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COMORBIDITIES AND QUALITY OF LIFE IN PATIENTS WITH MODERATE TO SEVERE PSORIASIS

Shilpa Soni[1*]

[1*]Assistant Professor, Department of Dermatology, Venerology and Leprosy, NIMS, Jaipur (Rajasthan)

***Corresponding Author:** Shilpa Soni
*Assistant Professor, Department of Dermatology, Venerology and Leprosy, NIMS, Jaipur (Rajasthan)

ABSTRACT
Psoriasis is a common, chronic inflammatory immunologically mediated disease of the skin, showing a high prevalence of associated comorbidities, and strongly affecting patients' quality of life (QOL), with profound impact on the psychological aspect. We aimed to establish the correlation between QOL and the associated comorbidities in patients with moderate to severe psoriasis. A cross-sectional, observational, epidemiological study was conducted. Adult patients diagnosed with moderate to severe psoriasis at least 6 months prior to the study visit and receiving or not receiving treatment for psoriasis were eligible for inclusion. A total of 146 patients were included. The study population showed mean 36-item short-form (SF-36) physical and mental health scores and Dermatological Life Quality Index (DLQI) of 49.7, 46.2 and 5.3, respectively. The multiple linear regression models showed that patients with moderate to severe psoriasis and a diagnosis of psoriatic arthritis (PsA), hypertension, diabetes mellitus, sleep disturbances or obesity were found to have lower SF-36 health physical scores. Female patients with depression or anxiety disorders had lower SF-36 health mental scores. Patients diagnosed with moderate to severe psoriatic disease and associated anxiety disorder had greater DLQI scores. Moderate to severe psoriasis has a significant burden on the QOL of patients. Regardless of sex, patients with several comorbidities such as PsA, hypertension or obesity were found to have worse scores in the physical component of the QOL questionnaire, whilst women were more affected in the mental health component than men.

Key words: arthritis, cardiovascular diseases, comorbidities, psoriasis, quality of life

Corresponding Author Details
Dr. Shilpa Soni
F-409, Ridhi Shidhi Tower,
Near Manipal Hospital, Vidhyadhar Nagar,
Jaipur (Rajasthan)-302039
Email- drshilpasoni@gmail.com

INTRODUCTION
Psoriasis is a chronic, multisystemic inflammatory disease of the skin, mediated by pro-inflammatory cytokines in combination with T-helper (Th) 1 and Th17 cells, [1] which has been estimated to affect

2–3% of the population worldwide.[2] There are different clinical psoriasis types, of which plaque psoriasis or psoriasis vulgaris is the most prevalent phenotype found in more than 80% of all cases.[4] This complex and immune-mediated condition, traditionally viewed as an inflammatory skin disorder, is increasingly recognized as a skin disease with far-reaching systemic effects.[5] Growing evidence is showing that the immune-mediated chronic inflammatory processes underlying psoriasis may contribute to a higher prevalence of associated comorbidities.[6] As such, psoriatic patients suffer from a spectrum of extracutaneous disease manifestations,[5,7] including psoriatic arthritis (PsA), metabolic syndrome, cardiovascular disease or malignancies, amongst others.[5,8–11] In addition to the physical impact, psoriasis has also been associated with certain psychopathological comorbidities that are not always influenced by disease severity,[12] and this is rated as one of the worst aspects of the disease.[13] Psoriasis is a serious condition that strongly affects the selfperception and is associated with greater negative impact on quality of life (QOL).[14] In fact, it has been shown that the effect of psoriasis on QOL is as great as that of other major medical conditions, such as cancer, heart failure, diabetes and depression.[15] Therefore, we aimed to analyze the clinical profile of patients with moderate to severe psoriasis in terms of associated comorbid diseases and to establish its correlation with their QOL.

MATERIALS & METHODS

This was a cross-sectional, observational, epidemiological study. All patients gave written informed consent for the use of their data prior to inclusion.

Objectives

The primary objective of this study was to establish the correlation between QOL and the associated comorbid diseases in patients with moderate to severe psoriasis. Secondary objectives were to describe the sociodemographic characteristics and the lifestyle habits, to evaluate the clinical features of psoriasis.

Study population

All adult patients diagnosed with moderate to severe psoriasis at least 6 months prior to the study visit and receiving or not receiving treatment for psoriasis at the moment of the inclusion on study were eligible. We defined patients with moderate to severe psoriasis as those with a Psoriasis Area and Severity Index (PASI) score of more than 10, and/or a body surface area (BSA) involvement of more than 10%, or a Dermatology Life Quality Index (DLQI) score of more than 10 at the initial diagnosis.

Assessment

The following information was retrospectively retrieved: sociodemographics (age, sex, employment status and level of education), lifestyle habits (consumption of alcohol, tobacco or regular exercise), history of psoriasis (type of psoriasis, assessment of severity and treatment) and comorbidities (e.g. PsA, obesity, hypertension, diabetes mellitus, dyslipidemia, cardiovascular disease, depression, anxiety). Patients were also given two questionnaires to measure the impact of skin disease on their QOL: the generic 36-item short-form (SF-36) to survey health status and the dermatology-specific instrument, the DLQI. The SF-36 is a widely used 36-item selfreported survey assessing eight domains of health status: physical activities, social activities, usual physical role activities, bodily pain, general mental health, usual emotional role activities, vitality and general health perceptions. A score from 0 to 100 is calculated for each item, with higher scores indicating better QOL.[16] The DLQI is a compact, self-reported questionnaire to measure QOL over the previous week in patients with skin diseases.[17] This is a 10-item questionnaire covering symptoms and feelings, daily activities, leisure, work and school, personal relationships and treatment. Each item is scored on a 4-point scale (range, 0–30), with lower scores indicating higher levels of QOL.[18]

Statistical considerations

Data for all evaluable patients was analyzed. Quantitative variables were described using means, standard deviations (SD) and confidence interval at 95% when they were normally distributed, or

medians and interquartile range when they were not. Qualitative variables were expressed as number of patients and relative and absolute frequencies. To analyze statistically significant differences between quantitative variables, we used Student's t-test or the Mann–Whitney U-test, according to the distribution of data; while for qualitative variables, Fisher's exact test or the v2 -test were used. Multivariate logistic regression analyses were used to assess the possible association between the comorbidities and QOL. The significance level was determined as $P < 0.05$.

RESULTS

Study population and lifestyle habits

In total, case report forms were fully completed for 146 patients with moderate to severe psoriasis. The sociodemographic characteristics of patients are presented in Table 1.

Table 1 Sociodemographic characteristics (n = 146)

	n (%)
Sex	
M	58(39.7)
F	88(60.3)
Age	
Less than 30	17(11.6)
31-49	72(49.3)
50-69	50(34.2)
70 & above	7(4.8)
Employment	
Employed	90(61.6)
Unemployed	23(15.7)
Student	12(8.2)
Housewife	21(14.9)
Education	
None	17(11.6)
Primary	50(34.2)
Secondary	42(28.8)
University	27(18.5)
Other	10(6.9)

The mean age of patients at study inclusion was 46.3 years. A total of 54 (36.9%) patients were smokers, half of whom reported smoking a mean daily number of 10–20 cigarettes. The number of patients who reported drinking alcohol on a daily basis was 52 (35.7%); of these, 8 (15.3%) admitted drinking more than 40 ml of alcohol per day. Nearly 43% of patients stated that they exercised regularly.

Disease characteristics

The median age at onset of psoriasis was 21.0 years (range, 15.0–32.0) and the median duration was 20 years (range, 11.4– 29.8). At initial diagnosis, plaque psoriasis was the most common phenotype of disease in almost all patients (89.1%), followed by guttate (3.6%), erythrodermic (1.5%), pustular (1.3%), palmoplantar (1.1%), inverse (0.6%) and other types (1.6%). According to our core definition, the majority of patients (61%) were initially diagnosed as having moderate psoriasis and the remaining 39% severe. We defined patients with moderate to severe psoriasis as those with a PASI score of more than 10, and/or a BSA involvement of more than 10%, or a DLQI score of more than 10 at the initial diagnosis. A total of 68 (47%) patients had a family history of psoriasis; in 76% of cases, these were first-degree relatives. At the time of the study visit, 54 (37.3%) patients were having an active psoriasis recurrence. The mean number of acute psoriatic recurrences experienced by patients during the previous 12 months was 2.8 ± 2.6. We found that disease severity was significantly greater in patients

experiencing an acute psoriatic recurrence episode than those who were not, across all the assessment tools for disease severity (PASI, BSA or Physician Global Assessment) (P < 0.001) (Table 2). During the 12 months prior to study initiation, the majority of patients (62.8%) had received topical treatments, followed by biologics (56.8%), conventional systemic therapies (42.6%) and phototherapy (19.0%).

Table 2 Psoriatic severity assessment at the study visit (n = 146)

	Patient in acute psoriatic recurrence episode, n (%)	
	Yes, n=55	No, n= 91
PASI score		
<10	25(45.4)	85(94.4)
>10	30(54.5)	5(5.5)
BSA involvement		
<3%	7(12.7)	58(64.4)
3-10%	17(30.9)	25(27.8)
>10%	31(56.3)	7(7.8)
PGA		
0-1	7(12.7)	71(78.8)
2-3	32(58.2)	18(20.0)
4-5	16(29.0)	1(1.1)

BSA, body surface area; PASI, Psoriasis Area and Severity Index; PGA, Physician Global Assessment.

Comorbidities

A total of 105 (72.0%) patients had at least one comorbid condition in addition to psoriasis; of these, 69 (47.3%) individuals reported more than one comorbidity. Elevated lipid levels, obesity (body mass index [BMI], ≥30 kg/m^2), PsA and high blood pressure were the most common comorbidities, reported in 28.1%, 26.0%, 21.8% and 18.3% of patients, respectively. Furthermore, a significant association was observed between patients with obesity and PsA in 11 (7.5%) subjects. Additionally, 19 (13.0%) individuals had a diagnosis of tuberculosis infection, and almost all of them (95.6%) had latent infections.

QOL

The overall study population showed mean SF-36 physical and mental health scores of 49.7 and 46.2, respectively, and a mean score of 5.3 in the DLQI. Statistically significant differences were found in mean SF-36 physical, mental health scores and DLQI in patients who were experiencing an acute psoriatic recurrence episode compared with those who were not, at 48.5 versus 50.4, (P < 0.01), 43.2 versus 48.0 (P < 0.001) and 9.3 versus 3.0 (P < 0.001), respectively. The multiple linear regression models using a backwards elimination approach, showed that patients with moderate to severe psoriasis and a diagnosis of PsA, high blood pressure, diabetes mellitus, sleep disturbances or obesity were found to have lower SF-36 physical component scores (P < 0.05). Similarly, those of female sex and affected by depression or anxiety disorder were more likely to have lower SF-36 mental component scores (P < 0.05), indicative of worse QOL. Moreover, those patients diagnosed with moderate to severe psoriatic disease and associated anxiety disorder had greater DLQI score (P < 0.05), thus indicating greater impairment in QOL.

A statistically significant association between comorbidities and psoriatic disease severity was found in anxiety disorder (PASI, P = 0.038; BSA, P = 0.005), dyslipidemia (PASI, P = 0.022) and chronic hepatopathy C (BSA, P = 0.014). A negative correlation was found between each psoriatic disease severity assessment and the SF-36 physical health score (PASI, r = -0.160 P = 0.0; BSA, r = -0.173, P = 0.0) and the SF-36 mental health score (PASI, r = -0.227, P = 0.0; BSA, r = -0.214, P = 0.0).

Conversely, a positive correlation between the DLQI and disease severity was observed (PASI, r = 0.628, P = 0.0; BSA, r = 0.609, P = 0.0).

DISCUSSION

The findings of the present investigation underscore the correlation observed between QOL and the associated comorbid diseases in patients with moderate to severe psoriasis. This is one of the most extensive works carried out concerning comorbidities and QOL and provides a new insight into this topic in psoriatic patients. As one might expect, the majority of patients in our investigation had been diagnosed with a concomitant disease in addition to psoriasis, and almost half of the study population suffered from more than one comorbid condition. That is the case of the significant association between obesity and PsA, found in 7.4% of the individuals diagnosed with moderate to severe psoriasis. Previous large, prospective, epidemiological studies conducted in young women in the USA confirmed that obesity precedes psoriasis. Specifically, increased adiposity, weight gain and higher BMI were directly associated with the risk of developing psoriasis. Similar results from the investigation carried out by Li et al.[18, 19] concluded that obesity was an independent risk factor for PsA.[20] This is stressed by the fact that obesity is related to persistent, low-grade inflammation characterized by increased levels of leptin and inflammatory cytokines, [21] which could fuel a pro-inflammatory status leading to psoriasis and PsA. Beyond the pathophysiological correlation between obesity, PsA and psoriasis, the clinical implication of these findings may prove useful to improve management of patients with psoriasis and/or PsA. Therefore, in the case of patients with moderate to severe psoriasis and an existing diagnosis of obesity, dermatologists should encourage patients to lead healthy lifestyles, regarding diet and exercise, in addition to emphasizing adherence to treatment. Moreover, the pattern of fat distribution not only correlates with the risk of developing psoriasis but also with the risk for developing metabolic diseases, and specifically metabolic syndrome. According to the National Cholesterol Education Program Adult Treatment Panel III, metabolic syndrome is defined as the presence of three or more of the following components, including abdominal obesity, increased insulin resistance (or elevated glucose level), abnormal lipids and elevated blood pressure.[22] The presence of metabolic syndrome increases the risk of developing coronary heart disease. However, this risk is not as great as the risk conferred by its component factors alone.[23] Even though data on the association between psoriasis and metabolic syndrome are scarce,[24] the findings from the National Health and Nutrition Examination Survey 2003–2006 conducted by Love et al. in a US population, concluded that the prevalence of metabolic syndrome among psoriatic patients was almost two fold greater than in those without psoriasis.[25] Love et al. also observed that the most common features of metabolic syndrome among these patients were abdominal obesity, hypertriglyceridemia and low levels of lowdensity lipoproteins.[25] In our investigation, we did not seek the diagnosis of metabolic syndrome itself, but we did search for the individual components collected as comorbidities, finding that obesity was the most common feature in 26% of the study population, followed by hypercholesterolemia (23%), hypertension (18%) and diabetes mellitus (8%). Given the implication of these associated comorbidities, a diagnosis of psoriasis should trigger the early suspicion of the coexistence of metabolic syndrome, as it has been categorized as an independent life-threatening factor for the risk of cardiovascular disease.[26]

An association between psoriasis and latent tuberculosis infection (LTBI) is supported by recent epidemiological studies conducted in populations. Results from the study carried out by Sanchez-Moya and Dauden, which included 144 patients with moderate to severe psoriasis treated with tumor necrosis factor antagonists, [27] showed that 29% of the study population was diagnosed with LTBI based on a positive tuberculin skin test and/or signs of past tuberculosis on chest X ray. Subsequently, in the investigation conducted in the BIOBADADERM (Spanish registry for systemic biologic and non-biologic treatments in psoriasis), including a total of 1425 patients, we found that the number of patients diagnosed with LTBI before starting biologic treatment was notably decreased, accounting for 163 (11.4%) subjects.[28] Likewise, in our investigation LTBI was found with a prevalence of almost 13% of patients with moderate to severe psoriasis.

This emphasizes the need for early LTBI screening at least before the administration of biologic agents, [29] as LTBI reactivation has been shown to be associated with the administration of immunosuppressive drugs, such as corticosteroids and/or biologic agents in immune-mediated inflammatory diseases.

In study, depression and anxiety disorder were found in 9% and 16% of patients, respectively.[31] These two conditions in women were associated with a decreased QOL in the SF-36 mental component score. Negative predictive factors for the SF-36 physical scores were the diagnosis of PsA, hypertension, diabetes mellitus, sleep disturbances and obesity. Therefore, psoriasis is presented as having a negative impact on physical, psychological and social factors that directly affects patients' QOL. Our findings are consistent with previous studies. Rapp et al., using the SF-36 questionnaire, demonstrated that the mean SF-36 mental health scores for patients with psoriasis were lower than those for patients suffering from heart disease, diabetes or cancer.[15] Likewise, Grozdev et al. in an attempt to determine whether patients' QOL, as assessed by the Short Form-12 Health Survey (a shorter version of the SF-36), was associated with psoriatic severity, highlighted that age was negatively associated with measures of physical functioning, but positively correlated with mental functioning. Simultaneously, men scored higher on both mental and physical components than women; whereas increased BMI was associated solely with a decreased physical health component.[32]

As expected, we found that psoriatic severity was associated with decreased QOL in patients with moderate to severe psoriasis. Particularly, mean PASI scores and DLQI correlated strongly in this group of patients ($R2 = 0.628$, $P < 0.05$). In line with our results, data obtained from the systematic review following the PRISMA guidelines to assess the correlation between PASI and DLQI, suggested that a reduction in PASI score could be translated into a significant QOL improvement ($R2 = 0.898$, $P < 0.01$), primarily recorded in patients who had achieved a reduction of at least 75% in their mean PASI score.[33] The long duration of the illness could mean an alteration of scores on QOL index, and that there is a linear relationship between the severity of psoriasis, duration of the illness and the degree of impairment of the QOL.[34]

The authors recognize some limitations in this study that should be considered when interpreting the results. First, it should be noted that the diagnosis of metabolic syndrome was not collected from the patients' medical records. Thus, the omission of this key feature in our study is likely to have resulted in a weaker correlation between comorbidities and QOL, besides the lack of data on the current prevalence of metabolic syndrome in patients with moderate to severe psoriasis. It is also worth acknowledging that certain biases could have been introduced when collecting data due to the retrospective design. These may affect the interpretation of the results and the extrapolation to similar populations. Also, nearly 50% of patients in our study had a family history of psoriasis, therefore, further analysis will be necessary to distinguish if this point influences the QOL of patients without familial antecedents.[35] However, conducting this type of studies is of great relevance as it allows us to learn about conditions from routine clinical practice in this group of patients.

CONCLUSION

In conclusion, moderate to severe psoriasis has a significant burden on QOL. Regardless of sex, those patients with several comorbidities such as PsA, hypertension or obesity were found to have worse scores in the physical component of the QOL questionnaire, whilst women were strikingly more affected in the mental health component than men.

CONFLICT OF INTEREST: None.

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