. 43.7%; $p = 0.006$). The prevalence of skin involvement, arthritis/arthralgia, and gastrointestinal symptoms (e.g., abdominal pain, hematochezia) was comparable between the two cohorts. However, renal involvement was significantly more common and severe in the adult group (39.1% vs. 21.1%; $p = 0.006$), with markedly higher rates of hematuria ($p < 0.001$), proteinuria ($p = 0.006$), acute kidney injury ($p < 0.001$), and acute nephritic syndrome ($p = 0.003$). Although renal and skin biopsies were more frequently performed in adults ($p = 0.002$ and $p < 0.001$, respectively), no statistically significant differences were observed in histopathological grading according to the ISKDC classification ($p = 0.097$). Laboratory findings also revealed a more unfavorable inflammatory and renal profile in the adult group, with significantly higher ESR ($p = 0.043$), serum creatinine ($p < 0.001$), and lower albumin levels ($p < 0.001$). CRP levels were elevated in adults but did not reach statistical significance ($p = 0.454$). Treatment patterns differed significantly between age groups. NSAID use was more common in pediatric patients ($p < 0.001$), whereas the need for corticosteroids and other immunosuppressive agents—such as colchicine, azathioprine, cyclophosphamide, and ACE inhibitors—was significantly greater in adults. Despite similar relapse rates, chronic kidney disease (13.2% vs. 0%) and mortality (7.4% vs. 0%) were observed exclusively in the adult cohort, both reaching statistical significance.

Conclusion: Our findings demonstrate that adult-onset IgA vasculitis presents with a more severe clinical course compared to childhood-onset cases, particularly in terms of renal involvement and treatment burden.
Disclosure of Interest: None Declared

PReS25-ABS-1498

EVALUATING NIH, ITAS, AND CARDS SCORES IN TAKAYASU ARTERITIS: CLINICAL AND RADIOLOGIC PERSPECTIVES

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Introduction: Takayasu arteritis (TA) is a chronic, granulomatous large-vessel vasculitis that primarily involves the aorta and its major branches. Clinical remission often does not align with radiological progression, posing a challenge for disease monitoring. This study aimed to compare the NIH, ITAS, and CARDS scoring systems in the evaluation of disease activity and vascular damage in TA.
Objectives: Takayasu arteritis (TA) is a rare, chronic large-vessel vasculitis that primarily affects the aorta and its major branches. Clinical remission and radiological progression often do not align, making disease monitoring particularly challenging. This study aimed to compare three scoring systems -NIH activity score, ITAS, and CARDS- in assessing disease activity, vascular damage, and distribution, using 100 observation timepoints from pediatric TA patients
Methods: This retrospective study included 100 clinical and radiological evaluations from TA patients followed in a single centre. Each observation was assessed for systemic symptoms, vascular involvement and laboratory markers. Vascular severity, extent and progression were assessed by clinicians and radiologists. Statistical analyses included Spearman correlation, logistic regression and ROC analysis.
Results: CARDS scores were significantly higher than NIH scores in 89% of observations ($p<0.001$) and better reflected vascular severity, extent, and progression. Logistic regression identified CARDS as a significant predictor of advanced vascular involvement and widespread disease, while NIH and ITAS scores did not demonstrate predictive value. NIH scores were significantly higher than vascular severity in only 10 cases ($p<0.001$). CARDS was also significantly associated with vascular worsening ($p<0.001$), whereas clinical scores were not. Correlation analysis showed weak negative correlations between CARDS and both ESR ($r = -0.30$, $p = 0.005$) and CRP ($r = -0.254$, $p = 0.017$). No significant correlations were found for NIH or ITAS with laboratory markers. Conversely, fatigue exhibited a paradoxical association with lower NIH and CARDS scores, thereby suggesting a dissociation between symptoms and objective findings.
Conclusion: This study highlights the limitations of symptom-based clinical scores in capturing subclinical vascular progression and chronic damage in TA. CARDS outperformed NIH and ITAS scores in predicting vascular severity, extent, and disease course, making it a superior tool for long-term disease monitoring. While NIH and ITAS remain useful in identifying inflammatory activity, CARDS provides a more comprehensive picture by incorporating chronic vascular damage. The integration of radiological scoring into routine clinical practice has the potential to enhance the development of personalised treatment strategies and to improve long-term outcomes for patients with TA.
Disclosure of Interest: None Declared

PReS25-ABS-1509

FACTORS ASSOCIATED WITH THE NEED FOR SURGICAL INTERVENTION IN PEDIATRIC PATIENTS WITH TAKAYASU ARTERITIS

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Introduction: Takayasu arteritis (TA) is a rare large-vessel vasculitis that may require surgical intervention in cases of critical vascular stenosis or aneurysm formation. However, surgery carries a high risk of complications, particularly during active inflammation. Identifying factors associated with the need for surgical intervention in pediatric TA may enhance understanding of the mechanisms underlying critical arterial changes and early clinical presentations.
Objectives: To identify clinical, laboratory, and imaging characteristics associated with the need for surgical intervention in pediatric patients with TA.
Methods: A retrospective case-control study included 47 children diagnosed with TA according to EULAR/PRINTO/PRES 2010 criteria. Twelve patients who underwent surgical treatment (group 1) were compared to 35 controls without surgery (group2). Demographic, clinical, laboratory, and imaging data were analyzed. Groups were matched by gender, age at onset, disease activity (ITAS.A score), and follow-up duration. Statistical analysis was performed using StatTech v.4.8.3.
Results: Patients requiring surgical intervention had a significantly longer disease duration before diagnosis (median: 22.5 months [IQR: 12.75–27], $p = 0.004$), a higher number of affected vessels at diagnosis (median: 6 [IQR: 4.75–7.25], $p = 0.048$), as well as elevated systolic blood pressure (mean: 161.42 mmHg [SD ±25.41], $p < 0.001$) and diastolic blood pressure (mean: 104.67 mmHg [SD ±16.37], $p < 0.001$). Fever was less frequently reported in Group 1 compared to Group 2 (33.3% vs. 80.0%, $p = 0.009$). In contrast, headache (83.3% vs. 45.7%, $p = 0.042$) and arterial hypertension (91.7% vs. 11.4%, $p < 0.001$) were significantly more common in patients undergoing surgical intervention. Involvement of the descending thoracic aorta (66.7% vs. 22.9%, $p = 0.012$), abdominal aorta (83.3% vs. 42.9%, $p = 0.020$), and renal arteries (66.0% vs. 2.9%, $p < 0.001$) was also significantly more frequent in Group 1. A total of 17 surgical procedures were performed in 12 patients, including balloon angioplasty (n = 2), bypass grafting (n = 4), prosthetic vessel replacement (n = 7), autologous vessel reconstruction (n = 3), and renal artery stenting (n = 1). Early postoperative complications occurred in 4 patients: occlusion of the operated segment in 3 cases and neck phlegmon in 1 case. One late complication — rupture of an anastomotic aneurysm — resulted in a fatal outcome.
Conclusion: In our cohort, elevated blood pressure, headache, delayed diagnosis, and a greater number of affected vessels, including renal arteries, descending and abdominal aorta were significantly more common in pediatric TA with the need for surgical intervention. The lack of typical symptoms may contribute to diagnostic delay and progression to severe vascular damage. Further research is needed to identify early diagnostic markers and optimal management strategies in pediatric TA patients.
Disclosure of Interest: None Declared

PReS25-ABS-1212

TEAR PROTEOMIC ANALYSIS IN UVEITIS ASSOCIATED WITH BEHÇET'S DISEASE: PRELIMINARY RESULTS

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Introduction: Behçet's disease (BD) is a multisystem inflammatory disorder with an incompletely understood pathogenesis. Ocular involvement occurs in 25–75% of patients and, if left untreated, may lead to blindness. The most common ocular manifestation is uveitis, typically presenting as bilateral, recurrent, and non-granulomatous panuveitis. In 10-year retrospective records of patients with Behçet's uveitis, approximately one-third had severe visual impairment at onset, with notable delays in diagnosis. Early and appropriate initiation of immunomodulatory

treatment is essential. If uveitis development can be predicted, treatment may be initiated earlier to prevent complications. However, no reliable biomarker currently exists to identify patients at risk.

Objectives: To identify potential protein biomarkers predictive of uveitis risk by analyzing proteomic alterations in tear samples of Behçet's patients with and without uveitis.

Methods: Fourteen Behçet's patients (7 with uveitis, 7 without), followed in rheumatology clinics, were included. Tear samples were collected using Schirmer's test paper and stored at –80°C. Tear proteins were extracted and separated using Bradford and SDS-PAGE methods, followed by comparative analysis. Differentially expressed proteins were excised from gels and analyzed via LC-MS/MS. Bioinformatic analysis was conducted using the STRING database.

Results: Proteomic analysis revealed 61 proteins with differential expression between the groups: 36 were upregulated and 25 downregulated in uveitis samples. Among the upregulated proteins, mucin-1, guanine nucleotide-binding protein, histone H1, and inter-alpha-trypsin inhibitor heavy chain showed the highest increases (up to 1000-fold). Other upregulated proteins exhibited 2–6.4-fold increases. Among the downregulated proteins, ganglioside GM2 activator, immunoglobulin lambda, and V-type proton ATPase subunit G1 demonstrated >1000-fold decreases, while the remainder had approximately 4-fold decreases. Bioinformatic analysis indicated that these proteins are mainly involved in peptidase regulation, endopeptidase inhibition, enzyme inhibition, and signaling pathways.

Conclusion: Although it remains uncertain whether tear protein expression changes reflect disease pathogenesis or chronic inflammation, the identification of tear-based biomarkers may provide insights into uveitis development in Behçet's disease. These findings may support earlier diagnosis and contribute to the development of targeted therapies.

References: 1.Ksiaa, I., Abroug, N., Kechida, M., Zina, S., Jelliti, B., Khochtali, S., Attia, S., & Khairallah, M. (2019). Eye and Behçet's disease. *Journal francais d'ophtalmologie*, *42*(4), e133–e146.

2.Zhong, Z., Su, G., & Yang, P. (2023). Risk factors, clinical features and treatment of Behçet's disease uveitis. *Progress in retinal and eye research*, *97*, 101216. https://doi.org/10.1016/j.preteyeres.2023.101216

Disclosure of Interest: None Declared

ePoster Short Communications -13: Bone diseases and Transitional Care

PReS25-ABS-1587

TOTAL VOLUME OF HETEROTOPIC OSSIFICATIONS UNDERLIES FUNCTIONAL IMPAIRMENT IN FIBRODYSPLASIA OSSIFICANS PROGRESSIVA

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Introduction: Fibrodysplasia ossificans progressiva (FOP) is an extremely rare genetic disorder which caused by mutation in the ACVR1 gene characterized by progressive heterotopic ossification (HO) and severe mobility restrictions. Low-dose whole body computed tomography (WBCT) is the most preferable option of observation the HO development. It seems that HO volume may be correlated with age and a cumulative analogue joint involvement scale (CAJIS).
Objectives: To evaluate HO volume and analyze correlations with age of pts and functional status according to CAJIS.
Methods: In single-center prospective study 32 pts with FOP were underwent WBCT without contrast in a 128-slice CT scanner. HO volume was determined by segmentation of each axial slice using semi-automatic algorithms in AW Server 3.2 with manual contouring for optimization. HO volume was calculated separately for each body region and then summarized. The CAJIS was used for functional status assessment.
Results: From July 2022 to March 2025 the WBCT was performed in 32 pts (15 female/17 male) with a verified FOP. 31/97% pts have «typical» c.617G>A (p.Arg206His) and 1 pt have ultra-rare (p.Gly356Asp) heterozygous missense substitution in the ACVR1 gene. All pts have congenital malformed great toes as a classic phenotypical FOP features. In 18 pts WBCT was done twice (9 female/9 male), in 4 pts 3 times (2 female/2 male), in 1 male pt – 4 times. HO volume was calculated in 23 pts (repeated in 13). WBCT was repeated after 1-year period. At the moment of first performed WBCT the median age of pts was 10 [interquartile range (IQR) 7;16] years, the median CAJIS was 7 [IQR 5;11], the median HO volume (n=23) was 89.7 [IQR 9.2;297.1]. We detected significant correlation between HO volume and CAJIS (r=0.554, p=0.006) and between age and CAJIS (r=0.554, p=00009). At the moment of second examination with WBCT the median age of pts was 11 [IQR 8;15] years, the median CAJIS was 7,5 [IQR 4;11], the median HO volume (n=13) was 89,7 [IQR 49,3;352,3]. We detected significant correlation between HO volume and CAJIS (r=0.741,p=0.003) and between age and CAJIS (r=0.656,p=0.003). Pts were compared into 4 age groups (at the moment of performing WBCT): 0-5 y.o. (n=5); 5-10 y.o. (n=12); 11-15 y.o. (n=6); >16 y.o.(n=9). Significant association with CAJIS was detected in two age groups: 5-10 y.o. and >16 y.o. (p=0.04). Tendency to significant association with HO volume was detected in other two age groups: 0-5 y.o. and 11-16 y.o. (p=0.08).
Conclusion: Our preliminary data confirmed that HO volume significantly increased according the age and correlate with CAJIS score. It is extremely needed to find medications that can prevent the development of HO with the possibility of their use in early childhood.
Disclosure of Interest: None Declared

PReS25-ABS-1180

EVALUATING BONE HEALTH IN FAMILIAL MEDITERRANEAN FEVER: IMPACT OF INFLAMMATION AND TREATMENT

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Introduction: Familial Mediterranean Fever(FMF) is an inherited autoinflammatory disorder characterized by recurrent episodes of hyperinflammation and persistent subclinical inflammation during attack-free periods. This chronic inflammatory burden has been implicated in various long-term complications, including impaired bone health. Current literature suggests that sustained inflammation may contribute to reduced bone mineral density(BMD) and an increased risk of vertebral fractures. However, the relationship between disease activity, treatment modalities, and bone health remains unclear.

Objectives: This study aimed to evaluate bone health parameters in pediatric FMF patients and explore their associations with inflammatory markers, disease severity (PRAS score), and MEFV mutations. Additionally, the potential protective effect of treatment on BMD and vertebral fracture risk was investigated.

Methods: A total of 87 FMF patients were included. Demographic and clinical data were retrospectively reviewed, while laboratory tests (CRP, ESR, SAA), bone mineral density (BMD) measurements (based on bone age, calendar age, and height age), and lateral vertebral radiographs were prospectively obtained during attack-free periods. PRAS scores were categorized as mild(≤5), moderate(6–7), or severe(≥8). To assess the impact of treatment on bone health, patients receiving colchicine or anti-IL-1 treatment (firstly anakinra, followed by canakinumab) were analyzed in separate subgroups.

Results: The mean age was 161.7±37.1 months, with a disease duration of 78.0±44.2 months. The gender distribution was 50.5% male and 49.5% female.

BMD z-scores for chronological age, height age, and bone age were recorded as -0.16±1.25, -0.10±1.34, and -0.31±1.29, respectively. The prevalence of vertebral fractures was 3.5% (n=4).

No significant associations were found between disease severity parameters, including inflammatory markers(CRP, ESR, SAA), MEFV gene mutations, and PRAS score, and bone health outcomes(BMD and vertebral fractures)($p > 0.05$ for all). Analysis of treatment subgroups revealed no significant effect of colchicine on BMD or vertebral fracture risk ($p>0.05$ for all). On the other hand, patients treated with anti-IL-1 treatment showed significantly higher BMD values adjusted for

both bone age and calendar age($p=0.037$ for both). However, no significant difference was observed in vertebral fracture risk($p=0.634$) or height age–adjusted BMD($p>0.05$) in this group.

Conclusion: Our findings did not reveal a significant association between disease severity and bone mineral density or vertebral fracture risk in FMF patients, suggesting that bone health may not directly reflect clinical or inflammatory burden. Notably, despite higher disease activity, patients receiving IL-1 blocking treatments exhibited higher BMD values, raising the possibility of a protective role of IL-1β inhibition in bone metabolism.

References: 1)Salah S, El-Masry SA, Sheba HF, El-Banna RA, Saad W. Bone Mineral Density in Egyptian Children with Familial Mediterranean Fever. Iran J Med Sci. 2016 Jan;41(1):2-8. PMID: 26722138; PMCID: PMC4691266.

2)Aydin, E.A., Baglan, E., Kocamaz, N.G. *et al.* The effect of canakinumab treatment on growth parameters in children with familial Mediterranean fever. *Clin Rheumatol* **43**, 387–392 (2024). https://doi.org/10.1007/s10067-023-06752-z

Disclosure of Interest: None Declared

PReS25-ABS-1170

CHRONIC RECURRENT MULTIFOCAL OSTEOMYELITIS (CRMO): TWO-YEAR POST-DIAGNOSIS OUTCOMES IN A PROSPECTIVELY IDENTIFIED INCEPTION COHORT FROM THE UNITED KINGDOM AND REPUBLIC OF IRELAND

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Introduction: Chronic Recurrent Multifocal Osteomyelitis (CRMO), also known as Chronic Non-Bacterial Osteomyelitis, is a rare autoinflammatory bone disorder primarily affecting children and adolescents. Data on short- to medium-term clinical outcomes remain limited to retrospective cohorts, commonly from specialist referral centres.
Objectives: To evaluate two-year clinical outcomes in a prospectively identified national cohort of patients diagnosed with CRMO across the United Kingdom (UK) and the Republic of Ireland (ROI).
Methods: A national prospective surveillance study was conducted between October 2020 to November 2022. Those under 16 years of age with a new diagnosis of CRMO were identified through monthly surveys sent via the British Paediatric Surveillance Unit and the British Society for Children's Orthopaedic Surgery to all paediatric consultants and paediatric orthopaedic consultants in the UK and ROI. Reporting clinicians completed standardised questionnaires at diagnosis (baseline), one-, and two-year follow-ups.
Results: During the 25-month surveillance period, 187 children and young people with confirmed CRMO were identified, with 6 patients reclassified later due to a change in diagnosis. Complete one- and two-year follow-up data were available for 153 of the remaining 181 patients (84.5%). The disease course reported at both year one and year two was similar with approximately a third in each category: 'Continuous', 'relapsing/remitting' and 'one-off episode'. Over the two-year period, 75% were treated with NSAIDs and/or bisphosphonates only. Biologics were used in 15/146 (10.3%) of patients. Of these, 9/146 (6.2%) had an additional diagnosis and 12/146 (8.2%) were treated with TNF-alpha inhibitors.
At the two-year follow-up, 47.3% were off medications. Among those still on medication, 41.8% received NSAIDs, 17.1% bisphosphonates, 2.1% corticosteroids, 7.5% methotrexate, and 6.8% biologics. No significant difference in outcomes was observed between pamidronate and zoledronate.
Functional outcomes improved from presentation to two-year follow up: the proportion of patients reporting normal mobility increased from 68% to 79%, and full-time school attendance rose from 89% to 93%. CRMO-related hospital admissions declined from 37.1% to 2.7%. Similarly, emergency department attendances decreased from 62.8% to 1.3%. Reported complications over two years included fractures in 4.7% and bone deformities in 6.1%.
Conclusion: This is the first national inception cohort followed for two years. Most patients improved clinically, with reduced healthcare use, better mobility, and school attendance. Nearly half required no medication at two years; however, almost two-thirds had relapsing/remitting or persistent disease. Findings support favourable CRMO outcomes with current treatments, though a subset of patients require more intensive therapy.
Disclosure of Interest: None Declared

PReS25-ABS-1590

VALIDATION OF THE EULAR/ACR CLASSIFICATION CRITERIA FOR CHRONIC NONBACTERIAL OSTEOMYELITIS IN A PEDIATRIC COHORT

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Introduction: Chronic nonbacterial osteomyelitis (CNO) is a rare autoinflammatory bone disorder primarily affecting children and adolescents. An international consensus group developed the EULAR/ACR Classification Criteria in order

to define a homogeneous group of patients diagnosed with CNO.
Objectives: This study aims to validate these criteria in a diverse pediatric cohort and compare their performance with the Jansson and Roderick diagnostic criteria.
Methods: A retrospective evaluation was conducted on 78 pediatric CNO patients and 99 mimickers in Hacettepe University department of pediatric Rheumatology from 2020 to 2024. Demographic, clinical, laboratory, and imaging data were analyzed, and the sensitivity, specificity, and predictive values of the EULAR/ACR criteria were assessed. Statistical comparisons were made against the Jansson and Roderick criteria.
Results: The EULAR/ACR criteria demonstrated high accuracy, with a sensitivity of 92.68% and specificity of 97.89%, outperforming the Jansson criteria (sensitivity: 88.46%, specificity: 72.73%) and aligning closely with the Roderick criteria (sensitivity: 96.15%, specificity: 96.97%). Key distinguishing features included multifocal and symmetric lesions, frequent involvement of high-scoring anatomical sites (e.g., clavicle and mandible), and the absence of exclusion criteria such as fever and markedly elevated inflammatory markers.
Conclusion: The newly validated EULAR/ACR classification criteria for pediatric CNO demonstrated high specificity and good sensitivity in our cohort. Their application facilitates the identification of homogeneous patient populations, aiding in research consistency and the development of standardized approaches to CNO classification and management.
References: 1. Jansson A, Renner ED, Ramser J, Mayer A, Haban M, Meindl A, et al. Classification of non-bacterial osteitis: retrospective study of clinical, immunological and genetic aspects in 89 patients. Rheumatology (Oxford). 2007;46(1):154-60.
2. Roderick MR, Shah R, Rogers V, Finn A, Ramanan AV. Chronic recurrent multifocal osteomyelitis (CRMO) - advancing the diagnosis. Pediatr Rheumatol Online J. 2016;14(1):47.
3. Zhao Y, Oliver MS, Schnabel A, Wu EY, Wang Z, Marino A, et al. EULAR/ACR classification criteria for paediatric chronic nonbacterial osteomyelitis (CNO). Annals of the Rheumatic Diseases. 2025.
Disclosure of Interest: None Declared

PReS25-ABS-1353

SCURVY MIMICKING CHRONIC NON-BACTERIAL OSTEOMYELITIS IN CHILDREN WITH NEURODEVELOPMENTAL OR BEHAVIORAL CONDITIONS

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Introduction: Chronic non-bacterial osteomyelitis (CNO) is a rare autoinflammatory bone disorder characterized by prolonged musculoskeletal pain and sterile bone inflammation. Its diagnosis relies on clinical presentation and imaging findings, often supported by whole-body MRI. Among these, scurvy—a rare but serious consequence of vitamin C deficiency—represents an important and well-recognized differential diagnosis, as also highlighted in current guidelines. Nevertheless, it remains underdiagnosed, particularly in at-risk pediatric populations.
Objectives: We present three pediatric cases in which scurvy closely resembled CNO in both imaging and clinical features. All affected children had underlying neurodevelopmental or neurological disorders, emphasizing the critical role of thorough nutritional assessment in children presenting with bone pain and imaging abnormalities suggestive of CNO.
Methods: This study presents a descriptive case series of three pediatric patients in two institutions. Clinical data were obtained from patient charts, including symptoms at presentation, diagnostic work-up, therapeutic interventions, and short-term outcomes.
Results: Three children were referred for evaluation of persistent musculoskeletal pain and functional impairment. Two

had autism spectrum disorder (ASD) and one had leukodystrophy. In the two most recent cases (diagnosed in 2024 and 2025), whole-body MRI revealed multifocal bone marrow edema and metaphyseal changes suggestive of CNO. In all three patients, a detailed dietary history revealed extremely selective food intake with little to no consumption of fresh fruits or vegetables. Clinical examination showed typical skin and gingiva manifestations. Laboratory testing confirmed severe vitamin C deficiency, with serum ascorbic acid levels below 0.5 mg/L. Following daily oral vitamin C supplementation, all patients experienced marked clinical improvement, and follow-up MRI showed resolution of bone lesions within six to twelve months. Non-steroidal anti-inflammatory drugs (NSAIDs) were administered occasionally for symptom relief.

Conclusion: Scurvy remains a relevant differential diagnosis in high-income countries, especially in children with neurodevelopmental or behavioral conditions that predispose to extreme dietary selectivity. Bone pain and MRI findings can resemble CNO, leading to misdiagnosis. In contrast to CNO, scurvy responds rapidly and completely to vitamin C supplementation, though imaging changes may lag behind clinical improvement. The presence of dermatological and intraoral signs, combined with restrictive eating, should prompt nutritional evaluation. In children with chronic musculoskeletal symptoms—particularly those with ASD, developmental delay, or neurological disorders—nutritional deficiencies must be considered. Early recognition and treatment are essential to avoid unnecessary interventions and ensure recovery. These cases highlight the need for interdisciplinary collaboration in assessing children with unexplained bone pain.

Disclosure of Interest: None Declared

PReS25-ABS-1717

PERCEPTIONS AND ATTITUDES TOWARD BIOLOGIC THERAPY AMONG FAMILIES OF PEDIATRIC RHEUMATOLOGY PATIENTS: A CROSS-SECTIONAL SURVEY STUDY

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Introduction: Childhood rheumatic diseases are chronic conditions that require long-term follow-up and may cause both physical and psychosocial challenges. In cases unresponsive to conventional treatments, biologic agents have become effective alternatives. However, treatment success depends not only on pharmacological efficacy but also on the child's and parents' adherence, knowledge, and attitudes toward therapy.

Objectives: This study aimed to assess parents' knowledge, attitudes, emotional responses, challenges, and satisfaction related to their child's biologic treatment using a structured questionnaire.

Methods: The study involved primary caregivers of 61 children on biologic therapy. After informed consent, participants completed a 64-item structured questionnaire covering six main categories with closed-ended, open-ended, and multiple-choice questions.

Results: Among participants, 70.5% were mothers and 65.6% of the children were girls. The most common diagnosis was juvenile idiopathic arthritis (57.4%). The most frequently used biologics were etanercept (34.4%), adalimumab (24.6%), and canakinumab (16.4%), mostly administered subcutaneously (88.5%) and weekly (32.8%). While 42.6% of parents reported sufficient knowledge, 88.5% cited the physician as their main information source, and 90.2% trusted the physician's decision. The most frequently requested topic for clarification was side effects (50.8%). Reported benefits included improved physical functioning (70.5%), school/social participation (55.8%), and family life (55.8%). Nevertheless, 24.6% experienced emotional distress and 50.8% reported feelings of loneliness and indecision. Adherence issues were noted in 14.8%, and 24.6% reported difficulties accessing treatment. Common

challenges included injection-related issues (24.6%) and the child's reluctance (21.3%). While 26.2% had attended an informational event, 80.3% were willing to join future sessions.

Conclusion: The findings underscore the need to address both medical and psychosocial aspects of parents' experiences during biologic treatment, supporting a more family-centered approach with structured information and caregiver support.

References: 1. Calvo Penadés I, Moreno Ruzafa E, Calzada-Hernández J, Mosquera Angarita J, López Montesinos B, Bou R, López Corbeto M, Sánchez-Manubens J, González Fernández MI, Carriquí Arenas S, Bittermann V, Estepa Guillén C, Rodríguez Díez L, Iglesias E, Marti Masanet M, LaCruz Pérez L, Peral C, De Lossada A, Valderrama M, Llevat N, Montoro M, Antón J. Real-world psychosocial impact among patients with juvenile idiopathic arthritis and families in Spain. Pediatr Rheumatol Online J. 2024 Nov 26;22(1):102. doi: 10.1186/s12969-024-01035-6. PMID: 39593042; PMCID: PMC11600913.

2. Lipstein EA, Lovell DJ, Denson LA, Kim SC, Spencer C, Ittenbach RF, Britto MT. High Levels of Decisional Conflict and Decision Regret When Making Decisions About Biologics. J Pediatr Gastroenterol Nutr. 2016 Dec;63(6):e176-e181. doi: 10.1097/MPG.0000000000001425. PMID: 27749390; PMCID: PMC5123667.

Disclosure of Interest: None Declared

PReS25-ABS-1235

COMPARISON OF KINESTHETIC AND VISUAL IMAGERY PERCEPTION IN JUVENILE IDIOPATHIC ARTHRITIS AND HEALTHY PEERS: A PILOT STUDY

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Introduction: Juvenile Idiopathic Arthritis (JIA) is a chronic condition that can impair physical activity, functional ability, and motor skill development, ultimately affecting quality of life (1). Kinesthetic and visual imagery are cognitive strategies known to support motor learning and performance, especially in children. However, limited evidence exists comparing these abilities between children with JIA and their healthy counterparts (2).
Objectives: The aim of the study was to compare kinesthetic and visual imagery abilities in children and adolescents with JIA versus healthy peers, and to examine the relationship between physical activity and imagery performance.
Methods: A total of 75 participants aged 7–18 years were included: 22 with JIA and 53 healthy peers. Physical activity was assessed using the Physical Activity Questionnaire for Children and Adolescents (PAQ-C/A), and exercise behavior was evaluated through the Exercise Stages of Change – Short Form (ESCSF) and the Exercise Stages of Change Questionnaire (ESCQ). Kinesthetic and visual imagery skills were measured using the Kinesthetic and Visual Imagery Questionnaire-20 (KVIQ-20).
Results: The mean age of the JIA group was 13.90 ± 3.25 years, and 15.19 ± 2.42 years for the healthy group. JIA participants exhibited significantly higher kinesthetic imagery scores compared to healthy peers ($t = -2.35$, $p = 0.027$), which may be attributed to increased bodily awareness, engagement in physiotherapy, or adaptive perceptual responses. PAQ-C/A scores did not significantly differ between groups ($t = -0.24$, $p = 0.808$). ESCQ analysis showed that 76% of the JIA group were in pre-contemplation or contemplation stages, while the healthy group was more frequently in action and maintenance stages. Exercise stage demonstrated a weak correlation with PAQ scores ($r = -0.295$) and kinesthetic imagery ($r = 0.028$).
Conclusion: Children and adolescents with JIA may demonstrate enhanced kinesthetic imagery abilities compared to their healthy peers, independent of physical activity levels. These findings suggest that cognitive and behavioral adaptations may contribute to motor imagery performance and underscore the need for comprehensive assessment strategies in pediatric rheumatology and educational settings. This enhancement in kinesthetic perception may stem from increased body awareness, regular physiotherapy, or adaptive sensorimotor mechanisms. Clinically, motor imagery techniques may
offer a promising, low-risk strategy in rehabilitation settings. Further longitudinal studies are warranted to examine how disease duration, treatment exposure, and imagery training influence these cognitive-motor skills.
References: 1. Hulsegge GH, et al. Fundamental movement skills, physical fitness and physical activity among Australian children with juvenile idiopathic arthritis. *J Paediatr Child Health.* 2015.
2. Paltiel O, Uziel Y. Juvenile idiopathic arthritis: Pathogenesis and rehabilitation perspectives. *Pediatr Rheumatol.* 2014;12(1):1–10.
Disclosure of Interest: None Declared

PReS25-ABS-1442

INVESTIGATION OF THE EFFECTIVENESS OF THE COGNITIVE EXERCISE THERAPY APPROACH IN PATIENTS DIAGNOSED WITH JUVENILE IDIOPATHIC ARTHRITIS: A PILOT STUDY

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Introduction: As emphasized in the guidelines of the Paediatric Rheumatology European Society (PReS), the multidimensional challenges caused by factors such as disease activity and chronic pain in juvenile rheumatic diseases require a holistic approach to disease management (1). It is emphasized that optimal disease management should combine pharmacological treatment with non-pharmacological approaches. In the pediatric rheumatology literature, non-pharmacological interventions with high levels of evidence are primarily active exercise and physical activity strategies, known for their anti-inflammatory effects (2). Cognitive Exercise Therapy Approach (BETY) is an innovative and original exercise method developed based on the biopsychosocial model. It has proven effectiveness in various adult rheumatic diseases (3).

Objectives: This pilot study aimed to investigate the effectiveness of the BETY on disease activity, pain, functionality, biopsychosocial status, and quality of life (QoL) in patients with Juvenile Idiopathic Arthritis (JIA).

Methods: Six individuals (four girls, two boys) diagnosed with JIA were included in the study. Demographic data were collected, and the following assessments were performed: disease activity using the Juvenile Arthritis Disease Activity Score-27 (JADAS-27); pain using the Visual Analogue Scale (VAS) and the Pain Catastrophizing Scale – child version (PCS-C); functionality using the Childhood Health Assessment Questionnaire (CHAQ); biopsychosocial status using the Juvenile Arthritis Biopsychosocial Questionnaire – Modified Version (JAB-Qm); and QoL using the Juvenile Arthritis Quality of Life Questionnaire (JAQQ). After the initial assessments, individuals with JIA participated in BETY group exercise sessions twice weekly for twelve weeks. The session content included a combination of BETY Nociplastic Pain Neuroscience Education, Function-Oriented Core Stabilization Exercises, and Dance Therapy Authentic Movement. At the end of the twelve weeks, all assessments were repeated. In addition, qualitative interviews were conducted with the patients and their families to explore their recovery experiences following the BETY sessions.

Results: Following the 12-week BETY intervention, statistically significant improvements were observed in general well-being (CHAQ; $p = 0.043$), psychosocial status (JAB-Qm psychosocial; $p = 0.027$), fatigue (JAB-Qm fatigue; $p = 0.027$), total biopsychosocial status (JAB-Qm total; $p = 0.046$), and QoL (JAQQ; $p = 0.046$). Qualitative feedback from both patients and families supported these findings, highlighting enhanced pain coping skills, increased physical capacity, improved social participation, and greater self-confidence.

Conclusion: This pilot study's findings can be interpreted as BETY positively affects fatigue, biopsychosocial status, and QoL in patients with JIA. Positive qualitative feedback from patients and their parents further supported the quantitative outcomes. Future randomized controlled trials with larger cohorts are planned to enhance the efficacy and clinical value of BETY as a biopsychosocial model-based exercise approach for patients with JIA.

References: 1) Foster HE, Minden K, Clemente D, et al. EULAR/PReS standards and recommendations for the transitional care of young people with juvenile-onset rheumatic diseases [published correction appears in Ann Rheum Dis. 2018 Jun;77(6):960. doi: 10.1136/annrheumdis-2016-210112corr1.]. Ann Rheum Dis. 2017;76(4):639-646. 2) Ringold S, Angeles-Han ST, Beukelman T, et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Treatment of Juvenile Idiopathic Arthritis: Therapeutic Approaches for Non-Systemic Polyarthritis, Sacroiliitis, and Enthesitis. Arthritis Rheumatol. 2019;71(6):846-863. 3) Unal E, Karaca NB, Saldirdak GA, et al. Investigation of the Effectiveness of a Biopsychosocial-Based Exercise Approach in Rheumatic Diseases: A Mixed Methods Research With Patients' Perspectives. *J Eval Clin Pract*. 2025;31(1):e70033.

Disclosure of Interest: None Declared

PReS25-ABS-1395

CLINICALLY FEASIBLE DETECTION OF COGNITIVE DYSFUNCTION IN ASSOCIATION WITH ABNORMAL CORTICAL MORPHOLOGY: A PROSPECTIVE STUDY IN ADOLESCENTS WITH CHILDHOOD-ONSET LUPUS

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Introduction: Clinical identification of diffuse neuropsychiatric syndromes like cognitive dysfunction (CD) in youth with childhood-onset SLE (cSLE) remains challenging due to limited resources and diagnostic tools. Computerized neurocognitive batteries such as the Pediatric Automated Neuropsychological Assessment Metrics (Ped-ANAM) show promise for time- and resource-feasible assessment of CD when neuropsychiatric SLE (NPSLE) is suspected. Ped-ANAM and quantitative neuroimaging present a potential clinically viable framework to improve CD detection and attribution in cSLE; however, they have not been assessed together in cSLE.
Objectives: To evaluate differences in Ped-ANAM and advanced metrics of cortical brain morphology between adolescents with cSLE and healthy controls (HC) and to examine the relationship between cognitive and brain metrics in each group.
Methods: Global performance (CPSMultiscore) and domain-specific cognitive efficiency throughput (TPstd) scores were calculated from Ped-ANAM in 68 adolescents with cSLE (10 females, 2 patients with NPSLE diagnosis; 15 patients with NPSLE concern) and 62 age/sex-matched HC, aged 11-17 years. T1w MRI was cross-sectionally acquired at 3T, and cortical brain metrics (volume and thickness) were calculated using Freesurfer. Group differences in cognitive and brain metrics were calculated with analyses of covariance. Associations between cognitive and brain metrics were evaluated with regression analyses, adjusted for covariates. Family-wise error corrections for multiple tests were performed.
Results: Compared to HC, adolescents with cSLE showed worse global and domain-specific (speed/efficiency, $t=4.23$; reasoning, $t=2.99$; $p<0.0042$) cognitive scores and similar age/sex/education distributions. They also showed both lower volume and thinner cortex in several clusters, mostly in frontal, as well as in parietal and occipital regions (all cluster areas>108 mm2; all stats *log10 p>2.32*). Higher speed/efficiency and reasoning associated with greater thickness on occipital (isthmus cingulate, lingual) and frontal (precentral/caudal middle frontal) clusters on the left hemisphere in HC (all cluster areas>56 mm2; all stats *log10 p>2.54*) while the inverse association (lower thickness) was observed in cSLE (all cluster areas>74 mm2; all stats *log10 p<-2.08*).
Conclusion: Patients with cSLE exhibited worse global performance, speed/efficiency and reasoning, regional atrophy, and cortical thinning compared to HC. By combining the strengths of ped-ANAM and MRI-based cortical morphology, we present a clinical framework for enhancing CD screening/monitoring in cSLE and potential cognitive training therapies. Next, this approach should be validated by comparing it to gold standards for CD screening and clinical neuropsychiatric diagnosis. The distinct relationships between cognitive speed, reasoning, and regional brain morphology in the cSLE and HC groups suggest a link to SLE pathology, treatment and/or comorbidities that requires further longitudinal investigation.
Disclosure of Interest: None Declared

PReS25-ABS-1507

HEART RATE PATTERNS AS INDICATORS OF PHYSICAL FITNESS IN JUVENILE IDIOPATHIC ARTHRITIS: INSIGHTS FROM A PRELIMINARY STUDY

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Introduction: Physical inactivity in children and adolescents is a global public health problem(1). Juvenile Idiopathic Arthritis (JIA) is characterized not only by joint inflammation but also by limitations in physical function and aerobic performance(2). Pedometric data such as step count are widely used to assess activity, whereas heart rate (HR) has not yet been fully investigated as a marker of physical fitness in pediatric rheumatology(3).
Objectives: This study aimed to investigate whether temporal HR patterns can discriminate between children with JIA and their healthy peers and provide predictive insight into underlying fitness levels.
Methods: 30 children aged 12–18 years with JIA and 24 healthy adolescents using Android-based mobile phones were included. Participants received smartwatches from four different brands and were trained in their usage and data management. The Pedi@ctivity mobile application developed by our team was synchronized with the Google Fit application on the Pedi@ctivity web platform for remote monitoring. Daily metrics (step count, movement speed, and heart rate) of participants were recorded for seven consecutive days from these watches. Step counts during the winter school period were recorded and analyzed remotely. Statistical analysis with SPSS Version 28.0., cluster analysis using only heart rate data further separated participants into two distinct groups corresponding to their clinical classification.
Results: Children with JIA exhibited consistently higher daily heart rate values compared to healthy controls, with statistically significant group differences on Monday ($p=0.029$), and non-significant differences on the remaining days (Tuesday to Sunday, $p>0.05$). Notably, Thursday was the only day showing similar group means. In the healthy control group, step count was significantly and inversely correlated with heart rate on Friday ($r=-0.84$, $p=0.001$), suggesting superior cardiovascular efficiency on days of peak activity. While similar negative trends were observed on Monday ($r=-0.66$, $p=0.074$) and Wednesday ($r=0.27$, $p=0.430$), with no statistical significance. K-means clustering based solely on heart rate data revealed two distinct physiological profiles: Cluster 0 (n=9) exhibited lower and more stable heart rates (66–75 bpm), comprising 6 healthy children and 3 with JIA, while Cluster 1 (n=3) showed markedly elevated and more variable HR (80–92 bpm), including 2 JIA and 1 healthy participant. Although clusters did not perfectly correspond to clinical groups, they reflected meaningful differences in cardiovascular efficiency.
Conclusion: The results suggest that HR monitoring using smartwatches, when combined with activity measurements, may be a valuable noninvasive biomarker for estimating physical fitness in children with JIA, with high and variable HR responses reflecting reduced cardiorespiratory efficiency. These findings support the continued exploration of HR analytics as a non-invasive clinical tool for assessing and monitoring physiological adaptation in children with JIA.
This study was supported by the TUBITAK 1001-Scientific and Technological Research Projects Support Program 121E690.
References: Guthold, et al. (2020). Global trends in insufficient physical activity among adolescents:A pooled analysis of 298 population-based surveys with 1.6 million participants. The Lancet Child & Adolescent Health
Pella, et al. (2023). Cardiorespiratory fitness assessed with cardiopulmonary exercise testing in patients with juvenile idiopathic arthritis:a systematic review and meta-analysis. Rheumatology
Nørgaard et. al. Accelerometry-based monitoring of daily physical activity in children with juvenile idiopathic arthritis. Scand J Rheumatol 2016

Disclosure of Interest: None Declared

PReS25-ABS-1242

''CONFUSED BY WHAT IT ALL MEANS'' –
USING A CREATIVE METHOD TO EXPLORE RHEUMATOLOGICAL CONDITIONS WITH CHILDREN

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Introduction: Living with a rheumatological condition is associated with a range of daily challenges. Children frequently experience higher levels of pain, fatigue, and physical disabilities despite access to treatments that aim to control disease activity [1,2].
Objectives: The IMPACT study is a UK wide study to design, develop and test a technology intervention to support parents of children with rheumatological conditions. As part of the first phase of this study we invited children to share with us their experiences and perspectives in focus groups. In order to support families better it is important to explore children's understanding of their conditions and how it affects them.
Methods: The children's groups were all conducted virtually on Teams. They were asked to consider how they would support a friend who has received a recent diagnosis. They were also encouraged to explore emotions and feelings associated with getting a diagnosis, but also the impact this may have on their 'friend's' everyday life. Using 'Teams Whiteboard' children were invited to share their thoughts and ideas as they were exploring different pre-written scenarios for their fictional character. The aim of using a storyboard was to ensure each child didn't feel they needed to share their own personal experiences, which they may have found upsetting.
Results: We conducted 3 focus groups with the help of one of our child representatives from the Steering Group who co-led the sessions. In total 10 children (aged 8-13 (*M* = 10.51, *SD* = 1.60); 58.33% were female), with a range of different rheumatological conditions (JIA (N=5), JDM (N=2) and other conditions such as Behcet's, fever syndromes, CRMO, and Scleroderma (N=5)) participated in the sessions. They discussed challenges and implications in relation to having a health condition, especially around taking medicines, and sometimes not understanding side effects. Most prominently, children were very encouraging and provided hints and tips on how to support their 'friend' when it comes to blood tests, taking medicines, and doing regular exercises. They explored advantages of telling their friends, and how informing school is important to get extra help where needed. The children voiced how they really enjoyed the opportunity to meet others during the focus groups, and some even swapped contact details to stay in touch.
Conclusion: It is crucial to understand children's views to know how to better support them. Providing them with creative ways to explore their ideas and share their emotions is important to allow children to discuss their thoughts freely in a
safe space. Using Teams Whiteboard as an interactive way for children to express themselves worked really well, with resultant high levels of engagement and energy in all three groups. Having a young Steering group member co-leading the sessions as both an expert as well as a peer, has provided a unique view and enriched the experience.
References: 1. Shaw KL, Southwood TR, Duffy CM, McDonagh JE. Health-related quality of life in adolescents with juvenile idiopathic arthritis. Arthritis Care & Research: Official Journal of the American College of Rheumatology. 2006 Apr 15;55(2):199-207. https://doi.org/10.1002/art.21852
2. Jones JT, Cunningham N, Kashikar-Zuck S, Brunner HI. Pain, fatigue, and psychological impact on health-related quality of life in childhood-onset lupus. Arthritis care & research. 2016 Jan;68(1):73-80. https://doi.org/10.1002/acr.22650
Disclosure of Interest: None Declared

PReS25-ABS-1237

CLINICAL INTERPRETATION OF FATIGUE IN PEDIATRIC RHEUMATOLOGY: PRELIMINARY RESULTS ON THE FEASIBILITY OF THE FATIGUE SEVERITY SCALE

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Introduction: Fatigue is a common and disabling symptom in pediatric rheumatology, significantly affecting daily functioning but often overlooked in clinical assessments (1). Although the Fatigue Severity Scale (FSS) is a widely used tool in adults, its application in pediatric populations remains limited, and its psychometric properties have not been sufficiently validated in children and adolescents with rheumatic diseases.
Objectives: This study aimed to evaluate the internal consistency of the FSS in pediatric rheumatic conditions and to investigate its correlation with the Visual Analog Scale (VAS) for fatigue, providing preliminary data on its clinical applicability.
Methods: Fifty-two pediatric patients diagnosed with rheumatic diseases completed the 9-item FSS, which assesses the functional impact of fatigue, and a 0–100 mm VAS to rate their current perceived fatigue. FSS scores ≥36 were considered clinically significant (2). VAS scores were classified as low (0–19), clinically relevant (20–49), and severe (≥50) (3). Internal consistency was assessed using Cronbach's alpha. Pearson correlation and cross-tabulation analyses were conducted to examine the relationship between the FSS and VAS scores.
Results: The FSS demonstrated strong internal consistency (Cronbach's $\alpha = 0.87$). According to the FSS, 30.76% of the participants experienced clinically significant fatigue, while 46.15% reported severe fatigue on the VAS. A moderate positive correlation was observed between FSS and VAS scores ($r = 0.38$, $p = 0.004$), and between VAS scores and age ($r = 0.33$, $p = 0.016$). Interestingly, several participants who scored below the FSS fatigue threshold still reported severe fatigue on the VAS, indicating a potential discrepancy in capturing acute fatigue experiences.
Conclusion: Preliminary findings suggest that the FSS is a reliable and feasible tool for assessing fatigue in pediatric rheumatology, with good internal consistency. However, its sensitivity to acute or fluctuating fatigue may be limited. Combining the FSS with real-time subjective measures like the VAS can enhance the comprehensiveness of fatigue assessment, capturing both functional and immediate fatigue experiences. Children generally understood the FSS items with minimal need for adaptation, supporting its potential utility in pediatric settings. The observed increase in fatigue perception with age may reflect behavioral factors, cumulative disease burden, or both. Further studies with larger cohorts are needed to validate these findings and explore the mechanisms underlying fatigue in pediatric rheumatologic conditions.
References: Vlist, et al.Fatigue in childhood chronic disease. *Archives of disease in childhood*. 2019.
Huether, et al.Screening cut-off scores for clinically significant fatigue in early Parkinson's disease. *Clinical parkinsonism & related disorders*.2023.
Pollard, et al.Fatigue in rheumatoid arthritis reflects pain, not disease activity. Rheumatology.2006.
Disclosure of Interest: None Declared

PReS25-ABS-1129

ORGANIZATION OF THE WORK OF THE FAMILY PATIENT SCHOOL IN COOPERATION WITH THE PATIENT ORGANIZATION OF PARENTS OF CHILDREN SUFFERING FROM JUVENILE ARTHRITIS

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Introduction: The organization of the work of the medical community in cooperation with patient organizations is a complex but necessary component of the extraclinical care of patients with chronic, potentially disabling, diseases. Patient organizations, uniting parents, aim to collectively resolve a number of issues related to the organization of out-of-hospital rehabilitation and drug provision issues. Involving the medical community in closer cooperation with patient organizations can significantly increase patients' awareness of their disease, the risks of complications, the need for therapy, its types and safety limits, as well as a number of other issues requiring special knowledge.
Objectives: The aim of the project, which was implemented within the region, was to develop and implement a series of measures that would significantly increase the awareness of patients with juvenile arthritis (JIA) and their parents about the characteristics of their condition, the importance of regular treatment, and the impact of adherence to medical advice.
Methods: To implement the action plan, a multidisciplinary team of doctors was formed, consisting of employees from the university, the university's clinic, and student volunteers. The main events of the program included the staging of theatrical performances on World Arthritis Day and World Young Rheumatic Disease Day, as well as the creation of a series of informative videos on various aspects of rheumatology.
Results: The theatrical events included information content on aspects of rehabilitation of patients with JIA. During their performance, patients with JIA became mandatory participants in the performance. This made it possible to demonstrate the integration of patients into society and the possibilities for achieving the desired goals with regular therapy. At least 13 videos were created in which doctors explained various aspects of pediatric rheumatology. Among the topics: historical aspects of rheumatology, issues of the pathogenetic aspects of JIA, treatment approaches, the specifics of the use of various drugs, the need for regular monitoring at the outpatient stage, possible complications of JIA and therapy. The issues of ophthalmological disorders were considered separately with the involvement of an ophthalmologist. Several videos were devoted to the issues of non-drug correction and rehabilitation of patients with JIA. The created video content was posted in the media communities of the patient organization, as well as on the medical websites of the University Clinic. The number of views and reactions gave a good understanding of the high demand for this information resource. Additionally, based on the results of familiarization of the patient community with these materials, answers were given to questions that arose (the most frequent among which were questions about prospects in "adult" life, social issues of adaptation).
Conclusion: The established system of the family patient school has demonstrated the need for additional contacts with the patient community. The results of its implementation have increased the level of awareness of patients about the
disease, which has improved compliance and will allow achieving better results in the treatment and rehabilitation of patients with JIA.
Disclosure of Interest: None Declared

PReS25-ABS-1636

CO-DESIGNING THE FUTURE OF TRANSITIONAL CARE: A PATIENT-CENTERED APPROACH FROM ERN RECONNET

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Introduction: Transition from pediatric to adult care remains a key challenge for patients with rare and low-prevalence connective tissue disorders (rCTDs). European Reference Networks (ERNs), including ERN ReCONNET, aim to improve patient care across Member States. However, significant differences persist in transition protocols and their implementation. The ERN ReCONNET Transition of care Task Force, composed of clinicians, patient representatives, and ERN ReCONNET coordination team members—in collaboration with ERN RITA—has undertaken a comprehensive assessment to develop a scientifically grounded, co-designed transition pathway that integrates perspectives of both patients and caregivers.

Objectives: The main objective of this initiative is to map existing transition pathways within ERN ReCONNET healthcare providers (HCPs) and identify the different unmet needs. A secondary goal is to co-design a harmonized transition model—incorporating direct input from young patients (YP) and caregivers—to be shared within and outside ERN ReCONNET centers and promote standardized, high-quality patient-centered care.

Methods: A two-phase survey approach was implemented. Phase I (December 2023–March 2024) targeted HCPs and collected 56 responses from 47 full members or affiliated partners of ERN ReCONNET (73% response rate). Phase II is currently ongoing, with the patient/caregiver survey being translated into 21 European languages. Distribution is scheduled for summer 2025, targeting at least 1,000 respondents overall. Once both datasets are available, their comparison will guide the development of a co-designed best-practice transition pathway for rCTDs, to be disseminated across the whole rCTD scientific and patient community.

Results: The HCP-directed survey revealed a marked heterogeneity in transition practices across centers, with critical gaps in patient identification, readiness assessment, and inter-center coordination. Notably, limited engagement from adult healthcare professionals and absence of formalized guidelines were reported. A lack of patient and caregiver input in current models further impedes effective transition. These findings underscore the need for a structured, co-designed approach that reflects the real needs and expectations of patients. Comparing the expectations and unmet needs of HCPs with those of YP and their caregivers will enable truly shared decision-making in the care transition process.

Conclusion: The HCP survey results demonstrate an urgent need for standardized, co-designed transition pathways for patients with rCTDs. A harmonised model, combining clinical expertise with lived experience, is being developed to enhance care continuity and patient satisfaction. The upcoming patient and caregiver survey will complete this process, resulting in a replicable framework to be adopted by ERN ReCONNET centers as well as by other centres taking care of rCTDs patients. As a next step, a dedicated meeting will be organized to share best practices and consolidate knowledge, fostering widespread implementation and collaboration.

References: 1) Marrani E, Zajc Avramovic M, Marinello D, Talarico R, Baldini C, Collado-González E, Fonseca JE, Schraven L, Oliveira Ramos F, Triggianese P, Vissink A, Mosca M, Avcin T, Simonini G. Challenges in the transition of care for rare

connective tissue diseases: results from the 2023 ERN ReCONNET Transition of Care Task Force survey. Rheumatol Adv Pract. 2025 Jan 11;9(1):rkae149. doi: 10.1093/rap/rkae149. PMID: 39886538; PMCID: PMC11780841.

Disclosure of Interest: None Declared

ABSTRACT ONLY

T01 - Non-systemic JIA (oligo, poly, psoriatic, undifferentiated)

PReS25-ABS-1058

IS OBESITY ASSOCIATED WITH TIME TO DIAGNOSIS AND DISEASE SEVERITY IN JUVENILE PSORIATIC ARTHRITIS?

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Introduction: Obesity is linked to delays in diagnosis, lower rates of minimal disease activity and poorer treatment response in adult-onset psoriatic arthritis, but its role in juvenile psoriatic arthritis (JPsA) is unclear.

Objectives: To examine the associations between obesity and JPsA features at initial presentation to paediatric rheumatology.

Methods: Children were recruited to the Childhood Arthritis Prospective Study, a UK multicentre JIA inception cohort, between 2001–2019. Participants selected had a physician's diagnosis of JPsA within one year of initial presentation to paediatric rheumatology. Demographic, clinical and patient-reported outcome data were collected at initial presentation.

Standardised BMI-z-scores at initial presentation were calculated using World Health Organization reference data and classified as 'underweight', 'healthy', 'overweight', or 'obese'.

Differences in JPsA features were compared between healthy and obese BMI-z-score groups descriptively and using Kruskal-Wallis (continuous variables) and Chi-squared tests (categorical variables).

Results: Among 111 children with JPsA, 48 (60.0%) had a healthy BMI, 18 (22.5%) were overweight, and 14 (17.5%) were obese. The proportion of overweight children exceeded the national average reported between 2001-2019 (11.5-15.5%), though the obesity rate was representative of national trends (14.0–18.5%).

Compared to children with healthy-weight-BMI, those with obese-range BMI had an older age of symptom onset (11.2 years, IQR: 10.2 to 14.6vs. 6.0 years, IQR: 2.7 to 11.2, p=0.010), and longer disease duration to diagnosis (6.6, IQR: 2.4 to 28.9vs. 5.1, IQR: 2.7 to 11.3, p=0.100), respectively.

Clinically, compared with children with healthy-weight-BMI, those with obese-range BMI had a higher ESR (26.0, IQR: 17.0 to 46.0 vs.10.0, IQR: 5.0 to 23.0, p=0.015). alongside clinically significant increases in active joint counts (4.0, IQR: 1.0 to 10.0 vs.3.0, IQR: 2.0 to 5.0), limited joint counts (2.0, IQR: 1.0 to 9.0 vs.1.0, IQR: 1.0 to 3.0), proportion of individuals with psoriasis (54.6% vs.37.8%, p=0.200), and nail abnormalities (20.0% vs.12.2%, p=0.700), respectively.

Patient-reported outcomes were worse in the obese-range BMI compared with the healthy-BMI group: parental global score (5.2cm, IQR: 1.8 to 7.6 vs. 1.8cm, IQR: 0.1 to 4.1, p=0.050); pain (5.4cm, IQR: 2.0 to 8.2 vs. 2.0cm, IQR: 0.4 to 3.5, p=0.050); and CHAQ scores (1.4, IQR: 0.3 to 1.9 vs. 0.31, IQR: 0.13 to 0.63, p=0.130), respectively.

Conclusion: In JPsA, obesity is associated with later symptom onset, increased inflammation, and worse wellbeing and pain. A larger sample size is needed to confirm these findings. This highlights the importance of holistic and developmentally appropriate care, including proactive weight management and early intervention strategies for young people living with JPsA.

Disclosure of Interest: None Declared

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PREDICTING CLINICAL RESPONSE TO ADALIMUMAB IN JUVENILE IDIOPATHIC ARTHRITIS WITH A MULTIDIMENSIONAL MODEL INTEGRATING DISEASE ACTIVITY AND PHARMACOKINETICS

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Introduction: Adalimumab, a fully human TNF-inhibitor, has revolutionized treatment of patients with juvenile idiopathic arthritis. The development of antidrug antibodies (AAA) has been reported in several paediatric inflammatory conditions. Most children treated with adalimumab respond within several months, but a minority of these may show loss of response (LOR) after continued exposure.
Objectives: The study describes clinical features in a single-centre cohort of JIA patients treated with adalimumab, grouped according to frequency (1W vs 2W), dose of drug administration (20 vs 40 mg) and disease activity (from inactive to high according to ACR-JADAS score). Subsequently, we investigated correlation between adalimumab levels and antidrug antibodies titres and the predictive covariates of clinical response.
Methods: Records of patients were retrospectively reviewed to identify patients with dosage of adalimumab and AAA in a 5-years-period. Clinical and demographic parameters were collected. Indirect E-max response model was created.
Results: From June 2019 to January 2024, we collected 445 samples in 110 patients (a median of 4 for each child). The majority of patient had ANA-positive oligoarthritis (55.4%) followed by RF- negative polyarthritis (24.5%). The median age at disease onset was 3.7 years. About 40% switched from drug originator to biosimilar. Pharmacokinetic analysis showed a moderately variable time-profile both of adalimumab concentration and ADA titres. Drug clearance was affected by 2 covariates: ADA titres (power increased 12%) and weight (allometric effect + 0.85 Kg/h). We observed a complete clinical response (CID) after only 3 months follow-up in 65% of children, who maintain remission also at 6 and 24 months. In the first 12 month of therapy, higher clinical inflammation at baseline is related to greater pharmacodynamic effect and better clinical response. The predicted adalimumab concentration (Css), at the same drug dose, were on average lower in patients with mild and high disease activity score. After 3 and 6 months of follow-up, the percentage of children with HDA was smaller in the upper drug exposition quantile than in lower one. However, the model did not predict (prediction rate 95%) long-term relapses (> 24 months).
Conclusion: This targeted risk analysis on the effect of ADA on the clinical incidence of loss of response has very important impact in our clinical practise. Our findings, together with target adalimumab ranges based on exposure-clinical response relationships, highlights the need of further pharmacological investigation to establish model-based personalized treatment approaches. The monitoring of the immunogenicity of the drug will therefore be implemented and will become the subject of future studies.
References: Marino A. *Anti-adalimumab antibodies in a cohort of patients with juvenile idiopathic arthritis: incidence and clinical correlations.* Clin Rheumatol 2018. Bartelds G.M. *Development of antidrug antibodies against adalimumab and association with disease activity and treatment failure during long-term follow-up.* JAMA 2011.
Disclosure of Interest: None Declared

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MULTIDIMENSIONAL ASSESSMENT OF DAMAGE AT TRANSITION IN JIA

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Introduction: Since Juvenile Idiopathic Arthritis (JIA) can persist into adulthood, these patients should be efficiently transitioned from paediatric to adult rheumatology services. Adult rheumatologists should evaluate not only the current disease activity but also consider the patient's long medical history and accumulated damage.

Objectives: The study aims to describe the outcomes and multisystem damage in a newly established cohort of patients with non-systemic JIA referred to the University Hospital of Padova. The assessment includes not only joint damage but also reproductive and ocular health.
Methods: At the transfer visit from peadiatric to adult rheumatology services, patients are prospectively enrolled and disease activity and damage are clinically scored by JADAS10-CRP, DAS28 and JADI. Multi-dimensional assessments include blood tests, magnetic resonance imaging (MRI) of the most affected joint through time, gynaecological or andrological referral. The MRI protocol includes T1, T2, STIR, PETRA, and DIXON sequences that have been blindly scored by a trained radiologist. The radiological score is an adapted version of the JAMRIS score for the knee in JIA without contrast enhancement. Gynaecological evaluation includes clinical evaluation, blood hormone levels and transaddominal ultrasound scan.
Results: The cohort consists of 82 patients transferred to our unit between 2017 and 2024, mostly females presenting with ANA positive oligoarticular JIA and treated with DMARDs. Almost 30% of patients had active disease with a median JADAS10CRP 8.5 (IQR 5.7). Among 50 patients with sufficient follow up time, nearly one-third relapsed within 3 years. The primary risk factor for relapse was a previous history of monoarthritis, independent of other disease characteristics, including ANA positive early onset classification. Among 82 patients, 57% (47) had JADI score >0. However no predictors for JADI A or JADI E could be identified among clinical and treatment variables, except for uveitis for JADI E. 19 patients (23.3%) underwent joint surgery before transition and 10% of patients had complicated uveitis. 22 patients underwent MRI of the most affected joint – mostly the knee-, diplaying at least 1 lesion in 21/22 cases. Residual joint effusion was found in 77% of cases, synovial thickening in 63%, bone marrow oedema in 40%, bone erosions in 22%. These lesions were found in clinically active but also in clinically inactive patients (12 patients), suggesting high rates of subclinical synovitis. Fitted models for MRI damage prediction could not find any significant result. 17 female patients underwent gynaecological evaluation finding high rates of dysmenorrhoea (71%) and polycystic ovary morphology (12%).
Conclusion: Patients transitioning from paediatric to adult rheumatology services exhibit high rates of residual joint activity and damage in their most affected joints. These findings emphasize the need for careful therapy management and highlight the risks of therapy reduction in this population.
Disclosure of Interest: None Declared

PReS25-ABS-1203

EXPERIENCE WITH JANUS KINASE INHIBITORS IN REFRACTORY JUVENILE IDIOPATHIC ARTHRITIS PATIENTS: A SINGLECENTER REAL-WORLD STUDY

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Introduction: Juvenile idiopathic arthritis (JIA) is a heterogeneous chronic inflammatory disorder in children, and a subset of patients remains refractory despite multiple biologic treatments. Janus kinase inhibitors (JAKi) have emerged as a promising therapeutic option for difficult-to-treat cases.
Objectives: To evaluate the effectiveness of JAKi in refractory JIA patients.
Methods: This cross-sectional study included a total of 27 refractory JIA patients who were initiated on JAKi (tofacitinib and/or upadacitinib) at a referral pediatric rheumatology center. JIA patients were categorized according to the ILAR criteria. Demographic, clinical and laboratory data, as well as treatment choices and switches, were recorded.
Results: Among the patients, 21 (77.8%) were female. The median age at diagnosis was 10.2 (IQR,5.4-11.9) years, and the median age at initiation of DMARD was 10.4 (IQR,5.4-12) years. The median age at initiation of biologic agents was 11.1 (IQR,7.8-14.5) years. Based on JIA subtypes, 14 (51.9%) had RF-negative polyarticular JIA, 5 (18.5%) had enthesitis-related arthritis, 4 (14.8%) had oligoarticular JIA, 2 (7.4%) had RF-positive polyarticular JIA, and 2 (7.4%) had juvenile psoriatic arthritis. The first-line biologic agents included etanercept in 19 (70.4%), adalimumab in 6 (22.2%), and infliximab in 2
(7.4%). JAKi were used as fourth-line (range, 2^{nd}-7^{th}) treatment. Except 2 patients, all had failed at least one anti-TNF therapy in addition to either tocilizumab or secukinumab. The median age at JAKi initiation was 15.6 (IQR,13-16.8) years. Tofacitinib was the first-choice in 24 patients (88.9%), while upadacitinib was preferred in 3 patients (11.1%).

17 (62.9%) patients experienced treatment failure with the initial JAK inhibitor. Of these, seven were switched to another JAKi—six to upadacitinib and one to tofacitinib. Among the switched patients, four are currently continuing JAKi, whereas the treatment of three has been switched to other biologic agents.

During follow-up, uveitis was observed in only two patients, both of whom had been diagnosed with uveitis prior to initiation of JAKi. In both cases, tofacitinib was initiated due to uveitis-related symptoms. One patient required a treatment switch due to uveitis reactivation, while the other continued to receive tofacitinib with sustained remission of uveitis symptoms. At the last visit, 14 patients (54.1%) were still on JAKi. All patients demonstrated full adherence to oral JAKi, and no difficulties in compliance were reported during the follow-up period.

Conclusion: This study highlights the promising effectiveness of JAKi in patients with treatment-resistant JIA. Approximately half of the patients who had failed at least three biologic therapies continued JAKi due to observed clinical benefit. However, larger randomized controlled trials are needed to validate these findings and to assess the long-term safety profile of these therapies.

Disclosure of Interest: None Declared

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DIFFICULT-TO-TREAT SUBGROUP IN THE SINGLE-CENTRE COHORT OF PAEDIATRIC STILL'S DISEASE

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Introduction: Difficult-to-treat (D2T) subgroup of Still's disease is characterised by failure to respond to IL-1 and IL-6 blockade, severe or recurrent macrophage activation syndrome (MAS) and lung disease (LD).
Objectives: Review of the presentation and disease outcomes of D2T paediatric Still's disease (SJIA) patients on the background of the SJIA cohort.
Methods: Retrospective electronic record review (2005-2020) and prospective (2021-2024) data collection on patients with SJIA.
Results: 66 patients (39 girls) fulfilling SJIA ILAR and/or PRINTO criteria were identified. Mean follow-up (F/U) time was 6.2±4.3 years, age at diagnosis 7.4±4.7 years. Initial systemic manifestation score (SMS) was 4.4 (SD 1.7). MAS developed in 25/66 (38%) patients, in 18/66 (27%) at SJIA onset. D2T disease was identified in 12/66 (18.2%) patients: Severe/recurrent MAS=6 (LD in 5), therapy failure=5 (one MAS episode in 3), LD with one MAS episode=1. MAS progressed to severe organ involvement in 4 cases: liver and respiratory failure (2 each), gut failure (3), CNS (seizures, coma,1). In one patient pulmonary hypertension (PH) developed. From 7 patients with LD 4 carried HLA-DRB1*15. During MAS, median (IQR) values of selected biomarkers were: Ferritin: 6,329 µg/L (3,674–18,524), IL-18: 15,437 pg/mL (9,904–20,006), CXCL9: 26,789 pg/mL (1,016–124,985), CXCL-10: 7,375 pg/mL (2,109.88–20,183.75), S100A8/9: 26.12 µg/mL (18.31–28.24), S100A12: 237.8 ng/mL (4.6–752.4). 59 patients were treated with anakinra (28 first-line,16 as monotherapy). Canakinumab was used in 17 patients as a 2nd or 3rd line biologic, 21 received tocilizumab,11 had TNF inhibitor, 2 abatacept. Haematopoietic stem cell transplantation (HSCT) was performed in 3 D2T patients (1 autologous), 5 received emapalumab for MAS, one was also treated with MAS825. 9/12 (75%) D2T patients received 3 or more different biologics. Other agents used included JAKi (n=8), cyclosporin A (n=14), etoposide (n=2), mycophenolate mofetil (n=3), cyclophosphamide (n=1). CID without CS at 6 months was achieved in 32/66 (48.5%) patients (none from D2T). At the last F/U 49/66 (74.2%) had
CID without CS, 30 (45.5%) were in full remission. From 12 D2T patients 2 died aged 4.5 (acute pneumonia) and 6 years (heart failure due to PH), both 3 years from SJIA onset. One patient is in full remission, 3 remain active after >5 years of therapy. From 6 patients who reached CID on therapy, 2 developed IBD.
Conclusion: Despite major advances in SJIA therapy, management of D2T subgroup remains a challenge. All 5/12 D2T patients with unfavourable outcome (active or dead) received all available therapies including experimental ones in 3. Our take-home message has been an earlier consideration of allo-HSCT in patients combining recurrent MAS and cardiopulmonary involvement.
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DON'T MISS THE BICEPS TENDON: A NEW CLUE TO ARTICULAR INVOLVEMENT IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Tenosynovitis is a recognized but often overlooked feature of systemic Juvenile Idiopathic Arthritis (sJIA). Regarding musculoskeletal or joint and tendon involvement, most literature has focused on large joint synovitis or tenosynovitis of the lower limbs, while inflammation of the long biceps tendon (LBT) remains poorly described (1), particularly in pediatric patients. This lack of attention may lead to underdiagnosis of LBT involvement.
Objectives: To assess the clinical and imaging involvement of LBT in sJIA. Secondarily, to explore whether LBT involvement is associated with a specific phenotype of the disease.
Methods: We retrospectively analyzed data from patients with sJIA followed at Bicêtre Hospital (France) between 1999 and 2023, and prospectively collected data from 2023 onward, with systematic assessment of ultrasound-detected LBT involvement. Patients were included if clinical or imaging evidence (ultrasound [US] and/or Magnetic Resonance Imaging [MRI]) of LBT involvement was available at disease onset or during flare-ups. Clinical, laboratory, and imaging data were collected at baseline and during the follow-up. US and MRI were performed based on clinical suspicion, particularly in cases of shoulder pain or reduced mobility. Imaging findings were reviewed using standardized pediatric definitions of tenosynovitis (2). Associations between LBT involvement and clinical phenotype (articular or systemic) were evaluated. **Results:** Out of 48 patients with sJIA, 33 were included in the analysis (15 excluded due to missing baseline data). Fourteen out of 33 patients (42%) showed evidence of LBT involvement, based on either clinical findings or imaging. Among these, 11/14 presented clinical signs. Eight patients (5 symptomatic) out of 14 underwent US examination, which was positive in 7 cases. For the remaining patient, no specific mention of LBT investigation was reported on US. MRI was performed only in 2 symptomatic patients and confirmed LBT tenosynovitis in both cases. Regarding the prospective analysis, among the eight newly diagnosed patients who underwent systematic US examination of the LBT, five (62.5%) showed LBT involvement (including two asymptomatic cases). In our cohort, two distinct ultrasound patterns were highlighted: typical tenosynovitis and bicipital synovial cyst. Notably, only 1/14 patients with LBT involvement developed Macrophage Activation Syndrome (MAS) (7% vs 93% without MAS, $p<0.05$), suggesting a potential inverse association between LBT involvement and MAS development.
Conclusion: LBT involvement may be an underrecognized marker of joint-predominant sJIA, particularly in patients without biological features of MAS. Its presence could help delineate a less inflammatory, more articular subtype of the disease. Given its frequency and diagnostic implications, we advocate for routine US assessment of the LBT in sJIA patients, even in those lacking overt arthritis, shoulder pain or systemic symptoms.
References: 1. Shimizu M, Yokoyama T, Wada T, Yachie A. Bicipital synovial cyst in systemic-onset juvenile idiopathic arthritis. J Pediatr. 2010 Jul;157(1):168. doi: 10.1016/j.jpeds.2010.02.014. Epub 2010 Mar 24. PMID: 20338579. 2. Collado P, Martire MV, Lanni S, De Lucia O, Balint P, Guillaume-Czitrom S, Hernandez-Diaz C, Sande NK, Magni-Manzoni S, Malattia C, Rossi-Semerano L, Roth J, Ting T, Vega-Fernandez P, Windschall D, D'Agostino MA, Naredo E; OMERACT Ultrasound Group. OMERACT International Consensus for Ultrasound Definitions of Tenosynovitis in Juvenile Idiopathic Arthritis: Systematic Literature Review and Delphi Process. Arthritis Care Res (Hoboken). 2023 Nov;75(11):2277-2284. doi: 10.1002/acr.25159. Epub 2023 Jun 26. PMID: 37221153.
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T04 - Autoinflammatory diseases

PReS25-ABS-1475

COMPARATIVE PERFORMANCE OF THE EUROFEVER/PRINTO CLASSIFICATION CRITERIA AND TEL HASHOMER CRITERIA FOR FMF DIAGNOSIS: A SYSTEMATIC REVIEW

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Introduction: Until recently, Familial Mediterranean Fever (FMF) diagnosis has primarily relied on the Tel-Hashomer criteria, historically recognized for high diagnostic accuracy [1]. In 2019, the Eurofever/Pediatric Rheumatology International Trials Organization (PRINTO) introduced new classification criteria for hereditary recurrent fevers, including FMF [2]. However, it remains unclear whether these updated criteria provide superior diagnostic accuracy compared to the traditional Tel-Hashomer criteria.
Objectives: In this systematic review, we aimed to directly compare the diagnostic accuracy of the Tel-Hashomer criteria and the Eurofever/PRINTO criteria for FMF.
Methods: We systematically searched PubMed, Embase, CINAHL, and Web of Science databases from inception to March 29, 2025, for relevant observational studies assessing diagnostic accuracy. The primary outcomes evaluated were sensitivity and specificity of the Tel-Hashomer criteria and the Eurofever/PRINTO criteria (clinical-only or clinical + genetic versions). True positives (TP), true negatives (TN), false positives (FP), and false negatives (FN) were calculated based on the reported sensitivity, specificity, and sample sizes.
Results: Out of 130 studies screened, four met inclusion criteria, comprising a total of 1,291 FMF patients and 373 controls. The Tel-Hashomer criteria demonstrated a sensitivity ranging from 82.6% to 96.0% and specificity from 73.1% to 92.6%, with the highest sensitivity observed in genetically confirmed cases [3]. The Eurofever clinical-only criteria had slightly lower sensitivity (70.0%-93.1%) but good specificity (80.5%-96.0%). When genetic testing was added (Eurofever clinical + genetic), sensitivity increased to 94.0%-96.0%, similar to Tel-Hashomer, while specificity remained high (82.9%-90.0%). Notably, false-negative rates were lower with Eurofever+genetic (FN = 7-9) versus Tel-Hashomer (FN = 17-224).
Conclusion: The Eurofever/PRINTO criteria demonstrate comparable diagnostic performance to Tel-Hashomer, particularly when incorporating genetic testing, offering a modern alternative for FMF diagnosis while maintaining high accuracy.
References: [1] Livneh A, Langevitz P, Zemer D, Zaks N, Kees S, Lidar T, et al. Criteria for the diagnosis of familial Mediterranean fever. Arthritis Rheum. 1997;40(10):1879–85. [2] Gattorno M, Hofer M, Federici S, Vanoni F, Bovis F, Aksentijevich I, et al. Classification criteria for autoinflammatory recurrent fevers. Ann Rheum Dis. 2019;78(8):1025–32. [3] Tanatar A, Sönmez HE, Karadağ ŞG, Çakmak F, Çakan M, Demir F, et al. Performance of Tel-Hashomer, Livneh, pediatric and new Eurofever/PRINTO classification criteria for familial Mediterranean fever in a referral center. Rheumatol Int. 2020;40(1):83-91. doi:10.1007/s00296-019-04463-w.
Disclosure of Interest: None Declared

PReS25-ABS-1140

INSIGHTS INTO CORTICOSTEROID USE FOR PFAPA: A STUDY BY THE JIR-CLIPS SURVEY

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Introduction: Periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis (PFAPA) syndrome is a recurrent fever disorder affecting young children. This study evaluates corticosteroid (CS) use in PFAPA, emphasizing the need for standardized treatment strategies to improve outcomes across diverse populations.
Objectives: This study aims to formulate Clinical Practice Strategies (CliPS) regarding CS use in patients with PFAPA that reflect real-life experience of physician in the field.
Methods: This study is part of the Juvenile Inflammatory Rheumatisms (JIR)-CliPS project, an international cross-sectional online survey led by the JIR-network (www.jircohorte.org) and conducted on 5 JIR medical conditions by a consortium of pediatric and adult rheumatologists and immunologists from Europe and beyond. Questionnaires on diagnosis, treatment and follow-up were sent to physicians taking care of PFAPA patients. Data were exported on September 18, 2024, yielding 313 responses from 41 countries. After excluding incomplete or irrelevant entries, 164 responses specifically addressing CS use in PFAPA were analyzed. The current analysis focused on 15 questions on CS use in patients with PFAPA. Analyses were conducted to explore associations between responses and factors such as professional experience, Gross Domestic Product (GDP), and Health Assessment Questionnaire (HAQ) indices.
Results: A total of 164 participants (117 women and 46 men) from 41 countries completed the survey. Seven countries— Türkiye, France, Brazil, Ukraine, Germany, Switzerland, and the UK—accounted for 58% (n=95) of responses. Among participants, 57% (n=94) had over 10 years of experience, 62.2% (n=102) worked in university hospitals, and 63.3% (n=103) were pediatric rheumatologists. A majority (92%, n=151) recognized CS response at the onset of flares as a key diagnostic tool for PFAPA, with no significant differences by professional experience.
Regarding CS prescription practices during flares, 60% (n=99) administered CS once or twice per flare. Child-friendly formulations, such as oral solutions, were available to 73% (n=119) of participants. Nearly half (49%, n=80) reported using CS no more than 5–10 times annually. Most participants (81%, n=133) observed clinical improvement within 3–4 hours of administration, or at most within 12 hours. Six CS formulations were identified and standardized for analysis, with no significant preference differences linked to professional experience. 32% (n=53) routinely prescribed CS at flares, while 68% (n=111) did so non-routinely. Complex Medical Reasons (such as combinations involving attack frequency and severity) tend to appear more frequently in high GDP categories. ($p<0.05$).
Criteria for nonresponse to CS included the need for more than two doses (50.6%, n=83), lack of fever improvement within 24 hours (38.4%, n=63) or 12 hours (36.6%, n=60), recurrence of fever after CS administration (35.4%, n=58), and the requirement for more than one dose of CS (12.8%, n=21). Regarding indications for alternative treatments, 57% (n=93) cited severe attacks, 36% (n=59) flare intervals shorter than two weeks, 27% (n=44) highlighted flare intervals shorter than three weeks or attacks persisting beyond three weeks, and 4% (n=6) noted attacks lasting over one year.
Conclusion: CS at flare onset is a treatment prescribed in most PFAPA patients from the 41 countries studied. However, we observed wide variations in the indication of CS treatment, the modalities of prescription and the criteria for treatment efficacy and failure. Our results emphasize the importance of individualized approaches, particularly in severe or frequent flares. Standardized clinical practice strategies (CliPS) are needed to optimize care and ensure consistent management across diverse healthcare settings.
Disclosure of Interest: None Declared

PReS25-ABS-1642

THE ADDI SCORE FOR ASSESSING DAMAGE IN AUTOINFLAMMATORY DISEASES: DATA FROM THE EUROFEVER REGISTRY

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Introduction: The Autoinflammatory Disease Damage Index (ADDI) is a validated and reliable tool used to quantify damage in patients with autoinflammatory diseases (AIDs). Currently, it has been validated in CAPS, FMF, MKD, and TRAPS [1, 2].
Objectives: This study aims to characterize the spectrum of damage in patients with AIDs and to highlight disease-specific relevant damage items not included in the ADDI.
Methods: The ADDI score, which ranges from 0 (no damage) to 27 (maximum damage), was applied to patients with the ten most prevalent diseases in the Eurofever registry at the time of enrolment. Patients were classified based on the presence or absence of damage. In addition, other clinical manifestations and laboratory data were evaluated to identify potential items for inclusion in future damage assessment tools.
Results: A total of 3211 patients with AIDs were assessed. The ten most prevalent diseases were: Behçet's disease (n=267), CAPS (n=131), CRMO (n=494), DADA2 (n=96), FMF (n=1484), MKD (n=100), PAPA syndrome (n=48), SURF (n=230), TRAPS (n=104), and undefined AID (n=257).
Overall, given the young age at enrolment, highest in PAPA with a median of 19.6 years [11.7; 31.9], the extent of damage was low, with the highest observed in CAPS and DADA2 (median ADDI of 1 [0.0; 3.0]). Among the diseases for which the ADDI was validated, FMF showed the lowest frequency of damage (338, 22.8%), whereas CAPS had the highest (77, 58.8%), followed by MKD (38, 38%) and TRAPS (27, 26%).
In CAPS, damage was predominantly due to hearing loss (37, 28.2%), while in TRAPS it was mainly related to renal involvement (11, 10.6%), particularly persistent proteinuria and renal amyloidosis. Growth failure was the leading cause of damage in FMF (192, 12.9%), MKD (17, 17%), SURF (52, 22.6%), and undefined AIDs (61, 23.7%). Musculoskeletal damage was most prevalent in CRMO (162, 32.8%) and PAPA syndrome (11, 22.9%), mainly due to chronic musculoskeletal pain.
In Behçet's disease, 105 (39.3%) had documented damage, primarily due to ocular involvement (43, 16.1%), including vision loss and blindness (39, 14.6%).
A significant proportion of patients with undefined AIDs had some degree of damage (134, 52.1%), mainly due to growth failure and renal involvement (47, 18.3%), particularly persistent proteinuria. Similarly, in DADA2, damage was relevant and detected in 50 (52.1%) patients, primarily related to neurological involvement (22, 22.9%), especially affecting the central nervous system (18, 18.8%).
Regarding items not included in the ADDI but persistent and relevant for damage we identified the following ones:
DADA2: peripheral neuropathy in 8 (8.9%), aplastic anemia in 4 (4.2%), and gastrointestinal perforation or tumors in 3 (3.1%)
PAPA syndrome: muscular atrophy in 4 (8.3%)
TRAPS: intestinal obstruction in 4 (3.8%)
CAPS: patellar overgrowth in 4 (3.1%)
MKD: camptodactyly in 3 (3%).
Conclusion: The ADDI is effective in assessing damage in validated AIDs and highlights key damage domains across other autoinflammatory diseases. Additional recurrent manifestations suggest the need to refine and expand damage indices to better capture disease burden in non-validated conditions. In the EuroFever cohort, damage was generally mild, also due to the young age at enrolment. **Trial registration identifying number:** NA
References: ter Haar NM et al, Ann Rheum Dis 2017,
ter Haar NM et al, Ann Rheum Dis 2021
Disclosure of Interest: None Declared

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A RETROSPECTIVE STUDY OBSERVING THE ROLE OF SERUM ACE, CHITOTRIOSIDASE AND SOLUBLE CD25 AS BIOMARKERS IN PAEDIATRIC SARCOIDOSIS

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Introduction: Paediatric sarcoidosis is a multisystem granulomatous inflammatory disease.[1] Several biomarkers to inform disease management in paediatric sarcoidosis have been researched, though their application can be limited.[2] Little is known of sarcoidosis biomarkers in children, and adult data is often used as a proxy.[3]
Objectives: This retrospective study observed three biomarkers, prominent within the adult literature (serum angiotensinconverting enzyme (ACE), chitotriosidase (CTO) and soluble CD25 (sCD25)), to assess their role in paediatric sarcoidosis. **Methods:** Electronic notes of patients in a large UK paediatric rheumatology centre over a ten year period (Apr 2015– Apr 2025) were accessed. Data were collected on patients with biopsy-proven sarcoidosis that had at least one simultaneous measurement of serum ACE, CTO and sCD25. Clinician determination of the child's clinical status (flare versus non-flare) was correlated.
Results: Twenty-six simultaneous measurements of serum ACE, CTO and sCD25 in 14 patients were identified. A flare was reported in 7 of the 26 measurements. In cases of flare, absolute values were significantly raised for both CTO ($p=0.004$; mean 680 [0-150nmol/hr/ml], IQR 1788) and sCD25 ($p<0.001$; mean 8023 [0-2500pg/ml], IQR 10873). Whilst mean serum ACE was raised in cases of flare, this was not significant ($p=0.093$). Further, a significantly higher proportion of measurements of CTO ($p=0.002$) and sCD25 ($p<0.001$) were above the upper limit of normal in cases of flare; this was not true for ACE ($p=0.069$).
When combining biomarkers, measurements were elevated in cases of flare most significantly using a minimum of two biomarkers ($p<0.001$) compared to a minimum of one biomarker ($p=0.026$) and when combining all three biomarkers ($p=0.014$), respectively.
Sensitivity and specificity analyses suggested CTO alone was highly specific but had low sensitivity. ACE had a sensitivity of 71% and specificity of 73%. Combining CTO with sCD25 had optimal combined sensitivity and specificity (71% and 95% respectively).
Conclusion: These preliminary data support the use of combining CTO and sCD25 biomarkers in children for the purpose of disease monitoring in sarcoidosis, whilst inclusion of serum ACE may also be beneficial if used in combination with at least one other. Measurement of serum ACE alone was not a reliable biomarker.
Few publications have addressed the area of sarcoidosis biomarkers in children. Whilst this study is limited by small sample size, and the retrospective design may be prone to bias, the results may serve as a promising start in understanding the role of biomarkers in the management of paediatric sarcoidosis.
References: [1] Chiu B, Chan J, Das S, Alshamma Z, Sergi C. Pediatric Sarcoidosis: A Review with Emphasis on Early Onset and High-Risk Sarcoidosis and Diagnostic Challenges. Diagnostics (Basel). 2019;25;9(4):160.
[2] Bazewicz M, Heissigerova J, Pavesio C, Willermain F, Skrzypecki J. Ocular sarcoidosis in adults and children: update on clinical manifestation and diagnosis. J Ophthalmic Inflamm Infect. 2023;13(1):41
[3] Nott K, Nott V, Lever E, Deakin C, Galloway J, Fisher C, Compeyrot-Lacassagne S. Pediatric Sarcoidosis: Retrospective Analysis of Biopsy-Proven Patients. J Rheumatol. 2023;50(7):924-933.
Disclosure of Interest: None Declared

PReS25-ABS-1225
COMPARATIVE EVALUATION OF CHATGPT AND LLAMA FOR RELIABILITY, QUALITY AND ACCURACY IN FAMILIAL MEDITERRANEAN FEVER

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Introduction: In the era of advanced technology, large language models (LLMs) such as OpenAI's ChatGPT and Meta's LLaMA offer rapid access to medical information for both patients and healthcare professionals. Unlike traditional search engines, LLMs empower clinicians to retrieve clinical data rapidly, facilitating decision-making processes. Despite their broad potential and widespread accessibility, studies have highlighted their accuracy and reliability concerns. The utilization of LLMs in rheumatology, particularly in the context of Familial Mediterranean Fever (FMF) remains underexplored.

Objectives: This study aims to evaluate and compare the accuracy, quality, and reliability of responses generated by ChatGPT-4o and LLaMA-3.1 405B models to medical questions related to FMF.

Methods: A total of 31 questions related to FMF were prepared from a clinician's perspective, based on the SHARE and EULAR guidelines. Each question was asked to ChatGPT-4o and LLaMa-3.1 405B only once in separate chat sessions. The randomized responses were independently and blindly evaluated by two pediatric rheumatologists, each with over 20 years of experience, in terms of reliability, quality, and accuracy. Reliability was assessed using the Modified DISCERN score, and quality using the Global Quality Scale (1). The accuracy of the responses was evaluated according to the evidence-based guideline on the genetic diagnosis of FMF published by SHARE and the guideline on FMF management published by EULAR (2,3). The Shapiro-Wilk test, the Intraclass Correlation Coefficient, and the Wilcoxon Signed Rank test were used to analyze the score distribution, inter-rater agreement, and the models' comparative performance, respectively. Readability was assessed using the Flesch Reading Ease, Flesch-Kincaid Grade Level, Gunning Fog Index, Coleman-Liau Index, and SMOG Index (4).

Results: Both models demonstrated moderate reliability according to the modified DISCERN score and high response quality on the Global Quality Score. Although both models aligned with guidelines in terms of accuracy on average, LLaMA exhibited notable inconsistencies. Despite achieving a high average score, some of its responses either directly contradicted guideline-based protocols or contained partially aligned guidelines but erroneous information. In contrast to LLaMA, ChatGPT's responses adhered to guidelines without contradictions; however, certain responses demonstrated informational gaps. Statistical analyses showed that ChatGPT's responses were superior to LLaMA's, with significantly higher scores in accuracy, quality, and reliability. Readability assessments showed that understanding the answers from both LLMs required at least a college-level education.

Conclusion: It is crucial for the clinicians to consider that LLMs may provide incomplete or misleading information.

References: 1. Charnock D, Shepperd S, Needham G, Gann R. DISCERN: an instrument for judging the quality of written consumer health information on treatment choices. J Epidemiol Community Health (1978) [Internet]. 1999 [cited 2025 Feb 4];53(2):105. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC1756830

2. Ozen S, Demirkaya E, Erer B, Livneh A, Ben-Chetrit E, Giancane G, et al. EULAR recommendations for the management of familial Mediterranean fever. Ann Rheum Dis [Internet]. 2016 Apr 1 [cited 2025 Feb 2];75(4):644–51. Available from:
https://ard.bmj.com/content/75/4/644
3. Giancane G, Haar NMT, Wulffraat N, Vastert SJ, Barron K, Hentgen V, et al. Evidence-based recommendations for genetic diagnosis of familial Mediterranean fever. Ann Rheum Dis [Internet]. 2015 Apr 1 [cited 2025 Feb 2];74(4):635–41. Available from: https://ard.bmj.com/content/74/4/635
4. Derivation of New Readability Formulas (Automated Readability Index, Fog Count and Flesch Reading Ease Formula) for Navy Enlisted Personnel [Internet]. [cited 2025 Feb 4]. Available from: https://apps.dtic.mil/sti/citations/ADA006655

Disclosure of Interest: None Declared

PReS25-ABS-1401

PAEDIATRIC UVEITIS - RETROSPECTIVE COMPARISON OF CATARACT SURGERY OUTCOMES WITH OR WITHOUT INTRAOCULAR LENS IMPLANTATION FROM TWO TERTIARY CENTRES IN THE UNITED KINGDOM

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Introduction: Cataract is one of the most common and visually debilitating complications of paediatric uveitis, developing as a consequence of chronic inflammation and steroid use. Cataract surgery can be technically challenging in patients with uveitis, and the outcomes are less certain. (1) Inserting an intraocular lens (IOL) is controversial for paediatric uveitis patients, leading to variable practice across different institutions. This study compares the outcomes of cataract surgery associated with paediatric uveitis with or without IOL implantation.

Objectives: To compare outcomes in children with uveitis undergoing cataract surgery with and without intraocular lens implantation.

Methods: A retrospective comparison study was conducted at two centres, Bristol Eye Hospital (Centre 1-Cataract surgery with IOL implantation) and Sheffield Children's Hospital (Centre 2-Cataract surgery without IOL implantation). All children below 18 years of age with uveitis who underwent cataract surgery between year 2011 and 2024 were included. Pre and post operative outcomes from the two groups were compared, including best corrected visual acuity (BCVA), LogMAR lines of improvement, ocular inflammation and complications. Follow up data upto 2 years post-surgery where available were recorded. Data was analysed using descriptive statistics.

Results: There were total 35 children (43 eyes) identified from both centres, 25 children (30 eyes) from centre-1 and 10 children (13 eyes) from centre 2. The median age at diagnosis in years was 5.5years (centre 1) and 5years (centre 2) and median age at surgery was 9 and 5 years with M:F=2:3 and 1.6:1 respectively. JIA was the most common etiology at both centres (60% and 90% respectively). Anterior uveitis was the most common subtype of uveitis at both centres (29 eyes, 9 eyes respectively). Median preoperative BCVA (IQR) was 0.84 (0.60-1.43) and 1.6 (0.92- 2.48) respectively. The median post-operative BCVA at 3 months, 12 months and 24 months at centre 1 was 0.20,0.2 and 0.10 and at centre 2 was 0.38,
0.50 and 0.15. Percentage of children with 2 or more lines of improvement at 3,12 and 24 months at centre 1 was 82.8%,
93.1% and 80.8% whereas at centre 2 was 84.6%, 75% and 81.8%. Surgical capsulotomy was required in 3 eyes (10%) by 24 months at centre 1. Active anterior chamber inflammation >1+ cells was recorded in 10(33%), 8(36.4%), 5(16.7%) in centre-1 and 1(7.7%), 2(15.4%), 1(7.7%) in centre-2 at 3,12 and 24 months.

Conclusion: Good visual improvement following cataract surgery in children with uveitis with and without IOL would support either of the practices. However, a caveat being that IOL insertion could potentially be associated with active inflammation.

References: 1. Quiñones K, Cervantes-Castañeda RA, Hynes AY, Daoud YJ, Foster CS. Outcomes of cataract surgery in children with chronic uveitis. J Cataract Refract Surg. 2009 Apr;35(4):725–31.

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SHARED TCR VB21.3+ T CELL IMMUNOLOGICAL SIGNATURE BETWEEN MIS-C AND MIS-A

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Introduction: Multisystem inflammatory syndrome in children (MIS-C) emerged shortly after the onset of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, characterized by life-threatening myocarditis and systemic symptoms. In adults, myocarditis was mainly associated to acute COVID-19 and mRNA-based coronavirus vaccines. Although extremely rare, a similar presentation to MIS-C with features of multisystem involvement and myocarditis was reported in adults and termed as Multisystem Inflammatory Syndrome in Adults (MIS-A). The pathophysiology of MIS is not fully understood. Several studies reported an aberrant immune activation in MIS-C involving autoantibodies, inborn errors of immunity, and a unique T cell signature defined by a polyclonal expansion of Vβ21.3+ T cells. In contrast, due to the rarity of MIS-A cases, T cell repertoire anomalies in MIS-A remain underexplored.
Objectives: We investigated the T cell response in a total of 16 cases of MIS-A to determine whether MIS-A shares the T cell receptor (TCR) Vβ repertoire skewing observed in MIS-C.
Methods: We explored the T cell response in cryopreserved peripheral blood mononuclear cells and fresh blood from Danish (n=5 patients) and French (n=11 patients) MIS-A cohorts, respectively. TCR Vβ repertoire and T cell phenotype were analyzed by spectral flow cytometry.
Results: Five Danish MIS-A patients were hospitalized between December 2020 and February 2022 upon SARS-CoV-2 infection. The patients presented with persistent fever, signs of hyperinflammation, gastrointestinal symptoms, and myocardial dysfunction. Laboratory results from the first days of hospital admission showed elevated levels of C-reactive protein in all five individuals. High levels of D-dimer, brain-type natriuretic peptide, and troponin were seen in several patients. Our data from the analysis of the TCR Vβ repertoire showed an expansion of Vβ21.3+ T cells in at least one of the three T cell subsets, CD3+, CD4+, or CD8+ T cells in 3 MIS-A patients. We also observed in all MIS-A patients an upregulation of the expression of activation and exhaustion markers (CD38, HLA-DR, TIM-3, and PD-1) on Vβ21.3+ cells compared to Vβ21.3- T cells. Additionally, we found a higher abundance of effector memory T cells (CD45RA-CCR7-) within the Vβ21.3+ T cells compared to the Vβ21.3- T cells.
To confirm these findings, we analysed data from the largest MIS-A published cohort to date (11 patients). TCR Vβ repertoire screening was performed in MIS-A patients and control cohorts including patients with COVID-19 associated myocarditis, post BNT162b2 mRNA vaccine-related myocarditis, and flu associated myocarditis. We found an expansion of Vβ21.3+ T cells in 6/11 MIS-A patients versus 3/15 control patients.
Conclusion: Our results highlight a skewing of the TCR Vβ repertoire towards a Vβ21.3 response in MIS-A similar to what was previously reported in MIS-C, in CD3, CD4, and CD8 T cells. Thus, the immunological signature of expanded and activated Vβ21.3+ T cells is also common between MIS-C and MIS-A and provide further evidence that these two medical conditions are highly similar and may be manifestations of the same immune dysregulation in children and adults.
Disclosure of Interest: None Declared

T06.b - Inborn errors of immunity and autoimmune diseases

PReS25-ABS-1374

EXPANDING THE SPECTRUM OF AIRE-RELATED AUTOIMMUNITY: A CASE OF PRIMARY SJÖGREN'S SYNDROME IN EARLY CHILDHOOD

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Introduction: Sjögren's syndrome (SS) is a chronic autoimmune disorder characterized by lymphocytic infiltration of exocrine glands, though its molecular pathogenesis remains unclear. The autoimmune regulator gene (AIRE) is crucial for central immune tolerance, and its dysfunction predisposes to autoimmunity, including SS. In AIRE-deficient mice, early lacrimal gland inflammation and signalling changes mimic SS, but in humans, this association is rarely reported.
Objectives: We describe a paediatric case of a primary SS most likely due to a heterozygous variant in AIRE gene.
Methods: Case-report
Results: We report a 4-year-old girl with no relevant past medical history and a family history of systemic lupus erythematosus (maternal grandmother), referred for bilateral submandibular swelling persisting for over a year, associated with intermittent parotid gland enlargement and episodes of unexplained high fever (~39ºC, 1–2 days/month). She also reported xerostomia, with no ocular symptoms. Physical examination revealed elastic, non-tender submandibular swellings (~3.5 cm). Laboratory workup was mostly unremarkable, except for a positive ANA (1:320) and elevated serum amyloid A (max 37 mg/L). ENA panel, anti-dsDNA, and rheumatoid factor were negative. IgG4 and ACE levels were normal. Cryoglobulinemia, monoclonal component (free light chain ratio), hepatitis C and HIV were excluded. Ultrasound revealed enlarged parotid and submandibular glands with heterogeneous echotexture and poorly defined hypoechoic areas, suggestive of chronic inflammation. Normal ophthalmologic evaluation. Submandibular biopsy showed dense B- and Tcell infiltration forming seven lymphoid aggregates (>50 cells) with germinal centres; focus score was 2.1, compatible with SS. No evidence of IgG4-related disease or lymphoma. Given the early onset and systemic features, genetic testing was performed and identified a heterozygous variant of uncertain significance (VUS) in the AIRE gene: c.816G>T (p.Arg272Ser), which has not been previously described in the literature. Pathogenic AIRE mutations have been reported in both autosomal dominant and recessive forms of autoimmune polyendocrine syndrome type 1 (APS-1). Cytokine profiling and familial segregation studies are pending. Treatment with hydroxychloroquine was initiated, with clinical improvement. **Conclusion:** This case highlights a rare paediatric primary SS likely associated with a previously undescribed AIRE gene variant, pending further clarification via familial segregation studies. It supports the hypothesis that AIRE dysfunction may contribute to early-onset autoimmunity beyond classical APS-1. Findings from AIRE-deficient mouse models reinforce a potential pathophysiological link with salivary gland inflammation. Further studies are needed to clarify the role of AIRE variants in isolated autoimmune phenotypes such as SS.
Disclosure of Interest: None Declared

PReS25-ABS-1098

GENOTYPE TARGETED MANAGEMENT FOR CHILDREN WITH MONOGENIC AUTOIMMUNE PHENOTYPE

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Introduction: Inborn errors of immunity (IEI) present clinically as increased susceptibility to infections, autoimmunity, autoinflammation, allergy, bone marrow failure, and/or malignancy.
Objectives: To study autoimmune manifestations and genotype-targeted management options for IEI children with autoimmune phenotype.
Methods: We have gathered a data of 14 children with a diagnosis of IEI with predominant autoimmune diseases , seen by us between August 2023 to April 2025. We have analysed their phenotype , immunotype , genotype and tried to see the response of genotype-targeted treatment options in some of the refractory autoimmune manifestations.
Results: Mean age of onset was 4.2 years. Male-female ratio was 2.5:1. Average delay between the onset of symptoms and the genetic diagnosis was 4.3 years. The commonest autoimmune manifestations were Lupus , Arthritis, Cytopenia/s, Enteropathy, Vasculitis , Interstitial Lung Disease and Endocrinopathy. Uncommon manifestations included granulomatous inflammation & primary sclerosing cholangitis. Few patients presented with overlapping phenotype. Immunoglobulin levels were normal in 4 patients, low in 3 patients , high in 2 patients and not available in 5 patients. Three patients were having low B cells and/or T cells. Out of 14 children , 4 were in clinical remission off glucocorticoids(GC) while rest of the 10 patients were either remained refractory to conventional agents or partially responded or having flare or were not able to wean GC prior to a genotype. Genetic tests revealed pathogenic variants in 8 patients which included LRBA ,RAG1,CTLA4 ,RELA,C1Q ,COPA,STXBP2, WAS and one patient had a likely pathogenic variant in RUNX1. Rest of the 5 patients had VUS in PSMB8 , FCGR2B , DOC8 , ADAMS17 & MMP2 , but except for MMP2, each VUS variant was matching with their respective phenotype. Four children (RELA,STXBP2,FCGR2B, ADAMS17) were in clinical remission off GC prior to a genotype, did not require any change but we have chosen the best possible agent in 2 children (TNFi for RELA & ADAMS17) in case of any flare. Out of 10 non-responding patients, two (LRBA & CTLA4 - Abatacept) could not afford the medications , one was lost on follow up (DOC8) ,one died (WAS) and one was having genotype-phenotype mismatch (MMP2). Five patients (Sirolimus-RAG1, FFP-C1Q, Tofacitinib-COPA, RUNX1, & PSMB8) were given genotypetargeted treatments. Three patients (COPA,RUNX1 & PSMB8) achieved clinical remission off GC and 2 patients showed significant improvement.
Conclusion: We should always keep a high index of suspicion of IEI when there is an early-age of onset (< 5 years) , polyautoimmunity , refractory autoimmune manifestations & overlaping features of autoinflammation , allergy , lymphoproliferation and susceptibility to infections/malignancy. Genotype may guide us to choose the best possible agent which might work better for some refratory autoimmune manifestations until the definitive therapy becomes available.
Disclosure of Interest: None Declared

PReS25-ABS-1478

SIGNIFICANCE AND ROLE OF HYPERFERRITINEMIA SCREENING IN PEDIATRIC PATIENTS

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Introduction: Hyperferritinemia is a key biomarker in the diagnosis of a broad spectrum of life-threatening cytokine storms, including hemophagocytic lymphohistiocytosis (HLH) and macrophage activation syndrome (MAS), and hyperinflammatory conditions, as Still's disease (SD). However, marked ferritin elevation may also be caused by a wide variety of other complex pediatric conditions, which differential is essential in clinical care.

Objectives: To investigate the underlying etiology of markedly elevated ferritin levels in a tertiary-level pediatric center

Methods: Data of patients evaluated in our center from 2020 to 2024 with at least 1 value greater than 1000 ng/ml were retrospectively reviewed. For each episode of hyperferritinemia, the highest value of serum ferritin available was selected and concomitant other laboratory parameters were collected, together with demographic data, diagnosis and outcomes. **Results:** We identified 169 episodes of ferritin > 1000 ng/ml, with a median value of 1785 ng/ml (range: 1007-75313 ng/ml). A total of 149 patients were included with a median age of 9.0 years (IQR, 3.0–14.0), 60% males.

Hyperferritinemia was related to inflammatory conditions in 36% of patients (24% HLH/MAS, 12% rheumatologic diseases), infections (25%), hemoglobinopathies (18%), malignancies (1%) and an heterogenous group of other conditions (30%). Among rheumatic patients, most had SD (67%) and multisystem inflammatory syndrome in children (24%), followed by systemic lupus erythematosus, juvenile dermatomyositis and ANCA-associated vasculitis (5%). Interestingly, within the "other" group hyperferritinemia was observed mainly in hemolytic uremic syndromes (HUS) (29%), chronic renal insufficiency (20%) and hepatological diseases (18%), followed by DRESS and myocarditis/pericarditis (6%)

The median ferritin in the MAS/HLH group was significantly higher (3793 ng/ml, IQR 1655-13513) than in the rheumatic group (1700 ng/ml, IQR 1111-3753) and in the other conditions (1491 ng/ml, IQR 1189-2674).

Most episodes (80%) required hospitalization (with a median length of 13.0 days). Intensive care (ICU) admission was required in 27% of cases. Four patients (2%) died (1 EBV-HLH, 2 severe liver insufficiencies and 1 sepsis in HUS), with a median ferritin of 14119 ng/ml (range 1420 – 51300 ng/ml).

Conclusion: Marked elevated ferritin is a sensitive critical biomarker for the detection of potentially deadly inflammatory conditions such as MAS/HLH. However, a sizable number of patients presented hyperferritinemia in the context of other pediatric disorders, suggesting the need of implementing a diagnostic rule to assist physicians in the early differential of hyperferritinemic conditions.

Disclosure of Interest: F. Lucioni: None Declared, M. Rossano: None Declared, F. Vianello: None Declared, F. Di Stasio: None Declared, S. Lanni: None Declared, G. Chidini: None Declared, G. Montini: None Declared, F. Salvini: None Declared, M. Fumagalli: None Declared, M. Aloi: None Declared, C. Agostoni: None Declared, G. Filocamo: None Declared, F. Minoia Consultant with: SOBI/NOVARTIS

PReS25-ABS-1505

VARIATIONS OF LYMPHOCYTE SUBPOPULATIONS IN MACROPHAGE ACTIVATION SYNDROME ASSOCIATED STILL'S DISEASE: POSSIBLE ROLE OF B CELLS, NK CELLS, AND CD38⁺HLA-DR⁺CD8⁺ T CELLS AS A BIOMARKER FOR THE DIAGNOSIS OF MACROPHAGE ACTIVATION SYNDROME

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Introduction: Early diagnosis of macrophage activation syndrome (MAS) is critically important. However, it remains challenging because clinical manifestations of active phase of Still's disease (SD) and MAS often overlap and also specific diagnostic biomarkers are still lacking. Recently, increase of activated CD8⁺ T cells co-expressing CD38 and HLA-DR (CD38⁺ HLA-DR⁺ CD8⁺ T cells) have been proposed as a characteristic feature with potential diagnostic value in primary or Epstein Barr Virus-associated hemophagocytic lymphohistiocytosis, However, its utility in MAS associated with SD has not been sufficiently investigated.
Objectives: This study aimed to identify some lymphocyte subpopulations as a useful diagnostic biomarker for MAS complicating SD and evaluating their diagnostic performance in differentiating MAS from active phase of SD.
Methods: Peripheral blood mononuclear cells were isolated from whole blood samples of patients with active SD (n = 18), MAS (n = 8), and disease controls (n = 13). Lymphocyte subsets were analyzed using multicolor flow cytometry. Markers that showed significant differences among the groups were further assessed by receiver operating characteristic (ROC) curve analysis to evaluate their sensitivity and specificity for distinguishing MAS from active SD. Serum or plasma levels of IL-18, CXCL9, soluble TNF receptor II, and IL-6 were quantified by Enzyme-linked immuno-sorbent assay. Correlation between cytokine levels and immune cell subsets was analyzed.
Results: In MAS patients, there was a marked reduction in NK cells, naïve B cells, and memory B cells, along with a significant increase in CD38⁺HLA-DR⁺CD8⁺ T cells compared with active SD. ROC analysis revealed area under the curve values, sensitivity and specificity of B cells, NK cell, and CD38⁺HLA-DR⁺CD8⁺ T cells were 0.83/0.63/0.94, 0.81/0.63/0.94, 0.83/1.00/0.61. Furthermore, the combination of these three markers yielded an AUC of 0.97, with a sensitivity of 0.88 and specificity of 1.00. A positive correlation between IL-18 and memory T cells and a negative correlation between IL-18 and NK cells, and a weak positive correlation between CD38⁺HLA-DR⁺CD8⁺ T cells and CXCL9 were observed.
Conclusion: A marked reduction of NK cells, naïve B cells, and memory B cells, along with a significant increase in CD38⁺HLA-DR⁺CD8⁺ T cells were characteristic in MAS. The combination of B cells, NK cells, and CD38⁺HLA-DR⁺CD8⁺ T cells demonstrated high diagnostic accuracy and may serve as a valuable tool to improve MAS detection in clinical practice.
Disclosure of Interest: M. Hatano: None Declared, S. Kaneko: None Declared, F. Miyaoka: None Declared, A. Shimbo: None Declared, H. Irabu: None Declared, Y. Akutsu: None Declared, Y. Hayashi: None Declared, M. Shimizu Grant / Research Support with: Medical and Biological Laboratories Co., Ltd, M. Mori Grant / Research Support with: AbbVie GK, Ayumi Pharmaceutical Corporation, Chugai Pharmaceutical Co., Ltd., CSL Behring K.K., Japan Blood Products Organization, Nippon Kayaku Co., Ltd., UCB Japan Co. Ltd., Asahi Kasei Corp.

PReS25-ABS-1656

EVALUATION OF THE GENERAL CHARACTERISTICS OF PATIENTS CONSULTED TO PEDIATRIC RHEUMATOLOGY FROM THE PEDIATRIC INTENSIVE CARE UNIT

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Introduction: Critically ill children with systemic inflammatory conditions may require specialized care by pediatric rheumatologists. Understanding the profile of patients consulted to pediatric rheumatology from the Pediatric Intensive Care Unit (PICU) can guide early recognition and appropriate treatment.
Objectives: This study aims to evaluate the demographic and clinical characteristics, treatment approaches, and outcomes of patients who were admitted to the PICU and consulted to pediatric rheumatology.
Methods: A retrospective review was conducted of patients admitted to the PICU of Ümraniye Training and Research Hospital between January 2016 and January 2025 and consulted to the pediatric rheumatology department. Data on age, gender, diagnosis, treatment, and survival status were collected from medical records.
Results: A total of 148 patients were evaluated. The mean age was 8.2 years (range 0–18); 67 were male and 81 female. At the time of PICU admission, 26 patients had an established primary rheumatologic diagnosis, including 7 cases of macrophage activation syndrome (MAS) secondary to systemic juvenile idiopathic arthritis (sJIA), 8 with systemic lupus erythematosus (SLE) experiencing disease flares, 1 with familial Mediterranean fever (FMF) presenting with ileus, 1 with interferonopathy (SPENCD) complicated by infections, and 9 with various forms of vasculitis manifesting as hypertension and altered mental status. Consistent with previous reports, SLE emerged as the most common rheumatologic condition requiring intensive care among pediatric patients, typically due to disease exacerbation or severe infectious complications [1], which aligns with our own findings.
Fourteen patients were diagnosed with a rheumatologic disease during their ICU stay, including sJIA (n=3), vasculitis (n=7), Tumor Necrosis Factor Receptor–Associated Periodic Syndrome (n=2), and SLE (n=2). Among 56 patients with prolonged fever, myocarditis, cytopenias, or elevated liver enzymes, 26 were diagnosed with multisystem inflammatory syndrome in children (MIS-C), and 30 with MAS secondary to infections or malignancies. The most frequent non-rheumatologic consult reasons were encephalitis/meningitis, viral myocarditis, and pneumonia with pleural effusion.
The mean ICU stay was 22.3 days. Plasmapheresis was used in 73 patients, hemodiafiltration in 24, mechanical ventilation in 64. Pulse steroid therapy was administered to 85 patients, IVIG to 101, and biologics to 66 (Anakinra in 58; 44.5%).
Overall mortality was 23% (35 patients). Mortality was 10% in MAS secondary to sJIA, 6.2% in vasculitis, and 44% in SLE. Among MIS-C patients, mortality was 11.5%; among secondary MAS cases, 41%. Of 36 patients with a primary rheumatologic diagnosis, 6 died (16.6%).
Conclusion: Rheumatologic diseases in critically ill children can lead to high mortality. Early diagnosis and prompt pediatric rheumatology consultation are essential for improving outcomes.
References: 1. Al-Mayouf SM, Fallatah R, Al-Twajery M, Alayed T, Alsonbul A. Outcome of children with systemic rheumatic diseases admitted to pediatric intensive care unit: An experience of a tertiary hospital. Int J Pediatr Adolesc Med. 2019 Dec;6(4):142-145.
Disclosure of Interest: None Declared

PReS25-ABS-1312

HEAD-TO-HEAD REAL-WORLD RETROSPECTIVE ANALYSIS OF OBINUTUZUMAB VERSUS RITUXIMAB IN CHILDHOOD LUPUS NEPHRITIS

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Introduction: B-cell depletion therapy represents a cornerstone in the management of systemic lupus erythematosus (SLE). Obinutuzumab (OBZ), a glycoengineered, type II anti-CD20 monoclonal antibody, has shown promising efficacy in autoimmune conditions[1,2,3].

Objectives: This study retrospectively compared the efficacy and safety of OBZ versus rituximab (RTX) in childhood-onset SLE (cSLE) lupus nephritis patients.

Methods: We conducted a national, retrospective cohort study of childhood-onset SLE patients with biopsy-proven lupus nephritis who received OBZ between January 1, 2019, and December 31, 2024, at French pediatric rheumatology and nephrology centers. We assessed clinical, serological, and therapeutic outcomes—including changes in global disease activity (SLEDAI-2K) at baseline (M0) and at 3, 6, 12, and 24 months; renal response and flare rates ; corticosteroid-sparing effects as measured by daily steroid dose at each timepoint ; and adverse event incidence — and compared these findings to those in a cohort of cSLE patients with lupus nephritis treated with RTX.

Results: Thirty-seven patients were included (OBZ, n = 16; RTX, n = 21). Baseline demographics, prior background therapy, age at diagnosis, and sex distribution did not differ between groups. Five patients in the OBZ cohort had previously been treated with RTX. At baseline, the OBZ cohort exhibited significantly higher median SLEDAI-2K scores than the RTX cohort (22 [IQR 15–34] vs. 12 [IQR 10–15]; $p < 0.001$). In the OBZ group, mean SLEDAI-2K declined markedly versus baseline at 3, 6, 12, and 24 months ($p < 0.001$), with no further significant changes among post-baseline visits. Mean daily corticosteroid dose fell from 1.21 mg/kg at baseline to 0.20 mg/kg at 24 months ($p = 0.005$). Renal outcomes were favorable: 31.2 % of OBZ-treated patients reached complete renal remission by 3 months and 62.5 % by 6 months, and the mean proteinuria/creatininuria ratio decreased from 499 mg/mmol at baseline to 21.8 mg/mmol at 24 months ($p < 0.001$). OBZ and RTX produced comparable reductions in SLEDAI-2K, corticosteroid tapering, and proteinuria at 3, 6, 12, and 24 months (all $p = 1$), but the median Δ SLEDAI-2K at 3 months was significantly greater with OBZ (–14 points, IQR –17 to –11) than with RTX (–6 points, IQR –8 to –4; $p = 0.002$). Median B-cell depletion duration was 15.0 months (SD 10.0) in the OBZ group versus 10.0 months (SD 5.0) in the RTX group ($p = 0.458$). Adverse events occurred in 43.8 % of OBZ patients versus 14.3 % of RTX patients ($p = 0.067$), with a higher rate of viral and bacterial infections in the OBZ cohort; no deaths were reported.

Conclusion: OBZ demonstrated efficacy comparable to RTX in childhood-onset lupus nephritis, achieving high rates of renal remission with marked reductions in proteinuria. It also produced significant and durable decreases in global disease activity and corticosteroid requirements. Although the OBZ cohort experienced a modestly higher rate of infections, its potent and sustained B-cell depletion supports its potential as an alternative to RTX in refractory SLE. Prospective, randomized trials are warranted to confirm these results and further characterize the safety profile of OBZ.

References: 1. Furie RA, Rovin BH, Garg JP et al REGENCY Trial Investigators. Efficacy and Safety of Obinutuzumab in Active Lupus Nephritis. N Engl J Med. 2025 Apr 17;392(15):1471-1483

2. Furie RA, Aroca G, Cascino MD, et al. Ann Rheum Dis 2022;81:100–107
3. Onuora S. Obinutuzumab effective for lupus nephritis. Nat Rev Rheumatol. 2025 Apr;21(4):193

Disclosure of Interest: None Declared

PReS25-ABS-1308

EFFICACY AND SAFETY OF A MODIFIED HIGH-DOSE PAMIDRONATE PROTOCOL IN PAEDIATRIC CHRONIC NONBACTERIAL OSTEOMYELITIS

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Introduction: Chronic non-bacterial osteomyelitis (CNO), including chronic recurrent multifocal osteomyelitis (CRMO), is a rare autoinflammatory bone disease in children. Pamidronate is a common second-line treatment, typically administered over three consecutive days every three months (CARRA protocol). [1] While effective, this protocol is logistically demanding requiring frequent hospitalizations and overnight stays. To date, no studies have evaluated a simplified oneday pamidronate protocol. This study compares this alternative approach to the traditional approach in clinical practice. **Objectives:** To assess the clinical efficacy and safety of a high-dose, single-day intravenous pamidronate protocol repeated once after three months, compared to the conventional three-day protocol, in paediatric CNO patients.

Methods: We conducted a single center retrospective cohort study of 36 paediatric CNO patients. Patients received either the standard protocol (1 mg/kg/day for three consecutive days, n=14) or a modified protocol (2 mg/kg as a single infusion, n=22), repeated once after three months. The primary outcome was treatment success at 6, 12, and 24 months, defined as absence of treatment escalation (i.e., no need for additional pamidronate infusions or initiation of TNF inhibitors), based on clinical and radiological response. Secondary outcomes included safety, infusion-related reactions, and adverse events. Statistical analyses included chi-square/Fisher's exact tests and Kaplan-Meier survival estimates.

Results: The modified high-dose pamidronate protocol demonstrated comparable efficacy to the standard protocol. There were higher efficacy rates for the modified protocol at 6 months (63.6% vs 30.8%, p=0.060), 12 months (50.0% vs 28.6%, p=0.211), and 24 months (37.5% vs 14.3%, p=0.227), but these differences were not statistically significant. Significantly fewer patients in the modified group required escalation to TNF inhibitors (36.4% vs 71.4%, p=0.040). No adverse events were observed after pamidronate use other than infusion reactions which were mild and similarly distributed over both groups.

Conclusion: The single-day, high-dose pamidronate protocol repeated once after three months shows similar efficacy as the standard multi-day protocol in achieving remission in paediatric CNO patients, with a similar safety profile. These findings support this new protocol as a potential treatment alternative to reduce hospitalization and healthcare costs without increasing adverse event risk.

References: 1. Zhao Y, Wu EY, Oliver MS, Cooper AM, Basiaga ML, Vora SS, et al. Consensus Treatment Plans for Chronic Nonbacterial Osteomyelitis Refractory to Nonsteroidal Antiinflammatory Drugs and/or With Active Spinal Lesions. Arthritis Care Res. 2018 Jul;70(8):1228–37.

Disclosure of Interest: None Declared

PReS25-ABS-1486

PREVALENCE OF LOW BONE MINERAL DENSITY AND DEVELOPING A NOMOGRAM FOR ITS EARLY IDENTIFICATION IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Juvenile idiopathic arthritis (JIA) affects bone health. Various factors in JIA, such as inflammation, disease activity, and limited mobility, contribute to low bone mineral density (BMD). Low BMD has a long-term implication in children with JIA, making them susceptible to fractures. There is a paucity of data on the prevalence and risk factors for low BMD in children with JIA. Though DXA is a preferred modality for identifying low BMD; however, given its accompanying radiation exposure, there is a need for guidance to optimize its rational use for identifying low BMD.
Objectives: To determine the prevalence and risk factors associated with low BMD in children with JIA. Using the factors associated with low BMD, we aim to develop a nomogram to predict the risk of osteoporosis in children with JIA.
Methods: This cross-sectional study was conducted at the Department of Pediatrics, All India Institute of Medical Sciences (AIIMS), New Delhi.
All children diagnosed with JIA as per ILAR criteria were screened. Children aged 5-18 years with JIA and a disease more than one year were included. Children with a history of bisphosphonate intake, bone damage due to infection, trauma, and JIA with overlap syndrome were excluded. Demographic details, clinical assessments, and laboratory investigations were recorded. Disease activity and functional disability were assessed using the cJADAS-10 and Steinbrocker, respectively. BMD was measured using DXA of the lumbar spine and left femoral neck, which was height-adjusted. Height adjustment ensures that children are evaluated based on their growth patterns. Low HA-BMD was defined as a Z-score ≤ - 2 SD at either of the two sites. Analysis was done using Stata 14.0 statistical software (Stata Corp, TX, USA). Stepwise multivariable logistic regression was done to identify factors associated with low HA-BMD.
Results: 101 children were enrolled in this study. The prevalence of low HA-BMD in our study population was 28.7% (29/101). On multivariable regression analysis, the higher cJADAS-10 score, Steinbrockers class, and systemic JIA were independently associated with low BMD. Using these factors, a nomogram to predict the probability of low BMD was developed. This nomogram quantifies the risk and predicts the likelihood of low BMD by assigning scores to each parameter and calculating a total score. The area under the ROC curve is 0.7883.
Conclusion: Significant children with JIA have low HA-BMD. Screening the children with identified risk factors might help in early identification and prevent long-term skeletal complications.

T12 - Genetics, genomics and environment

PReS25-ABS-1103

MAN1B1 MUTATIONS AND GLYCOSYLATION DISORDER: A NEW CAUSE OF MONOGENIC LUPUS?

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Introduction: Monogenic lupus, a specific form of lupus caused by single-gene mutations, has been reported to be associated with a broad range of metabolic disorders, including prolidase deficiency, chronic granulomatous disease and congenital disorders of glycosylation (CDG). While CDG-associated monogenic lupus has already been described, this association has been exclusively linked to *MAN2B1* mutations.
Objectives: To describe the first two cases of monogenic lupus associated with CDG caused by the same homozygous c.1833_1834del (p.Asp613fs) mutation in the *MAN1B1* gene.
Methods: Genetic, clinical and laboratory data, as well as therapeutic strategies, were retrospectively collected from two patients with MAN1B1-CDG who developed lupus.
Results: Patient 1, a 6-year-old female firstborn child of non-consanguineous parents, with genetically confirmed MAN1B1-CDG (homozygous frameshift mutation c.1833_1834del, p.Asp613fs), characterized by developmental delay and characteristic facial dysmorphisms, developed lupus symptoms. She presented with chilblains and malar rash in the presence of ANA, anti-dsDNA, and anti-Rib-P. She exhibited elevated type-I interferon signature (IS) at 50.9 (nv <2.3). Isoelectric focusing of transferin confirmed the diagnosis. A treatment with hydroxychloroquine (HCQ) was started, with positive response.
Patient 2, a 7-year-old female of Sudanese origin born to consanguineous parents, with a diagnosis of MAN1B1-CDG presented with severe multisystem involvement, including pancytopenia, diffuse alveolar hemorrhage, nephritis (24hproteinuria of 1 g) and neurological manifestations (white matter hyperintensities). Laboratory findings revealed positive ANA, anti-dsDNA, anti-Sm, anti-Ro, anti-La, anti-C1q, RF with low C3 and C4 levels. She also showed elevated IS (13.6) and the same *MAN1B1* mutation. She required intensive care and multiple immunosuppressive therapies (glucocorticoids, HCQ, cyclophosphamide, mycophenolate, plasma exchange, extracorporeal membrane oxygenation and anti-CD20) resulting in favorable clinical and biochemical response.
Conclusion: This report highlights the novel association between MAN1B1-CDG and monogenic lupus. α1,2-mannosidase participates in the retrograde transport of misfolded proteins from the Golgi to the endoplasmic reticulum by interacting with the gamma subunit of coat protein complex I (COPI). COPI mediates STING retrieval from the Golgi, a crucial negative regulatory mechanism under homeostatic conditions. MAN1B1 deficiency may impair COPI function, leading to STING accumulation and overactivation of the type-I IFN pathway, contributing to autoimmune dysregulation and lupus development. Further research is necessary to elucidate the precise mechanisms linking *MAN1B1* mutations to SLE.
References: - Han Y, Zhou Y, Pan J et al. MAN2B1 in immune system-related diseases, neurodegenerative disorders and cancers: functions beyond α-mannosidosis. *Expert Rev Mol Med*. 2025 - Pan S, Cheng X, Sifers RN. Golgi-situated endoplasmic reticulum α-1, 2-mannosidase contributes to the retrieval of ERAD substrates through a direct interaction with γ-COP. *MBoC*. 2013
Disclosure of Interest: None Declared

T14 - Juvenile dermatomyositis

PReS25-ABS-1399

EFFECTS OF HYDROXYCHLOROQUINE IN CHILDREN WITH JUVENILE DERMATOMYOSITIS IN NEPAL : A RETROSPECTIVE STUDY ON THE ONLY PEDIATRIC RHEUMATOLOGY CENTRE

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Introduction: Juvenile dermatomyositis (JDM) contributes to more than 3/4th of all juvenile idiopathic inflammatory myositis. Treatment of JDM is multi-pronged, comprehensive, and challenging due to inadequacy of data, heterogeneity of disease, and complications. The literature on hydroxychloroquine (HCQ) in JDM is limited.
Objectives: To study the effect of HCQ in patients with JDM
Methods: Ours is a single center for pediatric rheumatology in Nepal. We analyzed all cases diagnosed with JDM in our center as per modified Bohan and Peter criteria between August 2020 and March 2025. Cross-sectional data on demographics, disease activity, drugs, and course were noted. Bivariate analysis and multivariate logistic regression analysis were performed.
Results: As per the registry, a total of 61 children were diagnosed with definite JDM. All patients had features of dermatitis and myositis at the time of diagnosis. All patients were of age below 16 at the time of diagnosis. 55 (90.1%) had clear information about the use of HCQ and further courses. All patients were commenced on corticosteroids and immunosuppressants irrespective of being on HCQ. 35 (63.6%) patients had taken HCQ whereas 20 (36.4%) patients never used HCQ during their treatment period. A significant association was found between the use of HCQ and the improvement of any rash (malar erythema, Gottron's rash, heliotrope rash, or shawl/V signs) (p=0.012), CHAQ (p=0.024), calcinosis (p=0.044) and proximal myopathy (p=0.016). In multivariate analysis, only those patients with skin rashes (p=0.009) and calcinosis (p=0.021) were found to have a significant association with HCQ therapy. We could not find any association of HCQ therapy with improvement on large or small joint arthritis, vasculitis, lipodystrophy, major organ involvement, or complications.
Conclusion: There is a paucity of literature on the effect of long-term treatment of HCQ in children with JDM. Patients with dermatitis and calcinotic presentations were found to have benefitted from HCQ therapy whereas this drug was not found to leave a significant impact on other aspects like myositis, arthritis, vasculitis, CHAQ, and multi-organic complications. Due to the presence of many possible confounding factors and biases, a causal association cannot be promulgated. However, this study may be an addition to the scarce HCQ literature on JDM. Further longitudinal data will help to ascertain the benefits of HCQ in patients with JDM.
Trial registration identifying number: Not applicable
References: None
Disclosure of Interest: None Declared

PReS25-ABS-1181

PATIENT AND PUBLIC INVOLVEMENT (PPI) IN MYOSCOPE: A STUDY TO BRING A VISUAL MEASURE OF DISEASE ACTIVITY INTO CLINICAL PRACTICE TO HELP CHILDREN WITH DERMATOMYOSITIS

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Introduction: Nailfold capillary changes in juvenile dermatomyositis (JDM) associate with biomarkers of vasculopathy and disease activity[1.] MYOSCOPE is investigating feasibility and benefits of using nailfold capillaroscopy (NFC) in clinic in patients with JDM. Here we describe the patient and public involvement (PPI) which informed (and continues to inform) study design and delivery.

Objectives: 1. To co-design the study in partnership with patients/families, to ensure that all relevant data are captured. 2. To assess whether NFC is acceptable to patients/families, helps them understand their disease better, and improves adherence to treatment.

Methods: The study was co-designed with support of YourRheum (a group of 11-24 year olds with rheumatic disease), 'GenerationR Liverpool' (a network alliance of young people advisory groups which support paediatric health research) and a patient and parent lead, supported by our Patient and Family Coordinator. A new JDM advisory group was established to help further design the study, co-write materials and provide ongoing input (4 meetings over 2 years). 40 patients with JDM (≤18 years of age, any time point of disease) were recruited over 2 UK paediatric rheumatology centres. NFC was performed at clinic visits. Patients and carers were asked to complete age-appropriate questionnaires to explore feelings about NFC, with further evaluation through qualitative patient/family interviews.

Results: Discussion at PPI focus groups led to a fundamental change in study design. Our initial intention was to compare NFC changes to novel biomarkers of vasculopathy. Through PPI work we appreciated the importance of a visual tool, which patients/carers thought would aid understanding of their disease, self-management and empowerment. We changed our study design to evaluate impact of NFC through patient questionnaires/interviews. Age-appropriate information sheets, consent/assent forms and patient/carer questionnaires were co-written with our JDM advisory group. Allowing patients to have a copy of their NFC images, suggested during advisory groups, was added to the protocol. Our advisory group helped determine how images should be shown to patients, including examples of 'non-JDM' and JDM capillaries. A newsletter was produced as suggested after the mid-point PPI meeting. Preliminary data after visit 1 from 71 patient/carer questionnaires suggested that 64/71 (90%) felt "really good" or "fantastic" about NFC. 56/71 (79%) felt visualising their NFC helped them understand how active (or inactive) their JDM was currently and helped them know if they needed medications 63/71 (89%).

Conclusion: Co-design with PPI advocates ensured MYOSCOPE was acceptable and meaningful to patients/families, with further valuable opinions gathered through regular PPI meetings. Preliminary data from parent/carer questionnaires and qualitative interviews suggest an encouraging response to NFC performed in clinic.

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References: 1. Papadopoulou C, Hong Y, Krol P, Al Obaidi M, Pilkington C, Wedderburn LR, et al. The Vasculopathy of Juvenile Dermatomyositis: Endothelial Injury, Hypercoagulability, and Increased Arterial Stiffness. Arthritis Rheumatol. 2021;73(7):1253-1266

Disclosure of Interest: None Declared

T18 - Vasculitides

PReS25-ABS-1171

DEVELOPMENT OF AN INTERNATIONAL COLLABORATIVE STUDY GROUP AND REGISTRY FOR CHARACTERIZING CHILDHOOD-ONSET TAKAYASU ARTERITIS

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Introduction: The rarity of childhood-onset Takayasu arteritis (c-TAK) has resulted in small cohorts for study that has limited the potential for evaluating its course and outcomes.

Objectives: To engage Pediatric Rheumatologists internationally to contribute patient data to a research network targeted to characterizing c-TAK and improving disease outcomes. This will be achieved through the following: *Aim 1*: Create an international c-TAK registry, *Aim 2*: Evaluate the performance of existing disease activity measures, and *Aim 3:* Create and validate a preliminary disease activity score specifically for c-TAK.

Methods: Member sites of Childhood Arthritis Rheumatology Research Alliance (CARRA) and Pediatric Rheumatology European Society (PReS) are invited to enroll patients in this c-TAK registry. The registry is to capture children with a physician diagnosis of c-TAK aged ≤ 18 years at disease onset. Data entry is hosted on Research Electronic Data Capture (REDCap) platform. Registry data includes demographic characteristics, clinical symptoms, organ involvement, laboratory features, vascular imaging, treatment, physician global assessment (PGA) of disease activity, and the features needed to calculate the Pediatric Vasculitis Activity Score (PVAS), Indian Takayasu Activity Score (ITAS2010 and ITAS-A), and 2018 European League Against Rheumatism (EULAR) criteria for active large vessel vasculitis. The assessment of damage using the pediatric vasculitis damage index (PVDI) is collected at follow-up. Data is collected retrospectively from patient medical records at diagnosis, 12-months, and at the final visit on file beyond 15 months (if applicable).

Results: As of abstract submission, the registry has collected data on 72 patients from 12 countries and 31 unique clinical sites. Additional enrollment has begun at 40 other sites, including from 13 additional counties. To date the cohort comprises 80% females. The average age at diagnosis is 12.14 +/- 4.81 years; the average time to diagnosis after first symptoms is 7.53 +/- 13.07 months; 66% received intravenous pulse glucocorticoids (GC) at time of diagnosis, while 85% were started on oral GC. Primary treatments (n=63) prescribed at time of diagnosis include methotrexate (62%), anti-TNF biologic (27%) cyclophosphamide (24%), ongoing intermittent pulse IV GC (11%), and tocilizumab (11%). Secondary treatments included antihypertensives (54%) and anti-coagulants (48%).

Conclusion: Creation of an international c-TAK registry is feasible owing to global collaborations between member sites of CARRA and PReS, and the capabilities for electronic communications and data transmission. Registry data will improve knowledge of presenting symptoms and treatment of c-TAK and increase understanding of the value of current disease activity measures. The successful realization of further project aims is expected.

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PAINFUL SUBCUTANEOUS EDEMA IS ASSOCIATED WITH EARLY AGE AT DIAGNOSIS IN IMMUNOGLOBULIN A VASCULITIS PATIENTS: A MULTICENTER STUDY

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Introduction: Painful subcutaneous edema (PSE) in children and adolescents with immunoglobulin A (IgA) vasculitis (IgAV) occurs at disease onset, mainly in lower and upper limbs. While this feature has been described in case reports and case series,[1,2] to our knowledge, no studies have evaluated the risk factors associated with the presence of PSE in a large IgAV population.
Objectives: To evaluate initial factors of IgAV associated with PSE and its outcomes in children and adolescents in a multicenter study.
Methods: A multicenter study involving four university referral centers in Brazil evaluated 686 children and adolescents (≤ 18 years-old) with IgAV at first 3 months after diagnosis. All patients fulfilled validated EULAR/PRINTO/PRES classification criteria for IgAV. The charts were systematically and retrospectively assessed for demographic data, initial clinical manifestations, laboratory exams and treatments. IgAV patients with PSE were compared to those without PSE. The study received appropriate ethics approval by all participating centers. This study was supported by grants from Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) (#2022/13837-5 to KK & MC-S) and (#2022/12925-8 to NEA & CAS).
Results: PSE was found in 219/686 (31.9%) of IgAV patients during the first 3 months. The sites were lower limbs 192/214 (89.7%), upper limbs 85/214 (39.7%), face 29/214(13.5%), scalp 5/214 (2.3%), back 3/214 (1.4%) and chest 2/214 (0.9%). Multiple localizations of PSE occurred in 81/214 (37.8%). Persistent PSE (≥6 weeks of duration) was found in 4/215 (2%) and recurrent PSE was found in 7/217 (3%). The median age at IgAV diagnosis was significantly lower in PSE patients compared to those without this manifestation [5.0 (1.25-14.8) vs. 6.3 (0.25-17.5) years, p=0.001]. There was a higher duration of purpura and/or petechiae in the PSE group [15 (1-90) vs. 14 (1-120) days, p=0.03] and a significantly higher frequency of petechiae (52.5% vs. 41.3%, p=0.01). Increased CRP was significantly higher in IgAV with PSE compared to without PSE (52.6% vs 41.1%, p=0.03), likewise thrombocytosis (>400.000/mm3) (43.8% vs 35.1%, p=0.04). Logistic regression demonstrated that only age at IgAV diagnosis was inversely associated with PSE (OR=0.986; 95% CI 0.981-0.992; p<0.00001).
Conclusion: PSE occurred in approximately one third of IgAV patients at disease onset, mainly located on lower and upper limbs, and diagnosed predominantly at early age. Recognizing PSE as part of the clinical spectrum of IgAV may help tailor treatment strategies, especially in cases with persistent/recurrent PSE, avoiding prolonged discomfort.
References: 1. Shimizu A, Shimabukuro M, Shimizu M, Asai S, Tomizawa S, Hatakeyama S, Yamada Y. Painful subcutaneous edema of the lumbar region in IgA vasculitis. Pediatr Int. 2019;61(6):624-625.
2. Marcia M, Parodi E. Lumbar swelling and migrating edema in 3- and 4-year-old boys. SAGE Open Med Case Rep. 2022 25;10:2050313X221102112.
Disclosure of Interest: None Declared

PReS25-ABS-1402
GIANT CORONARIES IN CHILDREN WITH KAWASAKI DISEASE: A SINGLE CENTRE EXPERIENCE

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Introduction: Coronary artery abnormalities (CAA) are a dreaded yet potentially preventable stigmata of Kawasaki disease (KD). Timely treatment with IVIg decreases the frequency of CAAs from 25 to 5%[1]. Giant CAA are rare[2] but at higher risk of complications and adverse outcomes.
Objectives: To evaluate the medium-term outcomes of children with KD with giant coronary aneurysms (Z score >10).
Methods: KD cases registered in our tertiary care centre were retrospectively reviewed, and data of children with giant CAA was analysed.

Results: Of the 34 KD cases in our register (2018-2024), we encountered 5 children (14.7%) with giant coronaries (figures 1-5). All children presented as incomplete KD, with delayed immunomodulation and IVIg resistance. One patient had extensive systemic vascular involvement beyond the coronaries. The high proportion of children with giant coronaries as opposed to the reported literature might be due to a referral bias. The diagnosis of KD and initiation of immunomodulation took a median (IQR) of 12 (10-14) days. All received IVIg and oral steroids, with IV methylprednisolone pulse in two (Table 1). All but one received primary intensification with Infliximab. CAAs persisted in all, noted during the 22 patient-years of follow-up. There was one mortality owing to a cardiovascular event. The other four were leading ordinary lives at the last follow-up. Our experience, although limited, was concordant with published literature[3] suggesting that male sex, aneurysms at onset, delayed IVIG therapy, and IVIg resistance are heralds of giant CAAs in KD. Similarly, systemic vascular involvement was associated with a poor outcome.
Conclusion: Incomplete KD may have a high propensity to develop giant coronaries, possibly refractory to immunomodulation. Although rare, giant and systemic arterial aneurysms in KD are life-threatening and difficult to manage, and may progress despite appropriate immunomodulation. As is evident in our single-centre series, delayed diagnosis and immunomodulation are important factors determining CAA prognosis.
References: 1 Friedman KG, Gauvreau K, Hamaoka-Okamoto A, *et al.* Coronary Artery Aneurysms in Kawasaki Disease: Risk Factors for Progressive Disease and Adverse Cardiac Events in the US Population. *Journal of the American Heart Association* 2016; **5**: e003289. 2. Fukazawa R, Kobayashi T, Mikami M, *et al.* Nationwide Survey of Patients With Giant Coronary Aneurysm Secondary to Kawasaki Disease 1999–2010 in Japan. *Circulation Journal* 2018; **82**: 239–46. 3. Jiang S, Li M, Xu K, *et al.* Predictive factors of medium-giant coronary artery aneurysms in Kawasaki disease. *Pediatr Res* 2024; **95**: 267–74.
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PReS25-ABS-1057

PROLONGED SKIN INVOLVEMENT DISTINGUISHES ADOLESCENT FROM CHILDHOOD-ONSET IGA VASCULITIS: A MULTICENTER STUDY

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Introduction: Recently, a single-center study from Turkey on immunoglobulin A vasculitis (IgAV), formerly known as Henoch-Schönlein Purpura (HSP), demonstrated that adolescents exhibited more severe disease manifestations compared to children.[1] However, to the best of our knowledge, there is no multicenter study with a diverse ethnic background comparing demographic data, clinical and laboratory features, and treatments in children and adolescents.
Objectives: To compare demographic data, clinical and laboratory features, and treatments in children versus adolescents with IgAV/HSP in a large multicenter study.
Methods: A multicenter study involving four university and tertiary centers in Brazil evaluated 687 children and adolescents (≤ 18 years-old) with IgAV/HSP at first 3 months after diagnosis. All patients fulfilled the validated EULAR/PRINTO/PRES classification criteria for IgAV/HSP. The charts were retrospectively assessed for demographic data, initial clinical manifestations, laboratory tests and treatments. Data were compared between children (<10 years-old) and adolescents (≥ 10 years-old), according to WHO age range definition.The study received appropriate ethics approval by all participating centers. This study was supported by grants from Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) (#2022/13837-5 to KK & MC-S) and (#2022/12925-8 to NEA & CAS).
Results: IgAV/HSP was diagnosed in 599/687 (87%) children [5.33 (0.88-9.91) years-old] and 88/687 (13%) adolescents [11.33 (10-17.5) years-old]. The median duration of purpura/petechiae was significantly lower in children compared to adolescents [14 (1-120) vs. 15 (2-90) days, p=0.04]. The frequency of persistent purpura/petechiae (defined as ≥6

weeks of duration)[2] was significantly reduced in the former group (7.2% vs. 19.5%, p=0.002), as well as the frequency of gastrointestinal bleeding (17% vs. 34.1%, p=0.01) and proteinuria (49.7% vs. 84%, p=0.002). In contrast, the frequencies of arthritis/arthralgia (82.7% vs. 73%, p=0.03) and orchitis (16.6% vs. 4.8%, p=0.04) were significantly higher in children. Further analysis of laboratory tests showed that the median value of serum IgA was significantly lower in children than in adolescents [179.1 (40-1002.0) vs. 279.0 (104.0-488.0) mg/dL, p=0.01], whereas thrombocytosis was higher (40.1% vs. 23%, p=0.007). Logistic regression demonstrated that persistent purpura/petechiae after IgAV/HSP diagnosis (OR=18.337; 95% CI 1.245-270.137; p=0.034) was the only independently associated variable with dependent variable (adolescent). **Conclusion:** In this large multicenter cohort, IgAV/HSP onset occurred rarely at adolescence, but notably associated with a more prominent disease course compared to childhood onset. Prolonged purpura/petechiae after IgAV/HSP diagnosis was associated with adolescent-onset IgAV/HSP, reinforcing the need for vigilant monitoring in this subgroup.

References: 1. Coşkun S, Güngörer V, Ekici Tekin Z, Çelikel E, Kurt T, Tekgöz N, Sezer M, Karagöl C, Kaplan MM, Polat MC, Öner N, Acar BÇ. Preadolescent-versus adolescent-onset immunoglobulin A vasculitis: The impact of age on prognosis. Pediatr Int. 2023;65:e15426.

2. Roman C, Dima B, Muyshont L, Schurmans T, Gilliaux O. Indications and efficiency of dapsone in IgA vasculitis (HenochSchonlein purpura): case series and a review of the literature. Eur J Pediatr 2019;178:1275-1281.

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PReS25-ABS-1697

CHRONIC PAIN IN PATIENTS WITH CHRONIC NON-BACTERIAL OSTEOMYELITIS (CNO), INCIDENCE AND POTENTIAL RISK FACTORS.

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Introduction: CNO is a rare inflammatory bone disease predominantly affecting long bones[1-6]. Pain and bone swelling are typical presenting features[1-6]. In many, lesions are asymptomatic[1-6]. Whole-body MRI is now recognised as the gold standard for diagnosis[1-7]. Early reports suggested a self-limiting disease for the majority but more recent reports suggest many will still have radiological and clinically active disease into adulthood[7]. Chronic pain is reported but the incidence and risk factors remain poorly described to date.
Objectives: To evaluate chronic pain and identify potential risk factors in our cohort of patients with CNO.
Methods: Clinical,laboratory and radiological data was obtained retrospectively from patients health records,of patients diagnosed from 2019-2024. Patient's demographics and any reports of chronic pain defined as daily pain over three months in duration were noted, with current treatments and most recent whole body MRI imaging at their last clinical assessment.
Results: 33 patients were identified, 58%(N=19) females, 42%(N=14) males. Median age at diagnosis was 11-years (6-15 years). Average disease duration was of 4-years (1-6 years). At last follow up, 50%(N=17) reported pain. In total 15%(N=5) of patients met the criteria of chronic pain. 4 were female. Age at diagnosis was 9 to 12-years. Disease duration ranged from 1-4 years. Most recent WBMRI was, inactive disease =3, partial resolution =1, and worse =1. 4 patients required 1-2 second line agents: Methotrexate and / or anti-TNF therapy. In addition 60%(N=3) required one-year of Bisphosphonates treatment. 60%(N=3) of patients had raised inflammatory markers at time of diagnosis, measured with Erythrocytes Sedimentation Rate and / or C-Reactive-Protein. All five patients stopped regular physical activities, with reduced physiotherapy attendance. All had significant school absenteeism reported.
Conclusion: Female sex,12-years-of-age and above and raised inflammatory markers at diagnosis were identified as risk factors for chronic pain. Poor school attendance and inactivity was significant in those with chronic pain.Our study shows that chronic pain can develop in patients with CNO leading to a significant impact on quality of life and education.
Disclosure of Interest: None Declared

PReS25-ABS-1153

WHEN THE RIGHT DRUG IS OUT OF REACH: ETHICAL AND CLINICAL CHALLENGES IN MANAGING RARE PEDIATRIC RHEUMATOLOGIC DISORDERS IN LOW- AND MIDDLE-INCOME COUNTRIES

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Introduction: Rare rheumatologic conditions such as Complement Hyperactivation, Angiopathic Thrombosis and ProteinLosing Enteropathy (CHAPLE syndrome), and Hyperimmunoglobulin D Syndrome (HIDS) pose significant diagnostic and therapeutic challenges. These diseases demand early and precise initiation of targeted biologic therapies. However, in low- and middle-income countries (LMICs), access to these life-saving treatments is severely limited. Drugs such as pozelimab (anti-C5 monoclonal antibody) and canakinumab (IL-1β inhibitor) offer disease-specific efficacy, yet are often inaccessible. More commonly available alternatives like etanercept and anakinra provide only partial or non-specific immunomodulation, often resulting in suboptimal outcomes. In India, acquiring the appropriate targeted biologic remains a formidable challenge.
Objectives: To highlight the clinical and ethical challenges of managing rare autoinflammatory diseases in India when ideal biologics are unavailable or unaffordable, and to examine the consequences of using less effective substitutes.
Methods: A retrospective analysis was conducted on four pediatric patients—one with genetically confirmed CHAPLE syndrome and three with genetically confirmed HIDS. We evaluated clinical presentation, treatment strategies, drug procurement pathways, cost implications, and outcomes.
Results: The CHAPLE patient initially received steroids and etanercept with minimal clinical benefit. Upon genetic diagnosis, pozelimab was identified as the appropriate therapy and was acquired through a compassionate-use program enabled by international collaboration. Following treatment, the patient exhibited marked clinical improvement within two months.
Of the three HIDS patients, one child was from India and two were from the Maldives. The Indian patient was managed with etanercept due to unavailability of canakinumab. The disease remained refractory, and the patient succumbed within a year. In contrast, the two Maldivian children received canakinumab after genetic confirmation—one transitioned from anakinra, and the other was started promptly post-diagnosis. Both showed significant clinical improvement and achieved remission, with costs covered under the Maldivian national health insurance program
Conclusion: For rare pediatric rheumatologic disorders, access to the correct biologic is essential—not optional. Delayed or inappropriate therapy exacerbates morbidity, increases long-term costs, and undermines trust. LMICs like India require expedited drug approval processes, equitable access schemes, and enhanced international partnerships to address the stark disparities in rare disease care.
Disclosure of Interest: None Declared

PReS25-ABS-1149

CLOSED-LOOP ARTIFICIAL INTELLIGENCE MODEL 'MAVERIK' TO AID IN THE DIAGNOSIS OF CHRONIC NONBACTERIAL OSTEOMYELITIS IN CHILDHOOD: A NATIONAL MULTICENTER PERFORMANCE EVALUATION IN TURKEY

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Introduction: Childhood-onset Chronic Non-bacterial Osteomyelitis (CNO) is an inflammatory bone disease that has become better defined in the last two decades. It is frequently encountered in Pediatric Rheumatology practice. However, the disease is still poorly understood and often confused with malignancy and growing pains, so it can easily be missed in daily practice.

Objectives: We aimed to evaluate the performance of 'Maverik', a computer-based physician-friendly model for a diagnostic tool using closed-loop Artificial Intelligence (AI) by testing it on real patient data with national multicenter participation.

Methods: The study included data from 395 patients from 23 Pediatric Rheumatology centers, and 13 cities in Turkey.

Training of the Model: The model is based on the Python software language, the Tensorflow AI library, and the Recurrent Neural Network and has 12 inner layers and 1024 neurons. To train the model, 83 cases of CNO, 9 cases of growth pain, 9 cases of bone tumors (5 Ewing's Sarcoma and 2 Osteosarcoma, 2 Osteid Osteoma), 9 cases of Juvenile Idiopathic Arthritis (JIA) (5 oligo-JIA, three poly-JIA, 1 Crohn's related Arthritis) and 30 healthy control data were used. During the model's training, the number of data points was increased with the duplication method, and two different pediatric rheumatologists checked that it reflected the real data in the separation. The model was registered by the Turkish Patent and Trademark Office with the name 'Maverik' as a 'Utility Model' with the number 2025-X8XXX, 'Physician Friendly Closed Circuit Artificial Intelligence Software for the Evaluation of Medical Data in Childhood Chronic Non-bacterial Osteomyelitis Disease'.

Evaluation of Model Performance: Laboratory, clinical, sociodemographic, and clinical data of the cases and written details of imaging reports were digitized as 1 (abnormal), 0 (normal range), and -1 (abnormal). Duplication of real data was avoided to avoid 'overfitting' the model.

Results: Maverik processed data input of 395 patients from 23 centers in 0.042 seconds and produced output with a technical margin of error of 0.028. The model adopted a 70-100% prediction interval to recognize CNOs. Accordingly, the model recognized CNO patients with an average prediction rate of 0.7937. Interestingly, it gave a 'missing data-possible CNO' warning for 47 of the 65 outputs (72.31%). This output was the model's interpretation and was not

previously taught. Indeed, all forty-seven outputs had at least one input violation. Despite this, the model correctly recognized 368 outputs (93.17%).

Conclusion: Our study is the first in the literature to develop an AI model as a CNO diagnostic tool, analyze real patient data with multicenter participation, evaluate it, and demonstrate its performance in daily practice. This study shows that the model can help clinicians in the diagnostic stage and differential diagnosis of CNO disease and avoids 'overfitting' by continuing to train itself with real data.

References: 1. Winter, E., et al., *Expert consensus recommendations for the diagnosis and treatment of chronic nonbacterial osteitis (CNO) in adults.* Annals of the Rheumatic Diseases, 2025.

2. McMaster, C., et al., *Artificial Intelligence and Deep Learning for Rheumatologists.* Arthritis Rheumatol, 2022. **74**(12): p. 1893-1905.

Disclosure of Interest: None Declared

PReS25-ABS-1206

AI-BASED FLARE PREDICTION IN JUVENILE IDIOPATHIC ARTHRITIS USING SIMULATED SYMPTOM DATA: A MACHINE LEARNING APPROACH

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Introduction: Juvenile Idiopathic Arthritis (JIA) is a chronic inflammatory condition with unpredictable disease flares, which can result in joint damage and long-term morbidity. Timely identification of impending flares can improve treatment responsiveness and patient outcomes. With the increasing use of mobile health tools, artificial intelligence (AI) provides new opportunities to interpret subtle trends in daily patient-reported symptoms.

Objectives: To evaluate the feasibility of a machine learning model in predicting disease flares using simulated, daily patient-reported symptom data from virtual JIA patients.

Methods: A synthetic dataset of 100 virtual JIA patients was generated, each reporting daily scores for pain, fatigue, morning stiffness, and joint swelling across 180 days. Flares were defined based on clinical threshold combinations of these symptoms. All values were simulated using Gaussian distributions informed by typical clinical observations. A Random Forest classifier was trained on 80% of the dataset and tested on the remaining 20%. To address the highly imbalanced flare distribution (flare rate ~0.07%), the Synthetic Minority Oversampling Technique (SMOTE) was applied to the training data. The selected features were chosen for their relevance in clinical practice (e.g., JADAS components) and for their feasibility in self-reporting via mobile platforms. Laboratory markers such as ESR and CRP were intentionally excluded, as they are not routinely available in daily monitoring scenarios.

Results: The machine learning model achieved an F1-score of 0.81 for detecting flare days in the unseen test set. Precision and recall metrics also demonstrated acceptable performance. Feature importance analysis showed that pain and morning stiffness were the most influential predictors of flare occurrence.

Conclusion: This proof-of-concept study demonstrates that AI models can effectively detect flare risk using only daily patient-reported symptoms, even without clinical or laboratory input. With further validation on real-world data, this approach may support early, remote flare detection and improve digital disease management in children with JIA. Scientific writing assistance was supported by OpenAI's ChatGPT (GPT-4-turbo, May 2024), while model development was performed using traditional machine learning tools.

References: Consolaro A, Ruperto N, Bazso A, et al. Development and validation of a composite disease activity score for juvenile idiopathic arthritis. *Arthritis Care Res (Hoboken)*. 2009;61(5):658–666.

Guzman J, Oen K, Tucker LB, et al. The outcomes of juvenile idiopathic arthritis in children managed with contemporary treatments: results from the ReACCh-Out cohort. *Ann Rheum Dis*. 2015;74(10):1854–1860.

Miotto R, Wang F, Wang S, Jiang X, Dudley JT. Deep learning for healthcare: review, opportunities and challenges. *Brief Bioinform*. 2018;19(6):1236–1246.

Sarker IH, Ehsan M, Rahman MA, et al. A Comprehensive Review on Machine Learning in Healthcare Industry: Classification, Restrictions, Opportunities, and Challenges. *Healthcare*. 2025;13(5):4405. doi:10.3390/electronics13224405.

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