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Musculoskeletal and Rheumatic Diseases as Emerging Risk Factors for Reduced Fertility

Maedeh Farhadi[*1,2]

[1.] Department of Public Health, School of Health, Torbat Heydariyeh University of Medical Sciences, Torbat Heydariyeh, Iran.
[2.] Public Health Student, Students Research Committee, Faculty of Health, Torbat Heydariyeh University of Medical Sciences, Torbat Heydariyeh, Iran.
[3.] Public Health Research Center, Torbat Heydariyeh University of Medical Sciences, Torbat Heydariyeh, Iran.
Corresponding author: Maedeh Farhadi FarhadiM1@thums.ac.ir
No 02, Torbat Heydariyeh University of Medical Sciences, Vice Chancellor for Education, Research and Technology Mehr Blvd., Ferdowsi Blvd., Valieasr Twn, Torbat Heydariyeh, Iran.
† P.O. Box 9516160061; Tel: +98 (51) 52421240; Fax: Tel: +98 (51) 52421248.

ABSTRACT.

The importance of musculoskeletal diseases (MSDs) and related immune mediated rheumatic conditions in both women and men is becoming more widely recognized, but underappreciated, as significant contributors to decreased fertility and adverse pregnancy outcomes. During assisted reproductive technology (ART) cycles, there is evidence accumulating from population-based registries, systematic reviews, and clinical cohort studies that indicate that individuals with various conditions like rheumatoid arthritis, systemic sclerosis, juvenile idiopathic arthritis, and others experience elevated rates of subfertility, childlessness, miscarriage, and complications. The biological mechanisms that directly affect gamete quality, implantation, and placental function include hormonal dysregulation, oxidative stress, chronic systemic inflammation, and direct effects. Significant knowledge gaps persist, particularly regarding male fertility and specific nonautoimmune MSDs, despite recent clinical guidelines advocating integrated reproductive health care for these patients. To address this overlooked aspect of health promotion, this editorial calls for a greater level of clinical awareness, regular preconception counseling, multidisciplinary collaboration between rheumatologists, orthopaedists, and reproductive specialists, and dedicated research funding.

Keywords: musculoskeletal diseases; rheumatic diseases; infertility; pregnancy outcomes; assisted reproductive technology; reproductive health; inflammation.

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Introduction

For many years, patients with rheumatic and musculo-skeletal diseases have received much more attention for their joint pain, functional limitations, or systemic inflammations than for their reproductive health. However, increasing amounts of high quality research now show that these conditions many of which peak in the prime of reproduction are consistently associated with lower fertility, more pregnancies aborted and poorer outcomes after ART. This editorial summarises recent epidemiological, mechanistic and clinical findings to argue that the link between MSD and fertility should be a key component of integrated patient care and health promotion (Boussaid et al., 2022).

There is no longer any doubt about the connection between musculoskeletal conditions and abnormal reproduction. Skomsvoll et al. conducted a population-based study of women between the ages of 40 and 42. (2000) discovered that compared to women without MSDs, those with chronic musculoskeletal disorders had a much higher percentage of subfertility and longer intervals between pregnancies (Skomsvoll et al., 2000). More recently, a nationwide Finnish registry study encompassing 19 immune-mediated diseases (Kerola et

al., 2024) demonstrated increased childlessness and fewer children among patients with rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA), systemic lupus erythematosus (SLE), and several other inflammatory rheumatic diseases. Notably, similar patterns were observed in men, a group historically overlooked in fertility research. Chandrashekara et al. in systemic sclerosis. (2025) confirmed reduced fertility and increased rates of miscarriage, including higher rates of miscarriage and (Chandrashekara et al., 2024).

In this population, pregnancy complications also tend to cluster. Kerola and associates. (2024) found that women with inflammatory rheumatic diseases are more likely to experience pre-eclampsia, preterm delivery, small-for-gestational-age infants, non-elective cesarean sections, and admission to the neonatal intensive care unit; SLE and Sjögren's syndrome have the most severe effects (Kerola et al., 2024). Wider reproductive disorders such as endometriosis, adenomyosis, fibroids and polycystic ovarian syndrome, which share inflammatory and hormonal pathways with MSD, also increase the risk of preterm birth, foetal growth suppression and placental pathologies (Vannuccini et al., 2015).

The prognosis for patients with rheumatic or musculo-skeletal disorders undergoing ART appears to be less favourable than for the general population. Systematic review and meta-analysis by Kontogiannis (2026) found that immune-mediated rheumatic diseases, in particular Sjögren's syndrome and rheumatoid arthritis, are associated with a decrease in live births per embryo transfer and overall in live births across disease categories (Kontogiannis et al., 2026). In a single-centre ART cohort, Manouchehri et al. (2025) confirmed higher miscarriage risks and more frequent inadequate gestational weight gain among women with rheumatic diseases compared to controls(Manouchehri et al., 2026).

Similar patterns are seen in other long-term immune-mediated disorders. Although IVF pregnancy rates in non-operated ulcerative colitis may be similar to those in non-IBD populations, inflammatory bowel disease, especially Crohn's disease, is associated with decreased fertility when the disease is active (Vieujean et al., 2022). Large registry data in multiple sclerosis indicate that, after adjusting for confounders, there is no discernible difference in live birth or clinical pregnancy following ART; however, relapse risk may rise in the vicinity of ART procedures (Sparaco et al., 2023).

Disproportionately little research has been done on how rheumatic and musculoskeletal conditions affect male fertility. Boussaid et al. conducted a systematic review. (2022) found that men with autoimmune rheumatic diseases had higher rates of varicocele, hormonal abnormalities, and poorer semen quality (Boussaid et al., 2022). Moreover, it is evident that some medications that modify disease, such as cyclophosphamide, are gonadotoxic. Kerola and associates. (2024) found that men with inflammatory rheumatic diseases also have lower fertility and more childlessness, with impaired spermatogenesis and sexual dysfunction as potential causes (Kerola et al., 2024). In multiple sclerosis, population-based data suggest an association between MS and male infertility or fewer offspring, though altered sexual behaviour may contribute (Toljan & Briggs, 2024).

The main mechanistic theory for how rheumatic and musculoskeletal disorders affect fertility is chronic low-grade systemic inflammation, which interferes with the hypothalamic-pituitary-ovarian (HPO) axis, hinders

follicular development, and lowers oocyte quality. The endometrial environment can be directly harmed by pro-inflammatory cytokines, which can lower implantation receptivity and increase early pregnancy loss. MSDs and reproductive disorders share hormonal and inflammatory pathways (Vannuccini et al., 2015) offer a unifying framework: diseases like endometriosis and RA share prostaglandin dysregulation, interleukin-1, and tumor necrosis factor-α, all of which impact ovulation, fertilization, and placentation. Gamete DNA and mitochondrial function are further harmed in both sexes by oxidative stress, a feature of many MSDs.

Understanding the connection between MSD and infertility has immediate practical implications. Reproductive health is now specifically integrated into rheumatic and musculoskeletal care according to major guidelines. The American College of Rheumatology's 2020 Guidelines for Managing Reproductive Health in Musculoskeletal and Rheumatic Conditions emphasises contraception, preconception counselling, ART, fertility preservation, and multidisciplinary collaboration (Sammaritano et al., 2020). However, the same guideline highlights significant knowledge gaps and low levels of evidence, particularly for men and non-autoimmune MSDs (fibromyalgia, osteoarthritis, and chronic low back pain). Reproductive endocrinologists are rarely consulted by specialists in clinical practice, and many patients are never questioned about their reproductive plans.

For this reason, we recommend three concrete actions. First, all men and women of reproductive age who have been diagnosed with a serious MSD or rheumatic disease should receive regular fertility testing and preconception counseling. Second, it is necessary to create and assess integrated care pathways that connect rheumatology, orthopedics, obstetrics, and reproductive medicine. Third, specific funding for research is desperately needed to close the evidence gaps, especially for intervention trials that look at how disease control affects ART success and prospective cohort studies that quantify fertility risks across the whole spectrum of MSDs.

Conclusion

The evidence is now clear: musculo-skeletal and rheumatic diseases are not neutral in terms of fertility. They reduce the chances of conception, increase the risk of miscarriage and compromise the results of ART. These conditions pose an underestimated burden on reproductive health for both men and women. Health promotion in this context means moving beyond symptom-based treatment and embracing a holistic approach that includes family planning, fertility maintenance and coordinated multidisciplinary care. As acknowledged in the ACR 2020 Guidelines, knowledge gaps remain large--but the first and most important step is recognizing this as a problem. This editorial is a call to action for clinicians, researchers and policy makers to put reproductive health at the heart of their care for the musculoskeletal system.

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