



INTERRELATIONSHIP OF INSULIN RESISTANCE, OBESITY AND PSORIASIS SEVERITY

Dermatology

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ABSTRACT

Background: Insulin resistance and obesity are quite frequent in psoriasis patients. They mutually seem to be interdependent. **Objective:** To assess the insulin level and obesity in Psoriasis patients and to correlate them with psoriasis severity. **Method:** A total of 60 psoriasis patients aged >18 years were enrolled in the study. BMI was calculated and serum fasting glucose and fasting insulin levels were assessed. HOMA-IR was calculated. Psoriasis severity was assessed using Psoriasis Area Severity Index (PASI). A correlation between Psoriasis severity, BMI and HOMA-IR was explored. Data analysis was done using SPSS 21.0 software. ANOVA and Pearson correlation coefficient were used to compare the data. **Results:** Mean age of patients was 39.37 ± 16.53 years. Majority of patients were males (66.7%). As per BMI criteria, a total of 20 (33.3%) were normal weight, 30 (50%) were overweight and 10 (16.7%) were obese. Mean HOMA-IR of study population was 8.48 ± 5.32 . A total of 25 (41.7%) were insulin resistant. As per PASI, a total of 9 (15%) had mild, 35 (58.3%) had moderate and 16 (26.7%) had severe psoriasis. With increasing psoriasis severity, there was a significant increase in mean BMI and HOMA-IR levels. There was a moderate positive correlation of PASI with BMI and HOMA-IR. A mild positive correlation was also seen between BMI and HOMA-IR. On multivariate analysis, severe psoriasis showed a significant association with BMI. **Conclusion:** Obesity, insulin resistance and psoriasis severity are interrelated and demand for lifestyle interventions as part of treatment strategy.

KEYWORDS

Psoriasis, PASI, Obesity, Insulin-resistance, HOMA-IR.

INTRODUCTION

Psoriasis is recognized as a skin disease yet its chronic inflammatory nature. This chronic inflammatory nature of psoriasis is responsible for dysfunction in a variety of organ systems. Psoriasis is characterized by expansion and activation of Th-1 T cells, antigen presenting cells, and Th-1 cytokines^{1,2}. Th-1 inflammatory cytokines such as TNF- α are elevated in the skin and blood of patients with psoriasis and are critical to recruiting T cells to the skin and joints, promoting angiogenesis, and epidermal hyper proliferation. Similarly, TNF- α is secreted in adipose tissue and is an important feature of the chronic low level inflammation seen in obesity³. Insulin resistance, which is common to psoriasis, could be mediated in part through inflammatory cytokines such as TNF. TNF inhibits the tyrosine kinase activity of the insulin receptor by activating peroxisome proliferator-activated receptor (PPAR), which impairs the insulin signaling, and results in insulin resistance. PPAR is also responsible for promotion of epidermal proliferation and modulation of adipogenesis and glucose metabolism^{4,5,6}. Insulin resistance is reported to be highly prevalent in psoriasis patients⁷. Although insulin resistance is generally linked with obesity, however, in psoriasis patients it is frequently seen in non-obese lean patients too⁸. Considering the fact that insulin resistance, obesity and psoriasis have an interrelationship, the present study was carried out to assess the prevalence of obesity and insulin resistance in psoriasis patients and to seek a relationship of body mass index and HOMA-IR with psoriasis severity.

MATERIAL AND METHOD

The present study was carried out at Era's Lucknow Medical College & Hospital, Lucknow, as a retrospective chart review of records of all the adult psoriasis patients aged >18 years visiting the facility for treatment of psoriasis over the last one year. Demographic details (age and sex), weight and height (for calculation of body mass index), fasting glucose and insulin levels were assessed. HOMA-IR was calculated. Insulin resistance was defined as HOMA-IR ≥ 2 . Psoriasis severity was assessed in terms of PASI. Only those cases having complete records regarding the requisite details were enrolled. A total of 60 such records were identified.

Assessment of Psoriasis Severity

Psoriasis severity was assessed by Psoriasis area severity index (PASI)⁹. PASI ranges from 0-72 and it is calculated using following method:

	Thickness 0-4	Scaling 0-4	Erythema 0-4	$\times$ Area 0-6 Total	TOTAL
Head	a	b	c	$d(a+b+c) \times 0.1$	A
Upper limbs	e	f	g	$h(e+f+g) \times 0.2$	B
Trunk	i	j	k	$l(i+j+k) \times 0.3$	C
Lower limbs	m	n	o	$p(m+n+o) \times 0.4$	D

$$PASI = A + B + C + D$$

Where, 0-4 scaling for severity of thickness, scaling and erythema is as follows:

- 0 = none;
- 1 = mild;
- 2 = moderate;
- 3 = severe;
- 4 = Very severe

And, 0-6 grading of area is as follows:

- 0 = no involvement
- 1 = <10%
- 2 = <30%
- 3 = <50%
- 4 = <70%
- 5 = <90%
- 6 = <100%

Axillae = upper limb
Neck/buttocks = trunk
Genito— femoral = lower limb

Patients were classified as:

- Mild Psoriasis (PASI <5)
- Moderate Psoriasis (PASI 5-10)
- Severe Psoriasis (PASI >10)

DATA ANALYSIS

Data so collected was entered into computer. Data was analyzed using SPSS 21.0 software. Association between Psoriasis severity and lipid levels was analyzed using ANOVA. Correlation of PASI scores with lipid levels was established using Pearson's Bivariate correlation coefficient. A 'p' value less than 0.05 was taken as indicator of a significant association. For bivariate correlation, 'r' value >0.3 was

considered to be clinically relevant (mild correlation). Binary logistic regression was done to find out association of different study variables with severe psoriasis.

RESULTS

Age of patients enrolled in the study ranged from 18 to 80 years. Mean age of patients was 39.37 ± 16.53 years. Majority of patients were males (66.7%). The male-to-female ratio of study population was 2:1. Body mass index (BMI) of patients ranged from 20.1 to 34.4 kg/m^2 . Mean BMI of patients was $26.88 \pm 3.38 \text{ kg/m}^2$. According to BMI, a total of 20 (33.3%) had normal weight (BMI $18.5\text{--}24.9 \text{ kg/m}^2$), 30 (50%) were overweight (BMI $25.0\text{--}29.9 \text{ kg/m}^2$) and 10 (16.7%) were obese (BMI $\geq 30 \text{ kg/m}^2$) respectively. Mean fasting glucose and insulin levels were $117.61 \pm 54.71 \text{ mg/dl}$ and $8.48 \pm 5.32 \text{ mIU/L}$ respectively. Mean HOMA-IR values were calculated as 2.34 ± 2.27 . A total of 25 (41.7%) patients were diagnosed as insulin resistant (HOMA-IR ≥ 2). PASI scores ranged from 2.5 to 27.2 with a mean of 8.52 ± 4.09 (Table 1).

Table 1: General Characteristics and Clinical Profile of Psoriasis Patients

SN	Characteristics	Statistic
1.	Mean Age $\pm$ SD (Range) years	39.37 ± 16.53 (18-80)
2.	Male:Female	40 (66.7%):20(33.3%)
3.	Mean BMI $\pm$ SD (Range) kg/m^2	26.88 ± 3.38 (20.1-34.4)
	Normal weight ($18.5\text{--}24.9 \text{ kg/m}^2$)	20 (33.3%)
	Overweight ($25.0\text{--}29.9 \text{ kg/m}^2$)	30 (50.0%)
	Obese ($\geq 30 \text{ kg/m}^2$)	10 (16.7%)
4.	Mean fasting blood sugar $\pm$ SD (Range) mg/dl	117.61 ± 54.71 (74.48-352)
5.	Mean Fasting Insulin $\pm$ SD (Range) mIU/L	8.48 ± 5.32 (2.8-27)
6.	Mean HOMA-IR $\pm$ SD (Range)	2.34 ± 2.27 (0.1-14.1)
	No. of patients with HOMA-IR >2	25 (41.7%)
7.	Mean PASI $\pm$ SD (Range)	8.52 ± 4.09 (2.5-27.2)

As per PASI, a total of 9 (15%) had mild, 35 (58.3%) had moderate and 16 (26.7%) had severe psoriasis (Table 2).

Table 2: Distribution of Cases according to Severity of Psoriasis

SN	Severity	PASI Score range	No. of cases	Percentage
1.	Mild	<5	9	15.0
2.	Moderate	5-10	35	58.3
3.	Severe	>10	16	26.7

Mean BMI was found to be 25.59 ± 3.28 , 26.00 ± 2.76 and $29.53 \pm 3.39 \text{ kg/m}^2$ respectively for mild, moderate and severe grades of psoriasis. Mean HOMA-IR values were found to be 1.12 ± 0.74 , 2.11 ± 1.63 and 3.53 ± 3.37 respectively for mild, moderate and severe psoriasis. Both BMI and HOMA-IR levels showed a significant incremental trend with increasing severity of psoriasis (Table 3).

Table 3: Association of Psoriasis severity with BMI and HOMA-IR levels

SN	Parameter	Severity of Psoriasis			Statistical significance (ANOVA)
		Mild (n=9)	Moderate (n=35)	Severe (n=16)	
1.	BMI (kg/m^2)	25.59 ± 3.28	26.00 ± 2.76	29.53 ± 3.39	F=9.493; p=0.001
2.	HOMA-IR	1.12 ± 0.74	2.11 ± 1.63	3.53 ± 3.37	F=4.044; p=0.023

Table 4: Binary logistic regression exploring association of different study variables with severe psoriasis

Independent Variable	Unadj. Odds $\pm$ SE	'p'	Adj. Odds	95% Confidence intervals of OR	
				Lower Bound	Upper Bound
Age in years	$-0.004 \pm .02$	0.850	0.996	0.950	1.043
Sex	0.59 ± 0.83	0.476	1.811	0.354	9.255
BMI (kg/m^2)	$0.36 \pm .14$	0.012	1.434	1.082	1.899
Fasting blood sugar levels (mg/dl)	$-0.01 \pm .01$	0.634	0.994	0.970	1.019
Fasting Insulin (mIU/L)	$0.02 \pm .10$	0.876	1.016	0.836	1.233
HOMA-IR	$0.18 \pm .38$	0.635	1.198	0.568	2.525
Constant	-11.10 ± 3.82	0.004	0.000		

On evaluating the correlation of PASI with BMI and HOMA-IR, it was found to be moderately positive and significant ($r=0.515$ and 0.507 ; $p<0.001$). There was a mild positive correlation between BMI and HOMA-IR too ($r=0.459$; $p<0.001$) (Fig. 1).

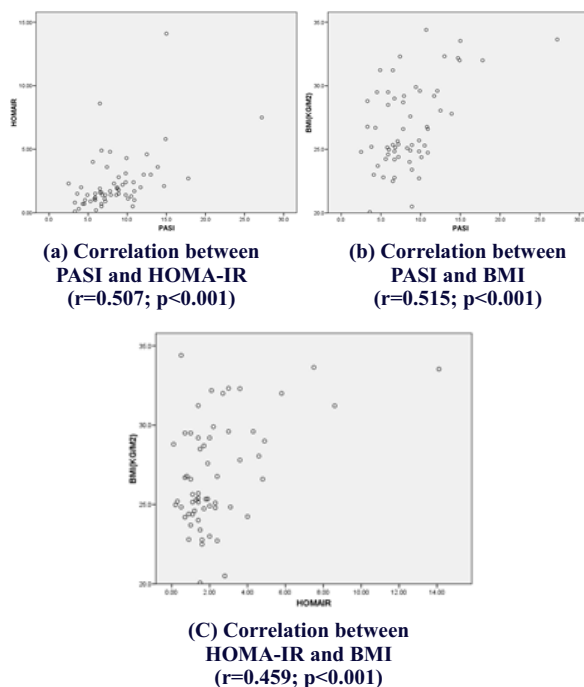


Fig. 1: Correlation between PASI, HOMA-IR and BMI

On binary logistic regression, where severe psoriasis was taken as a dependent variable on independent variables age, sex, BMI, fasting glucose, fasting insulin and HOMA-IR, only body mass index (BMI) was found to be significantly associated with psoriasis severity.

DISCUSSION

In present study problem of obesity (overweight and obese) as well as insulin resistance were found to be highly prevalent in psoriasis patients. Only one-third patients were non-obese normal weight patients while one-sixth of patients were obese (Mean BMI $26.88 \pm 3.38 \text{ kg/m}^2$). There was a dominance of overweight patients (50%). Overweight and obese together comprised two-third (66.7%) of study population. Moreover, 41.7% patients were insulin resistant too (Mean HOMA-IR 2.34 ± 2.27). As far as obesity is concerned, there is growing evidence suggesting a link between obesity and psoriasis. Obesity is recognized as a risk factor for incident psoriasis and its severity¹⁰⁻¹³. A high prevalence of overweight and obese persons in a series of psoriasis patients has also been reported by Sobhan and Farschian¹⁴ in their study in which as many as 69.1% patients were overweight and obese (Mean BMI 27.4 kg/m^2). In another study, Lara *et al.*¹⁵ also reported prevalence of overweight and obesity to be 62.5% in their series of psoriasis patients. Although, some studies have reported regional differences in prevalence of obesity in psoriasis patients¹³, still they also agree on the point that prevalence of obesity is higher in psoriasis patients as compared to normal population of that region. The findings of present study also indicate that most of the patients with psoriasis are either obese or tend to have obesity. With respect to insulin resistance, though the mean HOMA-IR value in present study was higher (2.34 ± 2.27) as compared to that reported by Alatas *et al.*¹⁶ in their study who reported the mean HOMA-IR values of psoriasis patients in their study to be 1.87 ± 1.05 yet they reported it to be significantly higher as compared to healthy controls. In present study, though we did not include a control population yet the high HOMA-IR values were depictive of a high prevalence of insulin resistance in our study population. Bhat *et al.*¹⁷ similar to our study found both obesity as well as insulin resistant to be highly prevalent in psoriasis patients. In their study they reported the prevalence of obesity and insulin resistance to be 37.2% and 27.3% respectively. The present study differed from their study from the point of view of a higher prevalence of insulin resistance (41.7%) as compared to obesity (16.7%), the fact that insulin resistance is often present in otherwise lean non-obese psoriasis patients too⁸. The mean HOMA-IR levels in

present study are in agreement with the mean HOMA-IR values for mild and severe psoriasis cases (2.21 ± 0.43 and 2.75 ± 0.51) as reported by Shivananda and Srikrishna in their study¹⁸. All these studies similar to our study show that insulin resistance is a common occurrence in a sizeable proportion of psoriasis patients and thus endorse the hypothesis that chronic inflammatory conditions might trigger insulin resistance^{19,20}.

In present study, we found a significant association between psoriasis severity and insulin resistance and obesity (HOMA-IR and BMI). We also found moderate positive and significant correlation of both HOMA-IR and BMI with PASI scores and a mild positive correlation between HOMA-IR and BMI. Association of psoriasis severity with obesity¹⁰⁻¹⁵ and insulin-resistance^{18,21}. In fact, psoriasis severity is often recognized as a risk factor of insulin-resistance independent of metabolic syndrome²¹. In present study too, the relationship between obesity and insulin resistance was not that strong as each of these two parameters had with psoriasis severity independently thus showing that both obesity and insulin-resistance have their independent effect on psoriasis severity. However, in present study, on multivariate analysis we did not find insulin-resistance to be an independent factor associated with severe psoriasis but instead observed BMI as the only independent factor associated with severe psoriasis. This finding indicates that though both BMI as well as insulin resistance could be independent risk factors for psoriasis, however, within psoriasis patients its progression seems to be dependent on the obesity status of the patients. The findings of the study support the viewpoint espoused by Jensen and Skov¹⁰ who reported that weight reduction may improve the severity of psoriasis in overweight individuals. They were also of the view that excess body weight could affect the efficacy of psoriasis treatment too and this could also be one of the reasons for its further progression and resultant severe psoriasis. The findings of present study thus highlight that obesity and insulin resistance have a significant association with psoriasis and its severity. Hence, psoriasis treatment, particularly in overweight and obese patients and those with insulin resistance should include appropriate lifestyle interventions focusing on reduction of weight and a better glycemic control in order to reduce the risk of further deterioration.

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