

Comorbidities in Iranian Obese Psoriatic Patients Compared With Non-Obese Patients

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Abstract- Psoriasis is a common chronic inflammatory skin disease, which is gradually being recognized as a systemic inflammatory disorder. Psoriasis and obesity are strongly linked, but there is not enough data whether obese psoriatic patients present differently from non-obese psoriatic patients. To compare the phenotype, clinical features, severity, baseline comorbidities and laboratory findings among psoriatic patients with/without obesity all the psoriatic patients, from three centers, who were receiving systemic therapy were included in the study. Patients were divided into two groups: those with obesity and those without obesity. We included 497 patients: 154 (31%) patients were obese and 343 (69%) were non-obese. Obese patients had more comorbidities, particularly hyperlipidemia, followed by hypertension and diabetes. Fasting blood sugar and serum lipids were significantly higher among obese subjects. Given the differences between obese patients and non-obese patients, the former group should be followed and managed more closely and with specific attention.

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Introduction

Psoriasis is a chronic inflammatory skin disease, affecting about 2-4% of the world population (1). In recent years, clear links have been established between psoriasis and a variety of diseases. Obesity, along with the metabolic syndrome and several other comorbidities are known to be associated with psoriasis (2,3). Obesity is an independent risk factor for psoriasis. In a meta-analysis of 16 observational studies, it has been shown that there is a pooled odds ratio (OR) of 1.66 for the association between psoriasis and obesity (4).

It is assumed that in both psoriasis and obesity, similar pathways of immune disorders occur. Psoriasis is an inflammatory condition associated with increased production of Th1 and Th17 cytokines, such as tumor necrosis factor (TNF)- α , interleukin (IL)-6, IL-17 and IL-23, among others. Some of these cytokines such as TNF- α and IL-6 are also involved in obesity (5,6).

In fact, the white adipose tissue is the largest endocrine organ. It has the ability to synthesize and

secrete inflammatory mediators such as TNF- α , IL 6 and also peptides such as adipokines, which have an impact on many physiological functions (7,8).

Epidemiological evidence has shown that obesity is linked to both pro-inflammatory and autoimmune diseases (9). However, the relationship between psoriasis and obesity is complex and there are still many unanswered questions about it. For instance;

- Do obese patients have the more severe disease?
- Are some specific variants more common in obese patients?
- Are some specific comorbidities more common in obese patients?
- Do they coexist because they have a common antecedent link?

To address these questions, we conducted a study to evaluate the relationship between obesity and clinical factors as well as comorbidities in patients with psoriasis.

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Materials and Methods

All patients with moderate to severe psoriasis on treatment with any systemic agents at three psoriasis clinics were selected for this cross-sectional study. The study was conducted from January to November 2017. These patients were classified into two mutually exclusive groups: (1) obese psoriatic patients or (2) non-obese psoriatic patients. Obesity was defined as a body mass index (BMI) greater than 30.

Diagnosis of psoriasis was according to the clinical findings, and if necessary, a skin biopsy was performed. Demographic data, family history of psoriasis, BMI, waist circumference (WC), age at onset, clinical phenotypes, Psoriasis Area and Severity Index (PASI) score and metabolic comorbidities were collected for all patients using a standardized form.

Weight and height were measured for each subject. BMI (as weight in kilograms divided by height in meters squared) was measured for all of the cases. Fasting blood sugar (FBS) and lipid profile was requested for each patient at the time of examination. All the laboratory examinations were performed in a single laboratory in each center.

Statistical analysis was performed using software

SPSS 18.0 (SPSS Inc., IBM Corporation, and Armonk, New York). Categorical variables were expressed as frequencies and percentages and analyzed by Chi-square test or Fisher's exact test. Normality of variables was verified by the Kolmogorov-Smirnov test. Quantitative variables were given as means (SD) or medians (range). T student test was used for quantitative variables with normal distribution. For quantitative variables with an abnormal distribution, the Mann Whitney test was performed. Statistical significance was considered at a level of 5% ($P < 0.05$) for all tests.

Results

A total of 497 patients were included in the study. Forty-nine percent were female. The mean age of patients was 45 ± 14.85 years. The mean PASI score was 11.31 ± 10.53 . Overall BMI was calculated as 27.98 ± 5.82 kg/m^2 . 31% of patients with psoriasis were obese. Obese psoriatic patients were more likely to be female (67%, $P = 0.001$). The severity of psoriasis was not significantly different between the two groups. Also, the mean age of onset and duration of psoriasis were similar between both groups (Table 1).

Table 1. Baseline characteristics according to BMI

	All patients (497)	Non-obese (N=343) (BMI<30)	Obese (N=154) (BMI≥30)	P
Age (yr.)	45.07±14.85	44.53±15.21	46.29±13.97	0.22
Gender (Female)	243(48.89%)	140(40.82%)	103(66.88%)	0.001
Age of onset (yr.)	29.80±16.20	29.03±16.21	31.53±16.11	0.12
Duration of disease	15.26±11.48	15.49±11.71	14.76±10.98	0.51
Smoking	138 (27.8%)	102 (29.7%)	36 (23.4%)	0.14
Alcohol	66 (13.3%)	47 (13.7%)	19 (12.3%)	0.67
PASI	11.31±10.53	11.27±10.67	11.38±10.26	0.93
BMI (kg/m^2)	27.98±5.82	25.03±3.15	34.55±4.97	0.001

PASI: psoriasis area severity index, BMI: body mass index

Table 2 shows anthropometric values in the two groups. The mean waist and hip circumferences in obese psoriatic patients were significantly higher than non-obese cases.

Overall, the most prevalent comorbidity among our patients was hyperlipidemia (13.5%). The prevalence of

diabetes mellitus, blood hypertension, hyperlipidemia, and hypothyroidism were significantly higher among obese psoriatic patients. While the prevalence of cardiovascular diseases was not significantly different between the two groups (Table 3).

Table 2. Anthropometric values of studied groups

	All patients	Non-obese	Obese	P
Weight (Kg) (N=497)	76.68±16.38	69.81±11.96	91.69±14.64	0.001
Height (cm) (N=497)	165.67±10.06	166.37±9.64	164.15±10.79	0.025
Waist circumference (cm) (N=439)	146±14.73	89.65±11.25	109.01±12.56	0.001
Hip circumference (cm) (N=429)	149±13.01	98.37±8.77	114.62±14.02	0.001

Table 3. Prevalence of comorbidities

	All patients (497)	Non-obese (N=343)	Obese (N=154)	P
DM	62 (12.5%)	34 (9.9%)	28 (18.2%)	0.01
HTN	65 (13.1%)	30 (8.7%)	35 (22.7%)	0.001
CVD	24 (4.8%)	16 (4.7%)	8 (5.2%)	0.79
HLP	67 (13.5%)	28 (8.2%)	39 (25.3%)	0.001
Hypothyroidism	25 (5%)	12 (3.5%)	13 (8.4%)	0.02

DM: diabetes mellitus, HTN: hypertension, CVD: cardiovascular disease, HLP: hyperlipidemia

Mean of FBS, triglyceride (TG), cholesterol (Chol) and low-density lipoprotein (LDL) were significantly higher in obese subjects ($P=0.02$, $P=0.002$, $P=0.03$ and

$P=0.03$, respectively). The mean of high-density lipoprotein (HDL) was lower in obese patients ($P=0.06$) (Table 4).

Table 4. Laboratory findings in the studied groups

	All patients (497)	Non-obese (N=343)	Obese (N=154)	P
FBS	104.65±35.41	101.59±31.16	110.70±42.07	0.02
TG	158.80±94.34	148.55±91.67	181.95±96.58	0.002
Chol	183.92±38.64	181.04±37.48	190.19±39.68	0.03
HDL	43.53±12.22	44.35±12.33	41.73±11.82	0.06
LDL	110.05±32.78	107.76±34.48	115.07±28.20	0.03

FBS: fasting blood sugar, TG: triglyceride, Chol: cholesterol, HDL: high-density lipoprotein, LDL: low-density lipoprotein

Chronic plaque type was the most prevalent type in both groups (Table 5).

Table 5. Phenotype of psoriasis in the groups studied

Type	All patients (497)	Non obese (N=343)	Obese (N=154)	P
Chronic Plaque	444 (89.3%)	299 (87.2%)	145 (94.2%)	0.02
Pustular	4 (0.8%)	3 (0.9%)	1 (0.6%)	0.79
Palmoplantar	48 (9.7%)	37 (10.8%)	11 (7.1%)	0.20
Flexoral	12 (2.4%)	6 (1.7%)	6 (3.9%)	0.14
Guttate	30 (6%)	17 (5%)	13 (8.4%)	0.13
Erythrodermic	18 (3.6%)	17 (5%)	1 (0.6%)	0.02

In this study, we could find a nonlinear correlation between BMI and PASI score ($P=0.034$, $R=0.021$), (Table 6, Figure 1).

Table 6. Model Summary and Parameter Estimates

Equation	Dependent Variable: BMI								
	Model Summary					Parameter Estimates			
	R Square	F	df1	df2	P	Constant	b1	b2	b3
Cubic	.021	2.925	3	406	.034	26.357	.415	-.021	.000

Psoriasis and obesity, more than comorbidity?

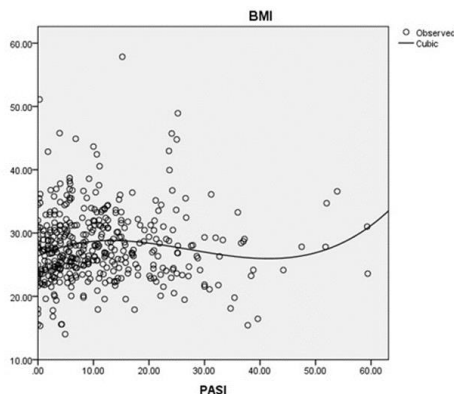


Figure 1. Estimation of PASI distribution curve

Spearman correlation coefficient was used for comparing PASI scores with other parameters in two groups of obese and non-obese psoriatic patients. Findings revealed that in obese psoriatic patients, PASI scores correlate with patients’ height, serum cholesterol, low-density lipoprotein, and blood urea nitrogen level, as well as blood hypertension and alcohol consumption. In contrast, in non-obese psoriatic patients, PASI correlates with patients' age, the age of onset of disease and serum uric acid level.

Both obese and non-obese patients were found to have correlations between PASI score and the age at the

onset of disease and the duration of disease (Table 7 and 8).

Canonic correlation coefficient revealed a strong correlation between the panel consisting of both PASI score and lipid profiles (Chol, HDL, LDL, TG) in comparison with the panel of the anthropometrics profile (BMI, weight circumference, hip circumference) (canonical correlation=0.424, $P=0.0001$, $r^2=0.18$). The correlation coefficient of the PASI score on the anthropometric indices was 0.13. Cholesterol had the strongest correlation followed by TG (Table 9).

Table 7. Correlation between the PASI score and quantitative variables in obese and non-obese psoriatic patients

		PASI score	
		BMI<30	BMI>30
Age	R	-.163	-.132
	P value	.006	.139
	Number	283	127
Weight	R	.099	.147
	P value	.099	.099
	Number	278	127
Height	R	.066	.224
	P value	.277	.011
	Number	273	127
Weight circumference	R	-.010	.031
	P value	.872	.735
	Number	259	120
Hip circumference	R	.084	.021
	P value	.181	.827
	Number	257	114
Age of onset	R	-.278	-.239
	P value	.000	.007
	Number	283	127
FBS	R	.026	-.049
	P value	.725	.633
	Number	189	96
TG	R	-.001	.149
	P value	.988	.148
	Number	222	96

Continuance of Table 7			
Cholesterol	R	.025	.232
	P value	.714	.021
	Number	219	99
LDL	R	.130	.288
	P value	.067	.006
	Number	201	90
HDL	R	-.046	-.064
	P value	.529	.561
	Number	189	86
BUN	R	-.054	-.217
	P value	.489	.048
	Number	164	84
Cr	R	-.023	.091
	P value	.738	.360
	Number	209	104
SGPT	R	.004	.056
	P value	.954	.544
	Number	250	119
SGOT	R	-.028	-.080
	P value	.665	.384
	Number	250	119
ALKP	R	-.030	.171
	P value	.661	.099
	Number	214	94
Uric acid	R	.176	-.197
	P value	.050	.122
	Number	125	63
Duration of disease	R	.161	.219
	P value	.007	.013
	Number	283	127
Weight to Hip ratio	R	-.073	.001
	P value	.246	.993
	Number	257	114

FBS: fasting blood sugar, TG: triglyceride, Chol: cholesterol, HDL: high-density lipoprotein, LDL: low-density lipoprotein, Cr: creatinine, BUN: blood urea nitrogen, SGPT: Serum glutamic-pyruvic transaminase, SGOT: Serum glutamic oxaloacetic transaminase.

Table 8. Comparison of PASI score and demographic variables in obese and non-obese psoriatic patients

		BMI					
		<30			>30		
		Mean±Standard Deviation	Median	P	Mean±Standard Deviation	Median	P
Sex	Male	11.86±11.51	8.20	.675	12.58±10.99	11.35	.247
	Female	10.30±9.05	8.20		10.74±9.86	9.20	
DM		12.60±10.50	8.20	.346	15.37±15.50	10.40	.339
HTN		9.61±7.75	7.80	.877	12.89±11.05	10.40	.318
CVD		13.37±9.84	12.60	.331	12.80±6.19	11.60	.256
HLP		12.10±7.49	9.20	.14	14.53±12.05	12.00	.01
Hypothyroidism		10.80±6.11	10.25	.492	9.38±6.16	9.90	.748
Family history		11.02±11.02	8.00	.659	12.68±12.05	9.90	.607
Smoking		11.19±9.91	8.20	.576	11.31±11.32	8.00	.702
Alcohol		12.42±9.25	11.00	.096	15.20±9.31	14.80	.019
Chronic plaque		10.80±10.14	8.10	.109	11.30±10.18	9.90	.968
Pustular		21.73±1.58	22.10	.044	9.10	9.10	.891
Palmoplantar		13.78±14.37	10.70	.631	3.78±2.32	4.35	.019
Flexural		20.90±9.74	20.10	.044	17.73±8.52	17.00	.140
Guttate		14.30±7.77	12.35	.075	21.38±9.65	21.45	.007
Erythrodermic		24.90±18.88	24.40	.004	2.20	2.20	.190

DM: diabetes mellitus, HTN: hypertension, CVD: cardiovascular disease, HLP: hyperlipidemia

Table 9. Standardized canonical coefficients section

Variables	Explained by the anthropometric variables	Unexplained by the anthropometric Variables
PASI	-0.133505	0.203532
FBS	-0.251819	-0.222742
TG	-0.478380	0.004409
Chol	-0.671355	0.066018
LDL	0.183803	0.006431
HDL	0.018109	0.964880
	Explained by the PASI and lipid profile	Unexplained by the PASI and lipid profile
Weight circumference	-0.816631	1.630921
Hip circumference	-0.049753	-1.028725
BMI	-0.174884	-0.871489

DM: diabetes mellitus, HTN: hypertension, CVD: cardiovascular disease, HLP: hyperlipidemia , BMI: body mass index

Discussion

Several studies have shown the association between obesity and psoriasis (10-13). Herron and colleagues demonstrated an almost two-fold risk of obesity in their psoriatic patients compared to the general population (34% vs 18%; $P=0.001$) (10). In our study, the prevalence of obesity in psoriatic patients was 31%, which is higher than the prevalence of obesity in the general population of Iran (21%, CI 95%: 18.5%-25%) (14). However, it seems that the prevalence of obesity in Iranian psoriatic patients is not as high as what was found in some other studies. For instance, Takahashi et al. and Warnecke *et al.*, reported a rate of 39.7% and 44% for obesity in patients with psoriasis respectively (15,16).

Some studies have revealed that the risk of psoriasis increases with higher BMI (17,18). The relationship between obesity and severity of psoriasis has been noted in a number of cross-sectional studies in which increased BMI coincides with a greater degree of psoriasis disease severity (10,18). We did not find such a relationship in our patients.

Most studies reported that obesity probably predates or co-exists with psoriasis. However, one study revealed new-onset obesity in patients with existing psoriasis, showing a slightly increased risk for developing obesity in psoriasis patients in comparison with controls (20). Behavioral factors, the unwillingness of psoriatic patients to participate in physical activities due to

psychological burden of visibility of the skin lesions, in addition to genetic and immune-mediated mechanisms, are possible mechanisms explaining the association between psoriasis and obesity (21-25).

It should be emphasized that a high BMI also has a negative impact on the response to treatment in patients with psoriasis (26). It has been revealed that response to treatment will be improved after a low-calorie diet-induced weight loss in subjects with psoriasis (27).

We found that hyperlipidemia, diabetes, hypertension, and hypothyroidism are all more common in obese psoriatic patients. However, we could not find any association between obesity and a higher risk of CVD. This data shows that perhaps the risk of CVD in psoriasis is independent of the metabolic syndrome and is related to the inflammatory nature of the disease itself. This is in accordance with a prospective, population-based cohort study conducted in the UK by Gelfand *et al.*, The cohort was adjusted for hypertension, hyperlipidemia, diabetes, history of myocardial infarction (MI), age, sex, smoking, and BMI. They showed that psoriasis may confer an independent risk of MI. Relative risk is especially higher in younger patients and in patients with more severe psoriasis (28). On the other hand, some studies have found no statistically significant association between psoriasis and cardiovascular events (29-31).

A pooled odds ratio (OR) for the association between psoriasis and hypertension of 1.58 (95% CI, 1.42-1.76) was found by a meta-analysis of 24 observational

studies (32). Alexandroff *et al.*, reported the increase in odds of hypertension among patients with psoriasis parallel to the increase in disease severity (ORs of 1.30 for mild and 1.49 for severe psoriasis) (33).

Independent of other risk factors, psoriasis is associated with an increased risk for DM. A meta-analysis of 5 cohort studies found a pooled relative risk (RR) for diabetes of 1.27 (95% CI, 1.16-1.40) among patients with psoriasis (34). The risk of insulin resistance and the likelihood of diabetes and its complications are increased with greater psoriasis severity as, independent of other risk factors such as BMI. Both means of FBS and prevalence of DM were significantly greater among obese psoriatic patients (35-37).

Dyslipidemia may be more prevalent among patients with psoriasis than others without (38). Lipid testing techniques have revealed atherogenic lipid profile and decreased high-density lipoprotein (HDL) cholesterol efflux capacity (CEC) among patients with psoriasis (39,40). In our study, the mean level of TG, Chol and HDL were all higher among obese psoriatic patients in comparison with non-obese patients.

Studies have shown an association between hypothyroidism and psoriasis. This association had been reported in both psoriatic patients with and without psoriatic arthritis (41,42). However, James *et al.*, found that rates of hypothyroidism in psoriasis patients were similar to rates of hypothyroidism in those without psoriasis (43). To the best of our knowledge, this is the first study that reported the association between hypothyroidism and obesity in psoriatic patients. Having

known that psoriasis has different clinical phenotypes, the present study examined the hypothesis that obese patients may present differently from non-obese patients. We did not find any data support this hypothesis.

We recognize that our study has some limitations. Regarding there is no psoriasis registry in Iran, our patients were only from three psoriasis clinics. Therefore, our data might not be generalizable to all Iranian psoriasis patients. Another limitation is that hypothyroidism was considered based on medical and drug history. Also, Hemoglobin A_{1c} might have been a better test for DM but was not routinely available.

In summary, a considerable proportion of patients with psoriasis have comorbid conditions. In obese psoriatic patients, the risk of these comorbidities is even higher. Psoriasis and obesity are interconnected through multiple aspects (Figure 2). Obese psoriatics should be considered as “at-risk” patients and special attention should be applied when formulating a treatment and management plan for them.

In this cross-sectional study, we found that comorbidities such as DM, HTN, HLP, and hypothyroidism are all statistically more common in obese as compared to non-obese psoriatic patients. Regarding the higher incidence of obesity in psoriatic patients and its association with other signs of metabolic syndrome, dermatologists should consider obese psoriatics as “at-risk patients” and initiate an interdisciplinary approach to the screening and management of their comorbidities.

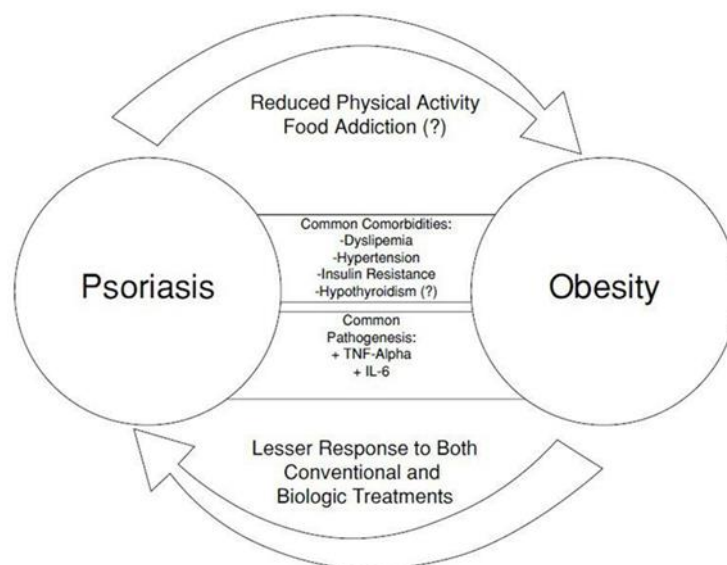


Figure 2. Multiple aspects of interconnection between psoriasis and obesity

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