Psoriasis in women with psoriatic arthritis: hormonal effects, fertility, and considerations for management at different stages of life

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SUMMARY

Objective. This review examines skin manifestations in women with spondyloarthritis, with a particular focus on psoriatic arthritis (PsA) and associated psoriasis.

Methods. A narrative review of the bibliography was conducted using the main databases (PubMed, Scopus, EMBASE).

Results. The review showed that the clinical course of PsA and psoriasis in women is influenced by hormonal fluctuations that occur at different stages of life, such as menstruation, pregnancy, postpartum, and menopause. Gender differences in the epidemiology of PsA and psoriasis are discussed and attributed to biological, hormonal, and environmental differences. The role of estrogen in modulating immune responses and its impact on the severity of PsA and psoriasis are reviewed. Special emphasis is placed on the psychosocial impact of visible skin lesions on women's quality of life and fertility problems associated with psoriasis. Treatment strategies are also taken into account, favoring personalized approaches that consider the safety of treatments during pregnancy and breastfeeding.

Conclusions. The review highlights the importance of a holistic and gender-sensitive approach to the management of PsA and psoriasis in women, promoting the integration of physical treatment with support for emotional well-being.

Key words: *Spondyloarthritis, psoriatic arthritis, psoriasis, women's health, hormonal influence, fertility, quality of life.*

Reumatismo, 2024; 76 (3): 196-204

INTRODUCTION

Spondyloarthritis (SpA), a complex group of inflammatory rheumatic diseases, is characterized by a range of different clinical manifestations, including involvement of the axial skeleton, peripheral joints, and entheses (1). This spectrum includes several conditions, such as ankylosing spondylitis, psoriatic arthritis (PsA), reactive arthritis, and arthritis associated with inflammatory bowel disease. Of these, PsA, with its dermatological manifestations, particularly psoriasis, represents a significant challenge for women. Psoriasis, a skin disease characterized by skin manifestations ranging from mild, localized plaques to severe, generalized forms, has a different clinical course and response to treatment in women and in men (2). This difference may be due to several factors, including different hormonal influences, as fluctuations in estrogen and other hormones can have a significant impact on the severity and progression of psoriasis (3). For example, hormonal changes during the menstrual cycle, pregnancy, postpartum, and menopause can alter the course of the disease and require an individualized approach to treatment. The effect of pregnancy on PsA and psoriasis is particularly significant. While some women experience an improvement in psoriatic symptoms during pregnancy, others may experience an exacerbation (4).

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This variability presents a challenge in the management of PsA in pregnancy, where the safety of medication for the fetus and the health of the mother become crucial considerations (5). After delivery, rapid hormonal changes can trigger psoriasis flares, requiring vigilant monitoring and adaptive therapeutic strategies. In addition to hormonal influences, genetic factors may also play a role in the gender-specific manifestations of PsA and its skin symptoms. Research suggests that certain genetic markers may predispose women to more severe forms of psoriasis associated with PsA. This genetic predisposition, combined with hormonal and immunological factors, makes the management of PsA in women even more complex (6). In addition, women with PsA and psoriasis often report a significant impact on their quality of life, not only because of the physical symptoms but also because of the psychological burden of the disease. Visible skin lesions can lead to self-consciousness, social stigma, and psychological distress, including anxiety and depression (7). These psychosocial factors need to be addressed as part of an integrated and comprehensive care pathway for women with PsA. In addition, the chronic nature of PsA and associated skin manifestations often requires long-term treatment plans that consider the patient's general health, comorbidities, and lifestyle factors. Women with PsA and psoriasis may also face challenges related to fertility, family planning, and parenting that need to be considered when managing the disease (8).

Epidemiology

Understanding the epidemiology of PsA and its cutaneous manifestations in women provides crucial insight into the prevalence, incidence, and gender-specific challenges of these conditions (9). PsA, as happens in conditions such as rheumatoid arthritis, lupus, and fibromyalgia, is known to disproportionately affect women. Recent data suggest that in the United States alone, approximately 53.2 million adults (21.2%) have been diagnosed with arthritis, and there is a significant gender gap, with a higher prevalence of physician-diagnosed arthritis in women than in men (10). On the other hand, psoriasis, which is often associated with PsA, affects more than 8 million Americans and 125 million people worldwide, or 2-3% of the world's population, and it is significant that approximately 30% of people with psoriasis also develop PsA (11). The manifestation of psoriasis in women, particularly those with PsA, is not just a skin condition but a global health problem that affects physical, psychological, and social well-being. This gender disparity suggests that there may be potential biological, hormonal, and possibly environmental factors that predispose women to a higher risk of developing arthritis (9).

Gender-specific presentation of skin manifestations in women with SpA

In women with SpA, and particularly in women with PsA, skin manifestations such as psoriasis may have a different clinical presentation compared to men (12).

Variability in severity and distribution

In women with PsA, the severity and distribution of psoriasis often differ from those of their male counterparts. Women tend to have more severe forms of psoriasis, which can cover larger areas of the body and involve more difficult-to-treat areas such as the scalp, nails, and creases (13). This increased severity can exacerbate the physical discomfort associated with psoriasis, such as itching and pain, and lead to more significant psychosocial effects, including anxiety, depression, and social isolation (14).

Hormonal influences

The role of hormones in the manifestation of psoriasis in women with PsA is particularly noteworthy. Hormones, particularly estrogen, play a key role in modulating immune responses in immune-mediated diseases. The intricate relationship between estrogen levels and psoriasis severity suggests a complex interaction between hormonal fluctuations and immune system activity that may influence the course of the disease in women at different stages of life (15, 16).

The role of estrogen in immune modulation

It is known that oestrogens have immunomodulatory effects, influencing both innate and adaptive immune responses. While elevated estrogen levels can exacerbate certain immune-related conditions, research suggests that high estrogen levels could be associated with a reduction in the severity of psoriasis. This suggests a potential protective role of these hormones in modulating the course of psoriasis throughout a woman's life (17).

The relationship between estrogen levels and psoriasis severity is particularly important in PsA. Higher estrogen concentrations tend to be associated with milder psoriasis symptoms. Conversely, low levels of estrogen, such as those that occur after childbirth or during menopause, can trigger or worsen psoriasis. This inverse relationship suggests that estrogen may have a protective effect against inflammation that characterizes psoriasis and PsA (3).

Estrogens affect several immune cells, including T cells, B cells, macrophages, and dendritic cells. They can modulate cytokine production, thereby influencing the central inflammatory processes of immune-mediated diseases such as PsA. Estrogen receptors expressed on these immune cells facilitate these modulatory effects, which can vary depending on the concentration of estrogen and the specific type of immune cell involved (18-20).

In addition, fluctuations in hormone levels at different stages of a woman's life have a significant impact on the course of PsA and its skin manifestations.

Menstrual cycle

Many women with PsA and psoriasis experience significant fluctuations in psoriasis associated with the menstrual cycle, a phenomenon closely linked to hormonal changes in their bodies. Estrogen, a key hormone, fluctuates during the menstrual cycle, and these fluctuations can profoundly affect the immune responses and inflammatory processes associated with psoriasis (21). During the menstrual cycle, estrogen levels rise and fall, reaching their lowest levels during menstruation. It is during this phase that many women with PsA report worsening psoriasis. The low estrogen phase is characterized by a reduction in the hormone's anti-inflammatory effects, which can lead to an increase in the inflammatory activity that underlies psoriasis. This results in more pronounced skin lesions, increased redness and scaling, and possibly increased discomfort or pain. These cycle-related changes highlight the complex interaction between hormonal dynamics and autoimmune diseases, such as PsA. They emphasize the importance of taking hormonal fluctuations into account when managing psoriasis in women with PsA, particularly when adapting therapeutic approaches to alleviate symptom flares during specific phases of the menstrual cycle. Recognizing these patterns may help to provide more effective and personalized treatment, thereby improving overall disease management and quality of life for patients (22).

Pregnancy

Pregnancy is a unique physiological state characterized by significant hormonal changes, particularly increased levels of estrogen, which can have a profound effect on several conditions, including PsA and psoriasis. During pregnancy, increased levels of estrogen generally have an anti-inflammatory effect, which can lead to a reduction in the severity of psoriasis. This improvement is thought to be due to estrogen's modulatory effect on the immune system, which helps to suppress the hyper-inflammatory responses characteristic of psoriasis. For some women, this can be a welcome respite from the persistent and often disabling symptoms of psoriasis, such as itching, scaling, and plaque formation. However, the relationship between pregnancy and psoriasis is complex and can vary greatly from person to person (23). In fact, contrary to the general trend of improvement, some women experience a worsening of their psoriasis during pregnancy. This may be due to individual differences in how the body responds to hormonal changes or may be influenced by other pregnancy-related factors such as stress,

dietary changes, or changes in immune function. During pregnancy, a woman's body is in an immune state designed to protect the fetus. This state involves a delicate balance between tolerance and immunity, which can have unpredictable effects on disease. Indeed, while the adaptation of the immune system during pregnancy is designed to prevent rejection of the fetus, these changes can alter the course of inflammatory diseases such as psoriasis, potentially triggering new flares or worsening existing symptoms. The variability of psoriasis responses in pregnancy highlights the need for careful monitoring and management of women with PsA during this period. Healthcare professionals need to be aware of the potential for improvement and worsening of psoriasis in pregnant patients. They must be prepared to modify treatment plans as needed, considering the safety of the mother and the developing fetus. This period requires a collaborative approach between dermatologists, rheumatologists, and obstetricians to ensure optimal outcomes for both mother and baby (24).

Postpartum

The postpartum period in women with psoriasis is characterized by a significant hormonal change, in particular a rapid drop in estrogen levels, which can have a direct impact on the course of the disease. This drop in estrogen alters the state of the immune system, reversing the immunomodulatory effects of pregnancy and potentially leading to increased psoriasis activity. Women who experience an improvement in their psoriasis during pregnancy may be particularly vulnerable to flare-ups after giving birth, experiencing a rebound effect where symptoms return with increased intensity. The additional burden of managing psoriasis flares during this time may increase stress and the risk of postpartum depression, especially in new mothers adjusting to the demands of caring for their newborn. Psoriasis flares can also pose a challenge to breastfeeding, particularly if lesions are present in the breast area, adding additional emotional distress and practical challenges to postpartum life (25). Effective management involves careful monitoring for early detection and treatment of flares, individualized therapeutic adjustments, and possible reintroduction of medications discontinued during pregnancy, with careful consideration for breastfeeding mothers. Topical therapies can be a safe and effective first line of treatment, and stress management support, including counseling or support groups, is useful. Advice on diet, exercise, and lifestyle changes can help manage stress and improve general health (26).

Menopause

Menopause, which marks the end of a woman's reproductive years, is associated with a significant reduction in estrogen levels, which has a profound effect on women with PsA, particularly in relation to psoriasis. The effects of menopause on psoriasis include an increase in psoriasis severity, as the anti-inflammatory and immunomodulatory effects of estrogen diminish with menopause, leading to increased inflammatory activity and an increased risk of psoriasis flares and more severe skin lesions (27). Postmenopausal women may experience not only more severe but also more frequent flares, as the loss of estrogen's regulatory influence on the immune system makes the skin more susceptible to psoriasis triggers, thus increasing the frequency of flares. Menopause also changes the skin, causing a reduction in elasticity, dryness, and thinning, which can worsen the discomfort associated with psoriasis, highlighting the importance of skin care in the management of psoriasis in postmenopausal women (28). Treatment considerations for postmenopausal women with PsA and psoriasis include the need for medication adjustment, as hormonal changes may alter the response to psoriasis treatments, necessitating adjustments or modifications to medications that were effective prior to menopause, and the consideration of new treatments to manage altered disease activity. Topical treatments may need to be re-evaluated due to menopausal skin changes, with more moisturizing and less irritating formulations being useful for increased skin sensitivity and dryness. Regarding hormone replacement

therapy (HRT), recent studies suggest that while it may improve menopausal symptoms in postmenopausal women, in some cases it may be a potential trigger for psoriasis flares. Therefore, the decision to use HRT should be made with caution, considering both benefits and risks and in consultation with healthcare professionals (29). Lifestyle changes such as a balanced diet, regular exercise, smoking cessation, and stress management techniques can help to ease the changes of menopause and potentially reduce the severity of psoriasis flares (30).

Quality of life

The impact of psoriasis on quality of life, particularly in women, shows a significant gender difference in disease burden (31). Psoriasis, characterized by red, scaly plaques, can have a significant impact on physical, emotional, and social aspects of life, with the burden often disproportionately high for women.

Physical effects

In women, psoriasis can be more aggressive and cover larger areas of the body, leading to greater physical discomfort. The presence of lesions in visible areas such as the face, hands, and scalp can be particularly distressing. In addition, women may experience more severe symptoms such as itching and pain, which can interfere with daily activities and sleep (32, 33).

Psychological and emotional distress

The psychological impact of psoriasis on women is profound. The visible nature of the condition can lead to feelings of self-consciousness and low self-esteem. Women may be subject to social pressure regarding appearance, and psoriasis lesions can have a significant impact on body image and self-confidence. The chronic nature of psoriasis, combined with the unpredictability of its manifestations, can lead to anxiety and depression. Younger patients going through critical developmental stages such as adolescence and young adulthood may be particularly vulnerable to these psychological effects (34-36).

Social and interpersonal relationships

Psoriasis can affect social interactions and relationships. The stigma associated with visible skin lesions can lead to withdrawal and social isolation. This social isolation can increase feelings of loneliness and depression. Younger patients, who are often more socially active and in the process of forming new relationships, may find these challenges particularly daunting (37).

Impact on work and education

Psoriasis can also affect work and education. Discomfort and visible skin lesions can lead to absenteeism or reduced productivity at work or school. Patients may feel the need to hide their condition, causing additional stress and anxiety. For those in customer-facing roles or professions where physical appearance is important, the challenges may be even greater (38).

Fertility challenge

Regarding the relationship between fertility and psoriasis, a 2020 study analyzed the impact of psoriasis on pregnancy outcomes and revealed some worrying trends. The study, which compared the reproductive patterns of women with and without psoriasis, found that women with psoriasis were younger at first birth and had longer intervals between pregnancies, but their total number of children was like that of women without the condition. Women with psoriasis had a higher risk of several adverse outcomes, including hypertensive disorders of pregnancy, premature rupture of membranes, and a higher incidence of cleft palate and unspecified malformations. These findings highlight the need for special monitoring and management of pregnancies in women with psoriasis, although there is no apparent effect on fertility (24).

In another recent population-based cohort study, researchers analyzed the impact of psoriasis on fertility rates and obstetric outcomes in women. The study used data from the UK Clinical Practice Research Datalink GOLD database, which includes records from 887 primary care practices and covers the period from 1998 to 2019. It included 63,681 female patients with psoriasis and

318,405 comparison patients without the condition, matched by age and general practice. The results showed that women with moderate to severe psoriasis had lower fertility rates than those without psoriasis. In addition, pregnancies in patients with psoriasis were associated with a higher risk of pregnancy loss, although no increased risk of antenatal hemorrhage, pre-eclampsia, or gestational diabetes was observed. This important study highlights the need for future studies to explore the mechanisms underlying the increased risk of pregnancy loss in patients with psoriasis to improve the understanding and management of fertility problems in this population (39). However, there is little evidence to support this claim, and more research is needed to better understand how psoriasis may affect women's fertility. Based on what is known, healthcare providers should monitor women with psoriasis during pregnancy to maintain maternal health and provide the safest possible environment for fetal development.

Treatment options

Treatment of the skin manifestations in women with psoriasis involves a variety of approaches, depending on the severity of the condition and the needs of the individual patient. Treatment options generally include topical therapies, phototherapy, systemic drugs, and biological agents (40) (Table I). The choice of therapy depends on the extent and severity of skin and joint involvement, response to previous treatments, comorbidities, patient preferences, and potential impact on quality of life. Regular monitoring and follow-up are essential to assess the effectiveness of treatment and make any necessary changes (40).

Table I - Treatment options.

Topical treatments
– Corticosteroids: widely used for their anti-inflammatory properties. They are effective for mild to moderate skin lesions. – Vitamin D analogs: such as calcipotriol, used alone or in combination with corticosteroids. – Topical retinoids: for example, tazarotene, used for plaque psoriasis. – Moisturizers and emollients: essential for maintaining skin hydration and barrier function.
Phototherapy
– UVB phototherapy: narrowband UVB is commonly used for moderate skin involvement. – PUVA therapy: combines UVA light with psoralen, a photosensitizing drug that is more effective than UVB therapy but has a higher risk profile.
Systemic treatments
– Methotrexate: often used for moderate to severe psoriasis or PsA. – Cyclosporine: effective for rapid control of psoriasis; especially useful in severe cases. – Acitretin: a systemic retinoid, useful in pustular and erythrodermic psoriasis. – Apremilast: oral small-molecule inhibitor of phosphodiesterase 4, used in the treatment of moderate to severe plaque psoriasis and active PsA.
Biological treatments
– TNF inhibitors: such as adalimumab, etanercept, infliximab, and certolizumab pegol. Effective for both skin and joint symptoms. – IL-17 inhibitors: including secukinumab and ixekizumab, which specifically target IL-17, a key cytokine in the pathogenesis of psoriasis. – IL-12/23 inhibitors: ustekinumab targets both IL-12 and IL-23 and is effective in the treatment of moderate to severe plaque psoriasis and active PsA. – IL-23 inhibitors: like guselkumab, tildrakizumab and risankizumab are newer agents for moderate to severe plaque psoriasis.
Lifestyle modifications
– Stress reduction – Smoking cessation – Weight management

UVB, ultraviolet B; UVA, ultraviolet A; PUVA, psoralen and ultraviolet A; PsA, psoriatic arthritis; TNF, tumor necrosis factor; IL, interleukin.

Treatment during pregnancy

Treatment of psoriasis during pregnancy involves several approaches (41).

Topical treatments

Topical corticosteroids are the main recommendation for psoriasis in pregnancy. They are well tolerated and do not significantly increase the risk of congenital malformations, premature birth, or fetal death. However, high-potency corticosteroids may slightly increase the risk of low birth weight when used at high doses (42).

Phototherapy

The controlled use of ultraviolet (UV) phototherapy during pregnancy is thought to be safe. It is important to monitor and supplement folic acid levels in pregnant patients receiving UVB therapy due to possible photodegradation of folic acid (43).

Biologic drugs

The use of biologics, particularly tumor necrosis factor-α (TNF-α) inhibitors, during

pregnancy and lactation in women with psoriasis requires careful consideration because of the potential risks and benefits. Currently, certolizumab-pegol is the preferred biologic treatment for use during pregnancy and breastfeeding. It has been shown that only negligible amounts of certolizumab-pegol cross the placenta to enter fetal circulation, and the levels found in breast milk are very low. This makes it a safer option for now (41).

Lactation considerations

Only small amounts of TNF-α inhibitors are expected to be excreted in breast milk. Therefore, systemic effects on the infant are not expected. The manufacturers of certolizumab-pegol and adalimumab do not object to their use during lactation (44), but in any case, the decision to treat women with psoriasis during pregnancy and lactation must include a thorough risk-benefit assessment.

Conclusions

Women with PsA and psoriasis may develop more severe skin manifestations, including increased extent and involvement of critical areas such as the scalp and nails. This increased severity may be due to hormonal fluctuations that women experience at different stages of life, such as menstrual cycle, pregnancy, postpartum, and menopause, which can significantly influence the severity and course of PsA and psoriasis. The postpartum period can often trigger an exacerbation of psoriasis due to rapid hormonal changes, requiring careful management and adaptation of therapeutic strategies. Menopause can also be challenging, with a drop in estrogen levels leading to more frequent and severe psoriasis flares. Furthermore, a recent study found that a longer reproductive lifespan in women is significantly associated with a lower risk of developing late-onset psoriasis and PsA (45). The psychological and social impact of psoriasis on women is profound and multifaceted. Visible skin lesions can cause significant emotional and psychological distress, including problems with body image, self-esteem, social stigma, and mental health problems such as anxiety and depression. These require a holistic approach to treatment that addresses both the physical symptoms and the emotional well-being of the patient. Treatment strategies need to be tailored to the individual, considering the severity of the condition, hormonal influences, and stage of life. During pregnancy, the safety of drugs for both mother and fetus is paramount. Some drugs, such as methotrexate, are contraindicated, while others, such as certolizumab-pegol, are preferred because of their minimal placental transfer. In conclusion, the management of women with psoriasis and PsA requires a comprehensive understanding of the interaction of the disease with female physiology, hormonal changes, and psychosocial factors. Treatment approaches need 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.

Contributions

All the authors made a substantial intellectual contribution, read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Conflict of interest

The authors declare no potential conflict of interest.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Funding

None.

Availability of data and materials

Data available from the corresponding author upon request.

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