PREVALENCE OF CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH PSORIASIS

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SUMMARY

Objectives: The main goal of the study was to describe the demographic, epidemiological, clinical and laboratory characteristics of a monitored group of patients with psoriasis to assess the prevalence of cardiovascular comorbidities and to define the cardiovascular risk profile.

Methods: One hundred and ninety outpatients aged over 18 were included in the prospective observational cross-sectional study. Demographic and clinical data were obtained from patients. The severity of psoriasis was evaluated using the Psoriasis Area and Severity Index (PASI) and the Dermatology Life Quality Index (DLQI). The results of laboratory testing were identified based on patient health records.

Results: Based on an evaluation of psoriasis phenotypes, 150 patients (78.95%) suffered from plaque psoriasis, 18 (9.5%) from palmoplantar psoriasis, 11 (5.8%) from guttate psoriasis, 6 (3.2%) from generalized pustular psoriasis, and 5 (2.6%) from erythrodermic psoriasis. The personal medical history discovered the occurrence of arterial hypertension in 83 patients (43.7%), the occurrence of depression in 49 patients (25.8%), type 2 diabetes in 29 patients (15.3%), and dyslipidaemia in 48 patients (25.3%).

Conclusion: It is noteworthy that psoriasis may be demonstrated as a multi-system disease which does not only affect the skin and its adnexa. The association of psoriasis with comorbidities may significantly increase morbidity and total mortality as well as the demands for health care provision.

Key words: psoriasis, comorbidities, arterial hypertension, depression, diabetes mellitus, metabolic syndrome

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https://doi.org/10.21101/cejph.a6806

INTRODUCTION

Psoriasis is a chronic, non-contagious disease of the skin and/or joints with a variable phenotype picture and a significant impact on the quality of the patient's life even with limited disability. At present, it seems to be the most studied chronic immune-mediated dermatosis. It represents a severe global problem, with a geographically manifold prevalence from 0.09% to 11.4% (1).

Despite the aetiopathogenesis of psoriasis still being unknown, genetic, immunological and environmental factors are known to contribute to its occurrence (2). The results of surveys in recent years in the field of the disease immunopathophysiology have changed the perception of psoriasis from that of an expressly hyperkeratotic disease of keratinocytes into a dysregulation of the immune system mediated by pro-inflammatory cytokines. The concept of psoriasis as system inflammation has significant consequences for the treatment of patients and overall disease management (3). Increasing evidence on the association of psoriasis with comorbidities that have significant impact not only on morbidity and overall mortality but also on the use of health care should result in actively searching for them and timely diagnostics, with the subsequent adequate therapeutic intervention (4). More than half of the patients suffering from psoriasis at the age of over 65 have at least two comorbidities, and two-thirds of them have one or more comorbidities (5). The association with comorbidities is assumed to contribute to a reduction of the average life expectancy (6).

MATERIALS AND METHODS

One hundred and ninety outpatients aged over 18 were included in the prospective observational cross-sectional study carried out from July 2014 to May 2015. Prior to inclusion in the study, each participant provided written informed consent. The study was carried out with the approval of the regional committee for ethics in medical research. Exclusion criteria included pregnancy and participation in another clinical trial. The main goal of the study was to describe the demographic, epidemiological, clinical and laboratory characteristics of the monitored group of patients with psoriasis, to assess the prevalence of cardiovascular comorbidities – arterial hypertension, type 2 diabetes, dyslipidaemia, obesity, and metabolic syndrome in the group, and to define the cardiovascular risk profile.

Patients were asked to provide the following demographic data: sex, age at the time of psoriasis onset, and disease duration. The occurrence of high blood pressure, dyslipidaemia, type 2 diabetes, psoriatic arthritis, and depression were determined from each patient's personal medical history, and concomitant therapy was identified. Patients were divided into three categories according to their smoking history: non-smokers, ex-smokers (not smoking for more than a year) and regular smokers. In smokers we found out whether they started smoking even prior to their psoriasis diagnosis. Based on the data on alcohol consumption, the patients were divided into occasional consumers (less than once a month), regular consumers (more than once a month) and non-consumers (including alcohol consumers in the past). The frequency of use in regular consumers was evaluated as: low (less than once a week), moderate (once to three times a week) and high (more than once a day).

The occurrence of psoriasis in first-degree and second-degree relatives and the occurrence of cardiovascular accident was queried in the family history. The physical examination was focused on risk factors of cardiometabolic diseases: blood pressure, anthropometric indicators aimed at overweight and obesity – body mass index (BMI) and waist circumference.

The severity of the psoriasis was evaluated using the Psoriasis Area and Severity Index (PASI) and the Dermatology Life Quality Index (DLQI). Psoriasis with PASI ≤ 10 was considered to be the mild form, psoriasis with PASI > 10 was considered to be the moderate to severe form. This group also included patients currently receiving systemic treatment, in compliance with the literature. These patients may have the disease stabilized due to therapy; thus, they do not fulfil the severity evaluation criteria according to PASI. All patients filled in the DLQI questionnaire validated in the Slovak language.

The results of laboratory testing, such as total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), triacylglycerols (TG), and fasting glycaemia, were identified based on the health records. Only the results from recent investigations were considered; the evaluation did not include results older than six months prior to the study beginning. Dyslipidaemia was stated if diagnosed in the past and treated by means of hypolipidemic drugs or in the case of identification of pathological values in the laboratory results. Metabolic syndrome (MetS) was diagnosed by applying the International Diabetic Federation criteria (7).

Moreover, we calculated the 10-year risk of coronary accident in percent. According to the calculated risk, the patients were stratified into three categories: low risk $< 10\%$, moderate risk 10% to 20%, and high risk $> 20\%$.

Statistical Analysis

The statistical analysis expressed the qualitative variables as absolute and percentage values. Quantitative variables were expressed as an average, standard deviation, median and interquartile range. The proportional comparison used the Chi-squared test; the Student's t-test was used to calculate differences between averages, and the Kruskal-Wallis test was used to test the significances of differences in the medians. The data were deemed statistically significant if the p value for the difference was less than 0.05 ($p < 0.05$). Statistical calculations were carried out in IBM-SPSS Statistics 21.0.

RESULTS

The study group included a total of 190 patients, 93 of whom were men (48.9%) and 97 women (51.1%). The average age of patients was 51.5 ± 14.0 (aged 18 to 92). The average disease duration was 15.8 ± 12.2 years, and the median was 13.0 years (interquartile range from 6.0 to 23.0). All patients were of the Caucasian race domiciled on the territory of the Slovak Republic.

Based on the evaluation of psoriasis phenotypes, 150 patients (78.95%) suffered from plaque psoriasis, 18 (9.5%) from palmoplantar psoriasis, 11 (5.8%) from guttate psoriasis, 6 (3.2%) from generalized pustular psoriasis, and 5 (2.6%) from erythrodermic psoriasis. The average PASI score was 3.4 ± 3.03 years, the median was 2.3 (0.9 to 4.5). During severity evaluation according to PASI, 17 patients (10.5%) had PASI ≥ 10, when evaluating according to the DLQI, and 26 patients (13.7%) had a DLQI ≥ 10. Out of the total number, 128 patients (67.4%) had moderate to severe psoriasis.

In terms of therapy, 79 patients (41.6%) were treated by applying local therapy, 59 (31.1%) by methotrexate, 27 (14.2%) by acitretin, 19 (10%) by UVB phototherapy, 16 (8.4%) by biologics, and only one by cyclosporine (0.5%). Fifty-seven patients (30%) proved a positive family history of psoriasis, 129 patients (67.9%) proved a negative family history, and four patients (2.1%) were unable to inform about the occurrence of the disease in the family. Psoriatic arthritis (PsA) was diagnosed in 37 patients (19.5%), 17 of whom (45.9%) suffered from asymmetric oligoarthritis, 10 (27%) from symmetric polyarthritis, 6 (16.2%) from interphalangeal joint arthritis, and 4 (10.8%) from spondylitis. No patient suffered from mutilating arthritis.

Out of the total number of patients, changes in nails were identified in 118 patients (62.1%). The most frequent sign was onycholysis (41.6% of patients) followed by pitting (21.6%), onychodystrophy (14.2%), subungual hyperkeratosis (11.6%), oil drops (4.2%), and subungual haemorrhage (11.1%).

Out of 190 patients, 39 (20.5%) were current smokers, 57 patients were ex-smokers (30%) and 94 (49.5%) were non-smokers. The average length of smoking was 22.3 years ± 12.0 years, with a median of 20 years. The majority of current smokers or ex-smokers (76.5%) started smoking even prior to the onset of psoriasis. The annual average of packs smoked was 21.3 ± 16. One hundred and five patients (55.3%) stated no alcohol consumption, 31 (16.3%) stated alcohol consumption in the past, 54 (28.4%) stated consumption less than once a week, and 18 (33.4%) one to three times a week. The clinical characteristics of patients in the group are provided in Table 1.

Comorbidity and Laboratory Findings

The personal medical history showed the occurrence of arterial hypertension in 83 patients (43.7%), the occurrence of depression in 49 patients (25.8%), type 2 diabetes in 29 patients (15.3%), and dyslipidaemia in 42 patients (25.3%). The laboratory findings revealed increased values of total cholesterol in 18.5% of patients, increased LDL values in 16.9% of patients and increased TG values in 33.7% of patients. Reduced HDL values were identified in 66 men (74.2%) and in 15 women (16.9%). The most frequent comorbidity was obesity (68.42% of patients). The waist circumference evaluation showed increased values in 68.8% of men and

Table 1. *Distribution of clinical characteristics in the group of patients with psoriasis (N = 190)*

Characteristics	n	%
Sex		
Men	93	48.9
Women	97	51.1
Phenotype of psoriasis		
Plaque	150	78.9
Palmoplantar	18	9.5
Guttate	11	5.8
Generalized pustular	6	3.2
Erythrodermic	5	2.6
Treatment		
Acitretin	27	14.2*
Cyclosporine	1	0.5*
Phototherapy	19	10.0*
Biological treatment	16	8.4*
Methotrexate	59	31.1*
Only local treatment	79	41.6*
Family history		
Positive	57	30.0
Negative	129	67.9
Missing data	4	2.1
Smoking		
Regular smoker	39	20.5
Smoked in the past	57	30.0
Does not smoke	94	49.5
Alcohol consumption		
Regular consumer	54	28.4
Consumed in the past	31	16.3
Does not consume	105	55.3
Psoriasis Area and Severity Index (n = 162)		
≥ 10	17	10.5
< 10	145	89.5
Dermatology Life Quality Index (n = 190)		
≥ 10	26	13.7
< 10	164	86.3

*categories are not mutually exclusive

Table 2. *Comorbidities and laboratory findings in the group of patients with psoriasis*

Characteristics	n	%
Depression	49	25.8
Type 2 diabetes	29	15.3
Arterial hypertension	83	43.7
Dyslipidaemia	48	25.3
Metabolic syndrome (n = 178)	80	44.9
BMI (n = 190)		
< 25	68	35.7
25.0–29.9	59	31.1
30.0–34.9	43	22.6
35.0–39.9	14	7.4
≥ 40	6	3.2
Waist circumference (cm)		
Men		
< 94	29	31.2
≥ 94 to < 102	28	30.1
≥ 102	36	38.7
Women		
< 80	13	13.2
≥ 80 to < 88	8	8.2
≥ 88	76	78.4
Total cholesterol (n = 178)		
Within the norm	145	81.5
Increased	33	18.5
Low-density lipoprotein (n = 178)		
Within the norm	148	83.1
Increased	30	16.9
High-density lipoprotein (n = 178)		
Men		
Within the norm	66	74.2
Reduced	23	25.8
Women		
Within the norm	15	16.9
Reduced	74	83.1
Triacylglycerols (n = 178)		
Within the norm	118	66.3
Increased	60	33.7

in 86.5% of women (p = 0.005), and 80 patients (44.9%) fulfilled the metabolic syndrome criteria (42.6% of men and 47.2% of women). Data of 178 patients were suitable for analysis (Table 2).

Framingham Risk Score

The Framingham Risk Score was calculated in 159 patients. According to the risk stratification, 38.4% showed moderate risk and 8.8% showed a high risk of probability of acute non-fatal and fatal coronary accidents within 10 years. The median was 8.0 (interquartile range from 4.0 to 13.0). Men had a median score of 10.0, and women showed a median of 7.0. The difference between the sexes was statistically significant (Kruskal-Wallis test = 8.6; p = 0.0033). The average was 10.5 ± 9.1.

Variable Analysis According to Psoriasis Severity

Out of the total number of 190 patients, 128 patients had moderate to severe psoriasis. In terms of severity, the following variables were statistically significant:

- disease duration: in patients with severe psoriasis the average duration of psoriasis was 17.5 ± 12.3 years compared to the

duration in patients with the mild form of 12.6 ± 11.2 years (p = 0.021);
- presence of PsA: 34 patients (26.5%) with moderate to severe psoriasis had PsA compared to three patients (4.8%) with the moderate form (p = 0.0008);
- nail disorder: 91 patients (71.1%) with moderate to severe psoriasis suffered from nail disorder compared to 27 patients (43.5%) with the mild form (p = 0.004);
- high BMI: 89 patients (69.5%) with BMI ≥ 25 compared to 33 patients (53.2%) with the mild form; in the case of analysis of obesity itself, no significant difference was identified (Table 3).

Variable Analysis According to Psoriasis Classification

Patients were divided into two groups based on the phenotype classification: patients with plaque psoriasis and patients with other phenotypes of psoriasis, with analysis of clinical and laboratory variables between the groups. Statistical significance was shown only by PsA: out of 37 patients with PsA, 35 suffered from plaque psoriasis and only two suffered from another form of psoriasis (23.5% vs. 4.9%; p = 0.0146). In patients with PsA, 34 patients (94.5%) had changes in their nails (p < 0.001).

DISCUSSION

The association of psoriasis and cardiovascular comorbidities has been described recently in many epidemiological studies. According to our knowledge concerning the occurrence of this association in the Slovak population, particular data are not yet available, and epidemiological studies in patients suffering from psoriasis have not been implemented. The average age of our patients was 51.5 (SD = 14), which likely contributed to the higher occurrence of comorbidities, such as arterial hypertension, type 2 diabetes and dyslipidaemia, whose prevalence increases with age. In compliance with the literature, no significant difference between the sexes was identified, since our sample included 48.9% of men and 51.1% of women.

The cardiometabolic comorbidities were dominated by obesity. Behavioural changes and changes in the quality of patients' life could contribute to increasing patients' weight. Similarly, obesity functions as a predisposition for psoriasis onset based on common inflammation mechanisms. Nearly two-thirds of the patients in our study (64.3%) had an increased BMI: 31.1% were classified as overweight and 33.2% as obese (22.6% of patients suffered from Class 1 obesity, 7.4% from Class II obesity and 3.2% from Class III obesity). Since this is a cross-sectional study, it is impossible to define whether skin changes are predispositions of obesity or vice versa. Contrary to the results of some studies, the presence of obesity in our group failed to correlate with the severity of psoriasis (8).

Visceral obesity increases metabolic and cardiovascular risk. The values of waist circumference at the level of 102 cm in men and 88 cm in women do not comply with the evaluation of each population. The International Diabetes Federation (IDF) criteria for diagnostics of metabolic syndrome modified for the European population provide waist circumference values of 94 cm for men and 80 cm for women (7). Based on these parameters, the increased values of waist circumference were discovered in 68.8% of men and 86.5% of women in our study. Considering the waist circumferences of 102 cm or 88 cm, respectively, which indicates even higher cardiovascular risk, increased values were identified in 38.7% of men and 78.4% of women. We found that, unlike men, the majority of women remained in the risk group despite the increase in the limit values.

The association of psoriasis and arterial hypertension is well documented. Our group of 190 patients showed hypertension in their medical history in 43.7% of patients, which corresponds approximately to the prevalence according to the KESHSR study (9). Newly discovered hypertension was diagnosed in five patients, who were then sent to a specialist. Contrary to the results of the published studies, we did not find any difference in the prevalence of hypertension in relation to the severity of psoriasis (10).

Type 2 diabetes is further an independent risk factor of cardiovascular diseases associated with psoriasis, probably based on common inflammatory pathways. Our study showed a diagnosis of diabetes in the medical history of 15.3% of patients, which is

Table 3. *Distribution of variables in relation to severity of psoriasis*

Characteristics	Moderately severe to severe n (%)	Moderate n (%)	Test statistics	p-value
Psoriatic arthritis				
Present	34 (26.5)	3 (4.8)	11.22[a]	0.0008
Absent	94 (73.5)	59 (95.2)		
Nail disorder				
Present	91 (71.1)	27 (43.5)	12.32[a]	0.004
Absent	37 (28.9)	35 (56.5)		
BMI				
< 25	39 (30.5)	29 (46.8)	4.15[a]	0.042
≥ 25 (overweight + obesity)	89 (69.5)	33 (53.2)		
Duration in years (median)	15.0 (8.0–25.0)[#]	8.0 (4.0–20.0)[#]	9.43[b]	0.021

[a]Chi-squared test; [b]Kruskal-Wallis test; [#]1st and 3rd quartiles

double the results of population studies in Slovakia (11). In eight patients with a negative medical history regarding diabetes, fasting hyperglycaemia was diagnosed but only in one evaluation, which is insufficient for diagnosing diabetes. These patients were sent to a diabetologist for further examinations. Type 2 diabetes is a comorbidity with the biggest number of reports from studies evaluating the association of its prevalence in relation to the severity of psoriasis (12, 13). Our study did not prove such an association.

Several studies confirm the association between psoriasis and alteration of lipid metabolism, such as HDL reduction and TG increase (14). In 48 patients (25.3%) in our study dyslipidaemia appeared in their medical history. According to laboratory findings, we discovered a high rate of men with low HDL compared to women (74.2% vs. 16.9%). In patients treated by acitretin, only five of them showed abnormal lipid levels, which probably did not affect the final data analysis. The MetS criteria according to IDF were fulfilled by 44.9% of patients. Compared to the 20.1% prevalence in the Slovak population (11), this is a significant difference ($p < 0.001$). Compared to the results of other studies, we did not find a correlation of MetS and the severity of psoriasis (13).

The relation between psoriasis and smoking has been confirmed by several studies (15). In our study smokers made up 50.5% of the sample (20.5% were regular smokers and 30% were ex-smokers). The majority (76.5%) in the group of 96 smokers (current or ex-smokers) stated the beginning of their smoking prior to the occurrence of the first signs of psoriasis. Based on the results of the 2014 European Health Interview Survey (EHIS 2014), the percentage share of regular smokers in 2014 amounted to 22.9% (16). Alcohol consumption, like smoking, may be a consequence of the negative impact of psoriasis on the life quality. It is difficult to quantify alcohol consumption due to existence of various alcoholic beverages with different alcohol content (17). Only 28.4% of patients mentioned regular alcohol consumption in our group, and none had a diagnosis of alcoholism.

Psoriasis, like other chronic diseases, may negatively affect all aspects of life, which results in the increased occurrence of psychiatric comorbidities. The prevalence of depression in patients suffering from psoriasis is approximately 20% and this may increase the risk of cardiovascular diseases (18). The prevalence of depression in our study was 25.8% without a relation to the severity or scope of the skin disorder.

In terms of the occurrence of severe cardiovascular accidents, three patients showed in their medical history that they had fought off acute heart attack requiring angioplasty, and one patient fought off ischaemic stroke. At the time of these accidents, all four patients had already been diagnosed with psoriasis.

Based on the evaluation, 67.4% of patients suffered from moderately severe to severe psoriasis. Some variables have a statistically significant relation to disease severity, e.g., disease duration: patients with severe psoriasis have been suffering from the disease for 17.5 ($SD = 12.3$) years compared to 12.6 ($SD = 11.2$) years in patients with the moderate form. This difference may be due to the fact that the patients with severe disease are subject to regular monitoring, while the patients with the moderate form and/or controlled course of the disease are often not monitored at all. The presence of PsA and nail disorder was significantly higher in patients with severe psoriasis ($p = 0.0008$ and $p = 0.0004$, respectively). These findings are compliant with the literature data. A further finding influencing the severity of psoriasis with statistical significance was overweight. Patients with a BMI ≥ 25 suffered from more severe psoriasis. However, an independent analysis of obesity did not find a statistically significant difference, which does not correlate with the results of multi-variant analyses (19).

Cardiovascular diseases are the main cause of morbidity and mortality worldwide. Thus, identifying individuals with a risk profile is inevitable. The most applied method is undoubtedly the Framingham Risk Score. The final score estimates the risk of mortal and non-fatal coronary accidents in the course of 10 years along with stratification of patients into risk categories. The score estimates a prognosis and indicates the required clinical intervention (20). Our study assessed 159 patients aged 30 to 74 without a disorder of the coronary arteries using the Framingham Risk Score; 47.2% of them showed moderate risk and 8.8% high risk of coronary accident in the course of the next 10 years. Forty-five patients (28.3%) showed a higher score compared to the expected one for individuals of the same sex and age. The average Framingham Risk Score was 10.5 ± 9.1, which is considered high. Our data are similar to the results of other studies on patients suffering from psoriasis (20, 21). Similarly, our study did not find any relation between the score and the severity of psoriasis. A limitation of the study was the lack of a control group.

CONCLUSION

In our study, we did not find the occurrence of arterial hypertension, type 2 diabetes, metabolic syndrome, and obesity to be higher in patients with psoriasis compared to the remaining population. Furthermore, we discovered a correlation between increased waist circumference and the more frequent occurrence of depression and regular alcohol consumption. The cardiovascular risk profile of patients according to the Framingham Risk Score was high compared to studies on the remaining population, and moderately or high 10-year risk of fatal and non-fatal coronary accidents was discovered in 47.2% of patients.

It is noteworthy that psoriasis may be demonstrated as a multi-system disease which does not affect only the skin and its adnexa. The association of psoriasis with comorbidities may significantly increase morbidity and total mortality as well as the demands for health care provision. The meaning of the risk profile definition, particularly in patients suffering from the severe form of psoriasis, is evident, and it becomes a medical obligation, as it allows simplification of the decision-making processes in the selection of therapy and intervention of risk factors. Dermatologists should be proactive in this field, at least in patients with the moderately severe and severe forms of psoriasis. A further step in management is then the proposal of an intervention that has the potential to reduce the identified risks. Though the results of some studies indicate a positive impact of treatment using methotrexate and biologics on cardiovascular risk in patients suffering from psoriasis, this impact is not clear and has not been sufficiently investigated. Such complex management, however, may not be feasible in the conditions of the common outpatient dermatological practise. A meaningful approach is to establish a network of specialized centres, at least for patients with moderately severe to severe psoriasis.

Acknowledgements

This work was supported by the grants: KEGA 007/UPJŠ-4/2018, KEGA 008UPJŠ-4/2020 and KEGA 010UPJŠ-4/2021 of the Ministry of Education, Science, Research and Sport of the Slovak Republic as well as project grants VVGS IPEL 2020/1485 and VVGS IPEL 2020/1662. We also thank the Directory Board of University Hospital in Košice for assistance with the organization of sample collection at the hospital wards.

Conflict of Interests

None declared

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Received February 20, 2021
Accepted in revised form November 30, 2021