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Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory disease predominantly involving the axial skeleton and sacroiliac joints. Although the exact aetiology remains largely unknown, there is thought to be an immune-driven element. Vitamin D deficiency has been associated with a number of autoimmune diseases and is thought to play an important role in modulating the immune system. Low vitamin D levels may contribute to the development and progression of axSpA¹.

Objectives: To study the possible associations between low vitamin D and disease activity in axSpA.

Methods: A systematic literature search using Medline, Embase and Cochrane was performed using MESH search terms "ankylosing spondylitis", "axial spondyloarthropathy" and "vitamin D". Articles examining disease activity measured by BASDAI, ASDAS-CRP, ESR and CRP identified through title/abstract screening, were included in the study, with relevant information extracted.

Results: Out of 495 articles identified from the initial search, 19 observational studies which were mostly (89%) cross-sectional studies were identified. There was considerable heterogeneity between studies, including in the definition of vitamin D deficiency, latitude where study took place and seasonal variation. Vitamin D levels were often lower in patients with axSpA compared to controls. Seventeen studies found no association with vitamin D deficiency and disease activity. The exceptions included one study which measured serum vitamin D receptor levels as opposed to serum 25 (OH) D or 1,25 (OH)₂ D concentrations, and another study whose recruitment occurred over four years and therefore seasonal variation may conflict results. Patients taking NSAIDs or anti-TNF had no difference in vitamin D levels.

Conclusion: Vitamin D deficiency is more prevalent in axSpA but does not seem to associate with increased disease activity. Longitudinal studies are required to better define these links.

References:

- [1] Sizheng Z, et al. Systematic review of association between vitamin D levels and susceptibility and disease activity of ankylosing spondylitis. *Rheumatology* 2014; 53:1595-1603.

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AB0674

CLINICAL AND IMAGING FEATURES IN SPONDYLOARTHRITIS PATIENTS WITH AND WITHOUT HLA-B27 AND HLA-B51

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Background: Despite being commonly expressed in the general population, the human leucocyte antigen (HLA)-B27 allele strongly increases the susceptibility to develop spondyloarthritis (SpA). Likewise, the association between the HLA-B51 allele and the development of Behçet's disease is well documented. However, the exact mechanisms responsible for their pathologic role are still a matter of debate. Moreover, anecdotal reports show an association between HLA-B51 and the clinical spectrum of SpA.

Objectives: To investigate the clinical and imaging findings of SpA patients according to the absence or presence of HLA-B27 or HLA-B51.

Methods: We retrospectively analyzed 236 patients with axial or peripheral SpA, according to the ASAS criteria, referring to two tertiary Rheumatology Clinics between 2017 and 2019. All patients had been tested for HLA-B alleles. Patients with HLA-B51 haplotype and fulfilling the criteria for Behçet's disease were excluded.

Results: Table 1 shows demographic and clinical features of patients, according with the HLA-B haplotype (neither HLA-B27 nor -B51, double negative; positive for HLA-B27 only, positive for HLA-B51 only). Inflammatory low back pain and sacroiliitis, assessed by X-ray or magnetic resonance imaging (MRI), were more prevalent in double negative and HLA-B27 patients, compared to HLA-B51 patients. In this regard, the presence of HLA-B51 was negatively associated with axial manifestations at onset (OR 0.347, 95% CI 0.200-0.604, p<0.0001) and in the course of the disease (low back pain: OR 0.395, 95% CI 0.225-0.689 p<0.0001; sacroiliitis on imaging: OR 0.342 CI 0.189-0.619 p<0.0005). When considering extra-articular manifestation, aphtous lesions were more prevalent in patients with HLA-B51 (p<0.0001), inflammatory bowel diseases in the double negative group

(p=0.0006), and increased C-reactive protein in double negative and HLA-B27 patients (p=0.02).

Table 1.

	All (236 patients)	Double-negative (101 patients)	HLA-B27 (53 patients)	HLA-B51 (82 patients)	p value
Female (%)	167 (71)	73 (72)	28 (53)	66 (60)	0.0024 (cumulative)
Age, years (mean±SD)	53.7±13.3	56.4±12.7 [#]	48.2±14.4 ^{\$}	54±12.7	[#] <0.01 vs HLA-B27 ^{\$} <0.05 vs HLA-B51
Age at diagnosis, years (mean±SD)	48±14.5	50.3±13 [*]	40.8±15.5 ^{\$}	50.2±14.3	[*] <0.001 vs HLA-B27 ^{\$} <0.001 vs HLA-B51
Time from symptoms to diagnosis, years (mean±SD)	3.8±5.7	3.6±4.8	3.2±3.7	4.4±7.5	ns
Type of onset:					0.0031 (cumulative)
-Axial (%)	129 (55)	67 (66)	31 (59)	31 (38)	
-Peripheral (%)	63 (27)	19 (19)	12 (23)	32 (39)	
-Axial and peripheral (%)	44 (19)	15 (15)	10 (19)	19 (23)	

Conclusion: The presence of HLA-B51 identifies a subgroup of SpA patients with peculiar features compared to double-negative or HLA-B27 SpA patients. HLA-B51-related SpA may be an additional condition to be included in the SpA spectrum.

References:

- [1] Bodis G, et al. Role of Human Leukocyte Antigens (HLA) in Autoimmune Diseases. *Rheumatol Ther* 2018;5:5–20.
- [2] Rudwaleit M, et al. The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part II): validation and final selection. *Ann Rheum Dis* 2009;68:777–83.
- [3] Rudwaleit M, et al. The Assessment of SpondyloArthritis International Society classification criteria for peripheral spondyloarthritis and for spondyloarthritis in general. *Ann Rheum Dis* 2011;70:25–31.
- [4] Maksymowych WP, et al. MRI lesions in the sacroiliac joints of patients with spondyloarthritis: an update of definitions and validation by the ASAS MRI working group. *Ann Rheum Dis*. 2019;78:1550-1558.

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AB0675

RED CELL DISTRIBUTION WIDTH AND FATIGUE IN AXIAL SPONDYLOARTHRITIS: A SLEEPER SIGNAL

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Background: Fatigue is a ubiquitous feature of autoimmune conditions, and axial Spondyloarthritis (axSpA) is no exception, with over 50% of patients reporting some degree of fatigue¹. Erythrocyte size variability (as measured by red cell distribution width (RDW)) has been found to correlate with fatigue in a cohort of systemic lupus erythematosus (SLE) patients and may reflect early iron deficiency². We investigate whether this finding holds true in axSpA.

Objectives: To investigate the relationships between fatigue, disease activity, and RDW (as a proxy for functional iron deficiency) in patients with axSpA.

Methods: Cross-sectional analysis performed on patients with axSpA, as defined by the Assessment of SpondyloArthritis international Society (ASAS) criteria, enrolled in a longitudinal data collection study from October 2017 until January 2020 in a single outpatient setting. Patients required a minimum of 1 set of patient-reported outcome measures (PROMs), including the completion of a Functional Assessment of Chronic Illness Therapy (FACIT) Fatigue Scale v4 (numerical score between 0–52 with a lower score indicating greater fatigue), and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). C-reactive protein (CRP) as a biochemical marker of disease activity, as well as Haemoglobin (Hb) and RDW performed within 3 months either side of a PROMs set were extracted and matched. Only one pair of matched data was selected per patient according to the least timeframe between a set of PROMs and bloods of interest (if multiple were available). Anaemia was defined according to World Health Organisation criteria, i.e., Hb <120g/L in

females and Hb <130 g/L in males. Non-parametric analysis of variables was performed using Spearman's rank correlation with significance defined at a p-value <0.05.

Results: 63 patients were included in the analysis (63.5% (40) male, mean time to diagnosis 11.46 (± 9.04) years, 79.4% (50) HLA-B27 positive, 46% (29) current or ex-smokers). Blood parameters showed mean Hb of 139.6 (± 16.03) g/L, mean RDW of 13.55 (± 1.46) %, mean CRP of 5.23 (± 10.82) mg/L. Mean BASDAI score of cohort was 3.69 (± 2.02) and FACIT score 34.18 (± 11.30). Mean absolute interval time difference between a PROMs set and bloods of interest was 16.14 (± 41.11) days.

Univariate analysis showed a statistically significant, negative correlation between fatigue (FACIT) and disease activity (BASDAI), ($p < 0.001$; $r = -0.63$), but failed to demonstrate an association between fatigue and Hb, RDW, or CRP. Sub-group analysis of 51 patients, following exclusion of patients with anaemia (12), engendered a significant and moderately negative correlation between fatigue and RDW ($p = 0.02$, $r = -0.32$) (Figure 1), maintained a significant correlation between fatigue and BASDAI ($p < 0.0001$, $r = -0.56$) and showed a non-significant association between RDW and BASDAI ($p = 0.07$, $r = 0.25$).

Figure 1. Negative correlation between FACIT score and RDW

Conclusion: These findings suggest that RDW may potentially represent a surrogate marker of disease activity in patients with axSpA. RDW may also be implicated in the multi-faceted aetiology of fatigue in axSpA patients, and may reflect functional iron deficiency. A recent cohort study of axSpA patients found anti-TNF therapy ineffective at alleviating fatigue in nearly 80% of patients¹. Management of potential functional iron deficiency as reflected by RDW may offer an alternative treatment target for fatigue in these patients.

References:

- [1] Bedaiwi M, Sari I, Thavaneswaran A, et al. *J Rheumatol*. 2015;42(12):2354.
- [2] Wincup C, Parnell S, Cleanthous B, et al. *Clin Exp Rheumatol*. 2019 Sep-Oct;37(5):852-54.

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AB0676

THE ROLE OF ACPA AND ANA IN SPONDYLOARTHRITIS: HOW THE AUTOIMMUNE DYSREGULATION CAN AFFECT THE COURSE OF DISEASE AND THERAPEUTIC SUCCESS OF MONOTHERAPY DMARDs AND bDMARDs

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Background: Occasional findings of anti-citrullinated-protein-antibodies (ACPA) and anti-nuclear-antibodies (ANA) were rarely described in literature on Psoriatic Arthritis (PsA) and on Spondyloarthritis (SpA) in general. How these autoimmune dysregulations can affect the course of them is not yet understood.

Objectives: The aim of our study is to evaluate if the presence of ACPA and ANA can determine different disease subsets and influence the DMARDs monotherapy (methotrexate) drug survival (DSM) and b-DMARDs multi-failure patients (MF).

Methods: We conducted a retrospective study on patients with Psoriatic Arthritis (PsA) and Spondyloarthritis that fulfilled the ASAS and CASPAR criteria. Patients with diagnosis of connective tissue disease and rheumatoid arthritis and patients ≤ 18 years old were excluded from the study. For each patient, the following variables were considered: age, ACPA, ANA, time between arthritis onset and start of DMARDs (start-time), DSM, switch to b-DMARDs (sw-bDMARDs), arthritis subset (oligoarticular (OA), polyarticular (PA), enthesitis (EA), axial involvement (AI)), number of comorbidities (NC), Charlson Comorbidity Index (CCI).

Results: 150 patients (55% with PsA and 45% with another SpA) were included in the study. No differences were found in age, ANA rate, ACPA rate, start-time, OA, PA, EA, AI, NC and CCI between the PsA and SpA groups.

In the whole group of patients, the ACPA+ subjects (11%) had a significant increase of NC (2.47 ± 1.5 vs 1.6 ± 1.4 , $p = 0.035$), a trend to higher CCI, to switch to b-DMARDs, and to be MF compared to those without ACPA. In the same group, the ANA+ patients (12%) showed shorter DSM (233.5 wk ± 45.9 vs 548.0 wk ± 56.8 , $p = 0.362$) with similar trend in each subgroup (PsA and SpA).

In SpA group, the ACPA+ patients (6.3%) had a trend to shorter DSM (269.0 weeks ± 125 vs 603.96 wk ± 92.8 , $p = 0.492$), to higher sw-bDMARDs, and to be MF, higher NC and CCI compared to those without ACPA. No differences in clinical subset (OA, PA, EA, AI) were observed. In the same group the ANA+ patients had significant higher rate of PA (100% vs 65%, $p = 0.026$) rather than OA (0% vs 35%, $p = 0.025$). No significant differences were found in NC, CCI, MF.

In the PsA group, ACPA+ patients showed a trend to develop PA and EA subsets, shorter DSM (187.5 wk ± 48.7 vs 299.6 wk ± 31.4 , $p = 0.415$), higher rate to sw-bDMARDs and to be MF. The ANA+ PsA patients had higher trend to develop PA and AI subsets rather than OA and EA. All ANA+ patients were MF (100% vs 42%, $p = 0.046$).

Conclusion: The ACPA and ANA positivity in PsA and SpA patients could be suggestive of more severe clinical disease manifestation, higher frequency of comorbidities and lower predicted 10-year survival (CCI). Moreover, this autoimmune dysregulation could be associated with worse drug survival in monotherapy with methotrexate and higher chance to be MF. Therefore, they can be taken into account for clinical management of these patients.

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AB0677

REVISING THE DEFINITION OF REACTIVE ARTHRITIS AND DIFFERENTIATION FROM UNDIFFERENTIATED SPONDYLOARTHRITIS

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Background: Reactive arthritis (ReA) is defined by 1999 ACR criteria as arthritis preceding a bacterial genitourinary (GUS) or gastrointestinal (GIS) infection in 3 days-6 weeks and evidence of triggering infection. Recently, ReA is classified as SpA and patients who do not fulfill SpA criteria are classified as undifferentiated spondyloarthritis (USpA) according to ASAS/EULAR SpA classification criteria.

Objectives: In several case reports which are associated with other infective agents are reported and the definition is extended for some clinicians so that SpA which is occurred after any infection is called as ReA. On the other hand, some researchers still accept the classical definition of ReA. The problem with the heterogeneity of opinions and unstandardized definition of ReA hinders studies about pathogenesis and standardization of treatments. In this study, we aimed to determine the spectrum of the use of the definition of reactive arthritis in publications in PubMed between 2009-2019.

Methods: The ReA keyword is searched in PubMed for the years between 2009-2019. 248 different publications have been identified and included in this research. 89 articles, 47 reviews, 108 case reports, 2 guidelines, and 2 editorials reviewed for the definition of ReA.

Results: Only 42.7% (106 patients) of these publications meet the classical definition which suggests ReA after only GIS and GUS infections. In 4 (1.6%) of the publications ReA was defined after GIS, GUS and oropharyngeal infections; in 3 (1.2%) of the publications after any bacterial infection; in 9 (3.6%) of the publications after any infection. In 8 (3.2%) of the publications, ReA and USpA was used correspondingly. In 39 (15.7%) of the publications the term agent related, ReA was used without making a general definition for ReA. 79 publications (31.9%) have not defined ReA.

According to causative agent and ReA relationship, in 64 (24.6%) general infective agents, in 75 (30.2%) classical agents, in 22 (8.9%) other bacterial agents, in 23 (9.3%) streptococcus, in 10 (4%) intravesical BCG, in 6 (2.4%) HIV, in 6 (2.4%) tuberculosis, in 12 (4.8%) clostridium difficile, in 2 (0.8%) parasites were