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Original Article

A clinical study of psoriasis and its association with co-morbid conditions

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Abstract

Objectives The study aimed (1) to compare incidence of co-morbidities among psoriatic patients (cases) and nonpsoriatic patients (controls), (2) to determine the association between psoriasis and various co-morbidities and (3) to determine the relationship between the severity of psoriasis and co-morbidities.

Methods We performed a hospital-based case-control study involving 100 psoriatic patients (cases) and 100 age- and sex-matched nonpsoriatic patients (controls) from the dermatology outpatient department in a government teaching institute. Detailed history and examination was followed by relevant investigations. The severity of psoriasis was assessed according to Psoriasis Area and Severity Index (PASI), and body surface area (BSA) measurement. Cardiovascular risk factors were assessed by using the definition for metabolic syndrome, which includes the presence of three or more of the National Cholesterol Education Program's Adult Panel III (ATP III) criteria.

Results The study revealed statistically significant association of psoriasis with metabolic syndrome (27% vs 8%, p = 0.0004) and psoriatic arthritis. Psoriatic patients had significantly higher levels of triglycerides (24% vs 8%, p = 0.002) and fasting blood sugar (23 % vs 8%, p = 0.003) along with significantly lower HDL levels (29 % vs 7%, p = 0.000, in males and 7% vs 2%, p = 0.043 in females). Abdominal obesity was more prevalent in psoriatic patients (24 % vs 9%, p = 0.02 in male and 9 % vs 3%, p = 0.033 in females). Neither metabolic syndrome nor psoriatic arthritis correlated with the severity of psoriasis.

Conclusion There was higher prevalence of metabolic syndrome in patients with psoriasis. However, its presence did not correlate with either severity or duration of the psoriasis. Hence, we suggest that all patients need to be evaluated for metabolic syndrome irrespective of severity of psoriasis which is the risk factor for systemic diseases.

Key words
Psoriasis, metabolic syndrome, comorbidities.

Introduction

Psoriasis is a chronic, inflammatory cell-mediated, genetically determined, common dermatological disorder affecting skin, nails, joints and associated with various systemic associations.[1,2] The disease is characterized by epidermal hyperproliferation, abnormal keratinocyte differentiation, angiogenesis with

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blood vessel dilatation, and Th1 and Th17 inflammation.[3] The chronic inflammatory nature of psoriasis is also thought to predispose patients to other diseases with an inflammatory component, the most notable being cardiovascular and metabolic disorders. This concept is supported by studies showing that psoriasis is associated with cardiovascular risk factors such as diabetes, obesity, hypertension, dyslipidemia, and smoking.[4,5] One of the strong predictors of cardiovascular disease is metabolic syndrome which is a cluster of risk factors including central obesity, atherogenic dyslipidemia, hypertension and glucose intolerance.[6] Hypertension which is a predictor of cardiovascular disease may be related to the increased levels of angiotensin-converting enzyme, endothelin-1(ET-1) and renin in patients with psoriasis,[7] whereas increased insulin resistance is due to TNF-α which plays a central role in the immune-pathogenesis of psoriasis.

The objectives of this study were to determine the association between psoriasis and various co-morbidities like diabetes mellitus, dyslipidemia, hypertension, cardiovascular disease etc., to compare incidence of comorbidities among psoriatic patients (cases) and nonpsoriatic patients (controls) and to determine the relationship between the severity of psoriasis and comorbidities.

Methods

This was a hospital-based case-control, observational, cross-sectional study involving a series of 100 psoriatic patients (cases) and 100 controls from the dermatology outpatient department in government teaching institute. The study was conducted from November 2012 to October 2014 after being approved by the Institutional Ethical Committee. Subjects of age 18 years and above with all clinical forms of psoriasis except for pustular and erythrodermic psoriasis were included in the study and patients who were pregnant or breast feeding or receiving disease modifying systemic therapy within 6 weeks from the date of enrolment were excluded. 100 age and sex-matched controls were enrolled among nonpsoriatic patients of other dermatological conditions attending the dermatology outpatient department.

After taking signed informed consent, a demographic and biometric data was collected. Detailed history including duration and course of the disease, severity of the disease, presence of nail or joint involvement, treatment history, concomitant illnesses, family history of psoriasis, diabetes, and cardiovascular disease and personal habits (smoking, alcohol, tobacco consumption) was taken. Complete systemic and cutaneous examination was done which was followed by relevant investigations. The severity of psoriasis was assessed according to Psoriasis Area and Severity Index (PASI), and body surface area (BSA) measurement. PASI score of less than 10% was considered as mild and more than 10% as severe. BSA involvement of less than 10% was taken as mild to moderate psoriasis and more than 10% as severe psoriasis. Body mass index (BMI) was calculated by using the formula [weight (kg) / height (m^2)]. To determine waist circumference, a measuring tape was placed at the level of the umbilicus and the widest part of the hip. Blood pressure was recorded as the average of two measurements. For assessing diabetic status and dyslipidemia, investigations like the fasting blood sugar, postprandial blood sugar and fasting lipid (cholesterol and triglycerides) levels were carried out. Liver function test (serum bilirubin, SGOT, SGPT, serum alkaline phosphatase), renal function test (serum creatinine, blood urea, serum uric acid) and X-ray of involved joints were also performed. Cardiovascular risk factors were assessed by using the definition for

metabolic syndrome, which includes the presence of three or more of the National Cholesterol Education Program's Adult Panel III (ATP III) criteria: waist circumference ≥ 102 cm or 40 inches (male), ≥88 cm or 36 inches (female); triglycerides≥150 mg/dl; reduced HDL≤40mg/dl in males and ≤50mg/dl in females, blood pressure ≥ 130/85 mmHg, and fasting plasma glucose ≥ 6.1 mmol/L (110 mg/dl).

Results

In our study, age of patients ranged from 18 years to 68 years. The mean age for cases and control group were 52 and 50 years, respectively, hence the difference was not statistically significant (p = 0.922) [**Table 1**]. Maximum number of patients (n=35) was in fourth decade followed by fifth decade (n=23). There were similar proportions of male and female patients in each of the study group (p = 0.645). Extent and severity of psoriasis was measured in PASI and BSA. Mean BSA was 32 and mean PASI was 15.75.

Duration of disease ranged from 2 months to 30 years, half of the patients (52%) had duration of the disease of more than 5 years. Chronic plaque psoriasis was the most common type of psoriasis contributing 91 (91%) cases. Two (2%) patients presented with guttate psoriasis and 7 (7%) with palmoplantar psoriasis. Eleven (11%) patients had joint complaints compared to 10 (10%) among controls. Among these 11 cases, 6 patients had mild psoriasis and 5 had severe psoriasis showing no association between psoriatic arthritis and severity of psoriasis. X-ray changes of involved joint were observed in all patients. Among cases, 1 patient had distal interphalangeal joint involvement (DIP arthritis alone), 2 patients had metacarpophalangeal and proximal interphalangeal joint involvement (symmetric polyarthritis), 1 patient had spondyloarthropathy, 8 patients had joint erosions, 5 patients had dactylitis and 3 patients had enthesitis. Among controls, only one patient had radiographic changes suggestive of osteoarthritis.

Table 1 Different clinical and laboratory parameters in cases and controls.

Characteristics	*Cases*	*Controls*	*P value*
Mean age (years)	52	50	0.922
Sex			
Female	29	32	0.645
Male	71	68	
Waist circumference (males)			
Normal	47	59	0.002
> 102cm	24	9	
Waist circumference (females)			
Normal	20	29	
> 88cm	9	3	0.033
Triglycerides			
Normal	76	92	
>150 mg/dl	24	8	0.002
Reduced HDL (males)			
Normal	42	61	0.000
<40	29	7	
Reduced HDL (females)			
Normal	22	30	0.043
<50	7	2	
Blood pressure			
Normal	79	83	0.471
> 130/85mmHg	21	17	
Fasting blood sugar			
Normal	77	92	0.003
>100mg/dl	23	8	
Metabolic syndrome			
Present	27	8	0.0004
Absent	73	92	
H/o smoking			
Absent	76	81	0.389
Present	24	19	
H/o alcohol			
Absent	78	73	0.596
Present	22	27	
Liver function tests			
Normal	98	98	1
Deranged	2	2	
Depression	19	4	0.48

Among 11 psoriatic patients, 7 (63.6%) patients had nail involvement along with history of joint pain compared to 34 (38.2%) patients with no history of joint pain (p = 0.740); hence there was no significant association between patients

with nail involvement and psoriatic arthritis. Nail involvement was seen in 41 (41%) patients. Among these, 17 patients had mild disease and 24 patients had severe disease. Among 59 patients without nail involvement, 35 patients had mild disease and 24 patients had severe disease showing no statistically significant (p = 0.079) association between nail involvement and severity of psoriasis. Among the nail changes, pitting was the most common finding followed by subungual hyperkeratosis, onycholysis and dystrophy.

Of 33 patients with raised waist circumference, 24 were male and 9 female and in control group there were 9 male and 3 female showing significant association of raised waist circumference in psoriatic cases compared to controls (p = 0.002). There were 24 (24%) patients with raised triglycerides compared to 8% controls (p = 0.002). The number of psoriatic patients with reduced HDL was 36, (29 males and 7 females) as compared to 9 (7 males and 2 females) among controls.

Twenty-one (21%) psoriatic patients had hypertension as compared to 17% controls (p = 0.471). Raised fasting blood sugar level (BSL) was observed in 23 (23%) patients compared to 8% controls (p = 0.003). Among 27 patients with metabolic syndrome, 15 (15%) patients had mild psoriasis and 12 (12%) patients had severe psoriasis (p = 0.665). Out of these 27 patients, 11 (11%) had psoriasis for less than 5 years and 16 (16%) had for more than 5 years (p = 0.878). Hence neither the severity nor the duration had any statistical association between metabolic syndrome, severity and duration of psoriasis. Association of hepatic system involvement was studied with the help of deranged liver function tests (LFTs). There were 2 patients with deranged LFT among cases and 2 patients among controls. There was no statistically significant difference between cases and controls (Fisher exact test, p = 1). In our study, 4 (4%) patients had raised uric acid levels among cases and none among controls. There was no significant association between depression and psoriasis (p = 0.48).

Discussion

Psoriasis is a multisystem inflammatory disease where the skin and the joints are the primary targets. There are many reports that psoriatic patients tend to have concurrent illnesses that are termed as comorbidities, though there are remarkably few studies from India. Comorbidities can be physical and psychological **(Table 2)**. Onumah *et al.*[8] observed that the severity of psoriatic skin disease portends a serious risk for the development of these comorbidities. Patients with moderate to severe psoriatic skin disease have a higher association with these comorbidities which may be related through common pathogenic mechanisms. Psoriasis has bimodal age of onset, first peak at 15- 20 years and second peak at 55-60 years but it can occur at any age. In Indians, highest incidence is reported in second decade or reproductive age group.[9] In one study, age of the patients ranged from 18 years to 68 years and maximum number were in fourth decade. A study done in North India by Bedi *et al.*[10] found the highest incidence to be in fourth decade which is similar to our study. Higher male: female ratio [2.4: 1] in our study group is similar to many studies reported from India.[9] Extent and type of involvement of different body surface areas with psoriasis has a huge bearing on the overall prognosis, as well as the choice of the treatment. For this purpose, psoriasis area severity index [PASI] and body surface area [BSA] involved are the most frequently used measures, which attempt to define the severity of psoriasis.[11] We classified our patients into mild [PASI of < 10%] and severe [PASI of > 10] type of psoriasis. Fifty-two patients had mild

Table 2 Comorbidities associated with psoriasis.

Psoriatic arthritis
Depression
Hypertension
Diabetes
Metabolic syndrome
Cardiovascular disease, such as coronary artery calcification and myocardial infarction
Dyslipidemia
Crohn's disease and ulcerative colitis
Autoimmune diseases
Non-alcoholic fatty liver disease
Chronic obstructive pulmonary disease
Obstructive sleep apnea

disease and 48% had severe disease. Most commonly, psoriasis presents as chronic, bilaterally symmetrical, well defined, erythematous, dry, red, scaly papules and plaques, Apart from this, there are several unique cutaneous manifestations, ranging from small papules (guttate psoriasis) to pustules (pustular psoriasis) and generalized erythema and scaling (erythrodermic psoriasis). In our study 91 cases [91%] presented with chronic plaque psoriasis, 2 cases (2%) had guttate psoriasis and 7% were diagnosed to have palmoplantar psoriasis. Bedi *et al.*[12] reported chronic plaque psoriasis as the commonest type [90%] followed by erythrodermic psoriasis in 3% cases and guttate psoriasis in 0.94%. Arthritis occurs in about 5% to 10% of patients of psoriasis.[13] In our study the number of patients with joint complaints[11] was not significantly higher when compared to control group.[10] Nail changes are seen in about 20% to 50% of psoriatics.[13] The common changes are pitting of the nail plate. The finger nails are more frequently involved than toe nails. The incidence of nail involvement is higher if there is associated arthropathy. Prasad *et al.*[14] studied 472 psoriatic patients. 40 patients had psoriatic arthropathy and out of these 40 patients, nail involvement was seen in 37 (92.5%) cases. In a study by Reich *et al.*[15] out of 1511 patients, 20. 6% had psoriatic arthritis and among these 68.6% showed nail involvement. In our study, out of 11 patients with psoriatic arthropathy, 7 (63.6%) patients showed nail involvement consistent with above-mentioned study. Comorbidities classically associated with psoriasis are psoriatic arthritis, Crohn's disease, psychological/ psychiatric disorders and uveitis. In recent years, the metabolic syndrome as a whole and its individual components has been associated with psoriasis.[16-18] Psoriasis is associated with metabolic syndrome, which encompasses obesity, raised triglycerides, low high density lipoprotein (HDL), insulin resistance, and hypertension. Its importance lies in its ability to predispose sufferers to cardiovascular disease.[19] There are some reports that the association is stronger for severe psoriasis than for mild psoriasis[20,21] but this association has still not been established beyond doubt as the number of studies are few and some studies have conflicting results. The updated Adult Treatment Panel III (ATPIII) criteria for the diagnosis of metabolic syndrome includes three or more of the following: triglyceride ≥ 150 mg/dl (1.7 mmol/l), HDL cholesterol < 40 mg/dl (1.03 mmol/l) in men and < 50 mg/dl (1.29 mmol/l) in women, fasting glucose≥100mg previously diagnosed with type 2 diabetes, blood pressure ≥ 130/85 mmHg or on antihypertensive medication, and central obesity (defined as waist circumference ≥ 90 cm in men and ≥ 80 cm in women, according to the ethnic criteria for Asians).[22] The International Diabetes federation (IDF) requires central obesity (defined as waist circumference ≥ 90 cm in men and ≥ 80 cm in women for Asians, except for Japanese) plus two of the following four factors: triglycerides ≥ 150 mg/dl, HDL cholesterol < 40 mg/dl in men and < 50 mg/dl in women, fasting glucose ≥ 100 mg/dl or previously diagnosed with type 2 diabetes, and blood pressure ≥ 130/85 mmHg or on treatment for hypertension.[23-25] The number of patients with increased waist circumference was 33, which is significantly more when compared

Table 3 Association of Metabolic Syndrome (MS) with psoriasis

Authors	*Year*	*TGL*	*HDL*	*DM*	*BP*	*Obesity*	*Severity*	*Duration*	*MS*
Gisondi *et al.* [6]	2007	S	NS	NS	NS	S	NS	S	S
Cohen *et al.* [29]	2008	S	S	S	S	S	-	-	S
Qureshi *et al*. [30]	2009	-	-	S	S	-	-	-	-
Nisa *et al.* [31]	2010	S	NS	S	S	NS	NS	NS	S
Ghiasi *et al.* [32]	2011	-	-	S	S	-	-	-	-
Pereira *et al.* [33]	2011	NS	NS	S	-	-	-	-	NS
Kutlu *et al.* [34]	2011	-	-	-	-	-	NS	NS	S
Madanagobalane *et al*. [7]	2012	S	NS	S	NS	S	NS	NS	S
Cenk Akcali [35]	2014	NS	NS	NS	S	NS	-	-	S
Ali *et al.* [36]	2014	S	S	NS	S	S	NS	NS	S
Our study	2014	S	S	NS	S	S	NS	NS	S

BP=blood pressure, DM= diabetes mellitus, HDL=high density lipoprotein, TGL=triglyceride lipids

to controls (12%). Similarly hypertriglyceridemia 24 patients and reduced HDL (36%) showed significant association with psoriasis. In a survey from Love *et al.*[26] The most common feature of the metabolic syndrome among patients with psoriasis was abdominal obesity, followed by hypertriglyceridemia and low levels of HDL cholesterol. Obesity itself is an independent risk factor for developing psoriasis. Sterry *et al*.[27] found that obese patients were more likely to have severe psoriasis (i.e. >20% body surface area). Intra-abdominal obesity was directly linked to the metabolic syndrome. Several studies have shown that psoriasis is associated with atherogenic dyslipidemia with increased blood levels of total cholesterol, triglycerides, low density lipoprotein (LDL), very low density lipoprotein, and lipoprotein A, and low levels of HDL and apolipoprotein B.[28] Though observational studies have detected independent associations between psoriasis and hypertension, our study showed no significant association. However, fasting BSL was increased in 23 cases as compared to 8 controls with P value of 0.003 indicating significant association with psoriasis. Multiple case control studies linking psoriasis and components of the metabolic syndrome have been done with variable results **(Table 3)**. Psoriasis is associated with low self-esteem and the prevalence of anxiety and depressive disorders is 30% and 60%, respectively. Recently, a high prevalence of alexithymia was observed.[37] About 10% of patients with psoriasis consider the possibility of suicide.[38-40] Recent data shows that depression and anxiety are mainly found in women with family problems.[41] In our study we found that incidence of depression was more among psoriatic patients (19%) compared to controls (4%). However, there was no statistical difference among the two groups in contrast to the study done by Esposito *et al.*[39] and Devrimci-Ozguven *et al.*[42] In conclusion, we have found higher prevalence of metabolic syndrome in patients with psoriasis. This association was not limited to severe cases but also occurs in mild cases and was not associated with duration of psoriasis. Hence, we suggest that all patients need to be evaluated for metabolic syndrome irrespective of severity of psoriasis which is the risk factor for systemic diseases.

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