Original Article / Orijinal Araştırma

Prevalence of Metabolic Syndrome and Insulin Resistance in Patients with Psoriasis

Psöriasisli Hastalarda Metabolik Sendrom ve İnsülin Direnci prevalansı

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ÖZET

Amaç: Son zamanlarda, Psöriasisdeki kronik inflamasyonun metabolik sendrom gelişmesine neden olduğu ileri sürülmektedir. Psöriasis ve insülin direnci arasındaki ilişki ile ilgili sınırlı veri bulunmaktadır. Bu çalışmanın amacı, psöriasis hastalarında insülin direnci ve metabolik sendrom sıklığı ve hastalığın şiddeti arasındaki ilişkiyi araştırmaktır.

Gereç ve Yöntem: Çalışmayı 48 psöriasisli hasta ve 45 sağlıklı birey oluşturmuştur. İnsülin direnci homeostasis model assessment (HOMA) formülü kullanılarak değerlendirildi. Psöriasis aktivitesi, psöriasis alan ve şiddet indeksi (PASI) ile değerlendirildi. Hastalar PASI skoruna göre 3 gruba ayrıldı.

Bulgular: Metabolik sendrom, 21 hastada (%43.75) ve 8 kontrol bireyde (%17.77) izlendi (p=0.007). İnsülin direnci, 16 hastada (%33.33) ve 5 kontrol bireyde (%11.11) izlendi (p=0.01). Metabolik sendrom ve insülin direnci sıklığı sağlıklı kontrollerle karşılaştırdığında psöriasisli hastalarda artmıştı. PASI, linear regresyon analizine göre insülin direnci gelişimi için bağımsız bir risk faktörüydü (p=0.003).

Sonuç: Metabolik sendrom ve insülin direnci insidansı kontrol grubuna göre psöriasisli hastalarda daha yüksek bulunmuştur. Özellikle psöriasis şiddeti ile insülin direnci riski arasında güçlü bir ilişki vardı. Bu nedenle, psöriasis sadece bir deri hastalığı olarak değil aynı zamanda bir metabolik ve kardiyovasküler hastalık olarak da düşünülmesi gereklidir.

Anahtar kelimeler: metabolik sendrom, psoriasis, insülin direnci, inflamasyon

ABSTRACT

Aim: Recently, it has been proposed that chronic inflammation in psoriasis lead to metabolic syndrome (MetS) development. There is limited data about the relationship between psoriasis and IR. Aim of the present study was to investigate the prevalence of IR and MetS in psoriasis patients and the association between the severities of illnesses.

Material and Method: The study consisted of 48 psoriasis patients and 45 healthy individuals. IR was estimated using homeostasis model assessment (HOMA) of IR formula. The psoriasis activity was evaluated by the psoriasis area and severity index (PASI). Patients were divided into 3 groups according to PASI scores.

Results: MetS was observed in 21 patients (43.75%) and 8 controls (17.77%) (p=0.007). IR was observed in 16 patients (33.33%) and 5 controls (11.11%) (p=0.01). The frequencies of MetS and IR increased in psoriasis patients compared to healthy controls. According to linear regression analysis, PASI was independent risk factor for IR development (p=0.003).

Conclusion: The incidences of MetS and IR were found to be higher in patients with psoriasis compared to control group. Especially there was a strong association between severe psoriasis and IR risk. Therefore, psoriasis needs to be considered as not only a skin disorder, but also a metabolic and cardiovascular disease.

Key Words: metabolic syndrome, psoriasis, insulin resistance, inflammation

Introduction

Psoriasis, Immune Mediated Inflammatory Disease (IMID), is a chronic inflammatory skin disorder in which proinflammatory cytokines including IL-6 and TNF-α increase both locally and systematically (1). Genetic and environmental factors are underlying in etiopathogenesis of psoriasis. Besides the skin symptoms and signs, systemic involvement and arthritis is common in patients, and disease is characterized with remission and relapses (2). Metabolic syndrome (MetS) was originally described as the clustering of four conditions (namely: glucose intolerance; hypertension, dyslipidemia and central obesity) which increase the risk of cardiovascular disease when present together in one individual (3). Recently, it has been reported that psoriasis patients have higher prevalence of MetS than general population (4). It was attributed to the effects of proinflammatory cytokines and chronic inflammations in psoriasis which are associated with development of atherogenesis, hypertension, type 2 diabetes mellitus and insulin resistance (IR) (1). There is limited data about the relationship between psoriasis and IR in the literature.

The aim of the present study was to investigate the prevalence of IR and MetS in psoriasis patients and the correlation between the severities of these illnesses.

Materials and methods

We designed a prospective study and a total of 48 patients and 45 healthy control subjects were recruited from Department of Internal Medicine and Dermatology outpatient clinics at Gaziosmanpasa University. The patient group consisted of the patients psoriasis diagnoses. The control group consisted of 45 healthy subjects who were matching with the patient group for age, gender and body mass index (BMI). All patients were assessed by medical history and physical examination. Each patient was examined by an experienced dermatologist. Extent of involvement was assessed using Psoriasis Area and Severity Index (PASI) that evaluates the erythema, induration, and scaling of the lesions in four body areas (head, trunk, arms and legs). A PASI between 0 and 7 was classified mild psoriasis, while scores between 8 and 12 moderate and >12 severe (5).

The patients with systemic or endocrine diseases such as diabetes mellitus, liver and renal dysfunction, thyroid disease, hyperprolactinemia, Cushing Syndrome, acromegaly, pregnancy, malignancy and the patients who are smoking, using hormonal medicines such as glucocorticoid, statins, oral anti-diabetics, insulin and severe systemic involvement of psoriasis (such as psoriatic arthritis, using anti-TNF agents) were not included in the study.

Demographic data and medical history of all subjects were recorded. Physical examination and anthropometric measurements were performed, and BMI was calculated (BMI = weight in kg/square of height in meters). The waist circumference (WC) was measured by placing the measuring tape snugly around the abdomen at the level of the iliac crest. The blood pressure (BP) was taken in the sitting posture twice and the average of two measurements was recorded.

Serum samples were taken from the patients for analysis of chemical parameters including triglyceride (TG), HDL-C and fasting blood glucose (FBG) levels. Serum HDL-C and TG were determined enzymatically (Olympus Diagnostica, Lismeehan, Ireland). For all laboratory parameters, venous blood samples were taken between 8.00 and 9.00 a.m. following 12-hour fasting. IR was estimated using HOMA-IR method. HOMA-IR index was calculated by [fasting insulin (μU/ml) X fasting glucose (mg/dl)/405] formula. Limit value for IR existence was accepted as 2.7 (6). MetS was diagnosed using the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria (7). If three or more of the following were present, the patient was diagnosed as having MetS: abdominal obesity (waist circumference ≥102 cm for males and ≥88 cm for females), blood pressure>130/85 mmHg, fasting blood glucose ≥110 mg/dl, hypertriglyceridemia >150 mg/dl, or low HDL cholesterol (<40 mg/dl for males and <50 mg/dl for females).

All subjects gave informed consent and the study protocol was approved by the local ethic committee (No: 11-BADK-026).

Statistical analyses

Statistical analyses were performed using the SPSS software, version 17.0 (SPSS Inc., Chicago, IL, USA). Normal distribution of the quantitative variables was analyzed by Kolmogorov-Smirnov test. Parametric tests were applied when variables distributed normally and non-parametric tests were applied when variables did not distribute normally. Parametric test results were given as means ± standard deviations (SD). Non-parametric test results were given as mean, minimum and maximum. Qualitative variables were presented as counts and proportions. For normally distributed variables, ANOVA was applied to evaluate the differences among groups and Bonferonni test was used for posthoc analysis. Comparison of variables which did not distribute normally was performed by using Kruskal-Wallis test. Linear correlations between clinical parameters were assessed within each group using the Pearson correlation. A multiple linear regression model was used to identify independent predictors of HOMA-IR. The value of $p<0.05$ was considered significant.

Results

A total of 48 psoriasis patients and 45 healthy controls enrolled in this study. Mean age of the patients was 39.8 ±14 years, BMI values were 27.83 ± 7.08 kg/m2. There was no difference between patients and controls in terms of age and BMI ($p>0.05$). Diastolic BP was significantly higher in patient group than the control ($p=0.01$). HDL-C was significantly lower in the patient group than in control ($p=0.005$). TG, HOMA, WC and FBG levels were similar in two groups ($p> 0.05$) (Table 1). MetS was observed in 21 patients (43.75%) and 8 controls (17.77%) ($p=0.007$). IR was observed in 16 patients (33.33%) and 5 controls (11.11%) ($p=0.01$). The frequencies of MetS and IR increased in psoriasis patients compared to healthy controls (Table 2).

Patients were divided into three groups according to PASI scores; patients in group 1 (n=28, F/M: 15/13) had PASI <7, patients in group 2 had PASI 7-12 (n=11, F/M: 6/5) and in group 3 had PASI>12 (n =9, F/M: 6/3). There were significant differences in BP, WC, BMI, FBG and HOMA among PASI groups. Systolic BP mean was significantly higher in group 3 than group 1, and diastolic BP was higher both in group 2 and 3 than in group 1. BMI, WC and FBG levels were significantly higher in group 3 than in other groups, and HOMA was significantly higher in group 3 than in group 1. TG and HDL-C levels were similar in three groups (Table 3). There was significant positive correlation between PASI and systolic and diastolic BP, TG, WC, FBG, BMI and HOMA (Table 4). MetS rates were 32.14% (n=9), 63.63% (n=7) and 66.66% (n=6) for group 1, 2, and 3, respectively. There was no significant difference in MetS rates among three groups. IR rates were 14.28% (n=4), 45.45% (n=5) and 77.77% (n=7) in group 1, 2 and 3, respectively. The difference was statistically significant ($p<0.001$). According to linear regression analyses, FBG ($p=0.001$), TG ($p=0.002$) and PASI ($p=0.05$) were independent predictors of HOMA, and PASI was independent risk factor for development of IR ($p=0.003$).

Table 1. The characteristics and clinical manifestations of the studied groups

	Patients with psoriasis (n=48)	Control group (n=45)	p value
Gender (male/female)	23/25	21/24	-
Age (years)	39.8±14	38.8±12.9	0.767
BMI (kg/m^2)	27.83±7.08	28.26± 4.92	0.490
WC (cm)	95.45±16.63	100.35±12.94	0.160
SBP (mmHg)	123.85±23.00	118.22±22.69	0.14
DBP (mmHg)	82.08±14.58	76.22±13.36	**0.01**
TG (mg/dL)	152.45±92.20	117.04+64.85	0.05
HDL (mg/dL)	44.45±10.44	50.42±12.96	**0.005**
FBG (mg/dL)	99.66±21.12	93.48±8.60	0.12
HOMA	2.62±1.56	2.26±1.18	0.33

BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, Triglyceride; FBG, fasting blood glucose; HOMA, homeostasis model assesment.

Table 2. Metabolic syndrome and insulin resistance in psoriasis patients and control

	Psoriasis (n=48) N %	Control (n=45) N %	p
MetS	21 (43.75%)	8 (17.77%)	**0.007**
IR	16 (33.33%)	5 (11.11%)	**0.01**

MetS, metabolic syndrome; IR, insulin resistance.

Table 3. The characteristics and clinical manifestations of the groups

	Group 1 (n=28)	Group 2 (n=11)	Group 3 (n=9)	p value
Age (years)	39.07±13.48	34±15.33	49.00±10.36	0.05
BMI (kg/m^2)	26.18±6.49	26.69±5.71	34.38±7.20	**0.006**
WC (cm)	91.14±16.59	94.63±15.61	109.88±9.53	**0.01**
SBP (mmHg)	116.96±17.91	126.36±20.98	142.22±30.32	**0.01**
DBP (mmHg)	75±12.32	90±10	94.44±13.33	**0.001**
TG (mg/dL)	145.21±96.54	138.63±70.58	191.88±100.3	0.36
HDL (mg/dL)	46.03±11.33	44±9.68	40.11±7.68	0.33
FBG (mg/dL)	94.92±9.79	95.81±13.20	119.11±39.44	**0.007**
HOMA	2.15±1.28	2.70±1.61	4.02±1.60	**0.005**

BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, Triglyceride; FBG, fasting blood glucose; HOMA, homeostasis model assesment.

Discussion

Psoriasis is a chronic, anti-inflammatory, multi-systemic disorder that progresses with flare ups and affects 1-3% of the population, and Th-1 immune cells play role in its pathogenesis (8). It has been proposed that chronic inflammation and pro-inflammatory cytokines in psoriasis lead to atherogenesis and peripheral insulin resistance and, hence, to development of MetS. Kaur et al. found that psoriasis develops with chronic inflammation and that plasma TNF-α, IL-6, IL-17, IL-22 and IFN-γ levels are higher in normal weight or obese psoriasis patients than in healthy control group (9).

Table 4. Correlation between PASI and metabolic risc factors

	PASI r-value	p-value
BMI (kg/m^2)	0.406	**0.004**
WC (cm)	0.540	**0.001**
SBP (mmHg)	0.387	**0.007**
DBP (mmHg)	0.409	**0.004**
TG (mg/dL)	0.491	**<0.001**
HDL (mg/dL)	0.157	0.287
FBG (mg/dL)	-0.200	0.173
HOMA	0.507	**<0.001**

PASI, psoriasis area and severity index score; BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, Triglyceride; FBG, fasting blood glucose; HOMA, homeostasis model assesment.

Inflammatory cytokines, whose releases increase in psoriasis patients, play role in etiopathogenesis of IR and MetS. Recansens et al. studied the association between chronic inflammation and metabolic syndrome and revealed associations between inflammation markers such as TNF α and IL-6 and IR, diabetes mellitus, hyperlipidemia and hypertension development (10). Similarly, Lobner et al. showed the role of subclinical inflammation in the pathogenesis of diabetes and atherosclerosis (11). Increased serum IL-6 concentrations in psoriasis have been shown to be related to IR (12).

There are limited studies indicating elevated IR and MetS frequency in psoriasis. In a study conducted by Uçak et al., IR was studied in non-obese psoriasis patients and was higher in patient group compared to healthy control group (13). In accordance with this study, we detected IR in 32 out of 48 patients (66%) and in 5 out of 45 healthy controls (11%). IR in patient group was significantly (p=0.01) higher than in control group. In addition, a significant positive correlation was detected between PASI score and HOMA-IR value (r=0.507, p<0.001).

Zindancı et al. found a MetS frequency of 53% in psoriasis patients and 39% in control group (1). In a similar study by Sommer et al., MetS frequency was 35% in psoriasis patients and 11% in control group (14). In both studies, MetS frequency was significantly higher in psoriasis patient group. Similarly, MetS frequency was significantly higher (p=0.007) in psoriasis patient group (43%) than in control group (17%) in the present study. Compared to healthy control group, psoriasis patient group had higher DBP and lower HDL-K levels. In addition, there were significant positive correlations between PASI, indicator of the disease severity, and TG, SBP, DBP, WC and FBG levels. Langan et al. similarly found higher incidence of MS in psoriasis patients compared to healthy control group and a significant positive correlation between MS frequency and PASI score (15). Similar significant correlations between indicators of insulin resistance and PASI score were detected by Boehncke et al. (16). In the present study, there were no significant differences in MetS rates among three groups. However, IR rates increased in the patients with severe psoriasis and higher PASI scores. PASI was an independent risk factor for development of IR (p=0.003). To our best knowledge, there is limited study about close relationship between PASI and IR in the literature.

Akhyani et al. compared lipid levels of 50 psoriasis patient with 50 healthy controls, and found

that TG levels were significantly higher and HDL-C levels were significantly lower in patient group (17). Unlike these studies, Farschian et al. found no significant differences in terms of lipid profiles between a group of 30 psoriasis patients and a group of 30 healthy controls (18). Slightly higher, but not significant, (p=0.05) triglyceride and significantly lower HDL-cholesterol levels were found in psoriasis patient group compared to control group in the present study.

Reich et al. reported that psoriasis is an inflammatory disease of IMID group and increase comorbidities; therefore, a timely and effective treatment prevents mortality and morbidity (19). In a study by Ormseth et al., HOMA-IR level was significantly higher in RA patient group compared to control group (20). Another study dealing with the frequency increases of MetS in rheumatoid arthritis patients found significantly higher incidence of MetS in rheumatoid arthritis patients than in healthy controls, which was attributed to systemic inflammation in those patients (21).

Conclusion

In the present study, MetS (p=0.007), and IR (p=0.01) incidences were higher in the patients with psoriasis compared to control group. In addition, there was a strong correlation between severe psoriasis and IR risk. Therefore, psoriasis needs to be considered as not only a skin disorder, but also a metabolic and cardiovascular disease with increased cardiovascular morbidity and mortality. Efforts to treat chronic inflammation in psoriasis patients might prevent development of MetS and IR.

Conflict of Interest: Non declared

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