

## Association of Metabolic Syndrome with Psoriasis Vulgaris: A Case Control Study

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### Abstract

**Introduction:** Psoriasis is a common, chronic, inflammatory, immune mediated, genetically determined skin disorder, the course of which is affected by multiple environmental factors. Psoriasis is associated with metabolic syndrome and its components, such as obesity, diabetes and hypertension independent of traditional risk factors for these disorders. These phenotypically diverse conditions share similar pathologic changes, selected susceptibility genes and loci.

**Aim:** To assess the association of Metabolic syndrome in patients of psoriasis vulgaris.

**Objectives:** 1. To select clinically diagnosed cases of psoriasis vulgaris.

2. To study and evaluate the profile of psoriasis vulgaris patients.

3. To compare the cases with age and sex matched control groups.

4. To study the association of psoriasis vulgaris with metabolic syndrome.

**Study Design:** Case Control study (200 cases and 200 controls). **RESULTS:** In our present study Metabolic Syndrome was present in 52(26%) of psoriatic cases in comparison to 20(10%) non psoriatic cases which came out to be statistically significant [Odds ratio (OR) - 3.162, Degree of freedom (df) -1, p - value-0.003, ? 2 -8.672].

**Conclusion:** There is possible association of metabolic syndrome with psoriasis.

**Keywords:** Psoriasis, Metabolic Syndrome, TNF-alpha, hyperlipidemia, Hypertension, BMI

### Introduction

Psoriasis is a common chronic, inflammatory, immune mediated, genetically determined skin disorder, the course of which is affected by multiple environmental factors. In recent years, psoriasis is being recognized as a systemic disease associated with numerous multi-organ abnormalities and complications, posing a lifelong burden for those affected.<sup>[1,2]</sup> Psoriasis is associated with metabolic syndrome, and its components, such as obesity, diabetes, and hypertension independent of traditional risk factors for these disorders. These phenotypically diverse conditions share similar pathologic changes such as chronic inflammation, angiogenesis, oxidative stress, and selected susceptibility genes and loci. TNF- $\alpha$  which plays a central role in the immunopathogenesis of psoriasis may be involved in the increased insulin resistance observed in patients with psoriasis.<sup>[3]</sup>

TNF may lead to insulin resistance by impairing insulin signalling by inhibiting the tyrosinase kinase activity of the insulin receptor; by activating peroxisome proliferator-activated receptor (PPAR  $\delta$ ) which promotes epidermal proliferation, modulates adipogenesis and glucose metabolism; and by suppressing adiponectin secretion from adipocytes, which is an important anti-inflammatory molecule that also functions in regulating insulin sensitivity.<sup>[4]</sup>

Finally, Genetics play a critical role in the susceptibility of psoriasis and metabolic diseases. For instance, the Psoriasis Susceptibility loci PSORS2, PSORS3 and PSORS4 are also associated with loci of susceptibility for disorders such as Diabetes Mellitus

type 2, Familial Hyperlipidaemia and Cardiovascular disorders.<sup>[5]</sup>

### Materials and Methods

This study was conducted in the Department of Dermatology, R.D. Gardi Medical College and C.R.G. Hospital and Research Centre, Ujjain, Madhya Pradesh, India within a duration of two years from October 2012-October 2014. The study was a hospital based case control study including a series of age and sex matched 200 cases of psoriasis and 200 controls of non-psoriatic patients (1:1 matching). Inclusion criteria for the psoriasis patients were all newly clinically diagnosed cases of psoriasis attending OPD and admitted in ward, psoriasis cases not taking any systemic drugs known to precipitate psoriasis or to cause hyperglycemia, deranged lipid profile and hypertension. Controls were patients of various dermatological disorder other than psoriasis. The source population for cases and controls was the same. An informed consent was taken from all cases and controls. Particulars of all patients were recorded in a standard proforma.

Relevant detailed history and clinical examination included age, sex, weight, height, smoking and alcohol habit, age of onset and duration of psoriasis, type and severity of psoriasis of all cases and controls was done. All cases and controls were subjected to Blood Pressure measurement, Waist Circumference and Body Mass Index (BMI). BMI was calculated as weight in kilograms/height<sup>2</sup> in meters. Waist circumference was obtained by measuring upper most part of hip bone

around the abdomen. Severity of psoriasis was assessed with psoriasis area and severity index (PASI). Routine investigations, Blood Fasting glucose level, Lipid profile was sent for all cases and controls. Metabolic syndrome was diagnosed by the presence of three or more of the five criteria of the National Cholesterol Education Programme's Adult Panel III i.e. abdominal obesity was modified using Asia Pacific WHO guidelines as waist circumference in cm for Men -  $\geq 80$  cm, Women  $\geq 90$  cm, Elevated triglycerides:  $\geq 150$  mg/dL (1.7 mmol/L), Reduced HDL ("good") cholesterol: Men  $< 40$  mg/dL (1.03 mmol/L) Women  $< 50$  mg/dL (1.29 mmol/L), Elevated blood pressure:  $\geq 130/85$  mm Hg or use of medication for hypertension, Elevated fasting glucose:  $\geq 100$  mg/dL (5.6 mmol/L) or use of medication for hyperglycemia.

Venous blood samples were taken after the subjects had fasted overnight. Serum cholesterol and triglycerides were measured with enzymatic procedures. Plasma glucose was measured using glucose oxidase method.

Approval from ethical committee was taken. Conclusion was established on the grounds of all findings. Analysis was done by using SPSS and EPI info software and necessary test of significance (chi square test) was applied.

## Results

The study included 200 cases and 200 age and sex matched controls with descriptive particulars and characteristics of all given in Table 1.

**Table 1:**

Particulars	Cases(n =200)	Controls(n =200)
Male/Female ratio	160/40	160/40
Age range(mean)	1-80(42.5)	1-80(42.5)
Alcoholic, n	44(22%)	50(25%)
Smoker, n	110(55%)	82(41%)
Body Mass Index (mean $\pm$ SD)	27.27 $\pm$ 6.66	24.81 $\pm$ 5.48

In our study we found disease duration in cases ranged from five months to twenty years and 65% of cases and controls were from rural areas.

Psoriasis area and severity index (PASI) score ranged from 0.8 to 47.7. Most of the cases were of chronic plaque type of psoriasis i.e. 176 (88%).

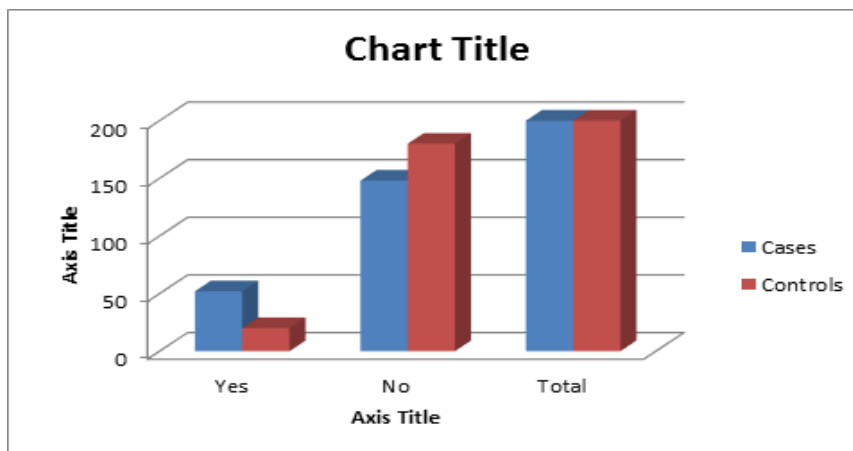
After comparing cases and controls for metabolic syndrome, we observed that there was more number of psoriatic cases associated with metabolic syndrome than the controls. In our present study Metabolic Syndrome was present in 52(26%) of psoriatic cases in comparison to 20 (10%) non psoriatic cases which came out to be statistically significant [Odds ratio (OR) - 3.162, Degree of freedom (df) - 1 p - value 0.003,  $\chi^2$  - 8.672] after adjusting for confounding by age.

Individual components of metabolic syndrome like dyslipidemia, obesity, impaired fasting glucose and hypertension were also more prevalent in cases than in controls. The prevalence of various components of metabolic syndrome in cases and controls along with odds ratio and p value are given in Table 2.

**Table 2:**

Clinical and Lab tests	Cases	Controls	OR	P-value
HDL cholesterol $< 40$ mg/dl(M) or $< 50$ mg/dl (F)	124	68	0.316	0.00
Fasting blood glucose $> 100$ mg/dl	56	30	2.204	0.025
Triglyceride levels $> 150$ mg/dl	72	10	5.062	0.00
Waist circumference $\geq 80$ cm (M), $\geq 90$ cm (F)	84	40	2.897	0.001
Blood pressure $\geq 130/85$ mm Hg	76	48	1.941	0.032
Metabolic syndrome	52	20	3.162	0.003

There was no difference regarding disease duration, gender or prevalence of smoking and alcohol. We observed an early onset of metabolic syndrome in patients of psoriasis.



## Discussion

The idea behind the current study is that comorbidities (atherosclerosis) and the psoriasis are two culprits of the same root cause. Psoriasis is associated with metabolic syndrome and its components such as obesity, diabetes and hypertension independent of traditional risk factors for these disorders. These phenotypically diverse conditions share similar pathologic changes such as chronic inflammation, angiogenesis, oxidative stress, and selected susceptibility genes and loci. Many diseases particularly heart disease, hypertension and diabetes mellitus showed the positive association.<sup>[6]</sup>

Similar studies done by Alexander E et al<sup>[7,8]</sup> in Indian population, the association of psoriasis with other diseases was established and with the highest frequency for diabetes mellitus. A study done by A Jucci et al indicate the existence of an endogenous insulin resistance in psoriasis.<sup>[9]</sup>

The metabolic syndrome or the insulin resistance syndrome or the syndrome X are the terms used to describe a constellation of metabolic derangements that includes insulin resistance, hypertension, dyslipidemia, central or visceral obesity, type 2DM or IGT/IFG, and accelerated cardiovascular disease.

TNF- $\alpha$  which plays a central role in the immunopathogenesis of psoriasis may be involved in the increased insulin resistance observed in patients with psoriasis.<sup>[3]</sup>

As one of the first to point out a possible cardiovascular risk in psoriasis patients McDonald et al. using data from three studies, showed that patients hospitalized for the treatment of severe psoriasis had an increased rate of chronic heart disease with fatal outcome. Recently, such data have been supported by analysis of patients investigated in a university dermatological practice. It was noted that a significant proportion of these patients had obesity, cardiac disease, hypertension and/or diabetes.<sup>[4]</sup>

Lipoprotein A which is a genetically determined molecule whose role has been implied in cardiovascular pathology, and whose levels have been reported to be elevated in patients of psoriasis may be a factor contributing to an increased cardiovascular risk in patients of psoriasis.<sup>[11]</sup>

The link between psoriasis and hypertension may be related to the increased levels of angiotensin converting enzyme, Endothelin 1(ET-1) and renin in patients with psoriasis.<sup>[3]</sup> Adipose tissue in psoriatic patients may serve as a major source of angiotensinogen, which is subsequently converted into Angiotensin II.<sup>[12]</sup>

Angiotensin II not only promotes salt retention by the kidneys, but it also stimulates T Cell proliferation.<sup>[13]</sup> Angiotensin II also appears to promote inflammation and the development of atherosclerosis.<sup>[14]</sup>

The association between psoriasis and hypertension may also be attributed to the increased oxidative stress in psoriasis patients. Greater levels of reactive oxygen species can damage endothelium dependent vasodilation.

It is also postulated that IL-6 induces insulin resistance, dyslipidaemia and a procoagulant effect. Increased IL-6 causes increased C- reactive protein level and erythrocyte sedimentation rate.<sup>[15]</sup>

Both psoriasis and metabolic syndrome are characterized by increased Th-1 and Th-17 activity. Cytokines, such as tumor necrosis factor (TNF)-alpha and interleukin (IL)-6 seem to play the essential role. However, psoriasis is also associated with increased levels of other cytokines, e.g., interferon (IFN)-gamma, IL-1, and IL-17).

A variety of cytokines generates a spectrum of pro-atheromatous changes including insulin resistance, dyslipidemia, clotting system activation, pro-oxidative stress, and endothelial dysfunction.

Cytokines affect metabolism already at low concentrations; thus, even slight yet chronic increases may be harmful and promote accelerated atherogenesis.<sup>[16]</sup>

It is reasonable to assume that if myocardial infarction is increased in patients with psoriasis, other manifestations of atherosclerosis, such as cerebrovascular disease and peripheral arterial disease, might also be increased. Not only are cardiovascular disease risk factors more prevalent, but even after these risk factors are controlled for, psoriasis confers an independent risk for myocardial infarction. Peripheral arterial disease, which can cause symptomatic claudication and may lead to amputation, is also associated with an increased risk of cerebrovascular disease, myocardial infarction, and death.<sup>[17]</sup>

**D. Cohen et al(2007)** demonstrated a possible association between psoriasis and the metabolic syndrome.<sup>[18]</sup>

**Thorvardur Jon Love et al (2011)** showed the prevalence of the metabolic syndrome according to the revised NCEP ATP III criteria was 40% among individuals with psoriasis and 23% among individuals without psoriasis.<sup>[19]</sup>

**Ilkin Zindanci et al (2012)** found a higher prevalence of MS in psoriasis patients than in controls (53% versus 39%) ( $P < 0.01$ ).<sup>[20]</sup>

**P. Gisondi et al (2012)** Metabolic syndrome was significantly more common in psoriatic patients than in controls (30.1% vs. 20.6%, odds ratio 1.65, 95% confidence interval 1.16–2.35;  $P = 0.005$ ).<sup>[21]</sup>

**Neema Muhammed Ali et al (2014)** They found that metabolic syndrome was more common in psoriatic cases than in controls and the differences were statistically highly significant ( $P = 0.005$ ).<sup>[22]</sup>

**Priya Prathap et al(2014)** There was an overall association of psoriasis with MS. Among the individual components of MS, increased waist circumference was significantly associated. Patients with greater duration or severity of psoriasis were more likely to have an association with MS.<sup>[23]</sup>

Furthermore, patients with severe psoriasis had higher rates of obesity and diabetes than those with mild psoriasis.<sup>[24]</sup> Similarly, in a case-control study in Israel with over 46,000 patients with psoriasis, investigators found the patients to be not only at an increased risk of diabetes, but of atherosclerosis, as well.<sup>[3]</sup> This increased risk of atherosclerosis was further supported by the work of Gelfand *et al.* who found that even after controlling for traditional cardiovascular risk factors, psoriasis conferred an independent risk for myocardial infarction.<sup>[25]</sup> The increased risk seems to be even higher in younger patients and in those with more severe disease.

Thus, as discussed above, additional epidemiological studies in broadly representative psoriatic populations are necessary to determine: the role of disorders such as Hypertension, Type 2 Diabetes

Mellitus and Dyslipidaemia in psoriasis: the role of co morbidities in modifying the severity of existing psoriasis: the role of psoriasis treatment in altering the risk of developing these serious comorbidities. It is thus, important to observe whether the treatment of these comorbidities forms an integral part in the management of psoriasis.

The knowledge that psoriasis can be associated with multiple comorbidities that have significant impact not only on morbidity and mortality but also on healthcare utilization, should lead us to early diagnosis and aggressive management of not only the psoriasis but also its associated comorbidities, like increased risk of cardiovascular mortality. We now know that psoriasis patients have increased rates of other risk factors, including diabetes, hypertension, hyperlipidemia, metabolic syndrome and smoking. Therefore, we as dermatologists not only need to notify our patients of these risks but also be proactive in our assessment and investigation of these patients. Knowledge of these risk factors is important with respect to the patients' general health but may also influence how we manage our patients.

## Conclusion

There is a significantly higher prevalence of metabolic syndrome and its component in psoriasis vulgaris patients as compared to general population. So it is necessary to determine the role of metabolic syndrome in psoriasis and the role of psoriasis treatment in altering the risk of developing these serious comorbidities.

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