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THU0689 ASTHMA AND ELEVATION OF ANTI-CITRULLINATED PROTEIN ANTIBODIES PRIOR TO THE ONSET OF RHEUMATOID ARTHRITIS

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Background: Anti-citrullinated protein antibodies (ACPA) are central to RA pathogenesis, with serum ACPA titers elevated years prior to clinical RA onset. Aberrant protein citrullination may occur in inflamed airway mucosa, forming neoantigens producing ACPA before articular involvement. Thus, individuals with inflammatory airway diseases, such as asthma, may be susceptible to RA-related autoimmunity.

Objectives: To investigate asthma as a risk factor for ACPA+ in serum prior to clinical RA onset.

Methods: We performed a cross-sectional analysis among women in the Nurses' Health Studies to examine whether asthma was associated with pre-RA ACPA+. Incident RA cases occurring after blood draw met research criteria and were each matched to 3 controls by age and menopausal status. Presence of self-reported asthma and potential confounders, including smoking pack-years, were assessed using questionnaires. The sensitive (primary) definition for ACPA+ was: >3 units on CCP2 or elevation (>99th percentile of the control distribution) on a research assay composed of autoantibodies targeting specific citrullinated protein epitopes. The specific (secondary) definition for ACPA+ was: >5 units on CCP2 or elevation of $\geq$2 different antibodies to citrullinated proteins on the research assay. Logistic regression was used to obtain ORs for ACPA+ independent of confounders. We performed secondary analyses using the specific definition for ACPA+ and in subgroups restricted to never smokers and pre-RA cases.

Results: We measured ACPA on 1,135 women, including 286 pre-RA cases. Serum was banked a mean of 9.7 years (SD 5.8) prior to RA diagnosis, mean age of 51.9 years (SD 7.9). Overall, 12% of pre-RA cases reported asthma compared to 7% of controls; pre-RA cases were heavier smokers than controls. Of pre-RA cases, 96 (34%) were ACPA+ by the sensitive definition and 60 (21%) by the specific definition. Among the entire sample, women with asthma were more likely to have ACPA+ (unadjusted OR 2.51, 95%CI 1.42-4.44) compared to those without asthma. After adjusting for age, smoking, BMI, and time to RA/matched date, asthma remained significantly associated with ACPA+ (OR 2.32, 95%CI 1.29-4.16). In the secondary analyses, we found similar associations of asthma with ACPA+ when using the specific definition for ACPA + (multivariable OR 2.28, 95%CI 1.11-4.69) and when restricted to never smokers (OR 3.11, 95%CI 1.29-7.47) and only pre-RA cases (OR 2.22, 95%CI 1.01-4.88).

Table: Odds ratios for elevated ACPA* by asthma status at time of blood draw.

	Unadjusted OR (95%CI)	Multivariable** OR (95%CI)
Entire sample (n=1,135)		
No asthma	1.00 (Ref)	1.00 (Ref)
Asthma	2.51 (1.42-4.44)	2.32 (1.29-4.16)
Never smoker subset (n=573)		
No asthma	1.00 (Ref)	1.00 (Ref)
Asthma	3.19 (1.37-7.39)	3.11 (1.29-7.47)
Pre-RA case-only subset (n=286)		
No asthma	1.00 (Ref)	1.00 (Ref)
Asthma	2.34 (1.13-4.87)	2.22 (1.01-4.88)

*ACPA positivity (sensitive version) was defined as >3 units on the commercial CCP2 assay or >99th percentile of control distribution on the research ACPA assay.

**Adjusted for age at blood draw, time to RA diagnosis/matched date for controls, BMI, smoking pack-years (continuous, pack-years).

Conclusion: Asthma may be a novel risk factor for elevation of ACPA prior to RA onset, independent of smoking. These findings encourage further research on the contribution of airway inflammation to RA pathogenesis.

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THU0690 DISEASE ACTIVITY CORRELATES WITH INSULIN RESISTANCE AND ADIPOCYTOKINES IN PATIENTS WITH DMARD-NAÏVE RHEUMATOID ARTHRITIS

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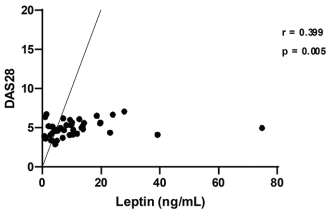
Background: Cardiovascular events such as myocardial infarction and stroke are frequent comorbidities in rheumatic diseases [1]. In relation, components of the metabolic syndrome (MS) including insulin resistance (IR), central obesity, high blood pressure, high triglycerides, and low high-density lipoprotein (HDL) are related to a high rate of endothelial dysfunction and atherosclerosis in patients with RA [2].

Objectives: We aimed to investigate the relationship between disease activity and insulin resistance (IR) and the levels of adipocytokines in non-diabetic patients with newly diagnosed rheumatoid arthritis (RA) who are naïve to disease modifying anti-rheumatic drugs (DMARDs).

Methods: Forty-seven DMARD-naïve patients with RA and 25 age-, gender-, and BMI-matched controls were included. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), 28-joint-count disease activity score (DAS28), serum lipids, glucose, HbA1c, insulin, leptin, resistin, visfatin, and RBP4 levels were measured. Homeostasis model assessment for insulin resistance (HOMA-IR) was calculated. Patients were studied before and 3 months after treatment with DMARDs.

Results: Levels of adipokines were similar in patients with RA and controls (p > 0.05 for all). However, RA patients with active disease (DAS28 > 3.2) had numerically higher levels of leptin (9.3 (3.7-17.4) vs. 7.6 (3.7-11.0), p = 0.289), insulin (8.0 (5.2-12.7) vs. 5.9 (4.2-8.7), p = 0.285), and HOMA-IR (1.9 (1.1-3.0) vs. 1.3 (1.0-1.9), p = 0.209). DAS28 was correlated with HOMA-IR (r = 0.356, p = 0.016), insulin (r = 0.323, p = 0.02), and leptin (r = 0.399, p = 0.005) in the study group (Figure-1). Regardless of the type of treatment modality, leptin levels (7.4 (4.4-13.4) vs. 6.4 (3.3-11.6, p = 0.047) decreased significantly after treatment, as did insulin levels (6.9 (4.9-12.5) vs. 5.9 (4.1- 8.8), p =0.01) and HOMA-IR score (1.7 (1.1-2.7) vs. 1.3 (1.0-2.0), p= 0.012). The reduction in leptin was more prominent in patients with active disease (9.3 (3.7-17.4) vs. 6.9 (3.1-11.4), p = 0.028). The reduction in ESR was correlated with ΔHOMA-IR (r = 0.308, p = 0.039), and CRP reduction was correlated with Δresistin (r = 0.288, p = 0.049) and ΔRBP4 (r = 0.456, p = 0.001).

Conclusion: Disease activity is associated with IR and correlates with circulating levels of adipokines in patients with RA. Treatment with DMARDs reduces leptin and improves IR.



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THU0691 CLINICAL, RADIOLOGICAL, THERAPEUTIC ASPECT AND PROGNOSTIC OF INFECTIOUS SPONDYLODISCITIS WITHOUT BACTERIOLOGICAL EVIDENCE

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Background: Early microbiological diagnosis and multidisciplinary management are the main predictive factor for successful treatment in septic spondylitis. However, the therapeutic management of spondylodiscitis without bacteriological diagnosis is not well codified.
Objectives: To evaluate whether there is clinical, biological or significant imaging between patients with infectious sondylodiscitis as they had or not a microbiological diagnosis.
Methods: Retrospective study including 107 patients hospitalized in our department between 1999 and 2018. The diagnosis was based on clinical, biological, radiological and bacteriological data.
Results: This study involved 107 patients, including 58 men (54.2%) and 49 women (45.8%) with a mean age of 55 years [16–86]. Spinal pain was observed in all cases and the lumbar spine was most affected (54.2%). A neurological deficit was noted in 16.82% of cases. The inflammatory syndrome was present in 90.6% of cases. Radiographs of the spine were abnormal in 83.1% of cases. CT and Spinal MRI were performed respectively in 60% and 78.8% of cases. Disco vertebral biopsy was performed in 73 patients and was contributory in 46.5% of cases.
We divided patients into two groups: patients with a confirmed biological diagnosis (group 1: 45.3%) versus patients in whom the diagnosis had been held on presumptive criteria (group2: 54.2%). There was no statically significant difference in the age (p=0.5), sex (p=0.3), risk factors such as diabetes (p=0.8), the start mode (p= 0.4), the presence of an impaired general condition (p=0.3), night sweats (p=0.1) and a neurological deficit (p=0.8), biological parameters (p=0.3) and the occurrence of complications (p=0.09) between the two groups. Vertebral condensation in radiographs of the spine was higher in group 2 and this was statically significant (p=0.03). In addition, the consumption of unpasteurized milk and positivity of wright serology was higher in the first group (p= 0.001 and p<0.001; respectively). Similarly, contributive histological result of vertebral biopsy was more frequent in group 1 (p=0.007).
Conclusion: Diagnosing infectious spondylodiscitis is facilitated by improved access to MRI testing. However, microbiological diagnosis is the main key to a successful management of this life threatening infection.
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THU0692 OCULAR MANIFESTATIONS IN BEHCET'S DISEASE MAY BE MORE COMMON IN CHILDREN THAN ADULTS: RESULTS OF A SYSTEMATIC REVIEW

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Background: Behcet's disease (BD) can develop in both children and adults, but they may have different clinical features. Ocular involvement is common in BD and causes substantial impairment. The frequency of ocular involvement in BD has a wide range (5 to 89%).
Objectives: This study determined the frequency and type of ocular manifestations in childhood and adult BD and compared prevalence of ocular manifestations by geographic location in those with BD.
Methods: The protocol of ocular conditions in rheumatic conditions was registered at clintrials.gov (NCT03753893). Search terms were: conjunctivitis, keratoconjunctivitis sicca, xeropthalmia, uveitis, eye hemorrhage, optic neuritis, papilledema, orbital disease, retinal artery/vein occlusion, macular edema, retinitis, chorioretinitis, scleritis, iridocyclitits, choroid hemorrhage, blindness and amaurosis fugax in patients with BD. The search was performed with the assistance of an information specialist. Medline, Cochrane and Web of Science were used searching papers that spanned from their inception (1966, 1991 and 1990 respectively) to October 5, 2018. Studies were included if they had a minimum of twenty patients and reported the frequency of ocular manifestations within BD. Random effects models were used to combine the prevalence of ocular manifestations using Revman 5.3. Heterogeneity was evaluated using I^2 and funnel plots.
Results: The search resulted in 3129 articles, of which 33 were included for meta-analysis. Eye manifestations were more frequent in childhood onset BD with the mean [95% Confidence Interval] frequency of 50 [38-63]% compared to 34 [25-43]% in adults. In both children and adults, posterior uveitis (children 27% vs. adults 25%) was the most common ocular manifestation, followed by anterior uveitis (children 18% vs. adults 23%). When comparing the distribution of ocular manifestations in Behcet's in adults, there was geographic variation higher along the ancient Silk Road with ocular manifestations occurring in 40% of patients from Turkey and the Middle East. Ocular manifestations were similar in Europe (36%) and North America (36%), but less frequent in North Africa (26%) and East Asia (20%).
Conclusion: The frequency of ocular involvement is higher in children when compared to adults with BD. The most common manifestation in the eyes is posterior and then anterior uveitis. Ocular involvement also presents regional differences.

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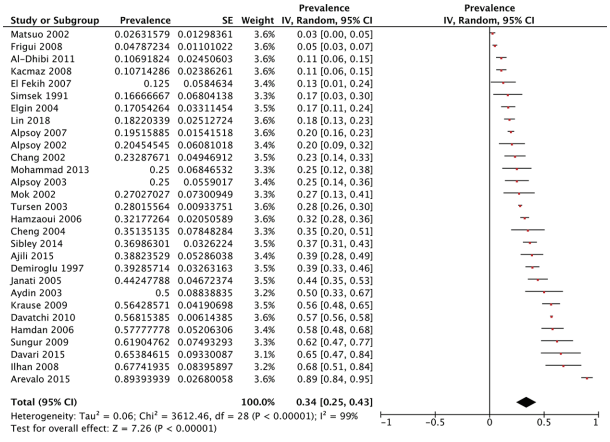

Figure: The prevalence (A) and geographic distribution (B) of ocular manifestations in adults with Behcet's disease.