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### <u>Original Article</u> Association between Psoriasis and Metabolic Syndrome and its Correlation with Disease Type and Severity: A Case Control Study

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### Abstract

**Introduction:** Psoriasis is an immune-mediated disease leading to increased susceptibility to cardiovascular disease. The risk factors predisposing to cardiovascular disease are described as a cluster of features referred to as metabolic syndrome (MS). Previous studies have shown an association between the two. **Methods:** The study was conducted in a tertiary hospital with 95 cases and 95 age and sex matched controls. A clinical examination of type and severity of disease was done. Blood pressure, waist circumference, fasting blood sugar and fasting lipid profile were assessed in all patients. Subsequently MS was diagnosed as per National Cholesterol Education Program (NCEP) - Adult Treatment Panel III as presence of 3 or more of the criteria.

**Results:** MS was found to be significantly more common in patients with psoriasis (p = 0.030). Of the individual components, those having significant association included hypertension (p=0.010), fasting blood sugar (p=0.021) and dyslipidemia (0.030). Increased waist circumference was more common in cases but association was not significant. Study had 77 (81.5%) males and 18 (18.95%) female patients with mean age of the psoriatic patients being 45.5 ± 9.5 years. Most cases having positive association were of chronic plaque type while guttate and inverse psoriasis had no association

**Conclusions:** *MS* has higher prevalence in patients having psoriasis. All patients should be screened and monitored for the same.

Keywords: Metabolic syndrome, psoriasis, diabetes mellitus, hypertension, dyslipidemia.

### Introduction

Psoriasis is a chronic inflammatory skin disorder affecting 2-4% of population across the world<sup>1,2</sup>. It is characterized by epidermal hyperproliferation, abnormal keratinocyte differentiation, angiogenesis with blood vessel dilatation and excess TH -1 and TH -17mediated inflammation<sup>3</sup>. Increasingly, association has been found between psoriasis and metabolic syndrome (MS) а cluster of risk factors including atherogenic dyslipidemia, obesity, hypertension and glucose intolerance - which is a strong predictor of cardiovascular diseases, typeand stroke<sup>4-5</sup>. Several studies have II diabetes consistently shown this association between metabolic syndrome and psoriasis<sup>6-14</sup>.

These phenotypically diverse conditions share similar pathological changes such as chronic inflammation, angiogenesis, oxidative stress and selected susceptibility genes and loci PSORS2-4, Apo $E4^{15}$ . CDKAL1 (for type 2-diabetes) and Metabolic syndrome has been defined by specific criteria for diagnosis<sup>16</sup>.Metabolic syndrome in psoriasis has been the main reason for increase in mortality in patients having this dermatosis $^{17}$ . Moreover, psoriatic skin lesions are more severe in those with underlying metabolic derangements. Recent studies have estimated a prevalence of metabolic syndrome varying from 11% to 41% of general population<sup>18</sup>. The incidence in of psoriasis associated metabolic syndrome is 20 to 40% as seen in international studies <sup>10,11</sup>. In Indian studies the incidence of this association is 25% to  $28\%^{13,14}$ .

The aim of our study is to find the incidence of metabolic syndrome in psoriatic patients, assess the predominantly deranged metabolic factors in our patients compared to those not having psoriasis and trying to establish a correlation between the severity of dermatosis with greater number of deranged metabolic factors.

### **Material and Methods**

This study was conducted in a hospital set up over a period of 12 months. After approval from Institutional Ethics Committee, 95 consecutive patients of psoriasis with age and sex matched controls were enrolled. Inclusion criteria for patients were age 16 years and above and those presenting with characteristic clinical features of psoriasis of any gender, type or severity, irrespective of treatment taken. Controls were also taken from Dermatology outpatient department and included patients suffering from any disease other than psoriasis.

Patients and control with medical diseases or on medications which can predispose or lead to abnormal lipid profile, blood pressure, blood glucose, or those taking hormonal therapy and pregnant and lactacting women were excluded from the study. Informed consent was obtained from all patients.

A detailed clinical history was taken including demographic details, disease history regarding duration, severity and treatment, family history, personal habits affecting metabolic profile such as diet and addictions. A thorough clinical evaluation inclusive of skin, nails and joints was done. General and systemic evaluation done including measurement of blood pressure, waist circumference, height, weight and calculation of Body Mass Index (BMI). Examination of cases for type of psoriasis and severity as per PASI score were recorded. Laboratory investigations such as fasting blood glucose and fasting lipid profile were sent for all patients. ECG was taken, fundus examination done in patients with DM and HTN and clinical photographs were taken. The findings were recorded in a specially designed proforma.

The most widely accepted criteria are issued by the National Cholesterol education program (NCEP) - Adult treatment panel III, which defines metabolic syndrome as the presence of at least three of the following conditions <sup>16</sup>

Waist	$\geq$ 102 cm in men (40 inch)		
circumference:	$\geq$ 88 cm in women (35 inch)		
Triglyceride plasma	$\geq$ 150 mg/dl		
levels	or on specific medication		
HDL Cholesterol plasma levels	< 40 mg/dl in men		
	< 50mg/dl in women		
	or on specific medication		
Elevated blood	Systolic > 130mmHg		
	Diastolic > 85mmHg		
pressure	Or on specific medication		
Fasting plasma	> 100mg/dl		
Fasting plasma	Or on specific medication		
glucose levels	Or known case of type - 2 DM		

**NCEP ATP III Criteria** 

Other organizations, such as the World Health Organization (WHO) and the European Group on Insulin resistance, agree with it in the essential components<sup>16</sup>

The data was analyzed using SPSS for Windows, version 20.0. Descriptive statistics were calculated including mean and standard deviation and frequency in the form of percentages. Chi-square test and Odd's ratio was used to test the association

between study variables and cases/controls. Uncorrected p value was entered.

### Results

During the study period of one year 102 patients were having skin manifestation of psoriasis. Of these, 95 adult patients of psoriasis formed the subject of our study. Males were the predominant sex in our study (81.05%) most belonging to age group 26-35 years (27.3%) closely followed by 56-65 years (25.9%) (Table 1).

Disease duration ranges from 6 months to 23 years. Out of the total 43 (45.2%) patients had skin lesions for more than 5 years, while only 6 (6.3%) patients had for less than 1 year. The commonest type of psoriasis seen in study population was chronic plaque type, seen in 81 (85.26%) patients, whereas Inverse being least common type. Most of the patients i.e. 33 (34.74%) had PASI score in the range of 13 to 24.

Table 1: Age and Sex Distribution of cases in study population

Age (in years)	Male	% (n = 77)	Female	% (n = 18)	Total	% (n = 95)
16-25	2	2.6	4	22.2	6	6.3
26-35	21	27.3	2	11.1	23	24.2
36-45	13	16.9	4	22.2	17	17.9
46-55	15	19.4	5	27.8	20	21
56-65	20	25.9	1	5.56	21	22.1
66-75	6	7.7	2	11.1	8	8.5
Total	77	100	18	100	95	100

The most common type of psoriasis in patients with metabolic syndrome was chronic plaque, seen in 20 (80%) patients. This was followed by erythrodermic and pustular types, each having 2 (8%) patients, while none of the patients with metabolic syndrome had guttate or inverse type of psoriasis. (Table 2).

Table 2 : Correlation Of Metabolic Syndro	ome With Types Of Psorias	is In Study Population
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Туре	Male	Female	Total	Percent
Chronic Plaque	16	4	20	80
Erythrodermic	2	0	2	8
Palmoplantar	0	2	2	8
Pustular	1	0	1	4
Guttate	0	0	0	0
Inverse	0	0	0	0
Total	19	6	25	100

Majority of cases with psoriasis and metabolic syndrome showed mean PASI score of 20.5. Study showed that 17 patients (68%) with metabolic syndrome had history of skin lesions for > 5 years suggesting that those with chronic disease are more likely to develop metabolic syndrome.

Based on National Cholesterol education program (NCEP) - Adult treatment panel III criteria metabolic syndrome was diagnosed in 25 (26.31%) patients as opposed to 13 (13.86%) in the control group. We also observed that higher prevalence of individual components of MS such as central obesity, hypertension, triglyceride levels, HDL cholesterol and fasting blood sugar in the cases compared to the control group. (Table 3).

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Metabolic Disorders	Cases	Controls	Odds ratio (95% CI)	P value
Hypertension	30 (31.58%)	15 (15.79%)	2.46 (1.16 to 5.35)	0.010
Obesity	19 (20.0%)	12 (16.84%)	1.23 (0.55 to 2.77)	0.575
Fasting blood sugar	32 (33.68%)	18 (18.95%)	2.17 (1.06 to 4.51)	0.021
Dyslipidemia	38 (40.00%)	24 (25.26%)	1.97 (1.02 to 3.85)	0.030
MS present	25 (26.32%)	13 (13.68%)	2.25 (1.02 to 5.16)	0.030

Dyslipidemia was the most commonly deranged component seen in 38(40%) patients. The mean age of psoriatic patients with MS was greater than those without MS, which suggest that increasing age is a risk factor for MS.

### Discussion

Psoriasis patients are known to be at increased risk of developing MS due to as yet unknown pathogenic mechanism. Certain proinflammatory cytokines like TNF-  $\alpha$ , IL- 6 found in psoriatic plaques have been found to contribute to features of MS such as hypertension, dyslipidemia and insulin resistance.<sup>19</sup>

We had 77 (81.5%) males and 18 (18.95%) female patients in the ages ranging from 16 to vears. We noted significant male 75 preponderance with male to female ratio of 4.27 : 1. Controls were taken to match this ratio. Similar male preponderance was noted by Nisan and Qazi et al<sup>13</sup>. The mean age of the psoriatic patients in our study was around  $45.5 \pm 9.5$  and control was 46.2±7.4. Most of the patients i.e. 23 (24.2%), belonged to the age group range of 26 to 35 years. This was followed by age group ranges 56 to 65 years, 46 to 55 years, 36 to 45 years, 66 to 75 years, and 16 to 25 years having 21 (22.1%), 20 (21%), 8 (8.5%), and 6 (6.3%) patients respectively.

Disease duration ranges from 6 months to 23 years, out of which 43 (45.2%) patients had skin lesions for more than 5 years.

We had a preponderance of patients with chronic plaque type psoriasis i.e. 81 (85.26%) patients. Other types seen were erythrodermic in 4 (4.3%) patients, guttate in 3 (3.1%) patients, pustular in 3 (3.1%) palmoplantar in 2 (2.1%) patients and inverse type of psoriasis in 2

(2.1%) patients. Similar types of skin psoriasis were mentioned by P. Gisondi et  $al^{10}$ .

In our study 70 (73.7%) patients had severe psoriasis with PASI score > 10, while only 25 (26.3%) patients had mild to moderate psoriasis with PASI score < 10.

Of these, 33 (34%) had PASI score in the range of 13 to 24. Mean PASI score in our study was 18.41, other studies <sup>9,10,13</sup> had mean PASI score in the range of 11.1 to 16.77.

In our study 19 (24.6%) male patients out of 77 had metabolic syndrome, while 6 (33.33%) female patients out of 18 had metabolic syndrome. It shows higher prevalence of metabolic syndrome in females as compared to male patients. Similar findings were reported by Sommer D.M. et  $al^7$ ,

We noted that, the association of psoriasis with metabolic syndrome is pronounced in patients after the age of 35 years, with 24 (96%) of patients with metabolic syndrome were more than 35 years old. These findings corresponds with those of P. Gisondi et  $al^{10}$ . However Nisa and Qazi et  $al^{13}$  observed the higher prevalence of metabolic syndrome in psoriasis patients in the age group of 18 - 35 years.

In our study, majority of patients with metabolic syndrome i.e. 17 (68%) had duration of psoriasis more than 5 years. It shows positive correlation between duration of psoriasis with metabolic syndrome

We noted that most of the psoriasis patients with metabolic syndrome i.e. 20 (80%) had chronic plaque type of psoriasis, showing it is the commonest type of psoriasis associated with metabolic syndrome. Similar findings were reported by Henseler and Christophers et al<sup>8</sup> and P. Gisondi et al<sup>14</sup>.

2019

Other less commonly associated types of psoriasis were erythrodermic, palmoplantar and pustular types seen in 2 (8%), 2 (8%) and 1 (4%) of patients respectively, while none of the patients with MS had Guttate or Inverse type of psoriasis.

We noted that 22 (88%) of patients with metabolic syndrome had severe psoriasis with PASI score more than 10, while only 3 (12%) patients had mild to moderate psoriasis with PASI score less than 10. This shows prevalence of metabolic syndrome increases with severity of psoriasis.

With reference to National Cholesterol Education Program (NCEP) - Adult treatment panel III criteria, our study shows that, 25 (26.3%) patients psoriasis had metabolic syndrome (MS) with was significantly more common which as compared to control group with incidence of 13 (13.68%). Our findings correlated with other Indian studies by Nisa and Qazi et al<sup>13</sup> with prevalence of 28% and S. K. Malhotra et al<sup>14</sup> with prevalence of 21.4%, while one other Indian study by S. Madanagobalane et al<sup>12</sup> reported high prevalence of MS i.e. 44%.

Zindancı *et al.*, after studied 115 plaque type psoriasis patients and 140 healthy individuals also found a higher prevalence of MS in cases (53%) compared to controls (39%), (P < 0.001 using International Diabetes Federation criteria) though prevalence was much higher than our study<sup>6</sup>. Gisondi *et al.* did a case control study comparing 338 patients with chronic plaque psoriasis and 334 controls and found statistically significant higher prevalence of MS in psoriatic patients compared with the controls (30.1% in cases and 20.6% in controls, P = 0.005)<sup>10</sup>.

In contrast, few studies have found no significant difference in incidence between cases and controls. In a study by Lakshmi et al. with 40 cases and controls, the frequency of presence of MS among patients with psoriasis was 32.5% and that in the control group was 30% (p=0.8094).<sup>19</sup>

Of the individual components, dyslipidemia was most common in 38 patients (40.0%). This was

significantly higher than control group with incidence of 24 (25.26%)with p=0.030. Hypertension was seen in 31.58% cases and 15.79% controls (p=0.010). Raised fasting blood sugar levels were seen in a significantly higher percentage of cases (33.68%) compared to controls having incidence of 18.95% (p=0.021). These findings were similar to other studies showing significant association in individual components<sup>7,20</sup>.

### Conclusions

Metabolic syndrome is associated with increased risk of mortality in psoriasis patients. Prevalence of metabolic syndrome was found to be significantly higher in cases of psoriasis compared to a control group and increases with age, duration of psoriasis, severity of psoriasis, and type of psoriasis. Hence it is prudent to evaluate all psoriasis patients for metabolic syndrome and correct aggressively their modifiable cardiovascular risk factors.

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