Cardiovascular and Metabolic Comorbidities in Patients with Plaque-Type Psoriasis Never Treated with Systemic Antipsoriatic Drugs: a Case-Control Study

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Abstract

Previous studies have shown a higher prevalence of cardiometabolic diseases among patients with psoriasis compared to non-psoriatics. However, little attention has been paid to the effects of systemic antipsoriatic drugs. The aim of this study was to investigate the association between psoriasis and these comorbidities, comparing untreated patients with psoriasis and population-based control non-psoriatic patients.

A hospital-based case-control study included 122 patients with plaque-type psoriasis and 122 age- and gender-matched controls. Patients who ever received systemic antipsoriatic drugs were excluded.

There were no significant differences between psoriatic patients and controls regarding the prevalence of hypertension (p=0.311), coronary heart disease (p=0.480), diabetes (p=0.641), myocardial infarction (p=0.71), stroke (2.4% vs. 2.4%, p=1.00) and metabolic syndrome (p=0.764). The prevalence of hypertriglyceridemia in patients with psoriasis and controls was 41.8% and 28.7%, respectively (OR 1.78, 95% CI 1.04-3.04, p=0.032). Furthermore, significant differences were observed in mean triglyceride levels (p=0.013). Smoking was significantly more often reported in psoriatic patients compared to controls. Patients with psoriasis also had a higher mean BMI (26.24, SD 4.42) compared with controls (24.73, SD 3.86), p=0.005. Psoriasis showed a statistically significant association with BMI obesity classification [$\chi2(4)$=11.560, p=0.02].

The prevalence of cardiovascular and metabolic comorbidities was not significantly higher in patients with plaque-type psoriasis who were never treated with systemic antipsoriatic drugs, compared to population-based non-psoriatic controls. Our data suggest that systemic antipsoriatic drugs may play an important role in the development of these comorbidities. However, this study confirms that untreated psoriasis patients have three major modifiable increased cardiovascular risk factors, such as smoking, obesity and hypertriglyceridemia.

Key words

Psoriasis is a chronic, relapsing, inflammatory skin disease with an estimated prevalence worldwide ranging from 0.91% (USA) to 8.5% (Norway) (1). The most common type of psoriasis is plaque psoriasis, accounting for around 80% of cases. Approximately 20% of affected individuals have moderate-to-severe psoriasis (2). The traditional belief about psoriasis is that it is a skin disease without visceral involvement. However, by the end of the 20th century, the psoriasis model had evolved to become a disorder of the skin and joints. Nevertheless, this concept has been challenged in recent years. Currently, psoriasis is considered to be a Th1/Th17-mediated inflammatory disease, characterized by chronically elevated levels of proinflammatory cytokines (3). Recently it has been classified as an immune-mediated inflammatory disease (IMID) with high risk of systemic comorbidities (4).

Comorbidity in psoriasis has become one of the most engrossing topics in dermatology in the past five years. A mere search of the terms "psoriasis and comorbidities" in Pubmed shows more than 300 articles published over the last decade.

In 2011, the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) identified comorbidities as one of three priority research areas in psoriasis and psoriatic arthritis (5). Traditionally, comorbidity has been defined as the presence of two or more diseases or conditions in the same individual at the same time (6). Klein et al. argue that comorbidity may occur for a variety of reasons. There is a possibility that comorbity occurs due to the following: conjuction of independent risk factors; shared or overlapping risk factors; one disorder causes another; variable expression of one disorder; independent coincidence (7).

There is a growing evidence that psoriasis is associated with a number of systemic comorbidities, including psoriatic arthritis (PsA), obesity, hypertension, diabetes mellitus, hyperlipidemia, metabolic syndrome, cardiovascular disease (CVD), Crohn's disease, lymphoma, malignancies and multiple sclerosis, as well as mental health comorbidity including anxiety, depression, smoking, alcoholism, and eating disorder (8-15). However, the exact mechanisms standing behind these associations are still uncertain.

The relationship between psoriasis and CVD is probably associated with the underlying chronic inflammation that exists in psoriasis, as a consequence of increased levels of proinflammatory cytokines (16). The elevated tumor necrosis factor-alpha (TNF-α) levels have been found in the skin lesions and sera of patients with psoriasis and increased serum levels have been shown to correlate with disease activity (17). The relationship between psoriasis and associated diseases is complex, making it difficult to identify direct relationships (Figure 1). Life style factors, impaired health-related quality of life, depression, and therapeutic interventions, may be confounding. Also, several biases, such as detection bias, may affect observational study results (18).

There is little information available on the effects of drugs on comorbidities. Drugs used in the treatment of psoriasis, such as acitretin, cyclosporine, and methotrexate, may adversely affect independent
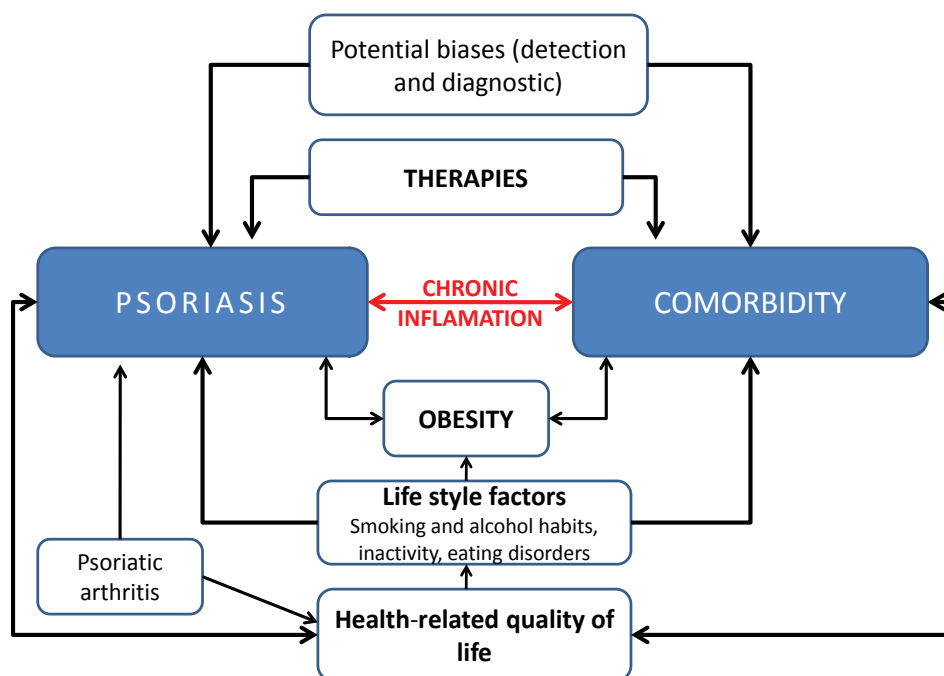

Figure 1. The complex relationship between psoriasis and comorbidity [Adapted from Wakkee et al, (18)]

cardiovascular risk factors such as blood pressure and lipid levels. Methotrexate increases homocysteine levels (19), whereas cyclosporine and acitretin induce hyperlipidemia (20). Thus, high prevalence of some comorbidities in patients with psoriasis may be, at least partly, due to systemic antipsoriatic drugs. Wakkee at al. argue that effects of systemic drugs on the cardiovascular risk represent a sum of anti-inflammatory effects and atherogenic side effects (18).

The objective of this study was to determine the prevalence of comorbidities in patients with psoriasis never treated with any systemic antipsoriatic drugs.

Material

Patients
One hundred and twenty two patients with plaque-type psoriasis and 122 age and sex-matched controls participated in the study. The group of psoriatic patients included 44 inpatients (36.1%) and 78 outpatients (63.9%), who were consecutively recruited from the University Clinic of Dermatology, at Skopje Medical Faculty from September 2011 to April 2012. The inclusion criteria were age > 18 years and clinical diagnosis of plaque-type psoriasis lasting at least six months. The study included only systemically untreated patients. Thus, patients who received systemic antipsoriatic drugs, (eg. acitretin, cyclosporine, methotrexate, ultraviolet therapy, corticosteroids) or biologics, were excluded. In addition, patients with other types of psoriasis (guttate, erythrodermic and pustular psoriasis), history of SLE, RA and other autoimmune disorders were also excluded. The control group was selected from patients from the same geographic region, who were consecutively admitted/visited the Public Health Center "13 Noemvri", during the same period. Each control was matched to a case according to age (+/-1 year) and sex. Controls visited general practitioners for: routine control (59 patients), viral infection (15 patients), bacterial infection (11 patients) and hypertension (10 patients), dermatologic condition other than psoriasis (8 patients), cardiomyopathy (8 patients), diabetes (4 patients), urology problems (3 patients), gastroenteritis (2 patients), and trauma (2 patients).

The study was conducted through a structured face-to-face interview and examination, and it was approved by the Ethics Committee of the Medical Faculty. All participants signed an informed consent.

Methods

Severity of psoriasis
The severity of psoriasis was assessed using the Psoriasis Area and Severity Index (PASI) and Body Surface Area (BSA). A PASI score ≤10 defines psoriasis as mild, whereas scores above 10 classify it as moderate or severe. Patients were classified in regard to the age of onset of psoriasis; type 1: onset before the age of 40 years, and type 2: onset after the age of 40 years (22). The diagnosis of psoriatic arthritis (PsA) was made using Moll and Wright criteria (23).

Comorbidity data
A list of clinically-relevant comorbidities was derived from diagnoses included in the Charlson Comorbidity Index (21). Chronic conditions were classified using diagnoses at discharge or drug prescriptions, for example: diabetes - if use of antidiabetic drugs was registered; hypertension - if BP ≥140/90 mmHg was found, and/or current use of an antihypertensive.

Metabolic syndrome
Metabolic syndrome was diagnosed by the presence of three or more of the following criteria of the National Cholesterol Education Programme's Adult Treatment Panel III (ATP III): waist circumference > 102 cm in men and > 88 cm in women; hypertriglyceridemia > 1.7 mmol/l (150 mg/dl) or ongoing drug treatment for elevated triglycerides; high density lipoprotein (HDL) cholesterol < 1.0 mmol/l (40 mg/dl) in men and < 1.3 mmol/dl (50 mg/dl) in women or ongoing antilipidemic treatment; blood pressure > 130/85 mmHg, or ongoing antihypertensive treatment; fasting plasma glucose > 6.1 mmol/l (100 mg/dl) or ongoing antidiabetic treatment (24).

Body mass index
The body mass index (BMI) was calculated as weight in kilograms divided by height in meters^2 and patients were classified as underweight (<18.5 kg/m^2), normal (18.5-24.9 kg/m^2), overweight (25–29.9 kg/m^2), and obese (≥30.0 kg/m^2).

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Blood pressure

Blood pressure (BP) was measured in sitting position using a standard mercury sphygmomanometer.

Smoking

Smoking habit was classified into two categories of never smokers and ex-smokers/current smokers.

Alcohol consumption

Alcohol consumption was classified into two categories of none/low/moderate: up to three alcoholic drinks per week, and regular/heavy: ≥ 4 alcoholic drinks per week.

Statistical analysis

Categorical variables were expressed as frequencies and percentages, and numerical variables as means, range and standard deviations (SD). Odds ratios (OR) were estimated using logistic regression models with conditional 95% confidence intervals (CI). The proportion of comorbidities in psoriatic patients was compared with their matched non-psoriatic controls. Comparisons were made by using the Student's t-test for parametric continuous variables, Mann-Whitney U test for nonparametric continuous variables and Chi-square test for qualitative variables. The limit for statistical significance was set at $p \leq 0.05$. The SPSS version 10 statistical software (SPSS Inc., Chicago, Illinois, USA) was used for statistical analysis.

Results

Baseline characteristics of the study group are shown in Table 1. One hundred and twenty-two patients with psoriasis (52 male and 70 female, the mean age 51.52 years, SD 15.56, range 19 -80 years), and 122 age- and gender-matched controls (52 males and 70 females, the mean age 51.98; years, SD 15.72, range 19 - 79 years, participated in the study. Figure 2 shows their age and sex distribution. A close match between the groups can be seen. No statistically significant difference was noted in the mean age and sex ratio between the groups (p=0.82 and p=1.00, respectively).

Disease characteristics

Type 1 psoriasis was found in 78 patients (63.9%). The mean age of psoriasis onset was 33.34 years (SD 17.14, range 1 - 76). The mean duration of psoriasis was 17.9 years (SD14.21, range 1 – 65 years). Psoriatic arthritis was present in 16 patients (13.1%). The mean age of PsA onset was 39.2 years (range 27 - 59). The mean interval between the onset of psoriasis and onset of PsA was 6.67 years (SD 6.6). In 2 patients, arthritis developed before psoriasis was diagnosed. A positive family history of psoriasis was reported by 21 patients (17.21%), with a 92% incidence in first-degree relatives.

PASI scores ranged from 2.4 to 62,0 (mean 14.75, SD 12.78) and 56 patients (45.9%) had moderate to severe psoriasis (PASI>10). BSA ranged
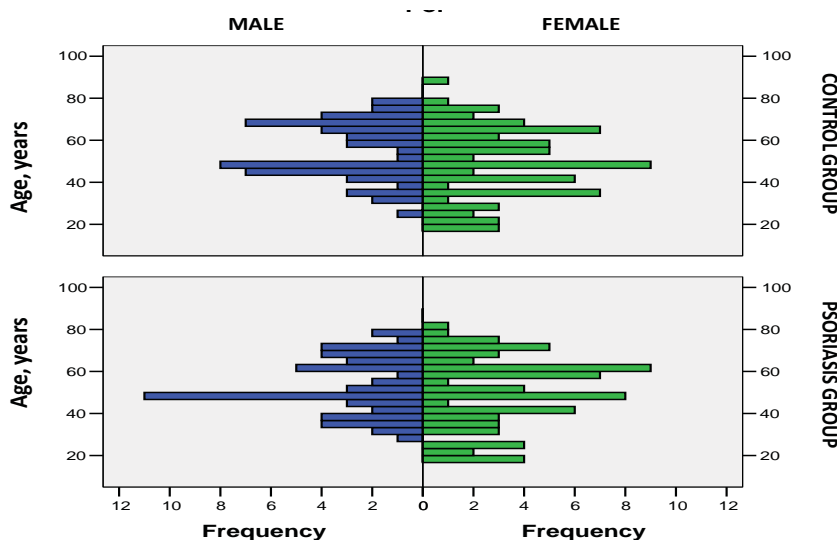

Figure 2. Age and sex distribution of patients with plaque psoriasis and controls

Histogram

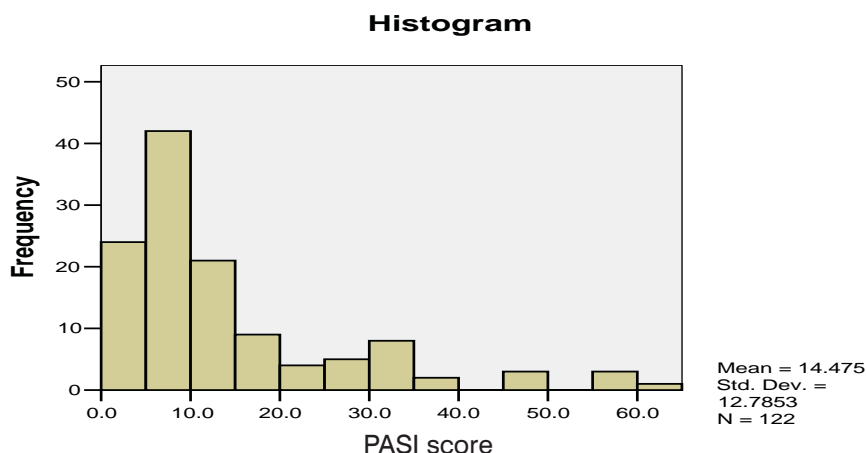Mean = 14.475
Std. Dev. = 12.7853
N = 122

Figure 3. Distribution of patients with plaque psoriasis according to PASI scores

from 2% to 85% (mean 15.23, SD 13.09), while 55 (45.1%) patients had > 10% of body surface area involved. Figure 3 shows distribution of patients according to the PASI score.

The prevalence of cardiovascular and metabolic comorbid conditions

There were no significant differences in the prevalence of hypertension (29.5% vs. 23.7%, p=0.311), coronary heart disease (13.9% vs. 17.2%, p=0.480), diabetes (9.0% vs. 7.3%, p=0.641), myocardial infarction (3.2% vs. 2.4%, p=0.71), stroke (2.4% vs. 2.4%, p=1.00) and metabolic syndrome (24.6% vs. 22.9%, p=0.764), between cases and controls (Table 2), (Figure 4).

The prevalence of hypertriglyceridemia in patients with psoriasis and controls was 41.8% and 28.7%, respectively (OR 1.78, 95% CI 1.04-3.04, p=0.032) (Table 2), (Figure 4). Furthermore, a significant difference was found in mean triglyceride levels of patients and controls (170.19±67.84 mg/dL vs. 149.27±81.15 mg/dL, p=0.013).

Lifestyle factors

Smoking was significantly more prevalent in psoriasis patients compared to controls (58.1% vs. 44.2%, OR 1.813, 95% CI, 1.091-3.013, p=0.021) (Table 1).

Regular and heavy alcohol consumption was infrequent and of similar prevalence in psoriasis cases and controls: 20.5% vs. 17.2%, p=0.513 (Table 1).

Patients with psoriasis had a higher mean BMI (26.24, SD 4.42) compared to controls (24.73, SD

3.86), p=0.005 (Table 1), (Figure 5). Furthermore, psoriasis showed a statistically significant association with BMI obesity classification [$\chi^2(4)$=11.560, p=0.02].

Discussion

Psoriasis and cardiovascular risk

The relationship between psoriasis and increased risk of CVD remains controversial (25). In general, most of the previous studies suggest that people with psoriasis are at increased risk of CVD (8-10, 16, 20, 26-28). This was not confirmed in a large prospective cohort study conducted by Stern and Lange (29). Furthermore, two recent studies of general population (30, 31) demonstrated that the relationship between psoriasis and cardiovascular risk (CVR) is insignificant, and that traditional cardiovascular risk factors are significantly associated with cardiovascular risk in psoriasis (30, 31). Moreover, two population-based database studies that included pharmaceutical data did not confirm the association between psoriasis and treatment of CVD (32, 33). Mallbris et al. found a 50% greater risk of death from CVD among psoriatic inpatients, compared with the general population. In contrast, the overall risk of cardiovascular death was slightly decreased among outpatients with psoriasis (27).

A recent meta-analysis of cardiovascular risk confirms that psoriasis is related with an increased risk of cardiovascular mortality (28). However, it remains unclear whether cardiovascular risk in

Table 1. Baseline characteristics of the study group

Baseline characteristics	Psoriatics (n=122)	Controls (n=122)	OR (95% CI)	p
Mean age (SD), years	51.52 (15.56)	51.98 (15.72)	NA	0.82
Sex M/F	52/70	52/70	NA	1
Smoking habit				
Current +ex-smoker, n (%)	51+21=72 (58.1)	42+12=54(44.2)	1.81 (1.09-3.01)	0.021
Never smoker	50 (41.8)	68 (55.7)		
Alcohol consumption, n (%)				
Moderate	97 (79.5)	101 (82.7)		
Regular/heavy	25 (20.5)	21 (17.2)	1.24 (0.65-2.35)	0.513
BMI obesity classification n (%)				
Underweight	4 (3.3)	5 (4.1)		
Normal	49 (40.2)	74 (60.7)		
Overweight	44 (36.1)	29 (23.8)	NA	0.02
Obese	20 (16.4)	12 (9.8)		
Severe obesity	5 (4.1)	2 (1.6)		
BMI, mean (SD), kg	26.24 (4.42)	24.73 (3.86)	NA	0.005

SD - standard deviation; OR - odds ratio; NA - not applicable; BMI - body mass index

psoriasis is increased beyond that conferred by traditional cardiovascular risk factors. Samarasekera et al. evaluated 15 cohorts and meta-analyses of the magnitude of CVD risk for the primary outcomes of CVD mortality, stroke and myocardial infarction and identified increased CVD risk only in people with severe psoriasis (defined as requiring systemic therapy or hospital admission). They detected that majority of studies failed to adequately adjust for key traditional risk factors (25).

In this matched case-control study, we found no differences between subjects with and without psoriasis, in regard to cardiovascular disease and major cardiovascular risk (CVR) factors.

Our study showed no significant difference in the prevalence of coronary heart disease (CHD) (p=0.48), hypertension (p=0.31), myocardial infarction (p=0.71), stroke (p=1) and metabolic syndrome (p=0.76), between patients with psoriasis and controls.

Psoriasis and diabetes
In recent years it has been recognized that patients with psoriasis carry an increased risk of type 2 diabetes. Two meta-analyses have examined diabetes in psoriatic patients. Armstrong et al. conducted a meta-analysis of 27 observational studies and found that psoriasis is associated with a relative risk of 1.27 (95% CI 1.16
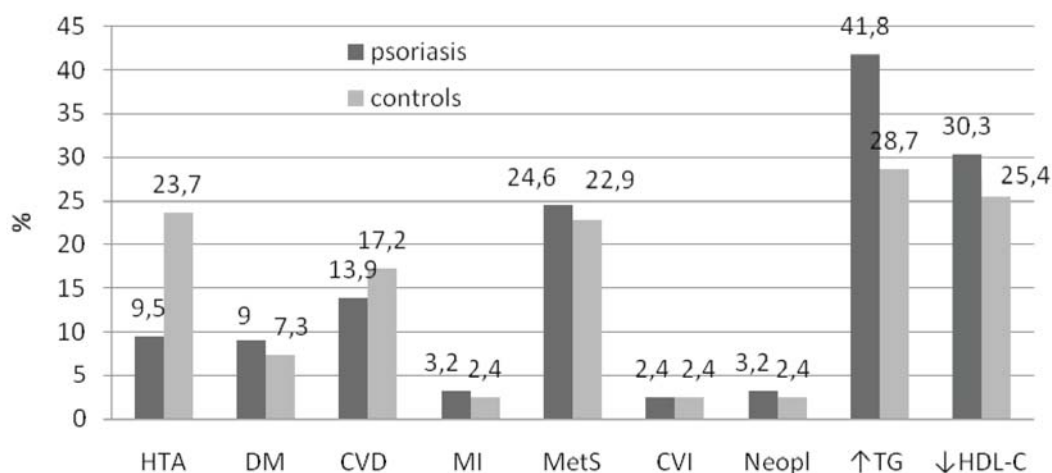
Table 2. Prevalence of cardiometabolic comorbidity conditions in psoriatics and controls

	Psoriatics N=122	Controls N=122	OR	95% CI	p
Hypertension	36 (29.5)	29 (23.7)	1.342	0.759-2.374	p=0.311 χ^2=1.029
Diabetes	11 (9.0)	9 (7.3)	1.244	0.496-3.119	p=0.641 χ^2=0.218
Coronary heart disease	17 (13.9)	21 (17.2)	0.779	0.388-1.561	p=0.480 χ^2=0.499
Myocardial infarction	4 (3.2)	3 (2.4)	1.345	0.295-6.138	p=0.71 χ^2= 0.147
Metabolic syndrome, n (%)	30 (24.6)	28 (22.9)	1.09	0.61-1.97	0.764 χ^2=0.090
Stroke	3 (2.4)	3 (2.4)	1.0	0.198-5.055	p=1 χ^2 = 0.0
Dyslipidemia, n (%)					
↑TG	51(41.8)	35 (28.7)	1.78	1.04-3.04	0.032
↓HDL-C	37 (30.3)	31 (25.4)	1.27	0.73-2.24	0.392

TG - Triglyceridemia > 1.7 mmol/L; HDL-C - high-density lipoprotein cholesterol < 1.0 mmol/L (Male) or < 1.3 mmol/L (Female)

- 1.40) for developing diabetes (34). Findings from a meta-analysis conducted by Cheng et al. suggested that individuals with psoriasis may have a slightly increased risk of diabetes (OR 1.42, 95% CI 1.40 - 1.45) (35). A cross-sectional study of Shapiro et al. performed using a database of a large health provider in Israel, showed that the incidence of diabetes was significantly higher in psoriasis patients in comparison with the control group (OR 1.27, 95% CI 1.1 - 1.48) (36). Interestingly, authors found an association between diabetes and multiple use of very potent topical steroids (P < 0.05) or systemic medications for psoriasis (methotrexate, cyclosporine or acitretin) (P < 0.001) (36). Brauchli et al. conducted a follow-up study with a nested case-control analysis within the UK-based General Practice Research Database. They found that the risk of incident DM increased with psoriasis duration and severity (37). It is well known that chronic systemic inflammation of psoriasis induces endothelial dysfunction, altered glucose metabolism, and insulin resistance which all together play a significant role in the development of obesity, diabetes mellitus, dyslipidemia, and cardiovascular disease (38). It is also possible that patients with psoriasis use topical corticosteroids for long periods of time, which are systemically absorbed and contribute to the development of diabetes (37, 39). However, several studies, failed to establish such a relationship

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HTA - hypertension; DM - diabetes mellitus; CVD - cardiovascular diseases; MI - myocardial infarction; MetS - metabolic syndrome, CVI - cerebrovascular insult; TG - Triglyceridemia > 1.7 mmol/L; HDL-C - high-density lipoprotein cholesterol < 1.0 mmol/L (Male) or < 1.3 mmol/L (Female)

Figure 4. Prevalence of comorbid conditions in patients with plaque psoriasis and controls

(40). In this case-control study, we found no differences between subjects with and without psoriasis in regard to diabetes (9.0% vs. 7.3%, p=0.641).

There are several possible explanations for the diversity of findings. Some studies are associated with high risk of selection and detection bias, due to the use of hospital records/administrative databases, and hospital/registry controls. Differences in various exposure factors, such as geographic-regional and ethnic, in genetic susceptibility and nutritional habits among different populations may affect the prevalence of cardiovascular diseases and diabetes. Thus, the prevalence of diabetes in the Macedonian population is considered to be about 7.7%, which is similar to our findings (41).

Finally, selection of untreated patients with psoriasis eliminates the influence of systemic antipsoriatic drugs on cardiovascular risks. To our knowledge, this is the first case-control study on comorbidities in untreated patients with psoriasis. Only few studies considered drugs as a factor contributing to the development of CVD (42). Gissondi et al. (42) and Nisa and al. (43) did not include patients receiving any systemic antipsoriatic treatment for at least one month before enrolment. Several other studies analyzed patients with new diagnosis of psoriasis (27, 44). On the contrary, some studies used systemic treatment as a measure of disease severity (45, 46). Traditional systemic therapies for psoriasis may aggravate cardiovascular risk factors (19, 20). Thus, high prevalence of CVD may be in part due to systemic antipsoriatic therapy. It is rather difficult to assess the independent contribution of systemic antipsoriatic drugs on the development of CVR in patients with psoriasis, since a certain number of concurrent factors, such as lifestyle factors, as well as other systemic drugs such as NSAIL, antidepressants and diuretics, needs to be taken into consideration, as these drugs are widely prescribed for patients with psoriasis (47).

Psoriasis and traditional cardiovascular risk factors
Our study confirms that psoriasis patients have three lifestyle/classic risk factors for CVD more frequently compared to controls: smoking, obesity and hypertriglyceridemia. The prevalence of smoking was higher in patients with psoriasis (41.8%) than in the control group (34.4%), and higher than in general population in Macedonia (35%) (48). Psoriasis showed a statistically significant association with BMI and obesity classification. This finding is in agreement with most of the previously published studies.

The major weakness of our study is its sample size, while its strength is its matched case-control design which controlled fundamental confounders of age and gender. Besides, both case and control subjects were selected from the same source population. All data
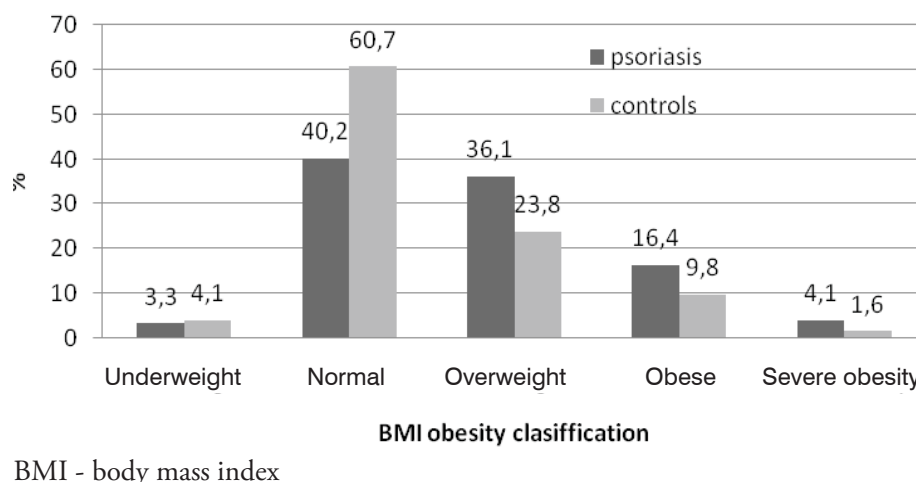
BMI - body mass index

Figure 5. BMI obesity classification among patients with plaque psoriasis and control group

were collected through interviews and measurements of disease activity were performed by an experienced dermatologist.

Conclusion

In conclusion, our data suggest that systemic antipsoriatic drugs may exert an important influence on the prevalence of cardiometabolic comobidity in patients with psoriasis. Furthermore, our study confirms that untreated psoriatic patients have three major increased lifestyle cardiovascular risk factors: smoking, obesity and hypertrigliceridemia. Further research will explore the effects of systemic antipsoriatic drugs on these comorbid conditions in psoriasis.

References

1. Parisi R, Symmons D, Griffiths CE, Ashcroft DM. Global epidemiology of psoriasis: a systematic review of incidence and prevalence. J Invest Dermatol 2013;133(2):377-85.
2. Nijsten T, Looman CW, Stern RS. Clinical severity of psoriasis in last 20 years of PUVA study. Arch Dermatol 2007;143(9):1113-21.
3. Ghoreschi K, Weigert C, Röcken M. Immunopathogenesis and role of T cells in psoriasis. Clin Dermatol 2007;25:574-80.
4. Davidovici BB, Sattar N, Prinz J, Puig L, Emery P, Barker JN, et al. Psoriasis and systemic inflammatory diseases: potential mechanistic links between skin disease and co-morbid conditions. J Invest Dermatol 2010;130(7):1785-96.
5. Armstrong AW, Callis Duffin K, Garg A, Gelfand JM, Gottlieb AB, Krueger GG, et al. Exploring priority research

areas in psoriasis and psoriatic arthritis from dermatologists' perspective: a report from the GRAPPA 2011: annual meeting. J Rheumatol 2012;39(11):2204-10.
6. Feinstein AR. The pretherapeutic classification of comorbidity in chronic disease. J Chronic Dis 1970;23:455-568.
7. Klein DN, Riso LP. Psychiatric disorders: problems of boundaries and comorbidity. In: Costello CG, editor. Basic issues in psychopathology. New York: Guilford; 1993. p. 19–66.
8. Pearce DJ, Morrison AE, Higgins KB, Crane MM, Balkrishnan R, Fleischer AB Jr, et al. The comorbid state of psoriasis patients in a university dermatology practice. J Dermatol Treat 2005;16(5-6):319-23.
9. Gelfand JM, Neimann AL, Shin DB, Wang X, Margolis DJ, Troxel AB. Risk of myocardial infarction in patients with psoriasis. JAMA 2006;296(14):1735-41.
10. Kaye JA, Li L, Jick SS. Incidence of risk factors for myocardial infarction and other vascular diseases in patients with psoriasis. Br J Dermatol 2008;159(4):895-902.
11. Zachariae R, Zachariae H, Blomqvist K, Davidsson S, Molin L, Mørk C, et al. Self-reported stress reactivity and psoriasis-related stress of Nordic psoriasis sufferers. J Eur Acad Dermatol Venereol 2004;18(1):27-36.
12. Bhole VM, Choi HK, Burns LC, Vera Kellet C, Lacaille DV, Gladman DD, et al. Differences in body mass index among individuals with PsA, psoriasis, RA and the general population. Rheumatology (Oxford) 2012;51(3):552-6.
13. Cheng J, Kuai D, Zhang L, Yang X, Qiu B. Psoriasis increased the risk of diabetes: a meta-analysis. Arch Dermatol Res 2012;304(2):119-25.
14. Dreiher J, Weitzman D, Cohen AD. Psoriasis and osteoporosis: a sex-specific association? J Invest Dermatol 2009;129(7):1643-9.
15. Gelfand JM, Shin DB, Neimann AL, Wang X, Margolis DJ, Troxel AB. The risk of lymphoma in patients with psoriasis. J Invest Dermatol 2006;126(10):2194-201.
16. Gottlieb AB, Chao C, Dann F. Psoriasis comorbidities. J

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Dermatol Treat. 2008;19(1):5-21.

17. Mussi A, Bonifati C, Carducci M, D`Agosto G, Pimpinelli D, D`Urso D, et al. Serum TNF-alpha levels correlate with disease severity and are reduced by effective therapy in plaque-type psoriasis. J Biol Regul Homeost Agents 1997;11(3):115-8.

18. Wakkee M, Thio HB, Prens EP, Sijbrands EJ, Neumann HA. Unfavorable cardiovascular risk profiles in untreated and treated psoriasis patients. Atherosclerosis 2007;190(1):1-9.

19. Naldi L, Griffiths CE. Traditional therapies in the management of moderate to severe chronic plaque psoriasis: an assessment of the benefits and risks. Br J Dermatol 2005;52:597–615.

20. Gisondi P, Cazzaniga S, Chimenti S, Giannetti A, Maccarone M, Picardo M, et al. Metabolic abnormalities associated with initiation of systemic treatment for psoriasis: evidence from the Italian Psocare Registry. J Eur Acad Dermatol Venereol 2013;27(1):e30-41.

21. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373–83.

22. Henseler T, Christophers E. Psoriasis of early and late onset: characterization of two types of psoriasis vulgaris. J Am Acad Dermatol 1985;13:450–6.

23. Moll JM, Wright V. Psoriatic arthritis. Semin Arthritis Rheum 1973;3(1):55-78.

24. Executive summary of the third report of the National Cholesterol Education Program (NCEP). Expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). JAMA 2001;285(19):2486-97.

25. Samarasekera E, Neilson JM, Warren RB, Parnham J, Smith CH. Incidence of cardiovascular disease in people with psoriasis: a systematic review and meta-analysis. J Invest Dermatol In press, doi: 10.1038/jid.2013.149.

26. Gelfand JM, Neimann AL, Shin DB, Wang X, Margolis DJ, Troxel AB. Risk of myocardial infarction in patients with psoriasis. JAMA 2006;296(14):1735-41.

27. Mallbris L, Akre O, Granath F, Yin L, Lindelof B, Ekbom A, et al. Increased risk for cardiovascular mortality in psoriasis inpatients but not in outpatients. Eur J Epidemiol 2004;19(3):225-30.

28. Armstrong EJ, Harskamp CT, Armstrong AW. Psoriasis and major adverse cardiovascular events: a systematic review and meta-analysis of observational studies. J Am Heart Assoc 2013;2(2):PMID 23447749.

29. Stern RS, Lange R. Cardiovascular disease, cancer, and cause of death in patients with psoriasis: 10 years prospective experience in a cohort of 1,380 patients. J Invest Dermatol 1988;91(3):197-201.

30. Jensen P, Thyssen JP, Zachariae C, Hansen PR, Linneberg A, Skov L. Cardiovascular risk factors in subjects with psoriasis: a cross-sectional general population study. Int J Dermatol 2013;52(6):681-3.

31. Maradit-Kremers H, Dierkhising RA, Crowson CS, Icen M, Ernste FC, McEvoy MT. Risk and predictors of cardiovascular disease in psoriasis: a population-based study. Int J Dermatol 2013;52(1):32-40.

32. Brauchli YB, Jick SS, Curtin F, Meier CR. Association between beta-blockers, other antihypertensive drugs and

psoriasis: population-based case-control study. Br J Dermatol 2008;158(6):1299-307.

33. Wakkee M, van der Linden M, Nijsten T. Psoriasis appears not to be directly related with using cardiovascular and antidiabetic drugs. J Invest Dermatol 2008;128:2548.

34. Armstrong AW, Harskamp CT, Armstrong EJ. Psoriasis and the risk of diabetes mellitus: a systematic review and meta-analysis. JAMA Dermatol. 2013;149(1):84-91.

35. Cheng J, Kuai D, Zhang L, Yang X, Qiu B. Psoriasis increased the risk of diabetes: a meta-analysis. Arch Dermatol Res 2012;304(2):119-25.

36. Shapiro J, Cohen AD, David M, Hodak E, Chodik G, Viner A, et al. The association between psoriasis, diabetes mellitus, and atherosclerosis in Israel: a case-control study. J Am Acad Dermatol 2007;56(4):629-34.

37. Brauchli YB, Jick SS, Meier CR. Psoriasis and the risk of incident diabetes mellitus: a population-based study. Br J Dermatol 2008;159(6):1331-7.

38. Cohen AD, Dreiher J, Shapiro Y, Vidavsky L, Vardy DA, Davidovici B, et al. Psoriasis and diabetes: a population-based cross-sectional study. J Eur Acad Dermatol Venereol 2008;22:585–9.

39. Naldi L, Chatenoud L, Linder D, Belloni Fortina A, Peserico A, Virgili AR, et al. Cigarette smoking, body mass index, and stressful life events as risk factors for psoriasis: results from an Italian case-control study. J Invest Dermatol 2005;125:61–7.

40. Kim GW, Park HJ, Kim HS, Kim Sh, Ko HC, Kim BS, et al. Analysis of cardiovascular risk factors and metabolic syndrome in korean patients with psoriasis. Ann Dermatol 2012;24(1):11-5

41. International Diabetes Federation [homepage on the Internet], [cited 2013 Jan 18]. Available from: http://www.idf.org.

42. Gisondi P, Tessari G, Conti A, Piaserico S, Shianchi S, Peserico A, et al. Prevalence of metabolic syndrome in patients with psoriasis: a hospital-based case-control study. Br J Dermatol 2007;157(1):68-73.

43. Nisa N, Qazi MA. Prevalence of metabolic syndrome in patients with psoriasis. Indian J Dermatol Venereol Leprol 2010;76(6):662-5.

44. Tekin NS, Tekin IO, Barut F, Sipahi EY. Accumulation of oxidized low-density lipoprotein in psoriatic skin and changes of plasma lipid levels in psoriatic patients. Mediators Inflamm 2007;2007:ID 78454.

45. Sommer DM, Jenisch S, Suchan M, Christophers E, Weichenthal M. Increased prevalence of the metabolic syndrome in patients with moderate to severe psoriasis. Arch Dermatol Res 2006;298(7):321-8.

46. Neimann AL, Shin DB, Wang X, Margolis DJ, Troxel AB, Gelfand JM. Prevalence of cardiovascular risk factors in patients with psoriasis. J Am Acad Dermatol 2006;55(5):829-35.

47. Gerdes S, Zahl VA, Knopf H, Weichenthal M, Mrowietz U. Comedication related to comorbidities: a study in 1203 hospitalized patients with severe psoriasis. Br J Dermatol 2008;159:1116–23.

48. Minov J, Karadžinska-Bislimovska J, Vasilevska K, Nelovska Z, Risteska-Kuc S, Stoleski S, et al. Smoking among Macedonian workers five years after the anti-smoking campaign. Arh Hig Rada Toksikol 2012;63(2):207-13.

Abbreviations

IMID - immune-mediated inflammatory disease
CVD - cardiovascular disease
TNF-α - tumor necrosis factor-alpha
UV - ultraviolet rays
GP - general practitioner
BMI - body mass index
BP - blood pressure
PASI - Psoriasis Area and Severity Index
BSA - body surface area
NCEP - National Cholesterol Education Program
ATP III - Adult Treatment Panel III
HDL - high density lipoprotein
SD - standard deviations
OR - odds ratios
CI - confidence intervals
PsA - psoriatic arthritis
CVR - cardiovascular risk
CHD - coronary heart disease
NA - not applicable
TG - triglyceridemia
MI - myocardial infarction
MetS - metabolic syndrome
CVI - cerebrovascular insult

Kardiovaskularni ili metabolički komorbiditet kod osoba sa plak-tipom psorijaze koje nikada nisu dobijale sistemsku terapiju za psorijazu: analitička studija slučaja

Sažetak

Uvod: Komorbiditeti su bolesti koje koegzistiraju sa bolešću koja je cilj ispitivanja; u ovom radu to je psorijaza. Sve su brojniji radovi u svetskoj literaturi koji doprinose stavu da je psorijaza značajno povezana sa nizom komorbiditeta kao što su psorijatični arthritis, debljina, hipertenzija, dijabetes, hiperlipidemija, metabolički sindrom, kardiovaskularne bolesti (KVB), Kronova bolest, limfomi, neoplazije i multipla skleroza, kao i anksioznost, alkoholizam, pušenje i neravnoteža u ishrani. Nije poznat tačan mehanizam odgovoran za ovu udruženost ali se ne može zanemariti direktni uticaj hronične inflamacije i povećani nivo TNF-α. Niz drugih faktora utiču na tu asocijaciju) (Shema 1). Malo je radova koji se odnose na uticaj lekova za sistemsko lečenje psorijaze na komorbiditete, ali je dobro poznato da metotreksat povećava vrednosti homocisteina u serumu, a ciklosporin i acitretin uzrokuju povišeni krvni pritisak i hiperlipidemiju.
Cilj: Ovo istraživanje je obavljeno sa ciljem procene prevalencije kardioloških i metaboličkih komorbidnih stanja kod bolesnika sa hroničnom plak-psorijazom koji nikada nisu lečeni antipsorijaticima za sistemsku primenu. Istraživanje je sprovedeno kao studija slučajeva – kontrola, a uparivanje kontrolne grupe po polu i uzrastu omogućilo je eliminaciju uticaja ovih kovarijabli na rezultate istraživanja.
Rezultati: Demografske i osnovne karakteristike ispitivane populacije su prikazane u tabeli 1. i shemi 2. Stepen težine psorijaze grafički je prikazan shemom 3. Prevalencije ispitivanih komorbiditeta date su u tabeli 2 i shemama 4 i 5. Nije utvrđena signifikantna razlika u odnosu na prevalenciju hipertenzije (29,5% vs. 23,7%, p = 0,311), koronarne bolesti srca (13,9% vs. 17,2%, p = 0,480), dijabeta (9% vs. 7,3%, p = 0,641), infarkta miokarda (3,2% vs. 2,4%, p = 0,71), cerebrovaskularnog inzulta (2,4% vs. 2,4%, p = 1) i metaboličkog sindroma (24,6% vs. 22,9%, p = 0,764), između ispitanika sa psorijazom i kontrolnih ispitanika. Prevalencija hipertrigliceridemije kod bolesnika sa psorijazom iznosila je 41,8%, za razliku od kontrolnih ispitanika kod kojih je iznosila 28,7% (p = 0,032). Značajna razlika utvrđena je i u odnosu na srednje vrednosti triglicerida (170,19 ± 67,84 mg/dl vs. 149,27 ± 81,15 mg/dl, p = 0,013). Pušenje je bilo češće kod bolesnika sa psorijazom (58,1% vs. 44,2%, p = 0,021). Osim toga, pacijenti sa psorijazom imali su veći prosečni indeks telesne mase, BMI (eng. *body mass index*) (26,24 vs. 24,73, p = 0,005) (Tabela 1).

Zaključak**:** Istraživanje je pokazalo da pacijenti sa plak psorijazom koji nikada nisu lečeni od psorijaze sistemskim lekovima nemaju statistički značajno češću pojavu kardiovaskularnih i metaboličkih komorbidnih stanja u odnosu na kontrolnu grupu.

Sistemski antipsorijatični lekovi mogu uticati na pojavu ovih komorbiditeta. Ipak, ova studija je pokazala da bolesnici sa psorijazom imaju povišena tri važna faktora rizika za nastanak kardiovasklarnih bolesti – pušenje, debljinu i hipertrigliceridemiju.

Ključne reči