Women and spondyloarthritis

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Spondyloarthritis (SpA) is an umbrella term for a heterogeneous group of chronic inflammatory diseases affecting the spine and/or peripheral joints, often associated with extra-articular manifestations, such as psoriasis, uveitis, and inflammatory bowel disease (1). Sex-related differences in patients with SpA are an emerging field in rheumatology (2). Women and men with SpA have different disease phenotypes, clinical courses, and responses to treatment, hence the need to increase awareness among clinicians. Furthermore, women more often have peripheral involvement, widespread pain and fatigue, symptoms that may lead the treating physician to misdiagnose them with fibromyalgia or nonspecific polymyalgia. Sex differences are a relevant and substantial source of variation also in disease experience and responses to therapeutic intervention.

This Special Issue of *Reumatismo*, *The Italian Journal of Rheumatology* provides an overview of sex-specific disparities among patients with SpA and their implications in the clinical setting.

From an epidemiological standpoint, the prevalence of SpA depends on the specific subset of patients considered. Although the occurrence of psoriatic arthritis (PsA) does not generally differ between males and females, axial SpA has long been considered to predominantly affect males. The review by Rizzo *et al.* indicates how these discrepancies may stem from longer diagnostic delays in women, associated with the higher prevalence of non-radiographic axial Spa in women; it also points to a gradual and progressive change toward a gender-equal prevalence of axial SpA (3).

The authors also describe new evidence accounting for an important role of genetics and epigenetics in driving the sex bias in the pathogenesis of SpA. In particular, epigenetics has emerged as an important mechanism for controlling gene expression in sex chromosomes (3).

Delayed diagnosis is a huge issue for women with SpA. In fact, Iagnocco *et al.* showed how musculoskeletal ultrasound may facilitate early diagnosis and prevent misdiagnosis in women (4). Ultrasound may be particularly useful in the detection of subclinical inflammation and structural abnormalities in sites particularly affected in women, such as joints, tendons and entheses. Conversely, magnetic resonance imaging (MRI) is a highly sensitive technique for the diagnosis of sacroiliitis in the early stages (5), although it might not be indicated in women during pregnancy and *postpartum*. Women are more prone to exhibit MRI changes associated with mechanical axial strain (6).

The study by Atzeni *et al.* investigates sex differences in relation to comorbidities frequently associated with SpA, including the increased risk of all-cause cardiovascular disease, obesity, and metabolic syndrome (7). Despite the conflicting results of the studies examined, the review gleaned some interesting evidence on how sex-gender aspects of cardiovascular comorbidities in PsA should be paramount with respect to personalized medicine (8).

The study by Zingone *et al.* discussed other

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comorbidities, particularly inflammatory bowel disease – often misdiagnosed as irritable bowel syndrome or fibromyalgia – which has a higher prevalence in women. This might cause a delay in diagnosis and, thus, a higher disease burden and poor prognosis. It is crucial that gastroenterologists and rheumatologists master all the available screening tools for early referral and better prognosis (9).

Psoriasis and skin manifestations in women with SpA constitute another prominent comorbidity and highlight how disease course, severity and treatment may be significantly influenced by hormonal fluctuations at different stages of life, such as menstruation, pregnancy, *postpartum*, perimenopause and menopause (10).

Patient-tailored counseling, particularly for women, must strive to address their unique needs concerning sexuality, fertility, pregnancy, and breastfeeding, as an essential aspect of holistic patient care. There is a growing focus on issues related to reproductive health in women with SpA, particularly contraception and fertility, which have been exhaustively reviewed by Andrisani *et al.* (11).

An important aspect of SpA patients is pregnancy and fertility issues in women of childbearing age. The patient's management should take into consideration both the need to keep the mother's disease under control and the way various therapies may affect the fetus or their chance of getting pregnant. Appropriate pregnancy planning, including sustained minimal disease activity before conception and during pregnancy, is paramount to minimize pregnancy-related adverse events (11).

The latest data on pregnancy in patients with axial SpA are described in the article by Tincani *et al.* which focuses on the recurrence of pregnancy-related complications and the disease activity throughout gestation and the *postpartum*, with a review of drugs indicated for future mothers (12).

During pregnancy, drug safety is of the utmost importance for both the mother and fetus. Treatment approaches ought to be flexible, and adaptable and include a range of treatment options to effectively address the different needs of female patients at different stages of life (13).

Finally, the study by Ristic *et al.* investigated the differences in health-related quality of life between males and females in a cohort of patients with SpA and found that female patients with axial SpA and PsA had worse scores overall (14).

The articles discussed in this special issue highlight how the ultimate goal of all research efforts is to deepen our understanding of the immunopathogenesis of SpA in women, towards precision medicine in SpA patients to reduce delayed diagnosis and misdiagnosis and preserve the fertility period.

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