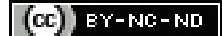


# Metabolic Derangements in Patients of Psoriasis and their Association with Psoriasis Area Severity Index Score: A Cross-sectional Study

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## ABSTRACT

**Introduction:** Psoriasis is a chronic inflammatory disease of skin associated with various metabolic derangements. These metabolic derangements increases the risk of cardiovascular diseases in psoriatic patients.

**Aim:** To study the metabolic parameters- Fasting Blood Glucose (FBS), serum lipid profile, serum uric acid, C-Reactive Protein (CRP) in psoriatic patients in relation to clinical disease severity- Psoriasis Area Severity Index (PASI) score.

**Materials and Methods:** The study was a hospital based cross-sectional observational study carried out over a period of 18 months in Department of Dermatology at Government Medical College and Rajindra Hospital, Patiala that included 250 psoriatic patients. Their percentage Body Surface Area (BSA) involved and PASI score were calculated as per the standard guidelines. The severity of psoriasis was divided into mild (PASI<7), moderate (PASI 7-12) and severe (PASI >12)

disease based on PASI score. Serum lipid profile was measured by enzymatic method, blood glucose by glucose oxidase method, serum uric acid by uricase method and CRP by latex slide agglutination method and the values obtained were compared with severity of psoriasis.

**Results:** There was a rise in the value of FBS, serum lipid profile, serum uric acid and CRP as PASI score increased and the difference between these values was statistically highly significant (p-value <0.001).

**Conclusion:** There was a significantly higher derangement of metabolic parameters in patients with higher PASI scores. So, patients with severe psoriasis have a higher risk of metabolic complications and cardiovascular diseases as compared to patients with mild disease. These patients should be advised lifestyle modifications and should be regularly monitored so that the metabolic derangements can be detected earlier and metabolic complications can be avoided.

**Keywords:** C-reactive protein, Fasting blood sugar, Lipid profile, Uric acid

## INTRODUCTION

Psoriasis is a common, chronic, disfiguring, inflammatory and proliferative condition of the skin, in which both genetic and environmental influences play a critical role. The characteristic lesions are red, scaly, sharply demarcated, indurated plaques present particularly over extensor surfaces and scalp [1]. The prevalence of psoriasis in different parts of the world ranges from 0.1%-3% [2]. It is almost equally common in males and females. Most of the Indian studies have reported the highest incidence of disease to be in second decade [3]. Common clinical types of psoriasis include plaque, pustular, guttate, and erythrodermic psoriasis, whereas psoriatic arthritis is encountered less commonly. Psoriasis unguis is the involvement of nail by the disease. Mucosal involvement, that is oral and genital mucosa, is uncommon in psoriasis [3]. Severity of psoriasis is calculated by the measurement of PASI score and percentage BSA involved. According to the Rule of 10, psoriasis is moderate to severe if BSA is >10%, PASI score is >10, Dermatology Life Quality Index (DLQI) >10 [4]. Psoriasis has been recognised as a complex systemic disease with various multiorgan abnormalities and complications. There is an increased risk of cardiovascular diseases, hypertension, dyslipidemia, atherosclerosis, type 2 diabetes mellitus, obesity, chronic obstructive pulmonary disease, cerebral stroke, osteoporosis, cancer, and depression in psoriatic patients [5].

Studies have shown that psoriatic patients have pro-atherogenic lipid profile with raised level of serum triglycerides, total cholesterol including Low-density Lipoprotein (LDL) and Very Low-density Lipoprotein (LDL) cholesterol and lower level of High-density lipoprotein (HDL-C) cholesterol [6]. It is still controversial whether

changes in lipid composition are primary events or secondary to psoriasis, or perhaps due to medications such as cyclosporine and retinoids [7]. The association between diabetes and psoriasis has not been clearly established. Tumor Necrosis Factor (TNF)- $\alpha$  involved in the pathogenesis of psoriasis has been shown to cause insulin resistance and hence diabetes mellitus [8]. CRP is an acute phase reactant and a well established biomarker of inflammation. It has been shown to be elevated in psoriasis patients and is a risk factor for cardiovascular diseases in psoriatic patients [9]. Rapid epidermal turnover in psoriasis might lead to an increased purine breakdown and thus, influence uric acid levels [10], so relationship can be expected between hyperuricaemia and extent of psoriatic skin involvement. The present study is undertaken in order to evaluate this relation. Whether metabolic derangements in psoriasis patients occur independently or they are associated with disease severity is still debatable. So, the present study was undertaken to establish an association between metabolic derangements and severity of psoriasis (PASI Score) by studying the metabolic parameters like FBS, serum lipid profile, serum uric acid and CRP in psoriatic patients.

## MATERIALS AND METHODS

This was a cross-sectional observational study carried over a period of 18 months from January 2016 to June 2017 comprising of cases of psoriasis who visited Department of Dermatology at Government Medical College and Rajindra Hospital, Patiala (Punjab). A total of 250 patients were enrolled using the convenience sampling method.

### Inclusion criteria

All new cases of clinically diagnosed psoriasis in the age group of age of more than 10 years.

### Exclusion criteria

- 1) Patients who were not willing to take part in the study.
- 2) Patients on drugs likely to interfere with the lipid profile, blood sugar level, uric acid and CRP.
- 3) Patients with metabolic syndrome.
- 4) Patients with history of smoking/alcoholism.

After obtaining clearance from Institutional Ethics Committee (TRG-8(109)2017/9436), cases of psoriasis who visited the Outpatient and Inpatient Department of Dermatology were included in the study. The cases comprised of chronic plaque psoriasis [Table/Fig-1], flexural psoriasis [Table/Fig-2], erythrodermic psoriasis [Table/Fig-3], pustular psoriasis [Table/Fig-4] and palmo-plantar psoriasis [Table/Fig-5,6]. A written informed consent and detailed history was taken. Diagnosis of psoriasis was established by history, clinical examination and biopsy. PASI score was calculated according to percentage BSA involved. The severity of psoriasis was divided into mild (PASI <7), moderate (PASI 7-12) and severe (PASI >12) disease based on PASI score [11].



[Table/Fig-4]: Pustular psoriasis.



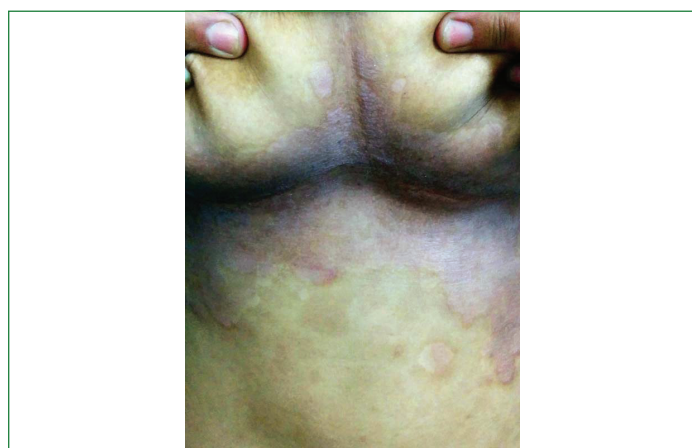
[Table/Fig-5]: Psoriasis of palms.



[Table/Fig-6]: Psoriasis of soles.



[Table/Fig-1]: Well defined scaly, erythematous, indurated plaques of psoriasis on back.



[Table/Fig-2]: Flexor involvement in psoriasis.



[Table/Fig-3]: Dystrophic nails in psoriatic erythroderma.

Levels of FBS, lipid profile, uric acid and CRP were studied in the patients and these values were compared with severity of the disease. Serum lipid profile was measured by enzymatic method, blood glucose by glucose oxidase method, serum uric acid by uricase method and CRP by latex slide agglutination method.

### STATISTICAL ANALYSIS

Statistical analysis was performed using Statistical Package For The Social Sciences (SPSS) version 22.0. Results were described as mean±standard deviation. Significance of mean difference among groups was compared using Pearson's Chi-square test. A p-value of less than 0.05 was considered significant. For comparing more than two mean groups, Spearman's rho and one-way ANOVA test was used.

PASI score is a tool used to measure the severity and extent of psoriasis. PASI combines the assessment of the severity of lesions and the area affected into a single score in the range 0 (no disease) to 72 (maximal disease). Four sites of affection- head (h), upper limbs (u), trunk (t), and lower limbs (l) are separately scored. Within each area, the severity is estimated by three clinical signs: Erythema (E), Induration (I) and Desquamation (D). Severity parameters are measured on a scale of 0 to 4, from none to maximum. The addition of these scores for each site is multiplied by the grading for area-wise percentage involvement of that particular site in the following manner: 1=<10% area, 2=10%-29%, 3=30%-49%, 4=50%-69%, 5=70%-89%, 6=90% or more area involved by psoriasis. Since the four body regions (head, upper limbs, trunk, lower limbs) represent about 10%, 20%, 30% and 40% of the BSA, respectively, they are given corresponding weightage in scoring by multiplying their scores by 0.1, 0.2, 0.3 and 0.4, respectively. The final formula for calculating PASI score is as follows [11]:

PASI=0.1 ( $E_h+L_h+D_h$ )  $A_h+0.2$  ( $E_u+L_u+D_u$ )  $A_u+0.3$  ( $E_t+L_t+D_t$ )  $A_t+0.4$  ( $E_r+L_r+D_r$ )  $A_r$

## RESULTS

Out of the total 250 patients, 51.2% (128) patients had mild disease (PASI <7), 24% (60) patients had moderate disease (PASI 7-12) and 24.8% (62) patients had severe disease (PASI >12). The age of onset of disease in patients with mild, moderate and severe disease was 27.0±7.5 years, 25.5±7.9 years and 28.1±8.8 years, respectively [Table/Fig-7]. A 60% (150) patients were male and 40% (100) were female.

Demographics	PASI categorised			p-value
	Mild (n=128)	Moderate (n=60)	Severe (n=62)	
<b>Gender</b>				
Female	49 (37.8%)	30 (50.0%)	21 (33.9%)	0.155 <sup>a</sup>
Male	79 (62.2%)	30 (50.0%)	41 (66.1%)	
Age (Years); Mean±SD	27.0±7.5	25.5±7.9	28.1±8.8	0.191 <sup>b</sup>
Mucosal involvement	1	3	20	-
Seasonal variation	81	49	47	-
Family history	5	5	6	-

**[Table/Fig-7]:** Demographic characteristics of study subjects in relation with severity of psoriasis.

a: Chi-Square test; b: p-value calculated using one-way ANOVA test; SD: Standard deviation; PASI: Psoriasis area severity index

The mean values of FBS, Triglycerides (TG), Total cholesterol, LDL, CRP and Uric acid with increasing severity of psoriasis are shown in [Table/Fig-8].

Metabolic derangements	Correlation with PASI score		PASI categories			p-value
	Spearman's rho	p-value	Mild (n=128)	Moderate (n=60)	Severe (n=62)	
FBS (mg/dL)	0.586	<0.001	94.8±14.4	109.6±15.6	122.5±15.0	<0.001 <sup>b</sup>
Uric acid (mg/dL)	0.574	<0.001	4.9±0.4	5.2±0.6	6.0±0.6	<0.001 <sup>b</sup>
TG (mg/dL)	0.721	<0.001	145.6±13.2	155.4±7.4	170.0±7.7	<0.001 <sup>b</sup>
Cholesterol (mg/dL)	0.665	<0.001	220.6±14.6	232.3±11.1	287.8±18.3	<0.001 <sup>b</sup>
LDL-C (mg/dL)	0.629	<0.001	138.3±14.4	147.6±13.6	186.3±17.2	<0.001 <sup>b</sup>
HDL-C (mg/dL)	-0.238	<0.001	42.9±7.3	40.5±5.0	38.2±6.2	<0.001 <sup>b</sup>
CRP positive	-	-	11 (8.7%)	14 (23.3%)	33 (53.2%)	<0.001 <sup>a</sup>

**[Table/Fig-8]:** Patterns of Metabolic derangements in study subjects across PASI scores.

[Figures in parentheses represent column-wise percentages; a: p-value calculated using Pearson's Chi Square test; b: p-value calculated using one-way ANOVA test]; PASI: Psoriasis area severity index; FBS: Fasting blood glucose; TG: Triglycerides; LDL-C: Low-density lipoprotein; HDL-C: High-density lipoprotein; CRP: C-reactive protein; less than 0.05 statistically significant

The mean FBS in cases of mild psoriasis was 94.8±14.4 mg/dL, moderate psoriasis was 109.6±15.6 mg/dL, severe psoriasis was 122.5±15.0 mg/dL. (p-value <0.001).

TG levels ranged from 145.6±13.2 mg/dL in mild, 155.4±7.4 mg/dL in moderate and 170.0±7.7 mg/dL in severe psoriasis. The total cholesterol levels in patients of mild, moderate and severe psoriasis in present study were 220.6±14.6 mg/dL, 232.3±11.1 mg/dL, 287.8±18.3 mg/dL, respectively. LDL cholesterol levels in patients with mild, moderate and severe psoriasis were 138.3±14.4 mg/dL, 147.6±13.6 mg/dL and 186.3±17.2 mg/dL, respectively. The HDL cholesterol levels in patients with mild, moderate and severe psoriasis were 42.9±7.3 mg/dL, 40.5±5.0 mg/dL and 38.2±6.2 mg/dL. The relationship of all these parameters of lipid profile with severity of psoriasis was statistically significant.

CRP levels were raised in 53.2% (33) patients with severe psoriasis, 23.3% (14) patients with moderate psoriasis and 8.7% (11) patients with mild psoriasis and this difference was statistically significant (p-value <0.001) [Table/Fig-8,9].

Metabolic derangements	Disease severity		
	Mild vs. Moderate	Mild vs. Severe	Moderate vs. Severe
FBS	<0.001	<0.001	<0.001
Uric acid	0.003	<0.001	<0.001
TG	<0.001	<0.001	<0.001
Cholesterol	<0.001	<0.001	<0.001
LDL-C	<0.001	<0.001	<0.001
HDL-C	0.049	<0.001	0.164

**[Table/Fig-9]:** Comparison of metabolic derangements in mild, moderate and severe disease (by Bonferroni method).

FBS: Fasting blood glucose; TG: Triglycerides; LDL-C: Low-density lipoprotein; HDL-C: High-density lipoprotein; less than 0.05 statistically significant

Uric acid levels in patients with mild, moderate and severe psoriasis were 4.9±0.4 mg/dL, 5.2±0.6 mg/dL and 6.0±0.6 mg/dL respectively and the difference was statistically significant (p-value <0.001).

## DISCUSSION

This work was undertaken to study the biochemical profile of psoriasis in 250 patients of the disease and to find out association of various metabolic derangements with PASI score in these patients.

**Metabolic derangements: [Table/Fig-10] [6,12-25]**

**Fasting Blood Glucose (FBS):** In the present study, the levels of FBS increased as the severity of psoriasis increased and the difference was statistically significant [Table/Fig-8,9]. This proves that psoriasis patients are predisposed to diabetes mellitus independent of the traditional risk factors for diabetes and the risk is associated with disease severity. This finding is in agreement

Studies	Year	Place	FBS	CRP	Uric acid	Lipid profile
Present study	2016-17	Punjab (India)	Raised	Raised	Raised	Raised
Neimann AL et al., [12]	2006	U.K.	Raised	--	--	--
Brauchli YB et al., [13]	2008	U.K.	Raised	--	--	--
Gelfand JM et al., [14]	2009	U.S.A.	Raised	--	--	Raised
PraveenKumar U et al., [15]	2016	Pondicherry (India)	Raised	--	--	Raised
Gui XY et al., [16]	2018	China	Raised	--	--	Raised
Maluki AH and Fulaih ZF [17]	2012	Iraq	Raised	--	--	Raised
Kothiwala SK et al., [18]	2016	New Delhi	Raised	--	--	--
Farshchian M et al., [21]	2016	Iran	--	Raised	--	--
Vadakayil AR et al., [22]	2015	Mangalore (India)	--	Raised	--	--
Chand R et al., [23]	1983	India	--	--	Raised	--
Li X et al., [24]	2016	China	--	--	Raised	--
Goldman M [25]	1981	Brazil	--	--	Raised	--
Ghafoor R et al., [19]	2015	Pakistan	--	--	--	Raised
Javidi Z et al., [6]	2007	Iran	--	--	--	Raised
Jamil A et al., [20]	2014	Pakistan	--	--	--	Raised

**[Table/Fig-10]:** Comparison of metabolic derangements in mild, moderate and severe disease (by Bonferroni method) [6,12-25].

FBS: Fasting blood glucose; CRP: C-reactive protein

with most of the previous studies. According to a study done by Neimann AL et al., it was reported that psoriasis was associated with diabetes independent of diabetes risk factors. This association was stronger in patients with severe disease [12]. Brauchli YB et al., reported that patients of psoriasis were prone to develop key components of metabolic syndrome particularly diabetes in future independent of the traditional risk factors for diabetes as found in our study [13]. The association of psoriasis with metabolic syndrome and a dose response relationship between psoriasis severity and hyperglycaemia was demonstrated by Gelfand JM et al., [14].

Praveenkumar U et al., studied 30 clinically diagnosed patients of psoriasis and reported that psoriasis was associated with elevated blood glucose levels but the difference was statistically insignificant ( $p$ -value=0.12). This may be due to their small sample size and time bound study [15]. A study on 859 Chinese psoriatic patients conducted by Gui XY et al., concluded that psoriatic patients had higher prevalence of hyperglycaemia than the controls and risk is more in patients with PASI >10 (severe psoriasis) [16]. Similarly Maluki AH et al., reported that psoriasis was associated with diabetes and association was stronger with severe disease (35.1%) as compared to mild disease (9.5%) and the difference was statistically significant ( $p$ -value=0.001) [17]. A study of 140 patients of psoriasis done by Kothiwala SK et al., found that type II diabetes mellitus was more common in psoriasis patients, that is 42.1% vs. 21.4% in controls. In addition, those with severe psoriasis had significantly higher prevalence of diabetes than those with mild psoriasis, the difference being statistically significant ( $p$ -value <0.001) [18].

**Lipid profile:** Psoriatic patients had a raised serum lipid profile in present study. The mean TG, total cholesterol and LDL cholesterol values were raised. Levels of HDL cholesterol were decreased and the derangements were more in patients of severe psoriasis as compared to mild psoriasis [Table/Fig-8,9]. This proved that psoriasis predisposes patients to dyslipidemia and the risk is associated with disease severity. These results are in concordance with the findings in previous studies. Ghafoor R et al., reported deranged lipid profiles in psoriatic patients. The total cholesterol levels (mg/dL) were  $203.43 \pm 11.43$  in cases and  $173.64 \pm 13.65$  in controls, TG levels (mg/dL) were  $178.87 \pm 43.60$  in cases and  $144.23 \pm 34.0$  in controls, High-Density Lipoprotein Cholesterol (HDL-C) levels were (mg/dL)  $37.81 \pm 10.78$  in cases and  $41.41 \pm 9.72$  in controls while Low-Density Lipoprotein Cholesterol (LDL-C) levels (mg/dL) were  $139.52 \pm 13.71$  in cases and  $109.44 \pm 13.80$  in controls. Each parameter had  $p$ -value <0.05 which was statistically significant. However, they did not compare the difference between mild, moderate and severe psoriasis [19].

Another study of 60 psoriatic patients done by Javidi Z et al., showed higher serum cholesterol, LDL-C and TG levels in psoriasis. The difference was statistically significant ( $p$ -value <0.05). The levels of total cholesterol and LDL-C increased with increase in disease severity. No significant relation was seen between disease severity and levels of HDL-C and TG. This might be due to small sample size [6]. Maluki AH and Fulaih ZF, reported higher serum cholesterol, TG, LDL-C values (mg/dL) in patients with severe psoriasis ( $215.51 \pm 51.51$ ,  $212.08 \pm 67.38$ ,  $143.10 \pm 51.80$ , respectively) as compared to mild psoriasis ( $176.80 \pm 46.51$ ,  $155.91 \pm 73.34$ ,  $100.48 \pm 40.56$ , respectively) and the difference was statistically significant ( $p$ -value=0.001). HDL-C (mg/dL) was higher in mild psoriasis  $43.20 \pm 9.13$  as compared to severe psoriasis ( $39.74 \pm 10.48$ ) [17]. Gui XY et al., in their study on Chinese psoriatic patients demonstrated higher prevalence of dyslipidemia in patients than controls and the derangements were more severe in patients of severe psoriasis (PASI >10) [16]. Similar results were reported by Gelfand JM et al., [14]. The prevalence of low HDL levels was found to be significantly higher in psoriatic patients as compared to controls (86.7% vs. 60%,  $p$ -value=0.02) by Praveenkumar U et al.,

in their study. However, they did not study its relationship to disease severity [15].

In a study of 120 patients of psoriasis conducted by Jamil A et al., it was found that raised serum lipid levels were there in 55.8% of the patients. A total of 34 (28.3%) patients had raised total cholesterol (>200 mg/dL), 32 (26.7%) had raised LDL-C (>130 mg/dL), 44 (36.7%) had hypertriglyceridemia (>150 mg/dL) and 35 (29.2%) patients had reduced HDL-C levels [20].

**C-Reactive Protein (CRP):** In present study, CRP levels were raised in 53.2% (33) patients with severe psoriasis, 23.3% (14) patients with moderate psoriasis and 8.7% (11) patients with mild psoriasis and the difference was found to be statistically significant ( $p$ -value <0.001) [Table/Fig-8,9]. These results are in concordance with findings of previous studies. Farshchian M et al., reported that patients with moderate to severe plaque psoriasis had active systemic inflammation which was demonstrated by elevated levels of CRP and the psoriasis severity correlated with CRP levels [21]. Significantly higher CRP levels in psoriasis patients than controls ( $p$ -value <0.003) were observed by Vadakayil AR et al., [22]. Further, they concluded that CRP might be used as a marker of disease severity and could be used to monitor psoriasis and its treatment. Also, it was postulated that elevated CRP levels might be an independent risk factor for cardiovascular diseases in patients with psoriasis [22].

**Uric acid levels:** There was a rise in the value of serum uric acid as the severity of disease increased and this correlation was statistically significant [Table/Fig-8,9]. These results are in concordance with findings of previous studies. Chand R et al., reported that serum uric acid in psoriatic patients was higher than the controls ( $p$ -value < 0.05). However, they did not find any correlation of raised serum uric acid levels and extent of skin involvement [23].

Li X et al., observed that the correlation between psoriasis and hyperuricaemia was either ethnicity or region dependent and that patients with psoriasis in Western Europe were more likely to have hyperuricaemia [24]. Goldman M studied uric acid in the aetiology of psoriasis. The study reported that patients who had both psoriasis and hyperuricaemia showed marked improvement in psoriasis lesions when hyperuricaemia was treated [25]. The above mentioned studies reported association of hyperuricaemia and psoriasis, but they did not find its association to severity of the disease. The present study clearly reported that as the severity of psoriasis increased, the levels of serum uric acid also increased significantly.

### Limitation(s)

The disease duration was not studied. Duration of disease could also have an impact on the metabolic parameters. So, it may act as a confounding factor. Also, family history of metabolic syndrome was not considered. So, future studies including these factors are recommended to evaluate the effect of disease duration and family history of metabolic syndrome in derangement of various metabolic parameters in patients of psoriasis.

### CONCLUSION(S)

The present study concluded that a definite association between PASI score and metabolic derangements like hyperglycaemia, hyperlipidemia, hyperuricaemia and raised CRP levels was present. Patients with severe disease (PASI >12) had a higher risk of metabolic derangements which predisposes them to cardiovascular disease. This association had not been clearly established in the previous articles. There were no previous Indian studies that provide data on metabolic derangements among psoriasis patients based on PASI score. Patients of psoriasis should be evaluated for these metabolic parameters at their disease onset or at their first visit to the hospital so that these cardiovascular risk factors and components of metabolic syndrome could be detected early. Patients with severe disease should be especially taken care of. They should be advised lifestyle modifications and should be regularly monitored.

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## PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Oct 05, 2020
- Manual Googling: Dec 04, 2020
- iThenticate Software: Dec 28, 2020 (25%)

## ETYMOLOGY: Author Origin

## AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Oct 04, 2020**  
Date of Peer Review: **Oct 30, 2020**  
Date of Acceptance: **Dec 05, 2020**  
Date of Publishing: **Apr 01, 2021**