Risk factors for comorbidities in Czech psoriatic patients: Results of a hospital-based case-control study

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Background. Psoriasis is now known to be associated with multiple other diseases/comorbidities - including the metabolic syndrome, atherosclerosis and gastrointestinal diseases which are all significantly higher in psoriasis patients. Research results however are highly variable and the conclusions are ambiguous. As no similar study has been performed to date in Czech psoriatic patients, this study aimed at identifying risk factors and early stages of selected diseases/comorbidities in the patients.

Methods and Results. The study was designed as a hospital-based case-control study. 131 patients with chronic plaque psoriasis formed the cases and 267 patients with other skin disorders formed the controls. A comparison was made of basic demographic and anthropometric indicators, metabolic parameters, the presence of specific antibodies (ASCA, AEP, p-ANCA, AGC, EMA, ARA, t-TG, AGA) and non-specific signs of gastrointestinal diseases. The chi squared, MWU tests and binary logistical model were used to evaluate the data. The results showed significant differences ($P<0.05$) for the following parameters: blood pressure, waist circumference, weight, BMI values, leucocytes values, HDL cholesterol level, glycemia and gliadine antibody IgA level. All differences were to the detriment of psoriasis patients. In the binary logistical model the following parameters were associated with psoriasis: diastolic blood pressure, leucocyte value and glycemia. For all variables included in the logistical model $P\leq0.001$.

Conclusions. The results were coherent and consistent with existing data. They indicate that psoriasis is interconnected with hypertension, higher BMI and a decreased level of HDL cholesterol. These parameters have been clearly demonstrated as risk factors for the development of cardiovascular diseases. Higher levels of gliadine IgA antibodies are one of the diagnostic markers of celiac disease. Higher values of leukocytes may be interpreted as a nonspecific indicator of gastrointestinal inflammatory diseases. The associations between psoriasis and diastolic blood pressure, BMI value and glycemia are statistically significant in the binary logistic regression model. Care for psoriatic patients should focus especially on secondary prevention of predisposing diseases.

Key words: psoriasis, co-morbidities, risk factors, hospital-based case-control study

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INTRODUCTION

Psoriasis is a chronic inflammatory skin disease, the prevalence of which is around 1.5% to 4.7% in Europe and in the USA. Some publications show that patients with psoriasis have a higher risk of developing systemic comorbidities such as metabolic syndrome, diabetes mellitus and cardiovascular diseases[1-4]. In contrast to this statement, other authors found no association between severe psoriasis and obesity or between obesity and cardiovascular mortality in their studies[5]. Recent studies show that patients with psoriasis have an increased risk of insulin resistance, obesity, dyslipidemia and hypertension. Obesity has been identified as an independent risk factor for the development of psoriasis. Psoriasis is associated with diabetes, coronary artery disease as well as with an increased risk of myocardial infarction. A possible reason for the coincidence of metabolic syndrome and psoriasis is that they share similar pathological changes such as chronic inflammation, angiogenesis and oxidative stress[6,7]. Higher mortality due to cardiovascular disease was observed in patients with the severe form of psoriasis[8,9]. The presence of psoriasis in the past medical history of a patient is considered to be one of independent risk factors of atherosclerosis[10].

A study of the Swedish and Finnish populations confirms the connection between psoriasis and inflammatory bowel diseases (IBDs), in which both have been associated with the IL23-R gene. So far there is no proven connection between celiac disease and psoriasis[11]. There is a possible association between celiac disease and psoriasis as seen by the fact that a gluten-free diet leads to a clear improvement and disappearance of psoriatic skin lesions in some patients[12]. Associated diseases significantly impair the quality of life of patients suffering from psoriasis and contribute to the increased morbidity and mortality

of these patients[13,14]. Based on the clinical experience and results of studies, we expected a higher prevalence of the metabolic syndrome and inflammatory bowel diseases in patients with chronic stationary form of psoriasis than in the general population. The aim of our project was to test the hypothesis that the prevalence of the metabolic syndrome and inflammatory gastrointestinal diseases is higher in patients with chronic stationary form of psoriasis than in the general population.

MATERIALS AND METHODS

The study was designed as a hospital-based case-control study. Patients with chronic plaque psoriasis were enrolled as cases. The control group, selected on the basis of a ratio of 1:2, was composed of patients with other skin diseases who complied with the same restrictive criteria used in cases. A comparison of basic demographic and anthropometric indicators, metabolic parameters, the presence of specific antibodies (ASCA, AEP, p-ANCA, AGC, EMA, ARA, t-TG, AGA) and non-specific signs of gastrointestinal diseases were carried out between cases and controls. The statistical significance of differences between cases and controls was tested by means of Chi-quadrat test or Mann-Whitney U test. We used the binary logistic regression to multivariate modelling of the association between psoriasis and the aforementioned indicators.

131 cases and 267 controls were included in the study. There were statistically significant differences between cases and controls with regard to a few important parameters. We found significant differences (P<0.05) for the following parameters: blood pressure, waist circumference, weight, BMI values, leucocytes values, HDL cholesterol level, glycemia and gliadine antibody IgA level. All differences were to the detriment of psoriasis patients of. In the binary logistical model the following parameters were associated with psoriasis: diastolic blood pressure, leucocytes value and glycemia (for all the parameters included in the logistical model P≤0.001).

Study population

Patients suffering from chronic plaque psoriasis were enrolled in this study. The controls were selected by means of frequency matching with a ratio of 2 controls for 1 case. They were selected among other dermatology patients not suffering from psoriasis. The cases and controls were subject to the same selection criteria. Al the persons suffering from chronic and autoimmune diseases, hypertension, diabetes mellitus, persons with centripetal obesity (men with a waist circumference greater than 102 cm and women greater than 88 cm) and patients with apparent signs for tested risk factors and diseases were excluded.

Scope of medical examination

In each study subject we determine the following:

- age, sex
- smoking
- 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), high density lipoprotein cholesterol (HDL), triacylglycerol (TAG)
- ASCA – Anti- Saccharomyces cerevisiae antibodies (Crohn's disease)
- AEP - Anti- acinar cytoplasmic granule pancreatic antibodies (Crohn's disease)
- p-ANCA - perinuclear antibodies to neutrophil granulocyte cytoplasm component (Ulcerative colitis)
- AGC- Anti - goblet cell antibodies (markers for inflammatory bowel disease)
- EMA – Anti – endomysium antibodies (celiac disease)
- ARA – Anti - reticuline antibodies (celiac disease)
- t-TG - Anti - transglutaminase antibodies IgA, IgG (celiac disease - U/mL)
- AGA – Anti - gliadine antibodies IgA, IgG (celiac disease- U/mL)
- nonspecific signs of gastrointestinal diseases
  - blood count (erythrocytes x1012/L, leucocytes x 109/L, thrombocytes x 109/L)
  - haemoglobin (g/L)
  - iron level (μmol/L)
  - total serum protein level(g/L)
  - C-reactive protein level (CRP - mg/L)

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 bivariate level. Simultaneous effects of the studied variables on the occurrence of psoriasis were studied by binary logistic regression. The point estimates of odds ratios and 95% CI describing the strength of association between independent predictors and Psoriasis are reported. Level of statistical significance in all tests was set to 0.05.

RESULTS

Data for131 cases and 267 controls are available. The main characteristics and the distribution of studied parameters are shown in Tables 1 and 2. Tests of statistically significant differences between cases and controls can be found in both tables.

The comparison revealed statistically significant differences for several variables (Table 1 and 2). Psoriasis cases had higher blood pressure than controls (Fig. 1), a bigger waist circumference and greater BMI (Fig. 2). The cases had a higher leucocyte count (Fig. 3) and titres gliadine IgA antibodies (Fig. 5) as well. In cases, the HDL level (Fig. 4) was significantly lower. Another difference between cases and controls was in glucose concentration

Table 1. Distributions of studied parameters and control comparison.

		Status		Total	OR	95% C.I. pro OR		Sig.
		Control	Case			Lower	Upper	
Gender	Man	136	81	217	1.00			
	Woman	131	50	181	0.64	0.42	0.98	0.040
Total		267	131	398				
ARA	Neg.	266	128	394	1.00			
	Pos.	1	3	4	6.23	0.64	60.52	0.072
Total		267	131	398				
ASCA	Neg.	261	123	384	1.00			
	Pos.	6	8	14	2.83	0.96	8.33	0.050
Total		267	131	398				
AEP	Neg.	265	131	396				
	Pos.	2	0	2	-	-	-	0.321
Total		267	131	398				
pANCA	Neg.	257	126	383	1.00			
	Pos.	10	5	15	1.02	0.34	3.05	0.972
Total		267	131	398				
AGCA	Neg.	255	123	378				
	Pos.	12	8	20	1.38	0.55	3.47	0.489
Total		267	131	398				

Table 2. Distributions of studied parameters and their comparison in controls and cases.

Variable	Status	N	Minimum	Median	Mean	Maximum	Range	Mann-Whitney U Test
Age (years)	Control	267	16.0	40.0	42.7	94.0	78.0	
	Case	130	17.0	39.0	41.7	81.0	64.0	0.969
	Total	397	16.0	39.0	42.4	94.0	78.0	
Systolic blood pressure (mmHg)	Control	267	90.0	120.0	120.4	170.0	80.0	
	Case	131	95.0	130.0	125.8	160.0	65.0	<0.001
	Total	398	90.0	120.0	122.2	170.0	80.0	
Diastolic blood pressure (mmHg)	Control	267	50.0	80.0	82.6	120.0	60.0	
	Case	131	60.0	80.0	82.6	120.0	60.0	<0.001
	Total	398	50.0	80.0	79.1	120.0	70.0	
Waist circumference (cm)	Control	267	60.0	84.0	83.8	102.0	42.0	
	Case	131	64.0	88.0	88.0	102.0	38.0	<0.001
	Total	398	60.0	85.0	85.2	102.0	42.0	
Weight (kg)	Control	267	46.0	74.0	75.3	126.0	80.0	
	Case	131	45.0	79.5	80.7	152.0	107.0	0.006
	Total	398	45.0	75.0	77.1	152.0	107.0	
Height (m)	Control	267	1.5	1.7	1.7	2.0	0.5	
	Case	131	1.3	1.7	1.7	2.0	0.7	0.734
	Total	398	1.3	1.7	1.7	2.0	0.7	
BMI	Control	267	17.6	24.5	24.7	34.5	16.9	
	Case	131	18.0	26.3	26.6	47.3	29.3	<0.001
	Total	398	17.6	24.8	25.4	47.3	29.8	
Leucocytes count ($x10^9$/L)	Control	267	3.5	6.5	6.9	15.4	11.9	
	Case	131	4.4	7.1	7.7	17.2	12.8	<0.001
	Total	398	3.5	6.7	7.2	17.2	13.7	
Erythrocytes count ($x10^{12}$/L)	Control	267	3.3	4.7	4.7	6.0	2.7	
	Case	131	3.2	4.8	4.8	5.9	2.8	0.396
	Total	398	3.2	4.7	4.7	6.0	2.8	
Thrombocytes count ($x10^9$/L)	Control	267	119.0	231.0	232.9	446.0	327.0	
	Case	129	108.0	238.0	243.1	435.0	327.0	0.167
	Total	396	108.0	232.5	236.2	446.0	338.0	

Table 2. Distributions of studied parameters and their comparison in controls and cases. (continued)

Variable	Status	N	Minimum	Median	Mean	Maximum	Range	Mann-Whitney U Test
Haemoglobin level (g/L)	Control	267	99.0	143.0	144.2	174.0	75.0	
	Case	131	101.0	148.0	146.4	181.0	80.0	0.093
	Total	398	99.0	145.0	144.9	181.0	82.0	
Total cholesterol (mmol/L)	Control	267	2.6	5.2	5.3	8.5	5.9	
	Case	131	3.2	5.5	5.4	9.5	6.3	0.372
	Total	398	2.6	5.3	5.3	9.5	7.0	
HDL cholesterol (mmol/L)	Control	267	0.7	1.5	1.5	2.6	2.0	
	Case	131	0.8	1.4	1.4	3.0	2.2	0.002
	Total	398	0.7	1.4	1.5	3.0	2.4	
LDL cholesterol (mmol/L)	Control	267	1.2	3.0	3.1	5.6	4.5	
	Case	131	1.3	3.1	3.2	6.0	4.7	0.167
	Total	398	1.2	3.0	3.1	6.0	4.8	
Triacylgycerol (mmol/L)	Control	267	0.4	1.2	1.5	7.6	7.2	
	Case	131	0.5	1.3	1.6	5.8	5.3	0.258
	Total	398	0.4	1.3	1.5	7.6	7.2	
Glycaemia level (mmol/L)	Control	267	3.1	4.9	4.9	9.4	6.3	
	Case	131	2.8	4.7	4.8	7.9	5.1	0.036
	Total	398	2.8	4.9	4.9	9.4	6.6	
C-reactive protein level (mg/L)	Control	267	0.1	1.7	3.0	26.5	26.4	
	Case	131	0.2	2.0	3.4	31.7	31.5	0.066
	Total	398	0.1	1.7	3.1	31.7	31.6	
Total serum protein level (g/L)	Control	267	63.0	75.0	75.1	88.0	25.0	
	Case	131	55.0	74.0	74.3	86.0	31.0	0.116
	Total	398	55.0	75.0	74.9	88.0	33.0	
Iron level (μmol/L)	Control	267	3.1	17.7	17.5	44.8	41.7	
	Case	131	2.6	16.7	17.6	40.1	37.5	0.925
	Total	398	2.6	17.4	17.5	44.8	42.2	
Anti gliadine antibodies IgA (U/mL)	Control	267	0.2	4.0	4.9	118.0	117.8	
	Case	131	0.0	4.3	5.6	39.5	39.5	0.039
	Total	398	0.0	4.1	5.1	118.0	118.0	
Anti gliadine antibodies IgG (U/mL)	Control	267	0.4	3.9	5.5	73.2	72.8	
	Case	131	0.0	4.3	5.5	26.5	26.5	0.062
	Total	398	0.0	4.1	5.5	73.2	73.2	
Anti-transglutaminase antibodies IgA (U/mL)	Control	267	0.4	2.2	2.0	9.7	9.3	
	Case	131	0.0	2.2	2.1	8.2	8.2	0.655
	Total	398	0.0	2.2	2.1	9.7	9.7	
Anti-transglutaminase antibodies IgA (U/mL)	Control	267	0.2	2.0	2.2	17.9	17.7	
	Case	131	0.0	2.1	2.4	26.3	26.3	0.164
	Total	398	0.0	2.1	2.2	26.3	26.3	

(Fig. 6). Using binary logistic regression psoriasis was positively associated with diastolic blood pressure, BMI value and leucocytosis (Table 3). The association between glucose concentration and psoriasis was negative.

DISCUSSION

The results show significant differences between psoriasis patients and control patients on several parameters: weight, waist circumference, BMI value, leukocytes, titres of gliadin and IgA antibodies, HDL cholesterol and glycemia. The association between psoriasis and diastolic blood pressure, BMI value and glycemia were statistically significant in the binary data logistic model as well.

Psoriasis therefore predisposes patients to hypertension, higher BMI values and lower HDL cholesterol. These parameters belong to the image of the 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) (ref.[15,16]). The finding that psoriasis patients had

Table 3. Binary logistic regress in model of the association between psoriasis occurrence and studied parameters.

		95% C.I. pro OR		
	OR	Lower	Upper	Sig.
Diast. Blood pressure (mmHg)	1.04	1.02	1.07	<0.001
BMI	1.11	1.04	1.18	0.001
Leucocytes count (x 10^9/L)	1.20	1.07	1.34	0.001
Glycaemia (mmol/L)	0.55	0.38	0.78	0.001
Constant	0.01			<0.001

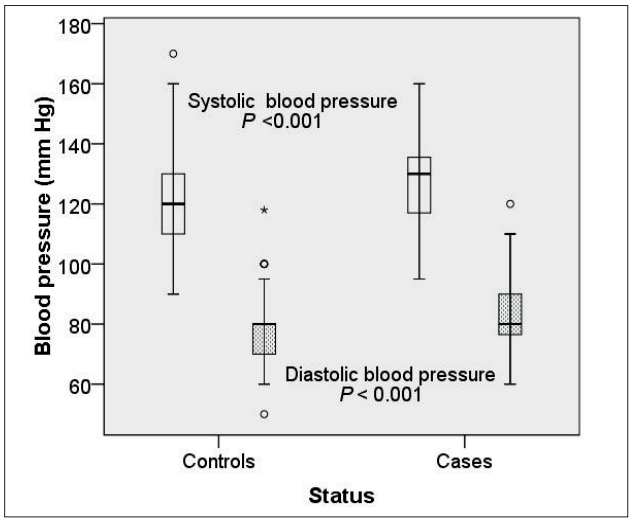

Fig. 1. Blood pressure in psoriatic patients and controls.

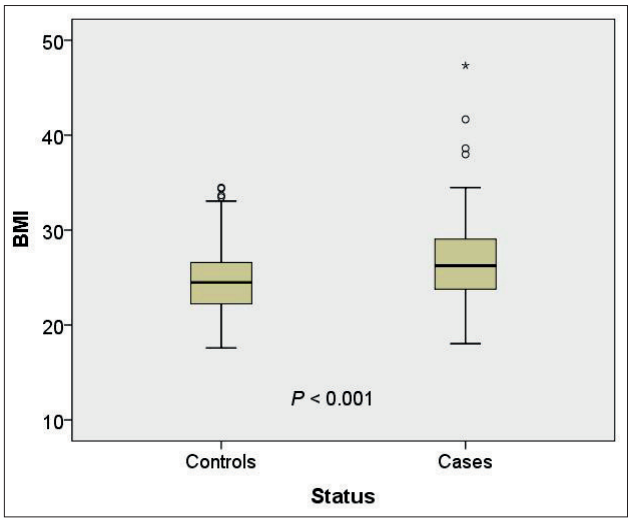

Fig. 2. Body mass index in psoriatic patients and controls.

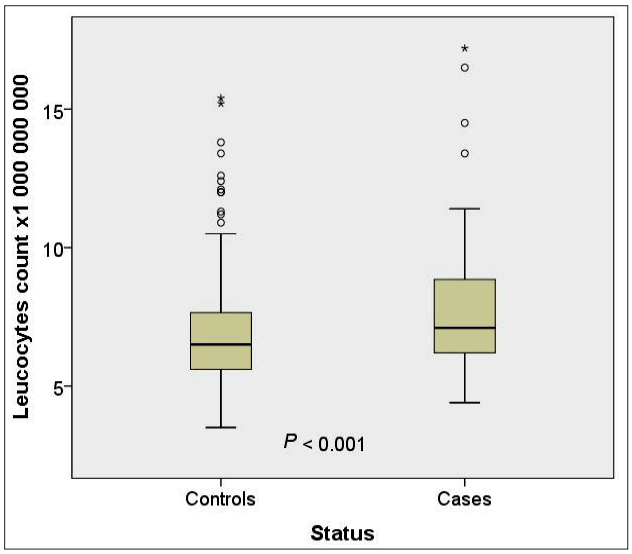

Fig. 3. Leucocytes count in psoriatic patients and controls.

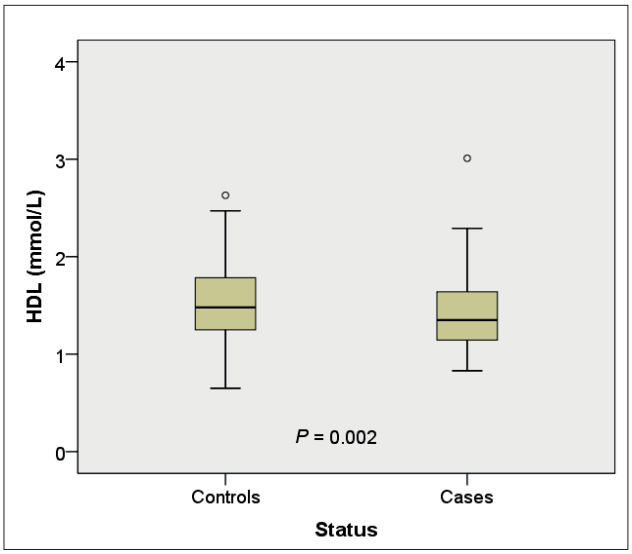

Fig. 4. High density lipoprotein concentrations in psoriatic patients and controls.

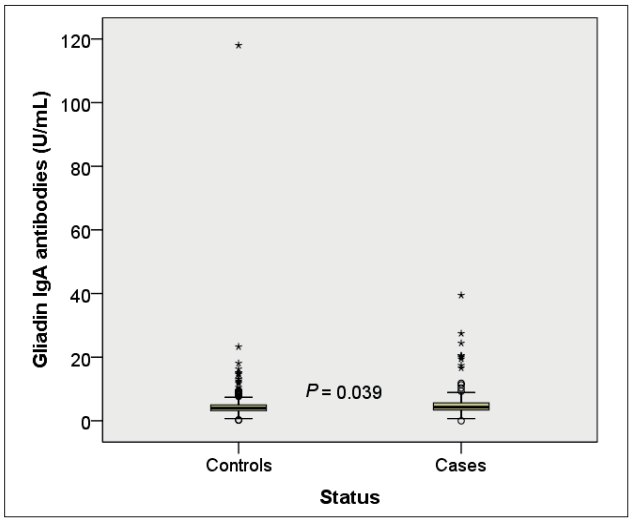

Fig. 5. Gliadin IgA antibodies in psoriatic patients and controls.

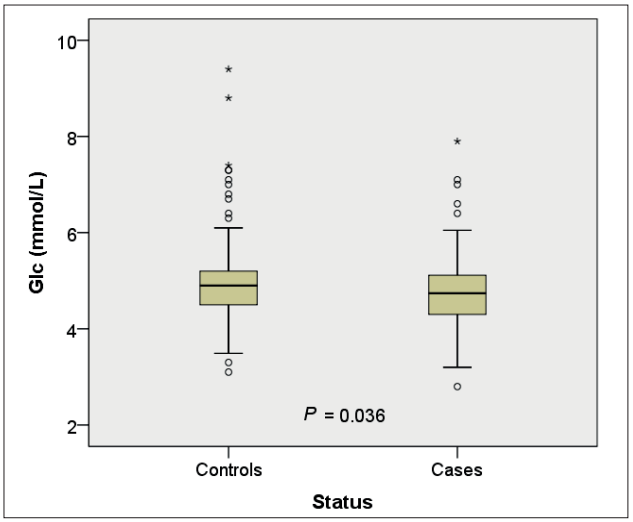

Fig. 6. Glycaemia in psoriatic patients and controls.

higher blood pressure than the control population is consistent with other published studies[17,18].

Significant differences in lipidograms of psoriatic patients and a control population are statistically important only in levels of HDL cholesterol, which is decreased in patients with psoriasis. We consider this finding to be important because the association between psoriasis and this parameter is very robust, given the evidence from the multivariate model. In addition to lower levels of HDL, other studies report elevated total cholesterol levels in psoriasis[19-21] and raised LDL and very low density lipoprotein (VLDL) cholesterol[19-23]. In this study, we also observed higher total cholesterol, LDL cholesterol and triacylglycerols. However, the differences between cases and controls were small and did not reach statistical significance.

Elevated baseline concentrations of CRP are associated with an increased risk of atherosclerotic events and serve as a predictive parameter both in primary and secondary prevention[24]. In this study, the increased levels of CRP in cases are borderline statistically significant (P=0.066).

BMI values as a sign of obesity in psoriatic patients is increased and achieves significance both at binary as well as at multivariate levels of analyses. The finding of higher BMI values correlates with the expectations and is consistent with previously published results[25,26].

Antigliadin antibodies (AGA) are diagnostic markers of celiac disease and several studies have reported an association between psoriasis and AGA, with improvements seen in the severity of psoriasis in patients on a gluten-free diet[27,28]. Our results seem to imply an association between psoriasis and asymptomatic coeliac disease.

Higher values of leukocytes in patients with psoriasis may be interpreted as a non-specific indicator of gastrointestinal diseases. This fact should be interpreted with caution however, as psoriasis is an inflammatory disease, and therefore the increased level of leukocytes may also be caused by skin disorders.

Despite the expectations arising from the published results of a number of studies[18,29,30], a higher level of glycemia was not found in patients with psoriasis in our study.

CONCLUSION

Relatively small differences between cases and controls in this study should be interpreted as a very conservative result, as selection criteria for entering the study decreased differences between cases and controls. Consequently it means that the differences between patients and controls are in fact bigger than described. The Bergson bias leads to distortion towards zero too, which is a consequence of a well-known fact that the hospital controls are often people with a number of risk factors. The results of a study conducted on Czech patients with psoriasis suggest that detection of elevated or pathological values in several investigated parameters reached levels of statistical significance. Therefore, a regular screening of patients with chronic stationary form of psoriasis should become a standard for dermatologists in cooperation with general practitioners. An early diagnostics of these diseases and risk factors greatly improves the future quality of life of the patient and, last but not least, the early treatment of comorbidities reduces the cost of treating complications of these diseases. It is also necessary to ensure the awareness of psoriatic patients about possible associated diseases and increase the patients' awareness that a healthy lifestyle may prevent the development of certain comorbidities.

Dispensary care of patients suffering from psoriasis vulgaris should focus on primary and secondary prevention of diseases, to which it creates a predisposition.

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CONFLICT OF INTEREST STATEMENT

None declared.

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