Cardiovascular Comorbidities in Patients with Psoriasis: Risk Profile Including Carotide Ultrasonography Assessed in Hospital-based Case Control Study

Jana Votrubova[1,2], Katerina Juzlova[1,2], Martina Dzambova[1,2], Jana Hercogova[1], Dana Gopfertova[2] Zdenek Smerhovsky[2]

[1]Department of Dermatovenereology, 2nd Faculty of Medicine, Charles University in Prague, Prague, Czech Republic; [2]Department of Epidemiology, 2nd Faculty of Medicine, Charles University in Prague, Prague, Czech Republic

Corresponding author:
Department of Dermatovenereology
2nd Faculty of Medicine
Charles University in Prague
Frantiska Krizka 15
Praha 7
Czech Republic
jana-votrubova@seznam.cz

Received: October 12, 2015
Accepted: July 1, 2016

ABSTRACT Psoriasis is a chronic inflammatory disease, and its comorbidities have attracted serious interest in recent years. The evidence that psoriasis is associated with systemic inflammation and significantly higher incidence of cardiovascular risk factors has already been described. The results of published studies are highly variable, the conclusions are ambiguous, and further epidemiological studies are needed for validation of published data. Therefore, we initiated a project aimed at identifying the association with cardiovascular risk factors, including early stages of atherosclerosis, that represent important comorbidities in patients with psoriasis. We carried out a hospital-based case-control study on 189 patients with chronic plaque psoriasis enrolled as cases. The control group consisted of 378 patients with other skin diseases complying with the same exclusion criteria who were recruited to the study as the controls. All participants underwent physical examination, blood tests, and measuring of blood pressure and waist circumference. Furthermore, we evaluated carotid intima-media thickness (CIMT) in a subset of 117 cases and controls (matched 1:2) with no history of cardiovascular disease. The results showed higher prevalence of hypertension, hyperlipidemia, waist circumference, weight, body-mass index (BMI), and C-reactive protein (CRP) level in patients with psoriasis than in controls. These parameters have been clearly demonstrated to be risk factors for the development of cardiovascular diseases. The associations between psoriasis and diastolic blood pressure, BMI value, and low-density lipoprotein (LDL) cholesterol were statistically significant in the binary data logistic model as well. CIMT was not significantly higher in patients compared with controls.

KEY WORDS: psoriasis; cardiovascular comorbidities; atherosclerosis; risk factors; case-control study

INTRODUCTION

Psoriasis is a chronic inflammatory disease, predominantly affecting the skin, and is included in the group of immune mediated inflammatory diseases (1). Its prevalence ranges from around 1.5 % to 4.7% in Europe and in the USA. Some experimental and epidemiological studies have linked certain interleukins, cytokines, and adipokines with cardiovascular disease, metabolic syndrome, obesity, and diabetes, making psoriasis a risk factor in developing systemic comorbidities (2-4). Inflammation also plays an

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important role in the pathogenesis of atherosclerosis (5,6). There are therefore striking similarities between molecular and inflammatory pathways in psoriasis and atherosclerosis (7).

The presence of psoriasis in the past medical history of a patient is, therefore, considered to be one of the independent risk factors of atherosclerosis (8).

In a recent published meta-analysis, the authors described that most of the studies reported a high prevalence of metabolic syndrome in patients with psoriasis, ranging from 14 to 40%, suggesting that metabolic syndrome is a common condition in patients with psoriasis (9).

In contrast to this statement, other authors found no association between severe psoriasis and obesity or between obesity and cardiovascular mortality in their studies (10).

As associated comorbidities significantly impair the quality of life of patients suffering from psoriasis and contribute to increased morbidity and mortality of these patients (11,12), it is at present common practice to administer a number of screening tests that detect asymptomatic patients at risk of cardiovascular comorbidities and atherosclerosis, such as measurements of carotid artery intima media thickness (13), basic blood tests (serum lipid levels, glycemia), and physical examination.

Based on the results of previous research and our own clinical experience, we designed a case-control study with the aim of contributing knowledge on the relationships described above. We tested the hypothesis that the prevalence of cardiovascular risk factors and atherosclerosis is higher in patients with the chronic stationary form of psoriasis than in the control population.

PATIENTS AND METHODS

The study was designed as a hospital-based case-control study, and 189 patients from Department of Dermatovenereology (Bulovka Hospital in Prague) with chronic plaque psoriasis were enrolled as cases. The control group consisted of 378 patients and was sampled at a 1:2 ratio from patients with other non-autoimmune and non-acute infectious dermatological and venereal diseases (e.g. patients with nevi in preventive care) according to the same exclusion criteria applied for the case group. All the patients suffering from chronic and autoimmune diseases, hypertension, and diabetes mellitus as well as patients with centripetal obesity (men with waist circumference greater than 102 cm and women greater than 88 cm) were excluded from the study. Due to comparison between cases and controls in the asymptomatic stages of cardiovascular diseases, patients with apparent signs of tested risk factors or patients already treated for cardiovascular diseases were excluded as well.

Scope of medical examination

In each study patient we determined the following parameters:

- age (all patients in study were 18-80 years old)
- sex
- waist circumference (cm)
- weight (kg)
- height (m)
- body mass index (BMI)
- blood pressure (mmHg)
- glycemia (mmol/L)

Blood lipids:

- total cholesterol (mmol/L)
- low-density lipoprotein cholesterol (LDL) (mmol/L)
- high density lipoprotein cholesterol (HDL) (mmol/L)
- triacylglycerol (TAG) (mmol/L)
- C-reactive protein (CRP) (mg/L)

The mean thickness of the right and left common carotid artery intima-media (IMT) were measured using color duplex ultrasound of the carotid arteries to compare carotid IMT values in a sample of participants (38 cases, 78 controls).

Statistical analysis

Due to asymmetric distribution of most of the studied variables, the differences between cases and controls were tested by means of Mann-Whitney U test at the bivariate level. Simultaneous effects of the studied variables on the occurrences of psoriasis were studied by binary logistic regression. The point estimates of odds ratios and 95 % confidence interval (CI) describing the strength of association between independent predictors and occurrence of psoriasis are reported. Level of statistical significance in all tests was set to 0.05.

RESULTS

Data on 189 cases and 378 controls are available. Differences in sex distribution did not reach the level of statistical significance. The main characteristics and the distribution of studied parameters are listed in the Table 1 and Table 2. Tests of statistically significant differences between cases and controls are displayed in both tables.

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The comparison of cases and controls revealed statistically significant differences in terms of several observed parameters (Table 1). Psoriasis cases had higher diastolic blood pressure than controls (Figure 1), a bigger waist circumference, and a higher BMI value (Figure 2). The cases had higher LDL cholesterol (Figure 3) as well. Using binary logistic regression, psoriasis was positively associated with diastolic blood pressure, BMI value, and LDL cholesterol (Table 2).

Table 1. Distributions of studied parameters and their comparison in cases and controls

Variable	Status	N	Mean	Median	Minimum	Maximum	Std. Deviation	Sig.
Age (years)	Controls	378	40.07	36.00	16	94	15.50	0.047
	Cases	189	41.88	39.00	17	84	14.24	
	Total	567	40.68	38.00	16	94	15.10	
Blood pressure systolic (mmHg)	Controls	378	120.73	120.00	90	170	13.61	0.000
	Cases	188	126.52	130.00	95	180	15.00	
	Total	566	122.65	120.00	90	180	14.34	
Blood pressure diastolic (mmHg)	Controls	377	78.06	80.00	50	118	9.14	0.000
	Cases	188	83.08	80.00	60	120	11.46	
	Total	565	79.73	80.00	50	120	10.24	
Waist circumference (cm)	Controls	378	83.16	82.50	58	117	11.81	0.000
	Cases	188	88.34	88.00	53	121	13.54	
	Total	566	84.88	85.00	53	121	12.64	
Weight (kg)	Controls	378	74.56	73.00	46	126	13.94	0.002
	Cases	188	79.58	78.00	45	152	17.76	
	Total	566	76.23	74.00	45	152	15.48	
Height (m)	Controls	378	1.74	1.75	1.38	2.00	0.10	0.381
	Cases	188	1.73	1.74	1.3	2.00	0.10	
	Total	566	1.74	1.74	1.3	2.00	0.10	
BMI	Controls	378	24.43	24.0	16.80	38.86	3.61	0.000
	Cases	188	26.32	26.11	17.76	47.34	4.63	
	Total	566	25.6	24.62	16.80	47.34	4.7	
Total cholesterol (mmol/L)	Controls	377	5.16	5.15	2.57	8.5	0.99	0.034
	Cases	186	5.37	5.35	2.23	9.52	1.10	
	Total	563	5.23	5.18	2.23	9.52	1.3	
HDL (mmol/L)	Controls	377	1.52	1.49	0.65	2.63	0.39	0.000
	Cases	186	1.4	1.35	0.78	3.1	0.34	
	Total	563	1.48	1.43	0.65	3.1	0.38	
LDL (mmol/L)	Controls	376	3.0	2.92	0.81	6.8	0.88	0.002
	Cases	186	3.23	3.11	1.00	5.97	0.91	
	Total	562	3.5	2.99	0.81	6.8	0.90	
TAG (mmol/L)	Controls	377	1.35	1.16	0.36	7.57	0.80	0.022
	Cases	186	1.53	1.3	0.45	5.76	0.94	
	Total	563	1.41	1.2	0.36	7.57	0.85	
glycemia (mmol/L)	Controls	377	4.83	4.8	2.6	9.4	0.73	0.901
	Cases	187	4.88	4.8	2.8	14.90	1,02	
	Total	564	4.85	4.8	2.6	14.90	0.84	
CRP (mg/L)	Controls	377	2.8	1.4	0.1	34.0	4.12	0.004
	Cases	186	3.71	1.95	0.2	71.1	6.50	
	Total	563	3.1	1.5	0.1	71.1	5.4	

*HDL: high density lipoprotein; LDL: low-density lipoprotein; TAG: triacylglycerol; CRP: C-reactive protein

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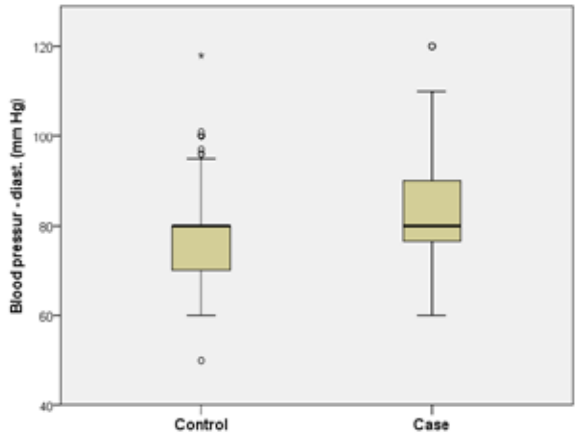

Figure1. Diastolic blood pressure in patients with psoriasis and controls (*P*<0.001).

DISCUSSION

The results of our study showed significant differences between the case group and controls at the bivariate level in several studied parameters: blood pressure, waist circumference, weight, BMI, CRP, total cholesterol, HDL cholesterol, LDL cholesterol, and triacylglycerols. The associations between psoriasis and diastolic blood pressure, BMI value, and LDL cholesterol remain statistically significant in the binary data logistic model.

According to our results, psoriasis predisposes patients at least to hypertension, higher BMI values, and elevated levels of LDL cholesterol. These parameters belong to the clinical picture of metabolic syndrome and they are proven risk factors for the development of cardiovascular diseases on the basis of atherosclerosis (myocardial infarction, stroke, and cardiovascular death) (14,15).

We consider the finding of elevated levels of LDL cholesterol to be important because the association between psoriasis and this parameter is very robust, given the evidence from the multivariate model. Results of other studies are in accord with our findings regarding elevated total cholesterol levels in psoriasis (16-18) and raised LDL and very low density lipoprotein (VLDL) cholesterol among participants with psoriasis (16-20). Elevated baseline concentrations of CRP observed at the bivariate level of analysis are associated with an increased risk of atherosclerotic events and serve as a predictive parameter both in primary and secondary prevention (21). In the present study, the increased level of CRP in the case group was borderline statistically significant (*P*=0.004). It can, therefore, be expected that if the case group grew sufficiently, the difference in this parameter would reach a level of statistical significance.

BMI values as a sign of obesity in patients with psoriasis were increased and achieved significance both at binary as well as at multivariate levels of analyses. The finding of higher BMI values correlated well with expectations and is consistent with previously published results (22,23).

Despite the expectations arising from the published results of numerous studies (24-26), a higher level of glycemia was not seen in patients with psoriasis enrolled in our study compared to the control group.

Regarding CIMT measurement, we did not find any statistically significant difference between cases and controls. This fact is in contrast with the majority of recent published studies – Balta *et al*. concluded that patients with psoriasis had a significantly greater CIMT compared with controls (27).

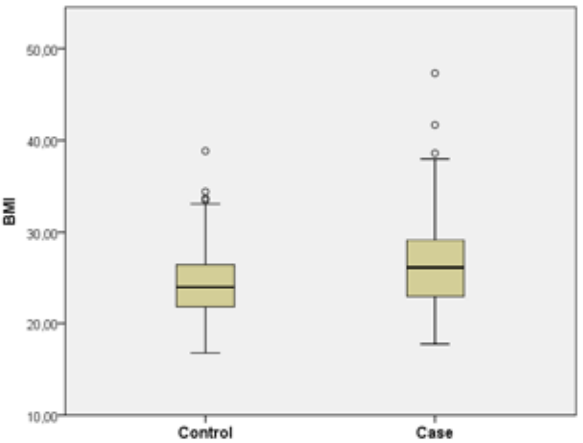

Figure 2. Body mass index in patients with psoriasis and controls (*P*<0.001).

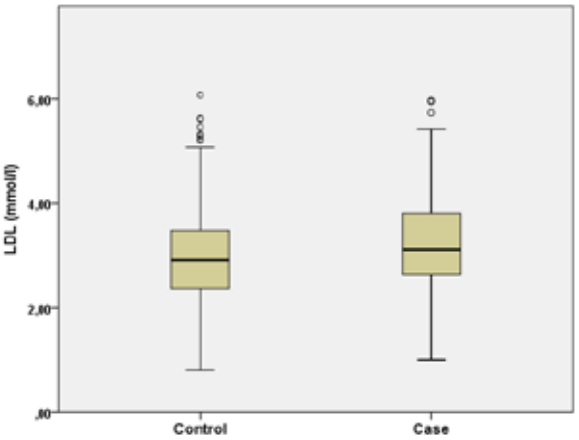

Figure 3. Low-density lipoprotein (LDL) cholesterol in patients with psoriasis and controls (*P*=0.002).

Table 2. Binary logistic regress in model of the association between psoriasis occurrence and studied parameters

	OR	95% CI for OR		
		Lower	Upper	Sig.
Blood pressure – diastolic (mmHg)	1.040	1.020	1.061	0.000
BMI	1.063	1.012	1.116	0.014
Leucocytes $\times 10^9$	1.222	1.109	1.346	0.000
LDL (mmol/L)	1.313	1.061	1.625	0.012

*BMI: body-mass index; LDL: low-density lipoprotein; OR: odds ratio; CI: confidence interval

Evensem *et al*., in accord with Balta *et al*., published in 2014 that the results of their study support previous evidence. They suggest that psoriasis is associated with an increased risk of atherosclerosis and subsequent cardiovascular disease (28).

Discrepancy between our results and previous published studies may be due to the systemic treatment of patients with psoriasis. In our study, 105 patients from the total number of 189 patients were treated with systemic agents. According to published results, the systemic treatment decreases the risk of atherosclerosis. The control group consists of patients (not of healthy population), so Bergson bias must be taken into account. The Bergson bias leads to distortion towards zero as well, which is a consequence of the well-known fact that hospital controls are often people with a number of risk factors.

Contrary to the majority of published studies, our results are supported by an extensive Rotterdam study, which did not find any significant difference between cases and controls. A total of 262 psoriasis (24% systemic/UV treatment) and 8 009 reference subjects were followed up for a mean of 11 years. The adjusted carotid intima-media thickness was 1.02±0.18 mm for psoriasis and 1.02±0.16 mm for reference subjects (29).

In the case of systolic and diastolic blood pressure, we found statistically significant differences. A statistically significant difference in the case of diastolic blood pressure was also found in the binary logistic regression. These results are in accordance with the majority of published studies (30-31).

CONCLUSION

The results of our study conducted on Czech patients with psoriasis suggest that detection of elevated or pathological values in several investigated parameters reaches the level of statistical significance.

Although no differences were found in the case of early stages of atherosclerosis and blood glucose, other modifiable risk factors such as hypertension, hyperlipidemia, elevated CRP, and centripetal obesity reached statistical significance. Our results are supported by the majority of published studies. Based on our findings, we suggest considering patients with psoriasis as an at-risk population for the development of cardiovascular disease. Performing preliminary diagnostics of concomitant diseases and referring the patient to an appropriate specialist should be the role of dermatologist. Primary prevention and early diagnostics of cardiovascular comorbidities benefit the health and quality of life of patients with psoriasis, but will also optimize available resources. Only a targeted individual approach to these patients can prevent their increased morbidity and mortality for cardiovascular diseases.

ACKNOWLEDGEMENTS

The project was supported by the Internal Grant Agency of the Ministry of Health of the Czech Republic (Grant NT 13275/4).

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