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PG Forum

International publications of interest from India (September–November 2014)

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1. **Grøn KL, Ornbjerg LM, Hetland ML, Aslam F, Khan NA, Jacobs JW, Henrohn D, Rasker JJ, Kauppi MJ, Lang HC, Mota LM, Aggarwal A, Yamanaka H, Badsha H, Gossec L, Cutolo M, Ferraccioli G, Gremese E, Bong Lee E, Inanc N, Direskeneli H, Taylor P, Huisman M, Alten R, Pohl C, Oyoo O, Stropuviene S, Drosos AA, Kerzberg E, Ancuta C, Mofti A, Bergman M, Detert J, Selim ZI, Abda EA, Rexhepi B, Sokka T. The association of fatigue, comorbidity burden, disease activity, disability and gross domestic product in patients with rheumatoid arthritis. Results from 34 countries participating in the Quest-RA program. Clin Exp Rheumatol. 2014;32:869–877.**

This large multinational study – Quantitative Standard monitoring of Patients with RA (QUEST-RA) – assessed the prevalence of co-morbidities and analysed predictors of fatigue including comorbidity burden, disease activity, disability and gross domestic product (GDP) in patients with rheumatoid arthritis (RA). The authors recruited 9874 patients from 34 countries, 16 with high GDP (>24.000 US dollars [USD] per capita) and 18 with low-GDP (<24.000 USD). The prevalence of 31 co-morbid conditions, fatigue (VAS), DAS28 score and physical disability (HAQ) were assessed. Patients reported a median of 2 co-morbid conditions of which hypertension (31.5%), osteoporosis (17.6%), osteoarthritis (15.5%) and hyperlipidaemia (14.2%) were the most prevalent. The majority of co-morbidities were more common in high-GDP countries. The median fatigue score was 4.4 (4.8 in low-GDP countries and 3.8 in high-GDP countries, $p < 0.001$). A high level of fatigue was more prevalent in low-GDP countries (25.4%) than in high-GDP countries (23%). In univariate analysis, fatigue increased with increasing number of co-morbidities, disease activity and disability in both high- and low-GDP countries. In multivariate analysis of all countries, these 3 variables explained 29.4% of the variability, whereas GDP was not significant. This large multi-centre collaborative study provides valuable insights into the common co-morbid conditions seen in patients with RA and their key role in explaining the fatigue which is an important component of this disease. It is interesting to note that the predictors of fatigue are similar in high and low-GDP countries and GDP itself does not correlate with fatigue levels.

2. **Performance of current guidelines for diagnosis of macrophage activation syndrome complicating systemic juvenile idiopathic arthritis. Davì S, Minoia F, Pistorio A, Horne A, Consolaro A, Rosina S, Bovis F, Cimaz R, Gamir ML, Ilowite NT, Kone-Paut I, Feitosa de Oliveira SK, McCurdy D, Silva CA, Sztajnbok F, Tsitsami E, Unsal E, Weiss JE, Wulffraat N, Abinun M, Aggarwal A, Apaz MT, Astigarraga I, Corona F, Cuttica R, D'Angelo G, Eisenstein EM, Hashad S, Lepore L, Mulaosmanovic V, Nielsen S, Prahalad S, Rigante D, Stanevicha V, Sterba G, Susic G, Takei S, Trauzeddel R, Zletni M, Ruperto N, Martini A, Cron RQ, Ravelli A; Paediatric Rheumatology International Trials Organisation, the Childhood Arthritis and Rheumatology Research Alliance, the Pediatric Rheumatology Collaborative Study Group, and the Histiocyte Society. Arthritis Rheumatol. 2014;66:2871–2880.**

In this study, a comparison was made between two different guidelines for discriminating macrophage activation syndrome (MAS) complication systemic juvenile idiopathic arthritis (JIA) from two potentially confusing conditions – active systemic JIA without MAS and systemic infection. The two guidelines compared were: the 2004 diagnostic guidelines

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for hemophagocytic lymphohistiocytosis (HLH-2004) and the preliminary diagnostic guidelines for systemic juvenile idiopathic arthritis (JIA)-associated macrophage activation syndrome (MAS). International pediatric rheumatologists and hemato-oncologists were asked to retrospectively collect clinical information from patients with systemic JIA-associated MAS and confusable conditions. The ability of the guidelines to differentiate MAS from the control diseases was evaluated by calculating the sensitivity and specificity of each set of guidelines and the kappa statistics for concordance with the physician's diagnosis. Owing to the lack natural killer cell activity, soluble CD25 levels and bone marrow aspirate data in all patients, the HLH-2004 guidelines were adapted to enable the diagnosis of MAS when 3 of 5 of the remaining items (3/5-adapted) or 4 of 5 of the remaining items (4/5-adapted) were present. The study included 362 patients with systemic JIA and MAS, 404 patients with active systemic JIA without MAS, and 345 patients with systemic infection. The best capacity to differentiate MAS from systemic JIA without MAS was found when the preliminary MAS guidelines were applied. The 3/5-adapted HLH-2004 guidelines performed better than the 4/5-adapted guidelines in distinguishing MAS from active systemic JIA without MAS. The 3/5-adapted HLH-2004 guidelines and the preliminary MAS guidelines with the addition of ferritin levels $\geq$500 ng/ml discriminated best between MAS and systemic infections. Early identification of MAS continues to be a diagnostic challenge in patients with systemic JIA. This comparison suggests that the preliminary MAS guidelines, possibly with the addition of hyperferritinemia, may prove to be most useful in identification of MAS in systemic JIA and its distinction from other similar conditions.

3. **Rosé CD, Pans S, Casteels I, Anton J, Bader-Meunier B, Brissaud P, Cimaz R, Espada G, Fernandez-Martin J, Hachulla E, Harjacek M, Khubchandani R, Mackensen F, Merino R, Naranjo A, Oliveira-Knupp S, Pajot C, Russo R, Thomee C, Vastert S, Wulffraat N, Arostegui J, Foley KP, Bertin J, Wouters CH. Blau syndrome: cross-sectional data from a multicentre study of clinical, radiological and functional outcomes. Rheumatology (Oxford). 2014 Nov 20. [Epub ahead of print]**

This three-year multicentric study assessed the articular, functional and ocular findings of the first international prospective cohort of patients with Blau syndrome (BS). A total of 31 patients (12 females and 19 males) were recruited from 18 centres in 11 countries. Of the 31 patients, 11 carried the p.R334W NOD2 mutation, 9 the p.R334Q and 11 various other NOD2 mis-sense mutations; 20 patients were sporadic and 11 from five BS pedigrees. Median disease duration was 12.8 years. Arthritis was oligoarticular in 7 patients and polyarticular in 23. The median active joint count was 21. Joints most often affected at presentation were wrists, ankles, knees and PIPs. Radiographs revealed a symmetrical non-erosive arthropathy. Newly described dysplastic bony changes were found in two-thirds of patients. Twenty five patients had ocular disease, with vitreous inflammation in 64% and moderate-severe visual loss in 33%. This series represents the largest report of children with this unusual granulomatour inflammatory disease which affects the skin, eyes and joints.

4. **Prakash J, Singh S, Gupta A, Bharti B, Bhalla AK. Socio-demographic profile of children with Kawasaki disease in North India. Clin Rheumatol. 2014 Nov 22. [Epub ahead of print]**

Based on their observations over a period of 18 years, the authors tested the hypothesis that children with Kawasaki disease (KD) in North India are of a higher socioeconomic status than children with other rheumatologic diseases. One hundred consecutive children with KD were enrolled as cases. Children with other rheumatologic diseases were taken as controls. Assessment of socioeconomic status was done by administering the Aggarwal scale. On univariate analysis, male sex, higher educational status of parents, urban residence, immunization status being complete, and higher scores on Aggarwal scale were found to be significantly associated with KD. On multivariate analysis, only male sex and urban residence were found to be significantly associated with KD. A larger sample size might provide more data on the relationship of Kawasaki disease and socioeconomic status.

5. **Gupta R, Yadav A, Misra R, Aggarwal A. Urinary sCD25 as a biomarker of lupus nephritis disease activity. Lupus. 2014 Oct 10. [Epub ahead of print]**

The authors classified patients with systemic lupus erythematosus as active LN (AN), inactive disease (ID) and active non-renal (ANR) based on baseline disease activity and renal involvement. Urine and serum samples were collected at baseline from all patients and at 3-monthly follow-up from patients with AN. SLE disease activity index (SLEDAI) was used for disease activity assessment at all visits. SCD25 was measured by ELISA and normalized to urinary creatinine excretion and expressed as pg/mg. Urine samples from 10 healthy individuals (HC) served as controls. There were 119 patients (111 females, median age 27 years, 57 AN, 43 ID, 19 ANR). Median SLEDAI was 18, 2 and 8 in AN, ID and ANR groups, respectively. Mean (±SD) urinary sCD25 in the AN, ID, ANR and HC groups at baseline was 741.1 (±794.9), 407.8 (±511.1), 735.4 (±667.7) and 250.9 (±122.2) pg/mg respectively ($p = 0.019$). Mean (±SD) serum sCD25 in AN, ID and ANR was 8285.25 (±5922.2), 6044 (±3501.92) and 6568.72 (±4333.62) pg/ml, respectively. Urinary sCD25 correlated with SLEDAI but did not correlate with serum sCD25 or proteinuria. In four patients who either had relapse, persistent disease activity or developed chronic kidney disease, urinary sCD25 showed rise preceding traditional abnormalities on urine examination. Urinary sCD25 may be a useful biomarker for predicting poor response and relapse in lupus nephritis.

6. **Tripathy R, Panda A, Das B. Serum ferritin level correlates with SLEDAI scores and renal involvement in SLE. Lupus. 2014 Sep 24. [Epub ahead of print]**

The authors studied 76 females with SLE and 50 age-matched healthy females from similar geographical areas. Serum levels of ferritin, IFN-α and IL-6 were quantified by ELISA. Clinical, biochemical, serological and other markers of disease activity (C3, C4 and anti-dsDNA) were also measured. Serum ferritin levels were significantly higher in patients with