

# Metabolic syndrome in patients with psoriasis: A comparative study

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## ABSTRACT

**Background:** Psoriasis patients are at increased risk of developing the metabolic syndrome (MS). Proinflammatory cytokines such as tumor necrosis factor- $\alpha$ , interleukin-6 that are increased in the psoriatic plaques are known to contribute to features of MS such as hypertension, dyslipidemia and insulin resistance. **Aims:** (1) To establish the frequency of MS in patients with psoriasis. (2) To study the risk factors associated with MS in psoriasis. **Materials and Methods:** A hospital based comparative study was conducted involving 40 adult patients with psoriasis and 40 age- and sex-matched controls. All participants were evaluated for components of MS. **Results:** Both groups included 31 males and 9 females. The mean age of the cases and controls were 49.95 years and 49.35 years, respectively. Psoriasis patients with MS had a statistically significant higher mean age ( $56.31 \pm 11.36$  years) compared with those without MS ( $46.89 \pm 11.51$  years). MS was present in 13 out of 40 (32.5%) patients with psoriasis and 12 out of 40 (30%) controls; this difference was not statistically significant. Higher age and female gender correlated with the presence of MS in psoriasis patients. The presence of MS in psoriasis patients was statistically independent of psoriasis area severity index score, body surface area involvement or psoriatic arthropathy. **Conclusion:** Our results suggest that there is no close correlation between psoriasis and MS in South Indian patients.

**Key words:** Comparative study, metabolic syndrome, psoriasis

## INTRODUCTION

Psoriasis is a chronic, T-cell mediated inflammatory disease of the skin and occasionally the joints.<sup>[1]</sup> Several observational studies have recently demonstrated that psoriasis is associated with systemic disorders such as cardiovascular disease, the metabolic syndrome (MS), cancer, chronic obstructive pulmonary disease, inflammatory bowel disease, depression and osteoporosis.<sup>[2,3]</sup> The suggested causal link between psoriasis and associated diseases is the presence of systemic inflammation and elevated levels of cytokines such as tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and interleukin-6 (IL-6).<sup>[2]</sup> There have been recent recommendations to “upgrade” psoriasis from a cutaneous to a systemic disease, but the topic remains contentious.<sup>[2]</sup>

MS, defined as a cluster of risk factors including central obesity, atherogenic dyslipidemia, hypertension and glucose intolerance, is a strong predictor of cardiovascular disease, that confers a cardiovascular risk higher than the individual components.<sup>[1,4]</sup> Increased mortality

from cardiovascular disease in patients with severe psoriasis has been documented and psoriasis may be an independent risk factor for myocardial infarction, especially in young patients.<sup>[1]</sup> Psoriasis is associated with MS, independent of its severity.<sup>[1]</sup> Several factors may contribute to an unfavorable cardiovascular risk profile in patients with psoriasis, such as cigarette smoking, alcohol consumption, obesity, physical inactivity, homocysteinemia, psychological stress, and depression, all of which are more prevalent in patients with psoriasis.<sup>[1,2]</sup> In addition, many traditional systemic therapies for psoriasis may also worsen cardiovascular risk factors such as hyperlipidemia, hypertension and homocysteinemia.<sup>[1,2]</sup>

Psoriasis affects about 3% of the population world-wide.<sup>[1]</sup> Recent studies have estimated prevalence of MS to be 15-24% in the general population and 30-50% among psoriasis patients. This increased frequency imposes a substantial burden on the overall health of psoriasis patients, which needs to be appropriately addressed during treatment of such patients.

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## AIMS

1. To establish the frequency of MS in patients with psoriasis
2. To study the risk factors associated with MS in psoriasis.

## MATERIALS AND METHODS

This was a hospital based comparative study, which was conducted over a period of two months between June and July 2012 at the Department of Dermatology. During the study period, psoriasis patients and controls attending the Dermatology Department were enrolled after obtaining informed consent.

### Cases

A total of 40 patients with psoriasis satisfying the following inclusion and exclusion criteria were enrolled:

- Inclusion criteria: Patients with psoriasis more than 18 years of age and those with psoriasis of at least 6 months duration.
- Exclusion criteria: Patients with psoriasis <18 years of age and those who have received cyclosporine or/and systemic retinoids therapy during the preceding one month.

### Controls

Forty age- and sex-matched controls satisfying the inclusion and exclusion criteria were enrolled.

- Inclusion criteria: Patients attending the Dermatology Outpatient Department suffering from skin diseases other than psoriasis.
- Exclusion criteria: Diagnosed cases of diabetes mellitus, hypertension and dyslipidemia attending special clinics in our hospital.

After obtaining informed consent from the patients, relevant data such as age, sex, occupation, age at the onset of psoriasis, percentage body surface area (BSA) of involvement, psoriasis area severity index (PASI), presence and distribution of psoriatic arthropathy and concomitant medications were collected in a proforma. Chronic plaque psoriasis was considered localized or generalised when it covers less or more than 10% of the BSA.

PASI was calculated as given below:<sup>[5]</sup>

Four sites of affection, the head (h), upper limb (u), trunk (t) and lower limbs (l), were separately scored by using three parameters, erythema (E), infiltration (I) and desquamation (D), each of which was graded on a severity scale of 0-4, where 0 = nil, 1 = mild, 2 = moderate, 3 = severe and 4 = very severe. The area-wise percentage involvement of the involved sites was calculated as: 1 ≤ 10% area; 2 = 10-29%; 3 = 30-49%; 4 = 50-69%; 5 = 70-89%; and 6 = more than 90%.

The final formula for PASI score: PASI = 0.1 (Eh + Ih + Dh) Ah + 0.2 (Eu + lu + Du) Au + 0.3 (Et + It + Dt) At + 0.4 (El + Il + Dl) A1.

For MS, following parameters were assessed: waist circumference, triglyceride level, high density lipoprotein (HDL) cholesterol level, blood pressure and fasting glucose. To determine the waist circumference, measuring tape was placed around the abdomen at the level of uppermost part of the pelvic bone, while ensuring that the tape measure remained horizontal and was snug without causing compression on the skin. Venous blood samples were collected from the patients after they fasted overnight (at least 8 h). Triglycerides and serum cholesterol were measured using standard enzymatic procedure. Blood pressure was recorded in a sitting posture and was calculated as an average of two measurements after the patients took the rest for 5 min. MS was diagnosed if three or more criteria of the National Cholesterol Education Program's Adult Treatment Panel III (ATP-III) were present, as given below:<sup>[6]</sup>

Ethics committee clearance was obtained prior to the study. Data was analyzed using SPSS (version 13, SPSS Inc. Chicago, Illinois, USA), Graphpad (version 3.06, Graphpad software, San Diego, California, USA). Descriptive statistics (mean, standard deviation, percentage), Student's *t*-test, Chi-square test and Fisher's exact test were used.

## RESULTS

Of the 40 cases and controls, 31 each were male and 9 female. The mean age of cases was 49.95 years ( $\pm 12.17$ ), with age ranging from 26 to 76 years. The mean age of male and female psoriasis patients were 50.26 years and 48.89 years, respectively. The mean age of the controls was 49.35 years ( $\pm 12.06$ ). There was no statistically significant difference in age between the cases and controls.

Psoriasis cases with MS had a statistically significant higher mean age ( $56.31 \pm 11.36$  years) compared with those without MS ( $46.89 \pm 11.51$  years), *P* value of 0.02. Controls with MS had a statistically significant higher mean age ( $54.57 \pm 9$  years) compared to those without MS ( $46.96 \pm 12.3$  years), *P* value of 0.038.

Age at the onset of psoriasis in patients with MS was  $52.15 (\pm 11.81)$  years and in those without MS was  $42.22 (\pm 12.73)$  years. The difference was statistically significant (*P* = 0.023).

Risk factor	Defining level
Abdominal obesity	Waist circumference Men >102 cm (>40 in) Women >88 cm (>35 in)
Triglycerides	≥150 mg/dL
HDL cholesterol	Men <40 mg/dL Women <50 mg/dL
Blood pressure	≥130/85 mmHg
Fasting glucose	≥110 mg/dL

### Education and socio-economic status

Seventy five percent of the cases were literate and 80% of the controls were literate. 95% of the cases belonged to the low income group and the remaining 5% belonged to the middle income group. Out of 40 controls, 87.5% belonged to the low income group and remaining 12.5% belonged to the middle income group.

### Occupation

Occupation groups of the cases were farmers (15%), labourers (15%) housewives (12.5%), retired employees (12.5%), cooks (10%), drivers and construction workers (5%) and others such as clerk, carpenter, conductor and launderer (10%).

In the control group, housewives (22.5%), retired employees (12.5%), tailor/security/construction workers (7.5%), attender/cook/clerk/shop owner (17%) were the main occupation groups seen.

### Type of psoriasis

Of the 40 cases, 36 had psoriasis vulgaris, two had psoriatic erythroderma and one patient each had acute generalized pustular psoriasis and palmoplantar psoriasis. Of the 36 cases with psoriasis vulgaris, psoriasis was stable in 33 patients and unstable in 3 patients.

### Duration of psoriasis

The mean duration of psoriasis was 4.5 years ( $\pm 6.52$ ). Mean duration in males was 3.94 years and in females was 6.44 years.

### Body surface involvement

The mean percentage body surface area (BSA) of involvement of cases having psoriasis was 38.50%. The mean BSA among patients with MS was 26.54% and in those without MS was 44.19%, but the difference was not statistically significant ( $P = 0.061$ ). Chronic plaque psoriasis was localized in 20% of cases and generalised in 80% of cases.

### PASI

The mean PASI among cases was 13.93. The mean PASI among psoriasis patients with MS was 9.99 and in those without MS was 15.83. The difference was not statistically significant ( $P = 0.061$ ).

### Psoriatic arthritis

Psoriatic arthritis was seen in 5 out of 40 cases of psoriasis, involving spine (1), knee joints (4) and small joints of hands (1).

### Usage of concomitant medication

Nine cases were on antihypertensives (atenolol, amlodipine, enalapril) anti-diabetics (metformin, glibenclimide), hypolipidemic drugs (atorvastatin), or drugs for thyroid disorders (thyroxine). Thirty one case were not on any concomitant medication.

### Height, weight, body mass index (BMI) and waist measurement [Table 1]

Weight was the only significantly different parameter between two groups, being higher in the control group ( $P = 0.0178$ ).

### Blood pressure, fasting lipid profile and fasting blood sugar [Table 2]

Low density lipoprotein (LDL) level was the only significantly different parameter between the two groups, being higher in the control group ( $P = 0.0381$ ).

### MS in cases and controls

The frequency of presence of MS among patients with psoriasis was 13 out of 40 (32.5%) and that in the control group was 12 out of 40 (30%), but this difference was not statistically significant ( $P$  of 0.8094 by Chi-square test).

The presence of MS in psoriasis was significantly associated with higher age of the patients (mean age in patients with and without MS was  $56.31 \pm 11.36$  years and  $46.89 \pm 11.51$  years, respectively,  $P = 0.02$ ) and female gender (6/9 in females vs. 7/31 in males,  $P = 0.021$  by Fisher's exact test). The presence of MS in psoriasis patients was statistically independent of PASI score, BSA involvement or psoriatic arthropathy.

Table 3 shows comparative characteristics of psoriasis cases with and without MS.

The age and fasting blood sugar were significantly higher in cases with MS ( $P = 0.02$  and  $P < 0.0001$ , respectively).

**Table 1: Average height, weight, BMI and waist measurement in cases and controls**

Parameters	Cases	Controls
Height (cm)	159.07	159.95
Weight (kg)	56.35	62.475
BMI (kg/m <sup>2</sup> )	22.47	24.45
Waist circumference (cm)	88.27	90.35

BMI: Body mass index

**Table 2: Average BP, fasting lipid profile and FBS among cases and controls**

Parameters	Cases	Controls	P value
Systolic BP (mmHg)	121.8	123.7	0.6585
Diastolic BP (mmHg)	78.9	75.95	0.2406
Triglyceride (mg/dL)	149.5	136.8	0.5176
Total cholesterol (mg/dL)	171.7	185.5	0.1181
HDL (mg/dL)	37.7	35.9	0.1874
LDL (mg/dL)	109.21	123.87	0.0381
VLDL (mg/dL)	25.45	27.15	0.5849
FBS (mg/dL)	104.02	104.82	0.9265

BP: Blood pressure, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, VLDL: Very-low-density lipoprotein, FBS: Fasting blood sugar

Proportion of female cases was significantly higher in cases with MS compared to those without MS ( $P = 0.021$ ).

Table 4 shows comparative characteristics of cases and controls having MS. Only total cholesterol and LDL were significantly different in between cases and controls with MS, both being higher in controls ( $P = 0.0170$ ,  $P = 0.016$ ).

## DISCUSSION

Psoriasis patients are at increased risk of developing MS. Although the exact pathogenic mechanism is not known, certain proinflammatory cytokines like TNF- $\alpha$ , IL-6 that are found in psoriatic plaques are known to contribute to features of MS such as hypertension, dyslipidemia and insulin resistance.

Several studies have found that MS is associated with psoriasis. Gisondi *et al.*,<sup>[1]</sup> studied 338 patients with chronic plaque psoriasis as well as 334 controls and found statistically significant higher prevalence of MS in psoriatic patients compared with the controls using National Cholesterol Education Program (NCEP) ATP III criteria (30.1% in cases and 20.6% in controls,  $P = 0.005$ ). Similarly, Zindanci *et al.*,<sup>[7]</sup> after studying 115 plaque type psoriasis patients and 140 healthy individuals found a higher prevalence of MS in cases (53%)

compared to controls (39%), ( $P < 0.001$  using International Diabetes Federation criteria). Nisa and Qazi<sup>[8]</sup> studied 150 patients with the chronic plaque psoriasis and 150 healthy individuals and found the prevalence of MS as 28% in cases and 6% in controls, ( $P < 0.05$ ).

Our study observed a higher prevalence of MS in cases (32.5%) compared to controls (30%) as per NCEP ATP III criteria, but the difference was not statistically significant. Mebazaa *et al.*,<sup>[9]</sup> studied 164 psoriasis patients and 216 controls and showed a marginally higher prevalence of MS in psoriatic patients (35.5%) compared to controls (30.8%). Kim *et al.*,<sup>[10]</sup> also have studied 490 patients with psoriasis and 682 controls and found no statistical difference in MS between patients with psoriasis and controls ( $P = 0.2$ ).

The absence of significant association between psoriasis and MS in our study may be attributed to several factors. Cases and controls for our study came from the South Indian population. According to Misra and Khurana,<sup>[11]</sup> South Asian population in general is inherently predisposed to an increased risk of MS and associated cardiovascular risk factor compared to the Caucasians. This could have increased prevalence of MS in the controls in our study, thereby negating an actual difference from that in psoriasis patients. Socioeconomic factors could have played a role in lowering the actual prevalence of MS in our psoriasis patients. Most of our cases (95%) and controls (87.5%) belonged to lower socio-economic status, which may explain the lower frequency of MS in our study population. While it is well-known that MS is more prevalent

**Table 3: Comparative characteristics of psoriasis cases with and without metabolic syndrome**

Parameters	Psoriasis (MS)		P value
	With	Without	
Number of patients	13	27	-
Age (years)	56.31±11.36	46.89±11.51	0.02
Gender	Male:7 Female:6	Male:24 Female:3	0.021
Psoriatic arthropathy (n=5)	2	3	-
PASI score	9.99±6.13	15.83±9.97	0.0606
BSA %	26.54±21.95	44.79±29.26	0.0612
Height (cm)	155.46±9.22	160.81±8.46	0.0767
Weight (kg)	58.31±11.36	55.41±10.75	0.4374
BMI (kg/m <sup>2</sup> )	24.41±5.69	21.53±4.81	0.1038
Waist circumference (cm)	92.31±13.45	86.33±10.78	0.1385
Systolic BP (mm Hg)	128.31±21.87	118.67±20.13	0.1757
Diastolic BP (mm Hg)	81.69±11.62	77.56±12.23	0.3154
Triglyceride (mg/dL)	174.77±116.36	137.44±84.69	0.2558
Total cholesterol (mg/dL)	166.77±33.85	174.07±37.99	0.5594
HDL (mg/dL)	35.54±7.53	38.81±6.37	0.1596
LDL (mg/dL)	103.25±22	111.96±28.01	0.3493
VLDL (mg/dL)	29.09±14.06	23.92±8.89	0.1853
FBS (mg/dL)	140.15±48.65	86.63±24.50	<0.0001

PASI: Psoriasis area severity index, MS: Metabolic syndrome, BSA: Body surface area, BP: Blood pressure, BMI: Body mass index, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, VLDL: Very-low-density lipoprotein, FBS: Fasting blood sugar

**Table 4: Comparison of cases and controls having metabolic syndrome**

Parameters	Metabolic syndrome		P value
	Cases	Controls	
Number of patients	13	12	-
Age (years)	56.30±11	54.57±9	0.6691
Gender	F:6, M:7	F:4, M:8	-
Height (cm)	155.46±9.225	159.71±12.425	0.3254
Weight (kg)	58.30±11.36	62.14±8.58	0.3295
BMI (kg/m <sup>2</sup> )	24.41±5.69	24.61±4.05	0.9147
Waist circumference (cm)	92.30±13.4	93.96±9.40	0.7123
Systolic BP (mm Hg)	128.30±21.87	134±15.82	0.4433
Diastolic BP (mm Hg)	81.69±11.62	77.85±10.12	0.3684
Triglyceride (mg/dL)	174.76±116.37	182.5±113.16	0.8625
Total cholesterol (mg/dL)	166.76±33.85	203.71±40.61	0.0170
HDL (mg/dL)	35.53±7.53	34.35±5.83	0.6514
LDL (mg/dL)	103.25±22	133±34.26	0.0164
VLDL (mg/dL)	29.09±14	36.28±22.46	0.3636
FBS (mg/dL)	140.15±48.65	127.35±50.37	0.5087

BP: Blood pressure, BMI: Body mass index, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, VLDL: Very-low-density lipoprotein, FBS: Fasting blood sugar

in higher socioeconomic classes, it is increasing in the middle socio-economic class also. Gupta *et al.*,<sup>[12]</sup> found that cardiovascular risk and hypertriglyceridemia was more common in the urban middle class of Jaipur, India. MS might have been influenced by occupational activity in our patients. In nearly one-third of psoriasis patients, occupation involved heavy manual work compared to the control group who generally had lesser physical activity. Crist *et al.*,<sup>[13]</sup> reported that increased aerobic exercises/work actually reduced the prevalence of MS.

MS in psoriasis was associated with higher age in our study. Age influences the occurrence of MS in the general population as the individual components of MS are more common in the elderly population. Cases and control groups with MS in our study had statistically significant higher mean age ( $56.31 \pm 11.3$  years and  $54.57 \pm 9$  years, respectively) compared to those without MS in their respective groups ( $46.89 \pm 11.5$  years and  $46.96 \pm 12.3$  years, respectively). Gisoni *et al.*,<sup>[1]</sup> found MS in psoriasis was more common after 40 years of age. Zindanci *et al.*,<sup>[7]</sup> found that MS was common in the age group of 40-59 years. Kim *et al.*,<sup>[10]</sup> found the prevalence of MS in patients older than 53 years age. Sumner *et al.*,<sup>[14]</sup> also concluded that the prevalence of MS increased with age - prevalence being 6.6% in young adults and 34% in older adults.

Our study found that MS was significantly more common in female psoriasis patients. Zindanci *et al.*,<sup>[7]</sup> found increased prevalence of MS in female patients ( $P < 0.05$ ). Mebazaa *et al.*,<sup>[9]</sup> found increased prevalence of MS in female patients with psoriasis (47.4%) compared to controls (30.1%), ( $P = 0.01$ ). However, Gisoni *et al.*,<sup>[1]</sup> Nisa and Qazi<sup>[8]</sup> and Kim *et al.*,<sup>[10]</sup> found no gender difference in the prevalence of MS. Zindanci *et al.*,<sup>[7]</sup> demonstrated higher prevalence of MS among women owing to higher BMI and waist circumference than men. Our study observed higher mean BMI and waist circumference in women compared to that in men, but the difference was not statistically significant ( $P > 0.05$ ).

MS was independent of PASI and BSA involvement of psoriasis in our study. Similar results were observed in studies performed by Gisoni *et al.*,<sup>[1]</sup> and Nisa and Qazi<sup>[8]</sup> They found no difference in the prevalence of MS based on PASI score and BSA involvement. Zindanci *et al.*,<sup>[7]</sup> and Mebazaa *et al.*,<sup>[9]</sup> also found that the prevalence of MS was independent of severity of psoriasis (PASI score). Kim *et al.*,<sup>[10]</sup> however, found that MS was associated with severe forms of psoriasis ( $P = 0.048$ ).

On analyzing the individual components of MS among psoriasis patients, we found that fasting blood sugar level was significantly higher among those with MS ( $P < 0.001$ ). Our study could not find a significantly higher prevalence of other components of MS such as obesity, hypertension and dyslipidemia among psoriasis patients with MS.

Several studies have demonstrated higher lipid levels in psoriasis. Dreier *et al.*,<sup>[15]</sup> found a significant increase in lipid levels among psoriasis patients than in controls ( $P < 0.001$ ). Shapiro *et al.*,<sup>[16]</sup> found that psoriasis was associated hyperlipidemia, but was not associated with an increase in LDL level. Cohen *et al.*,<sup>[17]</sup> have found that psoriasis is associated with dyslipidemia ( $P < 0.015$ ). In contrast, LDL and total cholesterol were significantly higher among controls with MS than among psoriasis patients with MS ( $P = 0.0170$  and  $0.0164$ , respectively) in our study. This might have been owing to the higher mean weight of controls compared to cases ( $P = 0.0178$ ) in our study.

## CONCLUSION

Our results suggest that there is no close correlation between psoriasis and MS in South Indian patients. This might have been due to a small sample size. However, the influence of race, socio-economic status and occupations involving heavy work on the occurrence of MS in psoriasis needs to be examined in larger studies.

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