FRI0304

SERUM IGG-UNDERGALACTOSYLATION PROFILES REFLECT CUMULATIVE EXPOSURE TO SYSTEMIC INFLAMMATION IN SPONDYLOARTHRITIS PATIENTS

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Background: Inflammation in spondyloarthritis (SpA) is often not reflected by elevated acute phase reactants such as C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR). It has been shown that IgG glycosylation patterns are subject to specific alterations (i.e. undergalactosylation) in chronic inflammatory diseases. Since these changes only occur in persistent inflammatory processes, lasting at least one to two $t_{1/2}$ of IgG (24 days), it was hypothesized that IgG-glycan profiles could serve as a surrogate marker for chronic inflammation in SpA patients.

Objectives: To assess the value of serum IgG-undergalactosylation in SpA patients in relation to outcome measures for disease activity, determined by patient reported outcomes, serum inflammatory markers and imaging outcomes.

Methods: Serum samples were obtained from SpA patients at the baseline visit of Be-Giant: a Belgian observational cohort including SpA patients who fulfill the ASAS classification criteria for axial or peripheral SpA. IgG Fc N-glycans were released directly in whole serum by endo- β -N-acetyl-glucosaminidase from *Streptococcus pyogenes* (EndoS), fluorescently labeled with ATPS and analyzed by capillary electrophoresis, rendering glycan profiles with six peaks (Figure 1). Relative peak heights were combined in the undergalactosylation score (UGS), capturing the relative upregulation of non-galactosylated glycans normalized to the total peak height (1). Baseline radiographs (X-SIJ) and magnetic resonance images (MRI) of the sacroiliac joints (SIJ) were assessed by three calibrated readers for sacroiliitis (fulfillment of the modified New York criteria; grading 0 to 4 per SIJ) and for inflammatory lesions according to the Spondyloarthritis Research Consortium of Canada (SPARCC) method (score from 0 – 72) respectively. Grades and inflammatory lesions that were seen by at least 2 readers were used for further analysis.

Figure 1. Example of a serum IgG-specific glycan profile. Adapted from (1), with permission.

Results: Glycan profiles were obtained from 376 SpA patients; UGS was scaled (mean = 0, SD = 1) for further analysis. UGS was independently associated with ASDAS-CRP ($\beta_1 = 0.15$, 95% CI 0.04 – 0.26, $p = 0.006$) and BASFI ($\beta_1 = 0.44$, 95% CI 0.16 – 0.72, $p = 0.002$) but not with BASDAI ($\beta_1 = 0.12$, 95% CI -0.13 – 0.38, $p = 0.34$). UGS showed a weak to moderate correlation with CRP ($R_s = 0.30$, $p < 0.001$) and ESR ($R_s = 0.27$, $p < 0.001$). In axial SpA, UGS was significantly higher in patients with ankylosing spondylitis compared to non-radiographic axial SpA (OR = 2.41, 95% CI 1.60 – 3.73, $p < 0.001$) and showed an independent association with the total grading of the SIJ ($\beta_1 = 0.44$, 95% CI 0.09 – 0.80, $p = 0.01$, Figure 2) and SPARCC score ($\beta_1 = 2.64$, 95% CI 0.98 – 4.31, $p = 0.002$). All models were adjusted for age, gender, BMI, CRP, anti-TNF treatment and symptom duration.

Conclusion: This study shows an independent association of serum IgG undergalactosylation with disease activity and functional impairment in SpA patients. Moreover, UGS was significantly higher in advanced compared to early-stage axial disease and therefore may reflect the cumulative exposure to systemic inflammation.

References:

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Figure 2. Correlation between UGS and X-SIJ total grading of sacroiliitis. R = Spearman's correlation coefficient.

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FERTILITY AND PREGNANCY OUTCOMES IN WOMEN WITH SPONDYLOARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Women with spondyloarthritis (SpA) are often affected by the disease during their reproductive years¹. However, little is known about the impact of the disease and its treatments on fertility and pregnancy outcomes, as well as the effect of pregnancy itself on disease activity².

Objectives: The aim of the study was to determine the effects of spondyloarthritis on fertility and pregnancy outcomes in women with SpA.

Methods: We searched Pubmed, Embase, and Web of Science until 1 November 2019, without any language restriction. All studies assessing fertility, pregnancy outcomes and disease activity during pregnancy in women with spondyloarthritis (axial SpA (axSpA) but also peripheral SpA, including psoriatic arthritis (PsA)) were eligible. The heterogeneity between studies was quantified (I^2), and multiple meta-regressions were carried out to identify potential sources of heterogeneity. In case I^2 was $< 50\%$, a random-effects model was used to pool the available data. Prevalence of events was described as percentages. The odds ratio (OR) and corresponding 95% confidence interval (CI) were used to assess the associations between the disease and the pregnancy outcomes.

Results: Within 4397 eligible studies, 21 articles fulfilling the selection criteria were included in the review, assessing overall 3306 patients (2578 with axSpA and 728 with PsA) and 4104 pregnancies compared to 42248 healthy controls (in 11 studies with a control group). Among the included studies, the risk of bias was evaluated as high, moderate and low in respectively 12, 1 and 8 studies. Regarding pregnancy outcomes, several studies report an increased risk of preterm birth, small for gestational age (pooled OR 2.05, [1.09-3.89], $I^2=5.8\%$ in axSpA) and caesarean section (pooled OR 1.77 [1.45-2.17], $I^2=27.5\%$ in axSpA and pooled OR 1.47 [1.22-1.76], $I^2=0.0\%$ in PsA), without any other unfavourable pregnancy outcome (miscarriage, stillbirth, gestational diabetes or preeclampsia). Further analysis found a significant higher risk for elective caesarean (pooled OR 2.64, [1.92-3.62], $I^2=0.0\%$ in axSpA and pooled OR 1.47, [1.15-1.88], $I^2=0.0\%$ in PsA), without increased risk for emergency caesarean. There was no substantial heterogeneity in the majority of meta-analyses.