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Risk factors and comorbidities for psoriatic arthritis. Literature review

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## **ABSTRACT:**

#### Introduction:

Psoriatic arthritis is a chronic disease involving peripheral arthritis, spondylitis, dactylitis (inflammation of the whole digit) and enthesitis. It is a disease equally prevalent in both genders. Psoriatic arthritis coexists with several conditions, including metabolic syndrome, obesity, cardiovascular disease, inflammatory bowel disease, and liver disease. The reciprocal effects of comorbidities with psoriatic arthritis are demonstrated by recent research. There are several risk factors associated with the condition that might hasten or worsen its symptoms.

## Aim of the Study:

The purpose of this paper is to present a thorough analysis of the research that has been done on comorbidities and risk factors for psoriatic arthritis. With an emphasis on changeable elements that might impact the disease's progression, the goal is to illustrate the multifaceted nature of psoriatic arthritis. The intention is also to highlight comorbidities that need to be considered while treating a patient with the illness.

### Materials and methods:

An analysis of papers available in PubMed and Google Scholar was performed using the following key words: psoriatic arthritis, psoriatic arthritis and lifestyle, psoriatic arthritis and comorbidities, psoriatic arthritis and cardiovascular risk, psoriatic arthritis and gastrointestinal diseases, psoriatic arthritis and physical activity, psoriatic arthritis and diet, psoriatic arthritis and alcohol, psoriatic arthritis and smoking.

## **Conclusions:**

Psoriatic arthritis is a chronic disease that affects many areas of patients' lives. It is critical to consider the connections that exist between this illness and other comorbidities. In order to provide a patient with this ailment with the best care possible, variables that might exacerbate the illness's progression must also be taken into consideration. Patients' mental health should get particular attention, and lifestyle modifications should be promoted.

**Keywords:** Psoriatic arthritis; cardiovascular risk; IBD; NAFLD; lifestyle modification; metabolic syndrome; obesity; seronegative spondyloarthropathies.

### Introduction

A long-term, inflammatory musculoskeletal condition linked to psoriasis is called psoriatic arthritis (PsA). [1] In Western adults, it is prevalent between 2-4 percent, and 20-30% of those with psoriasis will go on to develop psoriatic arthritis (PsA). From 40 to 50 years old, it affects men and women nearly equally. [2] In10-15% of patients, arthritis develops before psoriasis. [3] There are five non-exclusive clinical categories that can affect both axial and peripheral joints: asymmetric oligoarticular, symmetric polyarticular, distal interphalangeal joint-predominant, axial/SpA-predominant, and the infrequently found deforming/destructive subtype, or arthritis mutilans. [4] Peripheral arthritis, spondylitis, dactylitis (inflammation of the whole digit), and enthesitis (inflammation where a tendon, ligament, or joint capsule inserts into the bone) are musculoskeletal symptoms of PsA. [1] Early diagnosis and therapy might potentially avoid joint degeneration and disability caused by persistent inflammation. [5] Individuals diagnosed with psoriasis (PsO) or psoriatic arthritis (PsA) are more likely to experience extra-musculoskeletal inflammation and comorbidities, including depression, uveitis, inflammatory bowel disease, and metabolic syndrome.[6] Despite the early belief that PsA was a reasonably benign ailment, registry data has demonstrated the disease's destructive and progressive nature. [7] PsA is a common arthropathy that may be crippling and often goes untreated, although there are effective therapies for it. Treatment and early discovery are

likely to improve the situation. [8] Psoriatic arthritis (PsA) is a chronic inflammatory illness affecting several organs, causing physical and psychological symptoms in those who suffer from it. Pain alleviation ranks first for patients, followed by weariness and psychological anguish, as well as the capacity to function and engage in social life. [9] Psoriatic arthritis patients endure long-term pain, impairments in their physical function and capacity for employment, persistent exhaustion, and emotional and social disruptions. [10] According to the CASPAR (psoriatic arthritis classification criteria), the primary method of diagnosing PsA is clinical. [11] The etiopathogenesis of PsA is complex and not fully understood. It involves the interaction of genetic susceptibility factors (primarily human leukocyte antigens; HLA) B27, along with other HLA-B loci and the HLA-Cw \* 0602 allele) and environmental triggers (mechanical stress, dysbiosis, trauma, smoking, or infection), which results in the dysregulation of immunoinflammatory pathways and the development of the disease. [12]

#### Current state of knowledge

Numerous additional concomitant diseases, including obesity, sedentary lifestyles, excessive alcohol use, smoking, poor sleep, tiredness, and anxiety, are frequently linked to psoriatic arthritis. Consequently, there is an increased risk of mortality and morbidity, as well as a higher likelihood of metabolic syndrome and cardiovascular disease (CVD) in individuals with PsA. Therefore, it is essential to adopt healthy lifestyle adjustments, nonpharmacologic therapies, or psychological treatments. [13]

### Impact of obesity and nutrition on psoriatic arthritis

One of the risk factors for psoriatic arthritis is obesity. [14] According to studies, people with joint dysfunction may be less likely to be physically active, which might lead to weight gain as a result of these inflammatory disorders. [15] Weight on the joints, changed mechanics, and recurrent microtrauma are all possible consequences of obesity. Although this may trigger an inflammatory response, it can also result in osteoarthritis (OA). [16] In obese people, adipose tissue, which is metabolically active, results in a persistent low-grade inflammation. The higher risk of PsA, increased disease load, and poor response to therapy may be caused by this persistent low-grade inflammation; however, other variables (e.g., micro-injuries, general functional impairment owing to obesity and poorer PROs) may interact with this association. The cornerstones of treating obesity are diet and exercise, which can be difficult for patients to follow. In addition to improving PsA-related results, weight loss techniques should be supported for the benefit of patients' general health. [17] Important element in the shift from skin psoriasis to PsA may be obesity. A cohort research spanning 15 years that was carried

out for the general population in the UK revealed that PsA prevalence rose with BMI in both the general population (nearly 2 million) and 75,395 individuals who had psoriasis. After analyzing data on BMI, weight changes, and central obesity measurements in 89,049 women who participated in the US Nurse Health Study II over a 14-year period, Li et al. discovered a monotonic relationship between BMI and an elevated risk of PsA. [14] By encouraging patients to reduce body weight, which is a modifiable risk factor, the possibility of PsA can be reduced. In addition, weight loss in patients with PsA and overweight and obesity improves the pharmacological response. [18] Adopting a low-energy diet led to significant improvements in disease activity in the skin, entheses, and joints in obese individuals. PsA patients who weighed more than 33 kg/m2 had an extremely low energy diet, ingesting just 640 kcal a day. From 29% at baseline to 54% at the 6-month follow-up, there was a rise in the percentage of patients reaching little disease activity after six months. The significance of dietary modification for individuals with PsA and concurrent obesity was demonstrated by this study. [19]

### Psychological impact on psoriatic arthritis

Depression coexists in approximately 20% of patients with PsA. A common factor between psoriatic arthritis and depressive disorders is inflammation, which has a role in the occurrence of depression in these patients. [20] The incidence of anxiety and depression symptoms in PsA patients ranges from 7.9% to 36.6. According to research, those with PsA had greater rates of anxiety and depression (36.6% and 22.2%, respectively) than people with psoriasis (24.4% and 9.6%). [21] Furthermore, PsA patients are more likely to experience moderate to severe levels of depressive symptoms (25.1%) than RA patients (21.7% of whom had depression), particularly in those with polyarthritis (36.7%). [22] A cohort study investigating the relationship between endothelial dysfunction and depressional symptoms in patients with PsA showed the presence of a relationship between these conditions. This should encourage the systematic investigation of depressive symptoms as part of a proper cardiovascular risk assessment in PsA, contributing to increase the effectiveness of preventive strategies. [23] PsA's elevated emotional burden may be significantly influenced by pain. A very large percentage of psoriasis sufferers do not receive treatment for depression, neither recognized nor acknowledged. It's critical that medical professionals build a trustworthy therapeutic alliance with their patients, conduct regular mental health examinations, identify and manage pain symptoms, and, when necessary, offer psychiatric and psychotherapy services. [24]

#### Effect of psoriatic arthritis on sleep

According to published research, PsA patients experience more severe sleep impairment than individuals with only skin involvement. In instance, a Nordic study revealed that whereas 16% of psoriasis patients had sleep problems, 45% of PsA patients claimed the same. [25] Patients with PsA frequently have poor quality sleep, even though almost half of them do not use any medication for their sleep problems. In terms of the quality of sleep, emotional elements (worry, exhaustion) seem to be more significant than inflammatory ones. This symbiotic interaction between emotional disturbances, disease activity, and sleep quality emphasizes the necessity of a multidisciplinary approach to PsA. A crucial component of precision medicine's development to enhance patients' social functioning is the identification and management of comorbidities that may have an impact on PsA patients' activity levels. [26]

## Physical activity and psoriatic arthritis

Clinical recommendations for the therapy of inflammatory arthritis promote exercise as a means of symptom management, disability reduction, and comorbidity prevention and treatment. In this regard, guidelines for physical exercise were released by EULAR, with a particular emphasis on those suffering from inflammatory arthritis, such as PsA. [27] Exercise regimens can be very effective in lowering the risk of both the advancement of the illness and cardiovascular risk in PsA patients who may have subclinical atherosclerosis. According to EULAR guidelines, physical exercise can help manage cardiometabolic comorbidities in addition to lowering the burden of illness. [28] The results of the study demonstrated a correlation between reduced visceral fat mass and body fat percentage in both PsA patients and controls and moderate to high levels of physical activity. Individuals with PsA, particularly those under 40, exhibited more visceral fat mass and percentage body fat than controls in their age group. Additionally, they did not adhere to the suggested amounts of physical exercise. The study underlines how crucial it is to assess the variables behind these alterations and screen individuals with PsA for changes in their body composition. Individuals with PsA who have low levels of physical activity should receive treatment in clinical settings as this can affect key health outcomes and modify their body composition. [29]

### Smoking and psoriatic arthritis

In large cohort representative of the UK general population examining the connection between smoking and psoriasis discovered that while smoking was linked to a lower risk of PsA among psoriasis patients (HR 0.91; 95% CI 0.84 to 0.99), it was linked to an increased

risk of PsA in the general population (HR 1.27; 95% CI 1.19 to 1.36). Through mediation analysis, it was determined that smoking's impact on psoriasis mostly determined its impact on the likelihood of psoriatic arthritis. The results of sensitivity analysis for bias indicated that uncontrolled confounders might counteract the biased impact of smoking among psoriasis patients, even in cases where the correlation between the variables and smoking or PsA was minimal (both HR =  $\sim$  1.5). (HR = 0.9). [30] Smoking has a negative correlation with psoriasis sufferers, but a positive correlation with the condition in the general population. This behavior is known as PsA's "smoking paradox". Smoking may result in a poor reaction to therapy for PsA as well as poor adherence to it. Medical professionals should be aware of the smoking habits of their Psoriasis and PsA patients; if feasible, they should take smoking cessation programs into consideration. [31]

#### The effect of alcohol on psoriatic arthritis

A research conducted on 82,672 US women during a follow-up period (1991-2005) on the influence of alcohol and the risk of psoriatic arthritis identified 141 incident cases of PsA over a 14-year period. The multivariate HR for PsA was 4.45 (95% CI 2.07-9.59) for  $\geq$  30.0 g/day of cumulative average alcohol intake, 1.43 (95% CI 0.67-3.08) for 15.0-29.9 g/day, and 0.70 (95% CI 0.48-1.01) for 0.1-14.9 g/day. When updated alcohol use and baseline alcohol consumption from 1991 were considered as exposures, and when the analysis was limited to those who had psoriasis during follow-up, risk estimates were largely consistent. In a group of US women, excessive alcohol use was linked to a higher risk of PsA. [32]

#### Psoriatic arthritis and cardiovascular risk

PsA patients have higher cardiovascular risk due to the so-called classic cardiovascular risk factors, such as obesity, smoking, dyslipidemia, hypertension, and metabolic syndrome. [33] Compared to the general population, patients with PsA had a greater incidence and a higher prevalence of cardiovascular variables. The study compared 414 control people and 207 patients with PsA in order to evaluate the incidence of cardiovascular events and cardiovascular risk factors (CVRFs). The PsA patient group had a higher incidence of atherothrombotic illness after controlling for age and sex (SCORE p = 0.002, QRISK2 p = 0.001). The percentage of patients with high or very high cardiovascular risk in the PsA group rose from 39.3 to 45.3% with the use of SCORE-PsA. [34] In Pso/PsA, systemic therapy is linked to a statistically significant decrease in the risk of all cardiovascular events. [35] Patients with PsA may have an increased risk of atherosclerotic disease due to endothelial impairment. [36]

#### Psoriatic arthritis and metabolic syndrome

Metabolic syndrome and joint inflammation both cause cardiovascular disease through similar signaling mechanisms. [37] Metabolic syndrome, PsA, and atherosclerosis all exhibit similar patterns of T-cell activation. They enhance the production of Th-1-profile cytokines such as interleukin 10 (IL-10), interferon (IFN), tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), and interleukin 1 beta (IL1-β). [38] These cytokines cause skeletal muscle to become insulin resistant, boost the liver's production of procoagulant factors, block lipoprotein lipase, promote fatty acid oxidation, and raise blood levels of atherogenic lipoproteins. In a harmful positive feedback loop, the production of cytokines, insulin resistance, and endothelial dysfunction promote the development and accumulation of atheroma plaques. [39] Endothelial dysfunction is promoted by a chronic low-grade inflammatory state that has dysregulated immunoinflammatory pathways and fatty acid metabolism in the arterial wall. [40] PsA has been linked to an increase in the carotid artery intima-media thickness (c-IMT), a more sensitive marker of pre-atherosclerosis. [41] It has been demonstrated that in PsA patients, the presence of carotid atherosclerosis is clearly associated with CV events. This link is connected to the length of PsA as well as the inflammatory state, and it manifests independently of the presence of traditional CV risk factors.[42] Pharmacological intervention is frequently required for metabolic syndrome therapy, despite lifestyle modifications being the cornerstone of the approach. A verified diagnosis of psoriasis, however, should direct attention back toward inflammatory activity since psoriasis inherently promotes endothelial dysfunction, insulin resistance, and an environment that is prothrombotic. Thus, joint disease remission should be taken into account for proper metabolic syndrome management. [43]

## Psoriatic arthritis and gastrointestinal diseases

Numerous gastrointestinal disorders including inflammatory bowel disease (IBD) are linked to psoriasis and psoriatic arthritis. [44] IBD (inflammatory bowel disease) is a recurring, chronic immune-mediated gastrointestinal illness that includes Crohn's disease (CD) and ulcerative colitis (UC). [45] SpA patients have an up to four-fold greater chance of developing IBD compared to the general population because they share genetic and immunopathogenic pathways with IBD patients. While intestine involvement varies in frequency across different kinds of SpA, articular involvement is commonly seen in IBD. [46] The results of an MR investigation point to a causal relationship between psoriasis and IBD, as well as psoriatic arthritis. Specifically, the development of psoriasis and psoriatic arthritis appears to be linked to the subentity Crohn's disease. [47] Research has indicated that NAFLD is more common in

PsA patients than in the overall population. According to these authors, there is a 30% incidence of liver abnormalities in people with PsA, and these abnormalities are independently correlated with BMI, metabolic syndrome, disease activity, and CRP levels. [48] NAFLD affects around 47% of psoriasis patients, whereas NASH affects up to 15% of individuals. [49] NAFLD and the disease severity index (PASI) of psoriasis were shown to be substantially associated in PsA. Psoriasis raises the risk of advanced non-alcoholic fatty liver disease (NAFLD) by around 60% and enhances the risk of NASH development. [50]

#### Conclusions

Psoriatic arthritis is a disease with many comorbidities and has many risk factors. The treatment of a patient with this condition should be multidisciplinary. Above all, attention should be paid to the serious consequences of this disease, such as increased cardiovascular risk, atherosclerosis and increased risk of developing metabolic syndrome. Patients should be helped not only by providing pharmacological treatment focused on skin and joint lesions, but also by encouraging lifestyle changes to prevent the potential worse consequences of the disease. The systemic and inflammatory nature of the disease makes it necessary to look for co-morbidities. It is important to pay attention to the patient's lifestyle - their physical activity, diet or sleep and it is also important to pay attention to psychological aspects. Such management will modify the patient's prognosis and also influence therapeutic efficacy. Research that is exclusively devoted to treating these people non-pharmacologically is still lacking. There ought to be further investigation into this.

### Disclourse

## Supplementary materials

Not applicable.

## **Author's contribution**

Conceptalization, Aleksandra Pich-Czekierda and Zuzanna Kotowicz, methodology, Patrycja Proszowska, Adrianna Orzeł and Julia Sieniawska, software, Daria Sieniawska, check Magda Madoń and Aleksandra Pich-Czekierda, formal analysis, Zuzanna Kotowicz and Patrycja Proszowska, investigation Adrianna Orzeł and Julia Sieniawska, resources, Daria Sieniawska, data curation, Magda Madoń, writing-rough preparation, Aleksandra Pich-Czekierda, Zuzanna Kotowicz, visualization, Patrycja Proszowska, supervision, Adrianna Orzeł, project administration, Daria Sieniawska, Magda Madoń and Julia Sieniawska. All authors have read and agreed with the published version of the manuscript.

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