The Association between the Components and Features of Metabolic Syndrome in Patients with Psoriasis and Psoriatic Arthritis

Ghasem Rahmatpour Rokni[1], Maryam Mobini[2*], Adele Bahar[2], Reza Ali Mohammadpour[3], Aref Hoseinian Amiri[4], Alireza Mohseni[5]

1. Department of Dermatology, Mazandaran University of Medical Sciences, Sari, Iran.
2. Department of Internal Medicine, Diabetes Research Center, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran
3. Department of Biostatistics, Diabetes Research Center, Faculty of Health, Mazandaran University of Medical Sciences, Sari, Iran
4. Department of Internal Medicine, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran
5. Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran

***Correspondence:**
Maryam Mobini, Rheumatologist, Associate Professor, Diabetes Research Center, Mazandaran University of Medical Sciences, Sari, Iran.
Tel: (98) 113 335 0672
Email: mmobini50@yahoo.com

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Abstract

Objective: Psoriasis (Pso) is associated with an increased risk of cardiovascular involvement. Metabolic syndrome (MetS) includes a group of classic cardiovascular risk factors with pro-inflammatory condition. The aim of the present study was to evaluate and compare the frequency of MetS in Pso patients with and without arthritis.

Materials and Methods: This cross-sectional study was conducted on 48 Pso patients with psoriatic arthritis (PsA), 48 Pso patients without arthritis and 48 age matched controls. The demographic, clinical and laboratory features of the subjects were compared. Disease activity, damage and functional activity were assessed using functional indices. The MetS was diagnosed according to the definitions of the 2005 National Cholesterol Education Program (NCEP/ATP III) and International Diabetes Federation (IDF). The three groups were compared in terms of MetS components frequency. Data analysis was performed in SPSS (version 19) at a significance level of <0.05.

Results: The mean ages of the Pso and PsA groups were 42.40±8.8 and 45.00±10.3 years, respectively. Based on the NCEP/ATP III and IDF criteria, 21 (43.8%) and 26 (54.2%) Pso patients, 28 (58.3%) and 29 (60.4%) PsA patients, and 12 (25%) and 11 (22.9%) controls were diagnosed with MetS, respectively ($P< 0.05$). Furthermore, high waist circumference and hypertension were more prevalent in the PsA patients ($P< 0.05$).

Conclusion: The frequency of MetS was found to be more prevalent in the Pso and PsA groups compared to the controls. The relationship between MetS and cardiovascular consequences highlights the importance of investigating the role of this condition in the management of patients, especially PsA cases.

Keywords: Metabolic syndrome, Psoriasis, Arthritis, Epidemiology, Hypertension

Introduction

Psoriasis (Pso) is a common chronic inflammatory disease with skin and joint manifestations, affecting approximately 2% of the population worldwide. The annual incidence rate of psoriatic arthritis (PsA) in patients with Pso is about 2.7 cases per 100 Pso patients. The variables associated with the development of

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PsA include severe Pso, low level of education, use of retinoid medications, psoriatic nail pitting and uveitis (1).

Metabolic syndrome (MetS) is characterized by a combination of various risk factors (central obesity, insulin resistance, hypertension and atherogenic dyslipidemia). This condition is associated with additional cardiovascular morbidity that is greater than the sum of the risks associated with each individual component (2). There are different criteria for the definition of MetS. The International Diabetes Foundation (IDF) in 2004 and the Third Report of the National Cholesterol Education Program (NCEP ATP III) in 2001 are two useful criteria in this regard.

Evidence initially indicated a relationship between Pso and MetS. However, later, differences in the associations of Pso and PsA with MetS were raised (3). In a study, the PsA patients were reported to have an increased prevalence of MetS with significantly greater carotid intima-media thickness (CIMT) measurements, compared to patients with Pso. Furthermore, the PsA patients with MetS had higher CIMT measurements, compared to PsA patients without MetS and Pso patients with or without MetS (4).

The risk of myocardial infarction is higher in patients with severe Pso and early onset Pso (5). On the other hand, MetS is associated with a lower probability of achieving minimal disease activity in the PsA patients prescribed with anti-tumor necrosis factor alpha (TNFα) (6). Therefore, the evaluation and management of MetS and its biochemical components could be helpful in assessing the activity of Pso and PsA and the future development of cardiovascular events.

Compared with rheumatoid arthritis, PsA is associated with higher rates of obesity, diabetes mellitus and hypertriglyceridemia (7). It is important to investigate the association of MetS with Pso and PsA for the management, treatment selection and evaluation of cardiovascular risk factors. Few studies have examined the prevalence of MetS and its components in Pso patients with the consideration of disease activity, features and treatments.

There are some studies investigating the prevalence of MetS in Pso. Nonetheless, limited number of research has compared this prevalence among the PsA and Pso patients and controls. Considering the genetic and environmental specifications in different populations, it is important to conduct studies on the prevalence of MetS in Pso patients in association with the extent of the disease, joint involvement, and treatment types. Due to the paucity of such information, this research was performed to study the frequency of MetS in Pso and PsA patients and compare it with controls.

Materials and Methods

The present study was approved by the Ethics and Research Committee of Mazandaran University of Medical Sciences, Mazandaran, Iran (code: IR.MAZUMS.REC.1395.2403). This cross-sectional study was conducted (i.e., March-September 2016) on 48 consecutive Pso patients without articular manifestations, 48 PsA patients (30-60 years old) with articular involvement, and 48 age- and sex-matched eligible controls attending at two referral centres over a period of 7 months.

The PsA patients were diagnosed based on the classification criteria for psoriatic arthritis (CASPAR) (8). The controls included the patients without any inflammatory rheumatic diseases, such as osteoarthritis, mechanical low back pain and fibromyalgia. The exclusion criteria were: inflammatory joint disorders, current consumption of glucocorticoids for another disease and history of myocardial infarction, stroke and renal insufficiency. The controls were selected from the patients with mechanical or non-specific pain who referred to rheumatologist. The sample size was calculated according to the studies of Bostoen et al. and Pehlvan et al. with a confidence level of 95% and power of 80% (3,9).

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Patients

All participants, including Pso and PsA patients and controls were assessed clinically and biochemically to determine the metabolic profiles, infliction with type II diabetes (with or without treatment), arterial blood pressure, lipid profile (i.e., high-density lipoprotein cholesterol (HDL-c) and triglyceride (TG)), fasting blood glucose, and waist circumference. In addition, the patients' characteristics, including demographic and clinical features, and disease duration were recorded. The severity of skin disease was determined by the PASI (10). The definition of disease status in PsA was accomplished using the Disease Activity Score 28 (DAS28) (11) and health assessment questionnaire (HAQ) (12).

MetS was defined using the IDF 2004 and NCEP ATP III 2001. The IDF criteria comprise central obesity (waist circumference ≥94 cm for men and ≥80 cm for women) in addition to two of the following conditions: elevated TGs (>150 mg⁄ dL) or specific treatment for this lipid abnormality, reduced HDL cholesterol (<40 mg ⁄dL for men; <50 mg⁄dL for women) or specific treatment for this lipid abnormality, elevated blood pressure (>130 mmHg systolic or >85 mmHg diastolic) or treatment of previously diagnosed hypertension, and elevated fasting plasma glucose (>100 mg⁄dL) or previously diagnosed type II diabetes (13). The NCEP criteria was considered waist circumference ≥102 cm for men and ≥88 cm for women, in addition to other defining criteria of MetS (14).

Smoking status was categorised as current smoker or non-smoker. There were also other variables considered in the study, including the age, gender, disease duration, and treatment modalities (i.e., current therapies including the use of prednisolone, sulfasalazine, methotrexate, and biologic agents).

Assessments

Waist circumference was measured at the end of a normal expiration, in a horizontal plane around the abdomen at the level of the iliac crest, parallel to the floor. Blood pressure was assessed twice at rest, and the average of the two blood pressures was used for the determination of the systolic and diastolic blood pressure. In order to avoid bias, the measurements were performed by trained medical students who were unaware of the participants' illness.

After an overnight fasting period, blood sample was drawn from the subjects. Accordingly, the glucose and lipid profiles (i.e., total cholesterol, HDL, LDL and TGs) were measured enzymatically. The patients with Pso and PsA were also assessed for demographic and clinical data, as well as therapeutics and disease extent.

In the PsA patients, physical examination included recording the number of tender and swollen joints. The PASI is a quantitative rating score for measuring the severity of psoriatic lesions based on area coverage and plaque appearance. The DAS28 is a calculator for the measurement of the disease activity in the peripheral joints. The HAQ questionnaire is targeted toward the assessment of the functional disability of patients. This tool consists of eight categories, including dressing and grooming, arising, eating, walking, hygiene, reach, grip, and activities. Each category is scored in a range of 0-3 (3 is the worst), and the total score is obtained by the calculation of the mean of all sections.

The prevalence of MetS and its components, as well as the demographic and clinical features of the patients and controls were recorded. Subsequently, the patients with and without MetS were compared in terms of the clinical and demographic features.

Statistical analysis

Statistical analysis was performed by one-way analysis of variance (ANOVA), between the three groups and Tukey post-test by using SPSS version 19 (Chicago, USA). Results were considered significant at $P < 0.05$.

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Results

In this study, 48 patients with Pso, 48 patients with PsA, and 48 age-matched individuals as controls were compared with respect to the demographic and clinical characteristic. The mean age of the Pso and PsA groups were 42.40±8.8 and 45.00±10.3 years, respectively. In addition, 56.2% of the Pso patients and 64.6% of the PsA subjects were female. Furthermore, eight and three patients in the Pso and PsA groups were current smoker, respectively. The demographic data, clinical characteristics, and MetS components in the Pso, PsA, and control groups are summarized in Tables 1 and 2.

Medication history in the Pso and PsA patients was respectively positive for prednisolone in 1 (2.1%) and 21 cases (43.8%) (*P*= 0.0001), sulfasalazine in 0 and 9 subjects (18.8%) (*P*= 0.002), methotraxate in 2 (4.2%) and 31 (64.6%) participants (*P*= 0.0001), and biologic agents (infliximab or etanercept) in 2 (4.2%) and 4 (8.3%) patients (*P*= 0.399). Regarding the family history, 14 (29.1%) and 20 (41.6%) patients in the Pso and PsA groups had myocardial infarction or cardiovascular accident in their history (*P*=0.0001). The mean erythrocyte sedimentation rate (ESR) and PASI score were 17.15±9.6 mm/h and 24.67±13.7 in the Pso group and 3.46±3.95 mm/h and 6.51±10.7 (*P*= 0.067) in the PsA group (*P*= 0.003), respectively. Furthermore, the PsA patients had the mean HAQ of 0.63±0.8.

Differences among psoriasis, psoriasis arthritis, and control groups

Based on the NCEP criteria, 21 (43.8%) and 28 (58.3%) subjects in the Pso and PsA groups were diagnosed with MetS, while the frequency of this condition was 12 (25%) cases in the control group (*P*= 0.004) (Table 3). According to the results, the PsA patients had a higher frequency of hypertension and waist circumference, compared to the other two groups (*P*< 0.05). Furthermore, the mean of HDL cholesterol was significantly higher in the controls in comparison to those of the PsA and Pso groups (*P*< 0.05).

Table 1. Studied variables in Psoriasis patients and controls

Variable	Pso	PsA	Controls	*P*-value
Age(years)	42.40±8.8	45.00±10.3	42.27±7.6	0.242
Female, N(%)	27(56.2%)	31(64.6%)	27(56.2%)	0.632
Disease duration(years)	4.36± 5.07	8.20± 7.6	-	0.005
Current smoker, N(%)	8(16.66%)	3(6.25%)	3(6.25%)	0.138
History of diabetes mellitus, N(%)	2(4.2%)	6(12.5%)	4(8.3%)	0.80
History of dyslipidaemia, N(%)	11(22.9%)	12(25%)	5(10.4%)	0.149
History of hypertension, N(%)	7(14.6%)	10(20.8%)	6(12.5%)	0.510
Body Mass Index(Kg/m2)	28.12±4.2	29.93±5.7	28.48±5.0	0.211
Systolic BP(mm Hg)	126.96±14.2	132.08±15.7	120.21±12.8	0.000
Diastolic BP(mm Hg)	79.08±11.7	81.13±13.5	73.00±8.5	0.003
Cholesterol(mg/dl)	193.40±46.0	183.92±27.5	190.52±29.0	0.402
LDL°(mg/dl)	118.54±36.0	114.10±21.9	109.50±30.7	0.342
HDL(mg/dl)**	44.08±8.8	47.60±9.3	53.1. ±11.9	0.000
TG(mg/dl)	130.73±59.1	135.48±52.4	141.52±64.2	0.667
FBS*(mg/dl)	102.63±31.6	97.25±13.6	103.42±26.3	0.425

LDL=low density lipoprotein, **HDL=high density lipoprotein, *FBS= fasting blood sugar, NCEP=National Cholesterol Education Program, IDF=International Diabetes Federation.

Table 2. The metabolic syndrome components in three studied groups

Variable	Pso	PsA	Controls	*P*-value
Metabolic syndrome (according to NCEPT III), N (%)	21(43.8%)	28(58.3%)	12(25%)	0.004
Metabolic syndrome (according to IDF), N (%)	26(54.2%)	29(60.4%)	11(22.9%)	0.000
High waist circumference (according to NCEPT III), N (%)	23(47.9%)	32(66.6%)	20(41.6%)	0.039
High waist circumference (according to IDF), N(%)	40(83.3%)	39(81.2%)	25(52/0%)	0.001
Hypertension, N(%)	20(41.6%)	26(54.1%)	10(20.8%)	0.003
Low HDL, N(%)	34(70.8%)	31(64.5%)	21(43.7%)	0.018
Hypertriglyceridemia, N(%)	14(29.1%)	19(39.5%)	15(31.2%)	0.519
Hyperglycaemia, N(%)	17(35.4%)	17(35.4%)	17(35.4%)	1.000

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Table 3. Demographic and clinical data in Pso and PsA patients with vs without metabolic syndrome, according to the NCEP III Criteria

Variable	Pso(n=48)			PsA(n=48)		
	MetS+(n=21)	Met-(n=27)	*P*-value	MetS +(n=28)	MetS-(n=20)	*P*-value
Age, mean – SD (years)	45.43±9.5	40.04±7.3	0.031	48.79± 9.9	39.70± 8.2	0.002
Sex:F(%)	14(53.8%)	13(59/0%)	0.161	18(62.0%)	13(68.4%)	0.645
Waist circumference (cm)	100.38± 9.4	91.33± 8.0	0.001	106/00± 11.9	93.10± 12.9	0.001
BMI(kg/m2)	30.07±3.1	26.61± 4.3	0.004	30.54± 4.2	28.85± 7.2	0.314
Smoking(years)	1(3.8%)	7(31.8%)	0.055	2(6%)	1(5.2%)	0.551
ESR(mm Hg)	19.90± 9.6	15.00±9.1	0.079	23.93±12.9	27/00±14.27	0.449
VAS(cm)	-	-	-	4.18± 2.7	3.70± 2.5	0.545
PASI score	3.16± 2.2	3.70± 4.9	0.645	8.45± 13.4	4.01± 3.7	0.167
DAS-28	-	-	-	3.58± 1.34	3.45± 1.4	0.741
HAQ score	-	-	-	0.58± 0.8	0.70± 0.7	0.597

VAS=Visual analogue scale, PASI=Psoriasis Area and Severity Index, DAS 28=Disease Activity Score 28, HAQ=health assessment questionnaire.

Differences between patients with and without metabolic syndrome

As the results revealed, 49 patients with Pso or PsA met the NCEP criteria for MetS. The patients with MetS were older than those without such condition (P<0.05). Nonetheless, there was no difference between the patients with and without MetS in terms of ESR, visual analogue scale score, PASI score, DAS28, or HAQ score (Table 3).

Discussion

This study investigated the frequency of MetS in the Pso patients and compared it with controls while considering the association of this condition with joint involvement, severity of psoriatic lesions (based on the PASI), PsA joint involvement status (according to HAQ, and DAS 28). The MetS had the prevalence rates of approximately 43.8% and 58.3% in the Pso and PsA patients, respectively, which was significantly higher than the age-matched controls. The patients with PsA had a higher frequency rate of high waist circumference and both systolic and diastolic hypertension. Moreover, the lower level of HDL was more prevalent in the Pso and PsA patients than that in the controls.

The prevalence of MetS in the PsA and Pso patients have been reported to be 25.5-44% and 35.3-44.9%, respectively (3,15-18). In a study conducted in Turkey, 35.5% of PsA patients and 14.6% of healthy controls were identified to suffer from MetS based on the NCEP criteria (P= 0.004). In the mentioned study, no correlation was observed between functional indices and cardiovascular risk factors that are among the MetS components (17).

In another study carried out in Lebanon, patients with Pso were two times more likely to have MetS, compared with controls (35.3% vs 18.0%, P< 0.001), and all components of MetS were more prevalent in Pso patients than in controls. In the mentioned study, PASI score was higher in patients with MetS than in those without such condition (15). In addition, in a study performed in Morocco, MetS was more prevalent in Pso patients than in controls (44.7 vs. 2.7%) (16).

In the present study, MetS had the prevalence rates of 58.3% vs. 43.8% and 60.4% vs. 54.2% according to the NCEPT III and IDF criteria, respectively. As indicated, this rate was higher based on the IDF criteria due to more central obesity, which can be ascribed to the higher use of medication, especially systemic corticosteroids in the PsA patients. The MetS in PsA is shown to be associated with more severe PsA (18).

In the current study, there was no significant difference between the patients with and without MetS regarding the severity of skin or articular manifestations, which might be due to the small sample size. Table 3 presents the results of the literature regarding the frequency of MetS in patients with Pso and PsA. The MetS components may be different in PsA and Pso cases.

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In a cross-sectional study conducted on 104 patients with Pso (n=49) and PsA (n=55), the Pso patients (44.9%) had a significantly higher prevalence of MetS according to the IDF criteria, compared with the PsA group (25.5%) (*P*= 0.037). This discrepancy can be mainly attributed to the significantly higher prevalence of abdominal obesity in Pso (83.7%) vs. PsA (65.5%) (*P*= 0.034). However, in the mentioned study, no statistically significant differences were observed between the groups in terms of other individual components of the MetS, such as TGs, HDL, hypertension, and plasma glucose (3).

Furthermore, in a study carried out in Iran, the levels of TG, LDL, and smoking were significantly higher in Pso patients, compared with those in the controls. However, the levels of HDL and cholesterol was not significantly different between the two groups. Furthermore, in the mentioned study, the patients with Pso had an increased prevalence of hypertension (19). Premature atherosclerosis is a concern in Pso. A probable mechanism that may explain both Pso and atherosclerosis pathogenesis is the enhancement of Th1 and Th17 that lead to chronic inflammation. In addition, progressive adiposity and resultant MetS are the beginning steps in Pso (20).

The MetS is a cluster of classic cardiovascular risk factors caused by an imbalance between pro- and anti-inflammatory adipokines. Tumour necrosis factor-α is a pro-inflammatory adipocytokine, produced by monocytes and macrophages with a central role in inflammatory responses. This cytokine induces adipocytes apoptosis, promotes insulin resistance, and stimulates lipolysis (21). The levels of adipokines and insulin resistance are significantly higher in PsA, compared to those in Pso (22).

There are some controversies over the usefulness and efficacy of different MetS definitions. We chose the NCEP and IDF criteria because these criteria were used in the previous studies investigating MetS among the Pso and PsA patients, considering such parameters as hyperglycaemia, hypertension, hyperlipidaemia, and hyperglycaemia in their classification (3,4,13,14). There are various factors that seem to affect the prevalence of MetS. Diet, physical activity, age, medication, and genetics may influence MetS presentation.

To the best of our knowledge, there are few studies investigating the frequency of MetS in patients with Pso and PsA in comparison to that in the healthy people. There are some limitations in this study. In the present study, the controls had the MetS prevalence rates of 25% and 22.9% based on the NCEPT III and IDF criteria, respectively. These rates were higher than those previously reported in Iran. The prevalence rates of MetS in Iran were 10.88%, 13.03%, and 12.14% in the males, females, and in total, respectively (23). This might be due to the selection of controls, who suffered from mechanical pain and were more obese than normal population. Overweight can be associated with osteoarthritic pain and therefore induce patients to seek medical attention, osteoarthritis patients can have reduced mobility due to pain, depressive disorders are very often associated with fibromyalgia and may influence both physical activity and food intake.

Diet and physical activity werenot considered as variables in the examined groups, that may affect the outcome of the study. There was no significant difference between the Pso or PsA patients with and without MetS in terms of the clinical features of skin or joint disease. This may be due to low sample size. However, as long as more studies are performed with a larger sample size, the evaluation of MetS in patients with Pso and PsA seems logical.

Conclusions

As the findings of the present study indicated, the frequency of MetS was not significantly different between the patients with Pso and those with PsA. Nevertheless, this condition had a higher prevalence among the Pso and PsA patients than in the controls. About half of the patients with PsA and Pso patients fulfilled

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the MetS criteria. Given the relationship of MetS with cardiovascular consequences, this condition should be considered in the management of patients, especially those with PsA.

importance of antioxidant capacity and oxidant status as an effective assessment in diabetic patients. Besides, salivary measurement of redox status that has been a wide area of interest can be an effective tool in diabetic parameters assessment.

Conflict of Interest

The authors declare no conflict of interest with respect to the research, authorship or publication of this article.

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