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.

Keywords: Psoriasis; Obesity; Metabolic syndrome; Comorbidity

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)-a, interleukin (IL)-6, IL-17 and IL-23, among others. Some of these cytokines such as TNF-a 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.
Psoriasis and obesity; more than comorbidity?

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/m². 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) | Obese (N=154) | 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/m²)          | 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 (N=497) | Non-obese (N=429) | Obese (N=429) | P  |
|----------------------|----------------------|--------------------|---------------|----|
| Weight (Kg)          | 76.68±16.38          | 69.81±11.96        | 91.69±14.64   | 0.001|
| Height (cm)          | 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

| Comorbidity | 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

| Test     | 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±88.64       | 181.04±87.48       | 190.19±93.68  | 0.03|
| HDL      | 43.53±12.22        | 44.35±12.33        | 41.73±11.82   | 0.06|
| LDL      | 110.05±32.78       | 107.6±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 |
|----------|-------------------------|
|          | 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?

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**

| Variable                  | BMI<30  | BMI>30 |
|---------------------------|---------|--------|
| PASI score                | R       |        |
| Age                       | -.163   | -.132  |
| P value                   | .006    | .139   |
| Number                    | 283     | 127    |
| R                         | .999    | .147   |
| Weight                    | .999    | .999   |
| P value                   | 278     | 127    |
| Number                    | .966    | .224   |
| Height                    | .277    | .011   |
| P value                   | 273     | 127    |
| Number                    | .010    | .031   |
| Weight circumference      | .872    | .735   |
| P value                   | 259     | 120    |
| Number                    | .084    | .021   |
| Hip circumference         | .181    | .827   |
| P value                   | 257     | 114    |
| Number                    | -.278   | -.239  |
| Age of onset              | .000    | .007   |
| P value                   | 283     | 127    |
| Number                    | .026    | .049   |
| FBS                       | .725    | .633   |
| P value                   | 189     | 96     |
| Number                    | .001    | .149   |
| TG                        | .988    | .148   |
| Number                    | 222     | 96     |

Figure 1. Estimation of PASI distribution curve
Continuance of Table 7

|                      | R     | P value | Number | P     | Standard Deviation | Median | P     | Number | P     | Standard Deviation | Median |
|----------------------|-------|---------|--------|-------|-------------------|--------|-------|--------|-------|-------------------|--------|
| Cholesterol         | .025  | .232    | 219    | .714  | .021              | 99     | .130  | .288   | 201   | .006              | .90    |
| LDL                  | .067  | .232    | 90     | .714  | .021              | 201    | .288  | .288   | 90    | .006              | .90    |
| HDL                  | .046  | .232    | 86     | .714  | .021              | 201    | .288  | .288   | 90    | .006              | .90    |
| BUN                  | .529  | .232    | 86     | .714  | .021              | 201    | .288  | .288   | 90    | .006              | .90    |
| Cr                   | .738  | .232    | 86     | .714  | .021              | 201    | .288  | .288   | 90    | .006              | .90    |
| SGPT                 | .954  | .232    | 119    | .714  | .021              | 201    | .288  | .288   | 90    | .006              | .90    |
| SGOT                 | .655  | .232    | 119    | .714  | .021              | 201    | .288  | .288   | 90    | .006              | .90    |
| ALKP                 | .030  | .232    | .94    | .714  | .021              | .288   | .288  | .288   | .288  | .006              | .90    |
| P value              | .050  | .232    | .122   | .714  | .021              | .288   | .288  | .288   | .288  | .006              | .90    |
| Number               | 250   | 119     | 63     | 284   | 119               | 119    | 63    | 119    | 63    | 119               | 119    |
| R                    | .176  | .232    | .197   | .714  | .021              | .288   | .288  | .288   | .288  | .006              | .90    |
| Uric acid            | .007  | .232    | .013   | .714  | .021              | .288   | .288  | .288   | .288  | .006              | .90    |
| Number               | 283   | 127     | 127    | 384   | 114               | 127    | 127   | 127    | 127   | 127               | 127    |
| R                    | .073  | .232    | .001   | .714  | .021              | .288   | .288  | .288   | .288  | .006              | .90    |
| Weight to Hip ratio  | .246  | .232    | .993   | .714  | .021              | .288   | .288  | .288   | .288  | .006              | .90    |
| Number               | 257   | 114     | 114    | 114   | 114               | 114    | 114   | 114    | 114   | 114               | 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

|                      | Mean±Standard Deviation | Median | P     | Mean±Standard Deviation | Median | P     |
|----------------------|-------------------------|--------|-------|-------------------------|--------|-------|
|                     | <30                     | >30    |       | <30                     | >30    |       |
| Sex                  |                         |        |       |                         |        |       |
| Male                 | 11.36±11.51             | 8.20   | .675  | 12.58±10.99             | 11.35  | .247  |
| Female               | 10.30±9.05              | 8.20   | .675  | 10.74±9.86              | 9.20   | .247  |
| 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
Psoriasis and obesity; more than comorbidity?

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 |

| Variables     | Coefficient | Coefficient |
|---------------|-------------|-------------|
| Weightcircumference | -0.816631   | 1.630921    |
| Hipcircumference  | -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 A1c 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 psoriatrics 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 psoriatrics 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
Psoriasis and obesity; more than comorbidity?

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