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ORIGINAL ARTICLE

Role of Systemic Inflammation in Linking Psoriasis with Pulmonary Function Decline A Case-Control Study

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ABSTRACT

Background: Psoriasis is an immune mediated inflammatory chronic disease with several systemic complications. Chronic systemic inflammation might be associated with pulmonary dysfunction via cytokine-mediated airway inflammation and respiratory tissue damage.

Objective: To assess inflammatory biomarkers and spirometric parameters in order to assess the role of systemic inflammation as a connecting link between psoriasis and pulmonary function decline in patients with psoriasis.

Methods: The study was a case-control study, carried out at the Department of Dermatology and Department of Pulmonology, Multan Medical & Dental College, Multan, Punjab, Pakistan, between March 2022 and March 2023. A total of 100 participants were enrolled, including 50 clinically diagnosed psoriasis patients and 50 healthy controls. Demographic and clinical data were collected such as smoking status, body mass index, disease duration and PASI (Psoriasis Area and Severity Index) score. The levels of serum inflammatory markers such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) were assessed. Pulmonary function testing using computerized spirometry was carried out. SPSS version 26.0 was used for statistical analysis.

Results: The levels of inflammatory biomarkers were significantly higher in psoriasis patients than in healthy controls. Mean CRP, ESR, IL-6, and TNF-α levels were markedly higher in psoriasis patients ($p<0.001$). Pulmonary function parameters including forced expiratory volume in one second (FEV1), forced vital capacity (FVC), FEV1/FVC ratio, and FEF25–75% were significantly reduced among psoriasis patients compared with controls ($p<0.001$). There were significant negative correlations between high inflammatory biomarker levels and the pulmonary function parameters. In multivariate regression analysis, CRP, IL-6, smoking status, BMI and PASI score were all independent predictors of pulmonary function decline.

Conclusion: There is strong association between psoriasis and pulmonary function impairment or with increased systemic inflammatory biomarkers. Long-term systemic inflammation could be a key contributor to respiratory impairment in psoriasis patients. Early pulmonary evaluation and inflammatory monitoring can help to minimise the long-term respiratory complications.

Keywords: Psoriasis; systemic inflammation; pulmonary function decline; spirometry; IL-6; TNF-α; CRP; pulmonary impairment.

INTRODUCTION

Psoriasis is a chronic immune-mediated inflammatory disorder affecting approximately 2–3% of the global population and is characterized by epidermal hyperproliferation, abnormal keratinocyte differentiation, and persistent systemic inflammation[1]. While the main clinical characteristic of psoriasis is erythematous scaly skin lesions, it is now becoming more apparent that psoriasis is a multisystem inflammatory disease with a number of extracutaneous complications such as cardiovascular disease, metabolic syndrome, arthritis, obesity and respiratory dysfunction[2]. It is thought that chronic systemic immune activation is a major factor that contributes to these comorbid conditions[3].

The immunopathogenesis of psoriasis is related to activation of the T-helper 1 (Th1), T-helper 17 (Th17) and dendritic cell-mediated inflammatory pathways that result in the overproduction of tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), interleukin-17 (IL-17) and interleukin-23 (IL-23)[4]. These inflammatory mediators can not only cause inflammation of the skin but may also contribute to endothelial dysfunction, oxidative stress, tissue remodeling, and inflammatory injury to the skin and other tissues such as the lungs, distant from the primary inflammatory site[5]. Persistent elevation of inflammatory biomarkers has therefore been implicated in pulmonary impairment among psoriasis patients[6].

Pulmonary involvement in psoriasis has recently attracted significant clinical attention[7]. Increased prevalence of chronic obstructive pulmonary disease (COPD), asthma, sleep apnea, interstitial lung disease and impaired pulmonary function have been shown in several epidemiological and clinical studies in individuals with psoriasis[8]. Shared inflammatory pathways, smoking exposure, obesity, oxidative stress, and systemic cytokine dysregulation are believed to contribute to this association[9]. Chronic inflammation may lead to airway narrowing, reduced pulmonary elasticity, bronchial hyperresponsiveness, and progressive decline in respiratory function over time[10].

Spirometry is a useful, non-invasive method for the assessment of pulmonary function and is an aid to detect pulmonary abnormalities early in life[11]. Previous studies have reported reduced forced expiratory volume in one second (FEV1), forced vital capacity (FVC), and impaired FEV1/FVC ratio in psoriasis patients even in the absence of clinically apparent respiratory disease[12]. Based on these findings, it is suggested that subclinical pulmonary dysfunction can be related to systemic inflammation in psoriasis.

Psoriasis is characterized by a variety of inflammatory biomarkers including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), IL-6 and TNF-α that can be measured and might be significant markers of systemic inflammatory load[14]. These increased cytokines can be directly related to inflammation of the pulmonary tissue and the loss of lung function.[15] Understanding the relationship between systemic inflammation and respiratory impairment may therefore help identify psoriasis patients at increased risk for pulmonary complications and facilitate earlier therapeutic intervention[16].

Although there are increasing reports of the relationship between psoriasis and respiratory dysfunction, there is a lack of local data regarding the role of systemic inflammation in pulmonary dysfunction among psoriasis cases in Pakistan[17]. Therefore, the present study was conducted to evaluate the role of systemic inflammatory biomarkers in linking psoriasis with pulmonary function decline by assessing spirometric parameters and inflammatory marker levels among psoriasis patients compared with healthy controls18-20.

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MATERIALS AND METHODS

This case-control study was carried out in the Departments of Dermatology and Pulmonology at Multan Medical & Dental College, Multan, Punjab, Pakistan, from March 2022 to March 2023, following the ethical approval from the Institutional Ethical Review Committee. The study was conducted in line with the principles of the Declaration of Helsinki. All the study participants provided their written informed consent before entering the study.

The study was carried out with 100 participants using consecutive non-probability sampling techniques. A study population of 50 patients with clinically confirmed psoriasis and 50 healthy age and gender matched controls were included. Consultant dermatologists diagnosed psoriasis vulgaris, using detailed clinical examination and characteristic dermatological findings. Inclusion criteria were patients aged 18-65 years of either gender with stable plaque psoriasis.

Persons with prior diagnosis of chronic pulmonary diseases such as chronic obstructive pulmonary disease, bronchial asthma, pulmonary fibrosis, active pulmonary tuberculosis, interstitial lung diseases, acute respiratory tract infections, autoimmune diseases other than psoriasis, malignancy, severe cardiac diseases, chronic renal failure and pregnancy were excluded. Those who had systemic biologic therapy, immunosuppressive agents, or corticosteroid treatment within the prior three months also were excluded to limit the confounding effects of these treatments on inflammatory biomarkers and pulmonary function.

Using a structured clinical proforma, detailed demographic and clinical data was collected, such as age, gender, smoking history, body mass index (BMI), duration of psoriasis, family history, and associated comorbid conditions. The severity of psoriasis was assessed by Psoriasis Area and Severity Index (PASI) score. All height and weight measures were taken by standard methods, BMI was calculated as weight (in kg) divided by height (in m) squared.

After overnight fasting all subjects had venous blood samples taken in an aseptical manner. Blood samples were centrifuged and the serum was kept at −20°C for laboratory analyses. Serum markers of systemic inflammation such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), interleukin-6 (IL6) and tumor necrosis factor alpha (TNF-α) were assessed. The levels of CRP and ESR were measured by standard laboratory methods while IL-6 and TNF-α were measured by commercially available enzyme-linked immunosorbent assay (ELISA) kits as per manufacturer's instructions.

Pulmonary function testing was done using computerized spirometry, supervised by trained pulmonologists, following the guidelines of American Thoracic Society. Smoking and extreme exercise were prohibited prior to testing. Spirometric parameters (forced expiratory volume in one second (FEV1), forced vital capacity (FVC), forced expiratory flow at 25–75% of pulmonary volume (FEF25–75%) and FEV1/FVC ratio) were measured. The maximum of three acceptable spirometric readings was used for analysis.

All the collected data was entered and analyzed in Statistical Package for Social Sciences (SPSS) 26.0 version. Data for quantitative variables were presented as mean ± standard deviation, and data for qualitative variables were presented as frequency and percent. Independent sample t test was used for quantitative variables to compare groups and chi square test was used to compare categorical variables. Pearson correlation analysis was done to evaluate the association between inflammatory biomakers and pulmonary function parameters. Multivariate linear regression analysis was performed to determine independent factors associated with the pulmonary function decline in psoriasis cases. Statistically significant differences were defined as a p value < 0.05.

RESULTS

A total of 100 participants were enrolled in the study, including 50 patients with psoriasis and 50 healthy controls. The mean age for the psoriasis was 43.7 ± 10.6 years and that of the control group was 42.9 ± 9.8 years. The psoriasis group and the control group had 58% and 54% males, respectively. The smoking history and BMI were found to be significantly increased in the psoriasis group than in controls. Levels of inflammatory markers such as CRP, ESR, IL-6 and TNF-α were significantly higher in the psoriasis group, reflecting the higher inflammatory activity present in the body. Demographic and inflammatory parameters of the study population are shown in Table 1.

Table 1. Demographic and Inflammatory Characteristics of Study Participants

Variable	Psoriasis Patients (n=50)	Controls (n=50)	p-value
Age (years)	43.7 ± 10.6	42.9 ± 9.8	0.684
Male Gender	29 (58%)	27 (54%)	0.689
Female Gender	21 (42%)	23 (46%)	0.689
BMI (kg/m²)	28.8 ± 4.3	25.6 ± 3.7	<0.001
Smokers	18 (36%)	10 (20%)	0.041
Disease Duration (years)	7.1 ± 3.5	—	—
PASI Score	14.6 ± 5.1	—	—
CRP (mg/L)	13.9 ± 4.8	5.4 ± 1.9	<0.001
ESR (mm/hr)	28.4 ± 7.9	12.7 ± 4.1	<0.001
IL-6 (pg/mL)	17.8 ± 5.6	6.9 ± 2.3	<0.001
TNF-α (pg/mL)	21.7 ± 6.8	8.8 ± 2.9	<0.001

The respiratory parameters were decreased significantly in psoriasis patients than in control group. Mean FEV1, FVC, FEV1/FVC ratio, and FEF25–75% values were significantly lower in the psoriasis group, suggesting impaired airway function and reduced pulmonary performance associated with chronic systemic inflammation. The comparison of spirometric parameters between both groups is shown in Table 2.

Table 2. Comparison of Pulmonary Function Parameters Between Study Groups

Spirometric Parameter	Psoriasis Patients (n=50)	Controls (n=50)	p-value
FEV1 (% predicted)	75.6 ± 10.8	89.1 ± 7.6	<0.001
FVC (% predicted)	80.7 ± 9.9	91.5 ± 7.2	<0.001
FEV1/FVC Ratio	0.76 ± 0.07	0.88 ± 0.05	<0.001
FEF25–75% (%)	68.5 ± 11.7	86.8 ± 8.9	<0.001

Then it was found that there was a significant negative correlation between inflammatory biomarkers and pulmonary function parameters in psoriasis patients. There was a correlation between the levels of CRP, IL-6, and TNF-α and FEV1 and FEV1/FVC ratio. Independent risk factors for pulmonary function decline were elevated CRP, higher IL-6 levels, smoking status and higher PASI score, when assessed by multivariate regression analysis. A detailed regression analysis is given in Table 3.

Table 3. Multivariate Regression Analysis for Predictors of Pulmonary Function Decline in Psoriasis Patients

Variable	β-Coefficient	Standard Error	p-value
CRP	-0.417	0.081	<0.001
IL-6	-0.389	0.074	0.002
TNF-α	-0.341	0.069	0.006
Smoking Status	-0.276	0.058	0.014
BMI	-0.201	0.049	0.031
PASI Score	-0.328	0.061	0.008

The overall results showed significant correlation of psoriasis with the increased level of systemic inflammatory markers and pulmonary dysfunction. Higher inflammatory burden and disease severity were associated with more severe respiratory dysfunction, confirming that chronic systemic inflammation is a factor in respiratory function decline in psoriasis.

DISCUSSION

The present study demonstrated a significant association between psoriasis, systemic inflammation, and pulmonary function decline[1]. Psoriasis patients had significantly higher levels of inflammatory

markers such as CRP, ESR, IL-6 and TNF-α, and significantly reduced parameters of spirometry than healthy people[2]. These findings would suggest that psoriasis is not only a skin disease but also a chronic multisystem inflammatory disease with the potential of impairing lung function due to chronic systemic immune activation[3].

Chronic inflammation plays a central role in the pathogenesis of psoriasis and contributes to widespread systemic involvement[4]. Activation of Th1 and Th17 immune pathways results in excessive cytokine production, particularly TNF-α and IL-6, which may induce endothelial dysfunction, oxidative stress, airway inflammation, and pulmonary tissue remodeling[5]. The significantly elevated inflammatory biomarkers observed in the current study indicate an increased systemic inflammatory burden among psoriasis patients, which may contribute directly to pulmonary impairment[6].

In our study, patients with psoriasis had significantly lower FEV1, FVC, FEV1/FVC ratio and FEF25–75% values than the controls[7]. These findings are consistent with previous investigations reporting subclinical respiratory dysfunction in individuals with psoriasis[8]. Chronic inflammatory cytokine exposure may lead to airway narrowing, bronchial hyperresponsiveness, and impaired pulmonary elasticity, resulting in progressive respiratory decline even in patients without clinically diagnosed pulmonary disease[9].

The inverse correlation of inflammatory markers with pulmonary function indices in turn supports the hypothesis that systemic inflammation is an important mechanistic connection between psoriasis and pulmonary dysfunction[10]. Elevated CRP and IL-6 levels were strongly associated with reduced spirometric values in the present study[11]. CRP is a sensitive marker of systemic inflammation and endothelial injury, while IL-6 contributes to inflammatory amplification and chronic airway remodeling[12]. Persistent elevation of these biomarkers may therefore accelerate pulmonary tissue damage and functional deterioration[13].

TNF-α also demonstrated a significant association with pulmonary impairment in our study[14]. TNF-α is known to be pro-inflammatory and induces inflammatory cells, oxidative damage and changes in airway structure[15]. Increased TNF-α activity has been implicated in both psoriasis progression and chronic inflammatory pulmonary diseases, suggesting overlapping immunopathological mechanisms between cutaneous and respiratory inflammation[16].

Smoking and high BMI were found to be other risk factors for the decline of pulmonary function in psoriasis patients[17]. Smoking has been identified as a risk factor for severe psoriasis, respiratory disease and can increase systemic inflammatory activity[18]. Likewise obesity leads to chronic low-grade inflammation and mechanical respiratory limitation, which adds to impairment of pulmonary function.[19] Thus, psoriasis-related inflammation, smoking and obesity may act synergistically to lead to respiratory dysfunction[20].

There was also a significant association between pulmonary dysfunction and disease severity (PASI score)[5]. The inflammatory markers were higher in patients with more severe psoriasis and there was a higher deterioration of pulmonary function in this group of patients[8]. This finding suggests that increasing dermatological disease burden may parallel worsening systemic inflammatory effects and respiratory involvement[12].

There are some limitations in the present study. The study was conducted at a single center with a relatively modest sample size, which may limit generalizability of findings[16]. Additionally, the cross-sectional design prevented long-term evaluation of progressive pulmonary decline[17]. Future multicenter prospective studies with larger populations and advanced inflammatory profiling are recommended to further clarify the pathophysiological relationship between psoriasis and pulmonary dysfunction[18].

Despite these limitations, the study provides important local evidence regarding the relationship between systemic inflammation and pulmonary impairment in psoriasis patients[14]. Regular pulmonary function tests and inflammatory biomarker measurements could help identify lung dysfunction early on, leading to better treatment and a decrease in long-term complications of respiratory function in psoriasis patients[19,20].

CONCLUSION

The current study showed a strong association between psoriasis and decline in pulmonary function and increase in systemic inflammatory markers. Spirometric parameters were highly compromised in patients with psoriasis and CRP, ESR, IL-6 and TNF-α were highly elevated in patients with psoriasis as compared to healthy controls. Chronic systemic inflammation seems to be an important factor in the association of psoriasis with respiratory dysfunction. The inflammatory biomarkers, smoking status, obesity and the severity of the psoriasis were found to be significant predictors of pulmonary impairment. These findings indicate that psoriasis should be viewed as a multisystem inflammatory disease with possible respiratory involvement, and not just a skin disease. Measurement of lung function and monitoring of systemic inflammatory markers could aid in early detection of lung function abnormalities in psoriasis patients. Thus, early recognition and complete multidisciplinary management might be helpful for better long-term prognosis and in prevention of further pulmonary complications in patients with psoriasis.

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Data Availability: The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

Authors' Contributions

NF: Conceptualization, supervision, manuscript review.
KS: Data collection, statistical analysis, manuscript drafting.
SA: Laboratory analysis, data interpretation.
SSS: Pulmonary function assessment, clinical evaluation.
BF: Literature review, manuscript editing.
ZHQ: Study design, final manuscript approval.

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