DYSLIPIDEMIA AND HYPERGLYCEMIA IN PSORIATIC INPATIENTS

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Abstract

Clinical Study

Background: Psoriasis is a chronic cutaneous T-cell mediated disease, which has been associated with many comorbidities, such as metabolic disorders. Specific abnormalities include dyslipidemia, insulin resistance, obesity, and metabolic syndrome, many of which are themselves risk factors for other diseases. The goal of this study was to evaluate the presence of dyslipidemia and hyperglycemia in patients with psoriasis.

Methods: We compared 48 inpatients with plaque psoriasis aged 29-79, hospitalised between March 2018 and February 2019, to 48 age- and gender-matched controls. We evaluated dyslipidemia and hyperglycemia using enzymatic methods as part of a standard blood test or medication history indicative of ongoing treatment of dyslipidemia and/or hyperglycemia. Hypertension was evaluated by registering blood pressure greater than 140/90 mmHg or ongoing antihypertensive treatment. Smoking habits were also noted.

Results: There were statistically significant differences between psoriasis patients and controls for elevated total cholesterol (p=0.028), elevated low-density lipoprotein (LDL) (p=0.015), hypertriglyceridemia (p=0.006), and hyperglycemia (p=0.021). The two groups had statistically insignificant differences for lowered high-density lipoprotein (p=0.084), hypertension (p=1), and smoking (p=0.836).

Conclusion: Hypertriglyceridemia, hyperglycemia, and elevated LDL cholesterol were found to be more prevalent in the group containing psoriatic patients compared to the control group. This indicates that further investigation of metabolic abnormalities should be conducted in psoriatic patients, which could greatly benefit from early treatment of the aforementioned underlying conditions.

KEYWORDS: Psoriasis, Inpatients, Metabolic syndrome, Dyslipidemias, Hyperglycemia

Psoriasis is a chronic immune-mediated skin disorder, with a prevalence of 2% [2]. Tumor necrosis factor alpha, interferon alpha, interleukin 23, and T-helper 17 cells play an important role in the pathogenesis of psoriasis [3]. Recent evidence suggests that metabolic abnormalities are present in the milieu of chronic inflammation, as in the case of rheumatological diseases [4]. Chronic inflammation is thought to cause cytokine-induced changes in glucose and lipoprotein metabolism, alluding to a similar situation that happens in the case of insulin resistance caused by cytokines secreted by adipose tissue [5, 6].

The amount of data on the effect of psoriasis on metabolism is increasing, but various results have been reported. For triglyceride levels, there are studies that found increased levels as well as statistically insignificant changes [7-13]. There are studies that associated psoriasis with higher, and others with normal LDL (low-density lipoprotein) cholesterol levels [7-9, 14-18]. As for HDL (high-density lipoprotein) cholesterol, there are studies that associated psoriasis with lower HDL levels and studies that did not make that association [7, 9, 14-20]. A correlation was reported between psoriasis and diabetes mellitus in some studies, and in other studies, no such correlation was made [7, 8, 15, 19, 21-25]. Results on hypertension and psoriasis were also conflicting, as there are studies that established a link and studies that did not [16, 21].

Quantitative and qualitative changes in lipoprotein metabolism, caused by chronic inflammation, may be of potential clinical significance in patients with a high risk of cardiovascular comorbidity. This study was conducted to examine the correlation between psoriasis and abnormal glucose and lipid metabolism.

Methods

This retrospective study took into account 48 inpatients (27 males, 21 females) with psoriasis vulgaris (placata and nummularis type) aged 29-79, hospitalised in the University Clinic of Dermatology at the Medical Faculty in Skopje, between March 2018 and February 2019. Data were derived from the clinic's inpatient medical records. Psoriatic inpatients that had pustular psoriasis, psoriatic arthritis, erythrodermia, prior systemic treatment for psoriasis, concomitant tumours, chronic lung, heart, kidney, and rheumatological diseases were excluded from the study. These 48 inpatients were paired with another 48 inpatients, matched for age (±1 year) and gender, hospitalised within the same timeframe, and in the same clinic. The exclusion criteria were the same for this group. The diagnoses of the control group inpatients were the following (Figure 1): urticaria acuta (23), reactio anaphylactica (5), reactio allergica post ictus ab insectis (4), erythema multiforme (3), eczema chronicum (3), oedema Quincke faciei (2), erysipelas (2), vasculitis (2) dermatitis arteficialis (1), Linear IgA bullous dermatosis (1), lichen ruber planus (1), and ulcera crurum (1).

The variables of interest were triglyceridemia, LDL cholesterol, HDL cholesterol, glycemia, blood pressure, and smoking habits. Lipid parameters and blood pressure were evaluated according to cutoff values recommended by the National Cholesterol Education Program's Adult

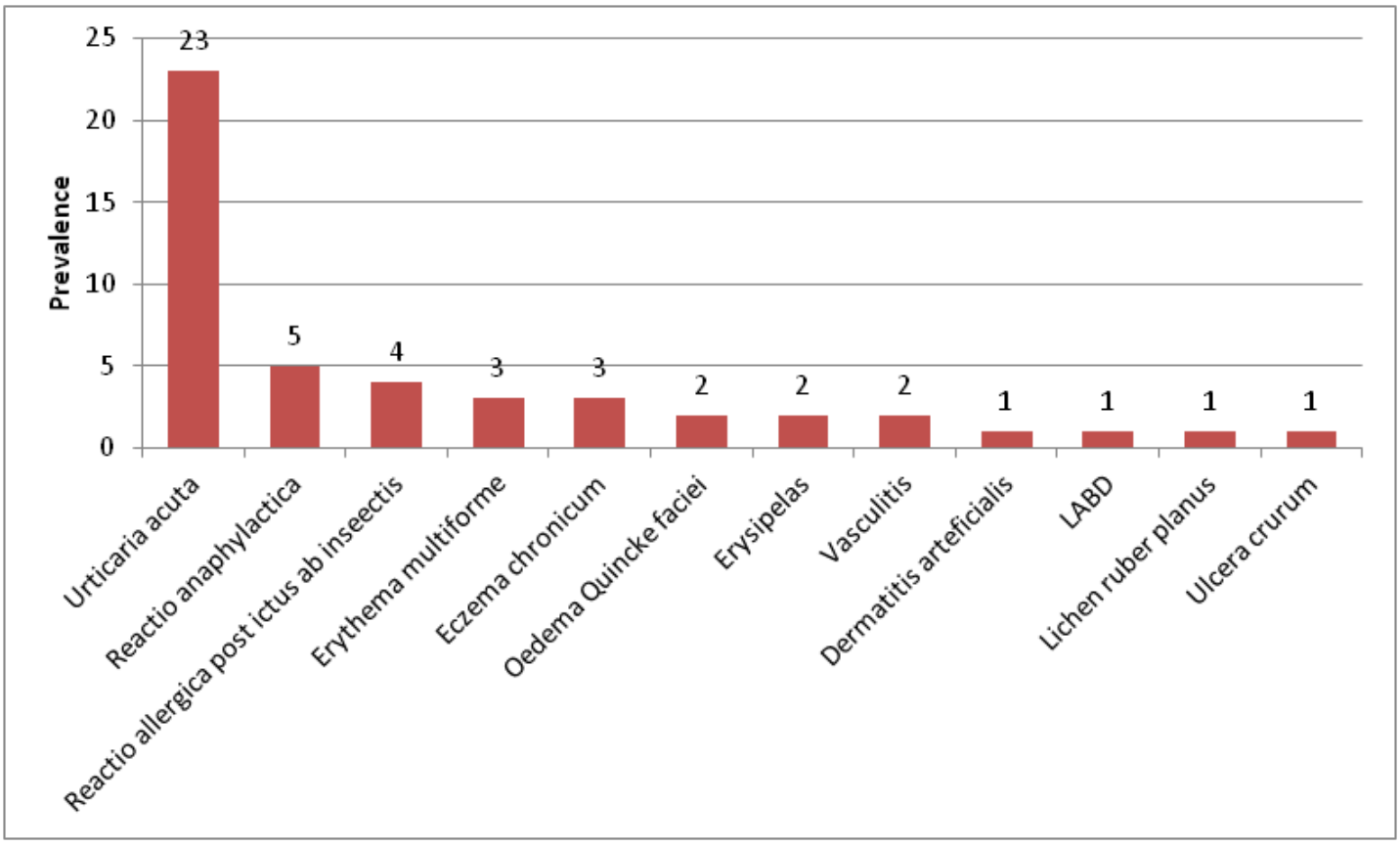

Figure 1: The diagnoses of the inpatients in the control group

Treatment Panel III, or ongoing antilipidemic and/or antihypertensive treatment according to the patient's medical history. These cutoff values were: 1.7 mmol/L for triglycerides, 3.3 mmol/L for LDL cholesterol, 1.0 mmol/L for HDL cholesterol, 140/90 mmHg for blood pressure. Glycemia was evaluated using the cutoff value of 6.1 mmol/L, recommended by the World Health Organization, or ongoing antidiabetic treatment [26]. Smoking habits were evaluated using two categories: patients who are non-smokers, and patients who are currently smoking or have smoked in the past. Glycemia and lipid parameters were measured using enzymatic methods. Blood pressure was measured with a standard mercury sphygmomanometer. RStudio was used to perform a Student's t-test and calculate the odds ratio with a 95% confidence interval.

Results

Among the 48 psoriatic patients, seven were aged between 29-39, 12 were aged between 40-49, 11 were aged between 50-59, 16 were aged between 60-69, and two were aged between 70-80. Identical distributions were present in the control group. In the psoriasis group, 14 patients (29.17%) had hyperglycemia, compared to five (10.42%) in the control group (p=0.021, OR 3.54, 95%CI 1.16-10.81). Hypertriglyceridemia was noted in 16 psoriatic patients (33.33%), and in five patients (10.42%) in the control group (p=0.006, OR 4.30, 95%CI 1.43-12.96). LDL cholesterol was increased in 16 psoriatic patients (33.33%), compared to 6 (12.5%) control patients, (p=0.015, OR 2.14, 95%CI 0.50-9.12). The differences between the psoriasis group and the control group were statistically insignificant for the remaining parameters. Ten (20.83%) psoriatic inpatients had lowered HDL cholesterol, compared to four (8.33%) control patients (p=0.084, OR 2.89, 95%CI 0.84-9.98). In the psoriasis group, 19 patients (39.58%) reported to have smoked or were current smokers, compared to 16 (33.33%) in the control group (p=0.836, OR 1.31, 95%CI 0.57-3.02). Finally, 16 patients in each group were found to have hypertension (p=1, OR 1.00, 95%CI 0.43-2.34) (Table 1).

Discussion

Despite the conflicting findings of the current body of research on this topic, there is a complex pathophysiological explanation for the quantitative and qualitative changes in the case of rheumatological diseases, which may also be true for psoriasis. Proinflammatory cytokines released during the course of these diseases change many aspects of lipid metabolism, such as increased very-low-density lipoproteins and triglyceride levels via increased hepatic fatty acid synthesis, decreased hepatic fatty acid oxidation, and increased adipose tissue lipolysis. This ultimately contributes to the increase of triglyceride content in LDL and HDL particles, which subsequently leads to the formation of small dense LDL particles. These particles are more atherogenic as a result of their high susceptibility to oxidation, high affinity for intra-arterial proteoglycans, and decreased clearance due to reduced affinity for LDL receptors. Additionally, lipoprotein lipase activity is reduced, which further reduces the clearance of LDL particles [4].

HDL particles are also subject to change in an inflammatory milieu, which equates to reverse cholesterol transport being severely impacted as a result. Apolipoprotein A-1 (Apo A-1) clearance is increased due to decreased synthesis and increased breakdown in the kidneys, which both lead to a lower affinity of Apo A-1 for HDL particles. Serum amyloid A, an acute-phase protein generated during inflammation, binds to HDL particles, which lowers the affinity of Apo A-1 for its receptor, and increases the clearance of HDL particles. Cholesterol ester transfer protein and lecithin-cholesterol acyltransferase levels are decreased, which lead to decreased cholesterol transport from HDL particles and decreased cholesterol ester

formation, respectively. Certain phospholipid and cholesterol membrane transport proteins, such as ATP-binding cassette transporter (ABC) A1, ABCG1, and scavenger receptor B1, have reduced activity, contributing to decreased hepatocyte uptake and decreased efflux from macrophages. Finally, lipoprotein (a) is generated, which has a high atherogenic potential [4]. This evidence of qualitative changes in lipoproteins suggests that perceived normal lipid levels may not be enough to exclude abnormalities in lipid metabolism.

The inflammatory pathogenesis of psoriasis suggests that, skin and joint lesions aside, many more less visible metabolic effects may be present. Psoriasis causes slight but clinically actionable alterations in certain metabolic parameters, which are relevant in terms of cardiovascular comorbidity.

This study could be improved by increasing the sample size to increase the accuracy of the data and to narrow down the confidence intervals. An important drawback represents its retrospective design. The data gathered were only the parameters that are measured during a routine examination. Additional useful parameters such as the Psoriasis Area and Severity Index and highly sensitive quantification of C-reactive protein to determine the extensiveness of the psoriatic lesions and the cardiovascular risk, respectively, could be measured and tested more appropriately in a case-control scenario.

Another aspect not covered in this study is disease progression. Our results are only indicative of one point in time, and the history of disease progress and treatment for each individual patient is unknown. Five of the previously mentioned studies stated that their objective was to determine the prevalence specifically of metabolic syndrome in psoriatic patients [15, 19, 21, 23, 24, 27]. Four of them associated psoriasis with metabolic syndrome, and one found no such link [15, 19, 21, 23, 24]. One of these previously mentioned studies established a dose-response relationship between the severity of psoriasis and the prevalence of metabolic syndrome, while another disproved that [24, 27]. One meta-analysis, taking 12 studies into account, also established a dose-response relationship [5]. These diverse findings pertaining to the metabolic syndrome, combined with the aforementioned diverse results on individual metabolic parameters, indicate that many other factors, such as the age of onset, duration, disease severity, and treatment, may play a role in terms of the order in which metabolic changes appear, and in the way they evolve over time.

Conclusion

The inflammatory pathogenesis of psoriasis suggests that skin and joint lesions aside, many more less visible metabolic effects may be present. Psoriasis causes slight but clinically actionable alterations in certain metabolic parameters, which are relevant in terms of cardiovascular comorbidity.

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Disclaimer

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Table 1: Quantitative outcomes between the intervention group and the control group

Parameter	Psoriasis	Controls	p-value	OR (95% CI)
Mean age	52,92	52,73	/	/
Sex (male/female)	27/21	27/21	/	/
Smokers	19	16	0,836	1.31 (0.57-3.02)
↑ gly	14	5	0,021	3.54 (1.16-10.81)
↑ TAG	16	5	0,006	4.30 (1.43-12.96)
↓ HDL	10	4	0,084	2.89 (0.84-9.98)
↑ LDL	16	6	0,015	2.14 (0.50-9.12)
↑ BP	15	16	1	1.00 (0.43-2.34)

Legend: OR - odds ratio, CI - confidence interval, ↑gly - hyperglycemia, ↑TAG - elevated triglycerides, ↓HDL - lowered HDL cholesterol, ↑LDL - elevated LDL cholesterol, ↑BP - hypertension

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CORRECT ANSWERS TO THE EXAM QUESTIONS

Answer question 1:
B. Fungal infections

Administration of the antibodies will lead to immunosuppression. The host's immune response against fungal infections is mostly regulated by neutrophilic granulocytes. These granulocytes are stimulated by the secretion of IL-17 by Th17-cells. Viral infections, on the other hand, are mediated by cytotoxic T-lymphocytes and natural killer cells.

For further reading:
Parham, P. Chapter 8: T-cel mediated immunity in The immune system, 4th edition. (Garland Science, New York, 2015)

During the exam, 87% of the participants answered this question correctly.

Answer question 2:
B. Primary EBV-infection

After the presentation of an antigen, the B-lymphocytes first produce IgM, which forms the start of the immune response. During the ongoing infection, IgG is formed through isotype switching, resulting in long-term immunity.

For further reading:
Parham, P. Chapter 4: Antibody Structure and the Generation of B-Cell Diversity in The immune system, 4th edition. (Garland Science, New York, 2015)

During the exam, 60% of the participants answered this question correctly.

The exam questions can be found back on page 10 in this journal.