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Serum pancreatic lipase [EC 3.1.1.3] activity, serum lipid profile and peripheral blood dendritic cell populations in normolipidemic males with psoriasis

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Abstract

The purpose of the study was to explore serum pancreatic lipase activity and the serum lipid profile in relation to peripheral blood dendritic cell subsets and disease severity in males with psoriasis.

Material and methods: The study population consisted of 22 normolipidemic males with psoriasis and 12 aged-matched and body mass index (BMI)-matched healthy males. The percentages of peripheral blood dendritic cell (DC) subsets were evaluated using appropriate monoclonal antibodies and flow cytometry. The serum pancreatic lipase activity and the lipid profile were determined using standard enzymatic and colorimetric techniques.

Results: Pancreatic lipase activity was increased ($p = 0.56421$), high-density lipoprotein (HDL)-cholesterol concentration ($p = 0.00584$) was significantly decreased, triglyceride ($p = 0.00766$) and VLDL-cholesterol ($p = 0.00765$) levels were significantly increased in serum of psoriatic patients compared to controls. The serum pancreatic lipase activity showed significant correlation with serum triglyceride ($r = 0.42$; $p = 0.04721$) and serum VLDL-cholesterol levels ($r = 0.42$; $p = 0.04721$) in psoriatic individuals. In psoriatic patients the percentage of myeloid DCs was increased ($p = 0.54932$), the percentage of lymphoid DCs was decreased ($p = 0.14210$) and myeloid DC/lymphoid DC ratio was significantly increased ($p = 0.03569$) compared to healthy individuals.

Conclusion: The direct cause of the abnormal lipid profile in psoriasis and its relationship with the immune system disturbances remains unclear. The reciprocal relationship between serum pancreatic activity and serum triglyceride level appears to confirm the hypothesis about abnormal lipid metabolism in psoriasis.

Keywords: Psoriasis; Pancreatic lipase; Lipids; Dendritic cells

1. Introduction

Psoriasis remains the common skin disease of unclear pathogenesis [1–3]. So far a substantial number of working hypotheses on biochemical, immune or genetic disorders have been proposed [1,4–6]. The future pathogenic concepts should try to combine different mechanisms.

There is a large body of literature concerning serious disturbances of lipid metabolism in the course of psoriasis, both at the level of involved epidermis and in peripheral blood [3–5,7–28]. However, it is still difficult to state whether it is primary event or secondary one to the disease onset, or perhaps due to consequences of its treatment [23,29,30]. The changes in lipid composition may be the result of aberrations in local lipolytic enzyme activity as well as of systemic lipid metabolism deviation. One should remember that the skin has the capacity to biosynthesise, convert and metabolise a variety of lipids, which may be implicated in abnormal lipid metabolism in psoriasis [7,30]. For example, psoriatic scales contain increased concentration of cholesterol and decreased concentration of free fatty acids in comparison to normal skin [31]. The loss of cholesterol with scales during the active disease was estimated at 1–2 g/day [32], whereas healthy skin secretes about 85 mg of

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cholesterol [33]. Interestingly, infectious agents may also contribute to anomalies of skin lipids. *Malassezia furfur*, which is present in many patients suffering from psoriasis, was found to secrete the enzyme possessing phospholipase A2 activity [34].

Considering serum lipid and lipoprotein pattern, many disorders have been revealed in psoriasis; including the most common findings of decreased concentration of high-density lipoprotein (HDL)-cholesterol [3,4,19,21–24,26–28], increased concentration of triglycerides [3–5,18,21,23,24,26,27] and/or low-density lipoprotein (LDL)-cholesterol [15,16,21,23,28], high levels of apolipoprotein B [3,14,18,19,23] or decreased apolipoprotein AI concentration [14,23]. Looking for the reasons of these changes, a variety of different factors and mechanisms should be taken into account. Many organs contribute to lipid metabolism, of which the most important are liver and pancreas. It should be stressed that both psoriatic and non-psoriatic pathology of these organs may affect a serum lipid profile. As for the liver, impaired hepatic enzyme function, unrelated to other factors, such as obesity, viral infection, medication or alcohol overconsumption, has been indicated in the course of psoriasis [35]. By contrast, according to Mingrone et al. [36] lipid synthesis is intensified in the liver of psoriatics; the phenomenon was documented by increased uptake of C14-labelled acetylocoenzyme A by hepatic lipids. Pancreas is another organ, which is essential in lipid metabolism. Exocrine pancreatic enzyme, lipase (triacylglycerol ester hydrolase, EC 3.1.1.3), plays the key role in dietary fats digestion and absorption. It is responsible for catalysing the breakdown of fats and oils in the intestinal lumen with subsequent release of free fatty acids, diacylglycerols, monoglycerols and glycerol [37,38]. Besides, lipases are also involved in various reactions, such as estrification, transestrification and aminolysis in organic solvents [38]. Psoriasis has been reported to disturb normal function of pancreas, especially high prevalence of low glucose tolerance and diabetes mellitus has been noted [39]. There is only few data concerning the activity and significance of pancreatic lipase (EC 3.1.1.3) in psoriasis [24,40]. The results of our previous research on this enzyme in psoriatics suggest the possible relationship between pathological psoriatic processes and excretory function of pancreas [20,41]. Since pancreatic lipase is essential for lipid metabolism, the current study tried to analyse the enzyme activity with regard to the serum lipid profile. The issue is particularly interesting in the context of a large body of literature concerning complex and difficult to explain alterations in serum lipids in the course of psoriasis [3–5,13–28,42,43].

Immune system disturbances are another factor considered to have extremely important implications for the pathogenesis of psoriasis. Potential disorders associated with pathological processes within involved skin include epidermal expression of chemokines recruiting immune cells into the skin, synthesis and release of pro-inflammatory mediators by activated immune cells or abnormal function of the immune synapse resulting in the emergence of self-reactive T cells. T lymphocytes and dendritic cells (DCs) seem to be most consistently linked to these events [6,44], and the latter are particularly interesting subject of current research. Dendritic cells play an important role in human immune system. These potent professional antigen-presenting cells are responsible for the initiation of immune response and probably for its polarisation toward a Th1 or Th2 profile [45,46]. Noteworthy, psoriasis is considered to be a Th1 disease [6]. A detailed investigation has revealed that human tissues contain distinct subpopulations of DCs, differing at the level of precursor cells, factors influencing growth and maturation, phenotype and function [46,47]. DC subsets, present both in the skin and peripheral blood, are derived from two lineages: myeloid or lymphoid and display different biological features [45,48].

Little is known about mutual relationship between the immune system and lipid metabolism; thereby effects of different lipid fractions on DCs in general and during the course of psoriasis in particular remain unclear. Recently dyslipidemia associated with atherosclerosis has been demonstrated to modulate DC function [49–51]. Furthermore, Weatherill et al. [52] and Zeyda et al. [53] have reported that saturated and polyunsaturated fatty acids differentially alter DC function. Since psoriasis is characterised by complex abnormalities in serum lipids and these molecules may be the potential source of reactive oxygen species, known to trigger changes in DC migration and function [54], the current study addressed the question about the distribution of blood DC subpopulations in the course of disease and its relationships with serum lipids.

Thus, the present study aimed to evaluate: (a) serum pancreatic lipase activity, (b) serum lipid levels, (c) subpopulations of peripheral blood dendritic cells, (d) reciprocal relation between studied parameters and (e) their relationships with disease severity in males suffering from psoriasis.

2. Material and methods

2.1. Subjects

The study comprised 22 normolipidemic males with active psoriasis vulgaris hospitalised in the Department of Dermatology, Medical University of Lublin, Poland. Inclusion criteria for the study were serum levels of total cholesterol <240 mg%, LDL-cholesterol <135 mg% and total triglycerydes <200 mg%. Values of total cholesterol <240 mg/dl were considered as normolipidemic, since the referential studies performed by local diagnostic centres had demonstrated higher total cholesterol levels in Lublin and nearby rural region compared to other parts of Poland [20,55]. Additional exclusion criteria included concomitant diseases potentially disturbing lipid metabolism (i.e. cardiovascular diseases, hypertension, diabetes mellitus, thyroid gland disorders, nephrotic syndrome, chronic kidney failure and obstructive liver disease) and a recent history of infections. Besides, none of the enrolled patients had received any topical treatment for at least 2 weeks, and any systemic medication known to affect lipid metabolism or evaluated immunological parameters for 2 months preceding the study. Informed consent was obtained from every participant and the study protocol was approved by the Ethics Committee at Medical University of Lublin.

The patients' age ranged from 18 to 64 years (32.27 ± 13.12 [mean value $\pm$ standard deviation]), with body weight ranging

from 54 to 95 kg (71.14 ± 10.58) and body mass index (BMI) ranging from 18.21 to 31.61 kg/m^2 (23.66 ± 3.94). Duration of the disease varied from 2 to 540 months (160.41 ± 149.45). The extent and severity of psoriasis was determined by the same investigator according to the Psoriasis Area and Severity Index (PASI) score and ranged from 10.20 to 48.00 (27.02 ± 7.68). The percentage of affected skin surface, calculated by using the rule nines, was 12–90% (35.98 ± 21.32). Twelve of the patients were smokers and declare smoking from 5 to 20 cigarettes per day. Eleven individuals were teetotallers, and alcohol consumption of the other 11 varied between 0.25 and 4 l of beer per month. The control group consisted of 12 healthy male volunteers fulfilling the required inclusion criteria, of ages ranging from 21 to 57 years (28.58 ± 9.93), body weight ranging from 50 to 90 kg (74.33 ± 10.37) and BMI varying between 17.71 and 28.41 kg/m^2 (24.10 ± 3.06). Six of them were smokers (3–20 cigarettes per day). Two persons were teetotallers and alcohol consumption of the other 10 varied between 0.1 and 4 l of beer per month. All participants were instructed to maintain their normal diet and drinking and smoking habits before the samples were taken. Systolic and diastolic blood pressure were measured with an electronic sphygmomanometer, in the lying position, after a rest period of 15 min; and were similar for both groups: patients 125.05 ± 16.46/79.00 ± 11.22 mmHg and controls 123.92 ± 14.85/79.25 ± 7.53 mmHg.

2.2. Collection and preparation of blood samples

Venous blood samples were taken after a 14-h overnight fast; moreover, participants were obliged not to smoke in the morning when the samples were drawn. Specimens were collected into tubes both without and with anticoagulant (EDTA and heparin) and immediately processed. Blood samples without anticoagulant were clotted, and then centrifuged for 15 min. Obtained serum samples were stored frozen at −20 °C until the time of analysis (no longer than 3 months). Anticoagulated blood was used for analysis of immune cell subpopulations.

2.3. Determination of serum pancreatic lipase (EC 3.1.1.3) activity

Pancreatic lipase (EC 3.1.1.3) activity in blood serum was determined by Enzyline® Lipase Color (BioMérieux, France). The kit enables the kinetic measurement of lipase activity in human serum using 1,2-diglyceride as a substrate [56,57]. The measurement was performed using Konelab 30 & 60 apparatus (BioMérieux) with Zymotrol® (BioMérieux) as reference. Intra-assay coefficient of variation at 38 U/l (control plasma) was estimated at 2.0% ($n = 3$) and inter-assay coefficient of variation at 19 U/l (control plasma) was 4.0% ($n = 3$). The detection limit was ≤1 U/l.

2.4. Serum lipid profile analysis

The serum concentrations of lipid parameters were assessed using standard enzymatic–colorimetric techniques. The serum levels of triglycerides and total cholesterol were measured with commercially available tests: Triglycérides Enzymatique PAP 150 (BioMérieux) and Cholestérol Enzymatique PAP (BioMérieux), respectively. Serum HDL-cholesterol was determined using ready-made reagent kit: HDL Cholestérol/Phospholipides (BioMérieux). Supernatant containing HDL fraction was obtained by precipitation of other lipoproteins with phosphotungstic acid in the presence of magnesium ions. Serum LDL-cholesterol was assessed in the fraction precipitated with amphipathic polymers with the use of commercial LDL Cholestérol/Phospholipides kit (BioMérieux). All analytical procedures were performed precisely according to manufacturer's recommendations. Spectrophotometer SPEKOL 11 (Carl Zeiss Jena, Germany) was used for the experiment; absorbance was determined at 500 nm wavelength. Serum VLDL concentration was calculated according to the formula: VLDL-cholesterol = triglycerides/5.

2.5. Analysis of blood dendritic cell subpopulations

Whole blood cell counts were measured using an automated haematology blood analyser Cell-Dyn 3700 (Abbott, USA). The mononuclear cells were isolated from heparinised blood by density gradient centrifugation on Lymphoprep (Nycomed, Norway) and next washed twice in phosphate-buffered saline (PBS) without Ca^{2+} and Mg^{2+} containing 0.5% bovine serum albumin (BSA) and 2 mM EDTA. The absolute number of peripheral blood mononuclear cells was calculated as the sum of lymphocyte and monocyte counts. The count of DCs was expressed as the percentage of the mononuclear cells. The phenotypes of DC populations were analysed with double-colour flow cytometry using following monoclonal antibodies: mouse anti-human BDCA-1-FITC (Miltenyi-Biotec, Germany), CD19-CyChrome (Pharmingen, USA), BDCA-2-FITC (Miltenyi-Biotec), CD123-PE (Becton Dickinson, USA). The staining procedure was performed according to the manufacturers' recommendations in the presence of FcR Blocking Reagent (Miltenyi-Biotec), to minimise non-specific FcR-monoclonal antibody binding. The immunolabelled cells were collected (300,000 events) using a FACSCalibur flow cytometer equipped with 488-nm argon laser (Becton Dickinson) and analysed with Cell-Quest Software. Myeloid DCs were defined as BDCA-1 positive and simultaneously CD19 negative cells, whereas lymphoid DCs as double BDCA-2 and CD123 positive cells, as described by Dzionek et al. [58].

2.6. Statistical analysis

Statistica 6.0 PL software was applied to statistical procedures. As the obtained data did not fit a normal distribution, numerical variables from the patients' and the control groups were compared using the Mann–Whitney *U*-test. Relationships among variables were assessed using Spearman's rank-order test. The results were expressed as mean value ± standard deviation, the p-value of <0.05 was considered significant.

Table 1
Serum pancreatic lipase activity and lipid levels in patients with psoriasis ($n = 22$) and control subjects ($n = 12$)

	Mean value ± S.D.	Minimum–maximum	p-Value
Pancreatic lipase (U/l)			0.56421
Psoriasis	23.45 ± 10.57	7.00–49.00	
Control	20.67 ± 8.63	6.00–35.00	
Triglycerides (mg/dl)			**0.00766***
Psoriasis	**111.93 ± 37.92**	**44.20–165.80**	
Control	**75.60 ± 34.94**	**40.60–153.50**	
Total cholesterol (mg/dl)			0.70513
Psoriasis	179.25 ± 32.79	120.00–234.20	
Control	182.03 ± 23.82	146.30–222.00	
HDL-cholesterol (mg/dl)			**0.00584***
Psoriasis	**50.05 ± 9.50**	**37.30–69.10**	
Control	**62.88 ± 12.97**	**43.30–87.70**	
LDL-cholesterol (mg/dl)			0.66542
Psoriasis	99.56 ± 23.22	63.90–129.60	
Control	96.16 ± 19.30	59.30–121.70	
VLDL-cholesterol (mg/dl)			**0.00765***
Psoriasis	**22.39 ± 7.58**	**8.84–33.16**	
Control	**15.12 ± 6.99**	**8.12–30.70**	

* $p < 0.05$ was accepted as statistically significant.

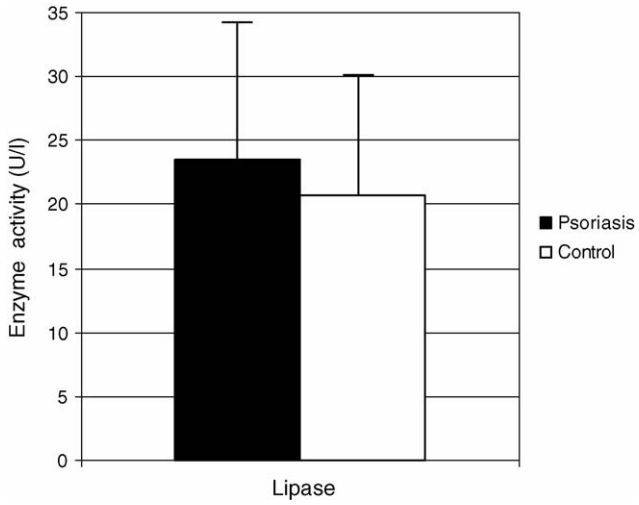

Fig. 1. Serum pancreatic lipase (EC 3.1.1.3) activity in psoriatic and control groups (mean value ± standard deviation).

3. Results and discussion

Pancreatic lipase activity and the levels of lipid parameters in serum of psoriatic patients and control subjects are summarised in Table 1.

As seen in Table 1 and Fig. 1, there is a slight tendency towards increased activities of serum pancreatic lipase in psoriatic group, but they do not differ significantly from those of control group. Corresponding phenomenon was observed in previous studies performed by our department. Toruniowa et al. [20] demonstrated a significant increase in serum pancreatic lipase concentration in normolipidemic males with psoriasis compared to carefully matched control group ($p < 0.05$). Moreover, Pietrzak and Lecewicz-Toruń [24] reported changes in EC 3.1.1.3 activity in normolipidemic psoriatics, observed an interesting gender difference. There was insignificant increase in the studied enzyme activity in psoriatic group. However, evaluation concerning gender criterion revealed significantly higher pancreatic lipase activity in psoriatic females than in appropriate control group and less pronounced increase in the enzyme activity in psoriatic males compared to respective control group (insignificant) [24]. The latter result is in full accordance with the present findings. Other studies regarding pancreatic secretion in psoriasis were confined to initial trials of the disease management by the administration of various pancreatic enzymes, including lipase [40]. Combes and Reisch [40] had found that lipase given orally had no effect on the blood level of native enzyme or serum lipids. Furthermore, the authors did not observe any significant improvement following the administration of enzyme preparation. To the best of our knowledge no other reports on serum pancreatic lipase activity in psoriasis have been

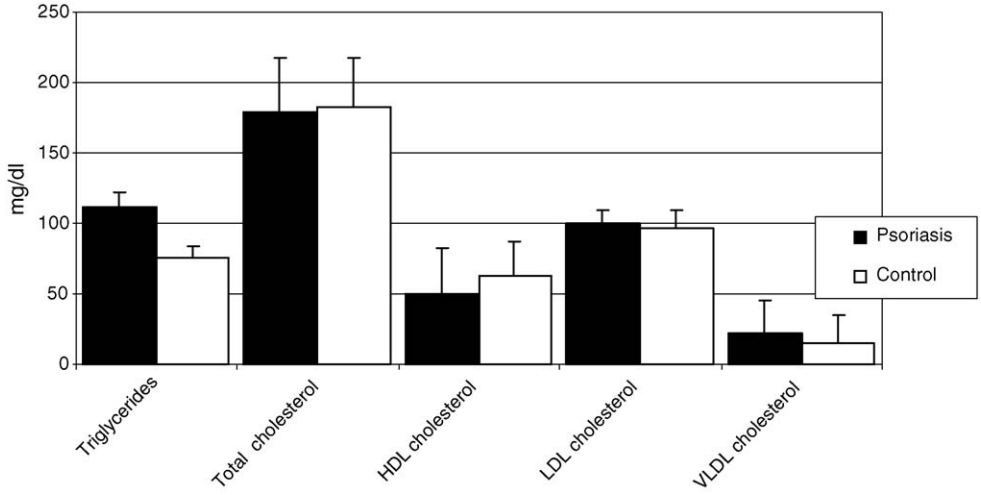

Fig. 2. Serum levels of triglycerides, total cholesterol, HDL-cholesterol, LDL-cholesterol and VLDL-cholesterol in psoriatic and control groups (mean value ± standard deviation). * $p < 0.05$ was accepted as statistically significant.

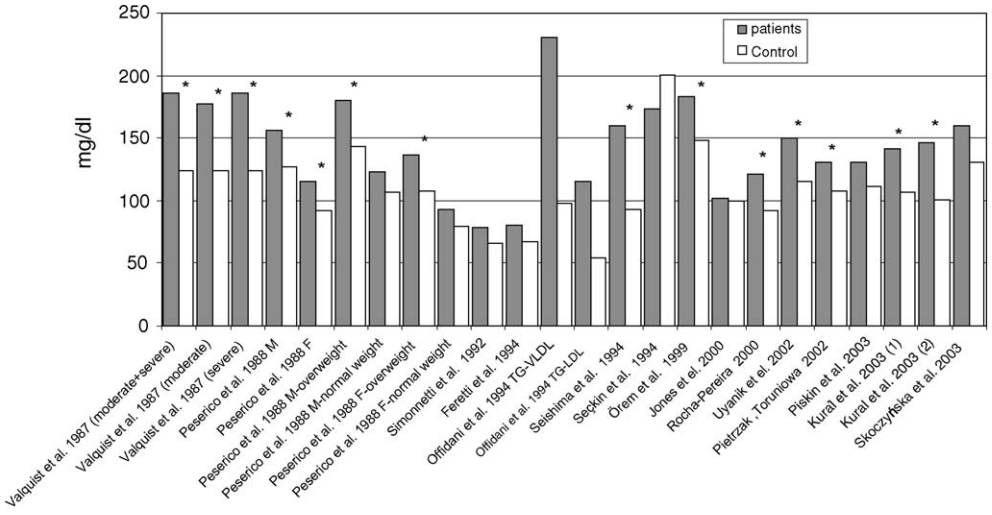

Fig. 3. Diagram illustrating mean triglyceride concentrations detected in previous studies analysing the lipid profile in patients suffering from psoriasis. The studies marked with asterisks noted significant differences between data from the psoriatic and control groups. If the values were expressed in mmol/l, they were converted into mg/dl according to the formula: mmol/l = g/l × 1.1293 [75].

presented, despite growing evidence in support of diverse abnormalities occurring in the digestive system in the course of the disease [41,59]. The direct cause of observed increase in EC 3.1.1.3 activity in psoriatics remains to be elucidated, it may be connected to disease-related pathological inflammatory condition of pancreas but probably it results from more complex disorders; for example, excretory hyperfunction of the organ due to excessive loss of lipids with psoriatic scales. Since the pancreas substantially contributes to lipid metabolism [37,38], there may be a functional relationship between the pancreatic lipolytic enzyme and a serum lipid profile.

The results of the current lipid profile analysis, presented in Table 1 and Fig. 2, seem to be on a close parallel with data published so far. Particularly marked are increases in serum triglyceride and VLDL-cholesterol levels ($p = 0.00766$ and 0.00765, respectively) and a decrease in serum HDL-cholesterol level

Table 2
Description of the study groups examined in previous studies analysing the lipid profile in patients suffering from psoriasis

First author (year)	Reference	Gender	Body mass index (kg/m^2)			
			Psoriasis group		Control group	
			Mean value ± S.D.	Range/comment	Mean value ± S.D.	Range/comment
Vahlquist (1987)	[4]	M	–	–/1.04[a] –/1.12[a]	–	–/0.99[a]
Peserico (1988)	[5]	M	26.25 ± 3.60	–	25.12 ± 3.12	–
		F	25.76 ± 5.12		25.03 ± 4.39	
Simonetti (1992)	[15]	M + F	–	–	–	–/non-obese
Ferretti (1994)	[16]	M + F	18.70 ± 2.70	–	16.60 ± 3.00	–
Offidani (1994)	[17]	M	–	–	–	–
Seishima (1994)	[18]	M	–	–	–	–
Seçkin (1994)	[19]	M	–	–/obese (2) + non-obese (30)	–	–/non-obese
Toruniowa (1997)	[20]	M	24.29 ± 3.30	–	23.17 ± 2.23	–
Örem (1999)	[21]	M + F	23.10 ± 4.80	–	23.40 ± 3.70	–
Jones (2000)	[22]	M + F	25.80 ± 5.60	–	24.60 ± 4.70	–
Rocha-Pereira (2000)	[3]	M + F	–	–	–	–/BMI-matched
Uyanik (2002)	[23]	M + F	–	–/<28	–	–/BMI-matched
Pietrzak and Lecewicz-Toruń (2002)	[24]	M	24.43 ± 3.25	18.62–33.02	23.25 ± 2.37	18.21–27.70
		F	23.25 ± 5.76	14.57–38.20	20.96 ± 1.98	17.97–25.16
Piskin (2003)	[25]	M + F	–	–/<30	–	–
Kural (2003)	[26]	M + F	–	–	–	–
Kural (2003)	[27]	M + F	–	–	–	–
Skoczyńska (2003)	[28]	M + F	–	–	–	–

–, no data; M, male participants; F, female participants; M + F, the study groups including both sexes.
[a] Broca's index—calculated according to formula: Broca's index = weight (kg)/height (cm) − 100.

($p = 0.00584$). As for a decrease in serum total cholesterol level and an increase in serum LDL-cholesterol level, the detected differences were not statistically significant (Table 1). Although previous studies on serum lipids in the course of psoriasis have reported divergent and sometimes conflicting findings, most authors agree that changes in lipid composition seem to be of atherogenic and prothrombotic character [3,26,60,61].

More specifically, the majority of researchers observed a significant increase in serum triglyceride concentration in psoriatic patients compared to healthy individuals [3–5, 18,21,23,24,26,27]. Several of them noted just a modest rise [15,16,22,25,28] whereas Seçkin et al. [19] detected slightly lower serum trigliceryde levels in psoriatics than in comparable controls (Fig. 3). Considering serum triglyceride levels, results of the current analysis remain fully consistent with findings published by Vahlquist et al. [4] and Seishima at al. [18], and additionally they confirm the findings of our previous investigation [24]. There is also a considerable similarity between the present study and studies by Örem et al. [21], Rocha-Pereira et al. [3], Uyanik et al. [23] and Kural et al. [26,27]. However, these authors performed analysis combining both sexes, whereas our investigation pertained exclusively to males with active psoriasis (Table 2). It should be highlighted that in studies combining both sexes female participants may mitigate serum lipid changes [62], which would be more noticeable if the examination comprehended only males. Thus, ignoring the differences in lipid referential values between sexes and analysing female and male participants collectively may considerably change the results. There are numerous reasons for hypertriglyceridemia. The raised triglyceride level may result from congenital lipid metabolism disorders, and the detailed classification of primary hypertriglyceridemia is based on lipoprotein phenotype and genetic defects [63]. Secondary hypertriglyceridemia, by contrast, may be caused by a whole panoply of factors; of which the most common are presented in Table 3. Indeed, to attribute the condition to psoriasis, other reasons, especially causative factors for secondary hypertriglyceridemia, have to be eliminated. Furthermore, "psoriatic hypertriglyceridemia" may be inextricably related to the study design or mode of the data analysis, not to real changes in serum triglyceride concentration. For example, some studies tend to make a direct comparison between patients' group consisting of individuals with normal and abnormal lipid profiles and normolipidemic control group, or compare obese psoriatics with non-obese healthy individuals (Table 2). Other reasons include a fair number of individuals with latent abnormal glucose tolerance or alcohol abuse among patients recruited for the study.

Even more controversy exists regarding total cholesterol level and concentration of separate cholesterol fractions in serum of patients suffering from psoriasis. The current investigation showing an insignificant decrease of total cholesterol in male psoriatics compared to healthy individuals is in general agreement with the results of Seishima at al. [18], Seçkin et al. [19], Jones et al. [22], Skoczyńska et al. [28] and our previously reported data [24]. Other authors have documented that serum total cholesterol concentration in psoriasis may be markedly decreased [5] or quite the contrary it may be increased

Table 3
Genesis of hypertriglyceridemia

Factors contributing to hypertriglyceridemia	Reference
Extrinsic	
Inappropriate diet	[63,76]
Excessive alcohol intake	[13,76]
Medications—diuretics, β-antagonists, corticosteroids, retinoids and cyclosporine	[3,4,63]
Intrinsic	
Obesity	[30,63]
Metabolic diseases—low glucose tolerance and diabetes mellitus	[63,76]
Biochemical disorders	
Increased triglyceride synthesis and increased hepatic secretion of VLDL	[30,63,76]
Abnormal distribution of triglyceride-rich lipoproteins	
Pancreatic lipase malfunction	[18,63,76]
Decreased activity of lipoprotein lipase	[64]
Genetic defect of lipoprotein lipase	[63,76]
Genetic defect of apolipoprotein CII	[64]
Blocking the ability of substrate to interact with endothelial lipase by activated adhesion molecules, such as ICAM, ELAM, VCAM, bound to the active sites on the enzyme	[62,76]

The condition may be attributed to psoriasis after elimination of other reasons, especially causative factors for secondary hypertriglyceridemia. *Abbreviations*: VLDL, very low-density lipoprotein; ICAM, intercellular adhesion molecule; ELAM, endothelial-leukocyte adhesion molecule; VCAM, vascular cell adhesion molecule.

[3,15,21,25–27]. Discrepancies between the cited reports may be due to mentioned above causative factors for "psoriatic hypertriglyceridemia". Besides, the phase, activity and form of psoriasis, and thereby an amount of lipids lost in shed psoriatic scales, also should be taken into account (Table 4). Since scales contain five times as much cholesterol as healthy skin surface [31], there is the potential for the loss of scales to affect serum lipids, especially serum cholesterol concentration. The majority of authors attributed increased total cholesterol concentration to atherosclerotic disease. The issue is further complicated by detailed analysis of cholesterol fractions. The observation that there is significantly decreased serum HDL-cholesterol concentration ($p = 0.00584$) in psoriasis is not unexpected. Many researchers have reported lower levels of this cholesterol fraction in psoriatics than in healthy controls [4,18,23,25], although only differences noted by Rocha-Pereira et al. [3], Örem et al. [21], Jones et al. [22], Kural et al. [26,27] and Skoczyńska et al. [28] were statistically significant (Fig. 4). The current data confirm our previous report [24], simultaneously both of them conflict with Simonetti et al. [15], Seçkin et al. [19] and Ferretti et al. [16], who detected an increase in serum HDL levels in psoriatics compared to healthy individuals, with insignificant differences between the studied groups. According to literature data decrease in serum cholesterol level may result from liver diseases, anomalies in HDL, VLDL and chylomicron metabolism, especially from decreased synthesis of HDL,

Table 4
Description of the study groups examined in previous studies analysing the lipid profile in patients suffering from psoriasis

First author (year)	Reference	PASI		Percentage of the body area covered by lesions
		Mean value ± S.D.	Range	
Vahlquist (1987)	[4]	–	–	>25[a] >30[b]
Peserico (1988)	[5]	–	–	–
Simonetti (1992)	[15]	–	–	<25
Ferretti (1994)	[16]	–	–	>30
Offidani (1994)	[17]	–	–	–
Seishima (1994)	[18]	–	–	>30
Seçkin (1994)	[19]	–	1.00–64.20	–
Toruniowa (1997)	[20]	27.78 ± 6.50	16.20–40.50	–
Örem (1999)	[21]	14.80 ± –	–	–
Jones (2000)	[22]	3.30 ± –	0.00–8.70	–
Rocha-Pereira (2000	[3]	–	–	>10[c] <10[d]
Uyanik (2002)	[23]	–	–	–
Pietrzak and Lecewicz-Toruń (2002)	[24]	M: 28.28 ± 6.96 F: 26.46 ± 7.29	M: 17.80–40.40 F: 18.00–48.00	–
Piskin (2003)	[25]	–	–	<25
Kural (2003)	[26]	5.80 ± 5.00	0.80–10.80	–
Kural (2003)	[27]	5.52 ± 3.63	1.89–9.15	–
Skoczyńska (2003)	[28]	–	–	–

–, no data; M, male participants; F, female participants.
[a] Data reported in the study are for mild-moderate/stable psoriasis.
[b] Data reported in the study are for severe psoriasis.
[c] Data reported in the study are for severe/active psoriasis.
[d] Data reported in the study are for mild/inactive psoriasis.

or changes in particle structure [64]. Noteworthy, low circulating levels of HDL-cholesterol were demonstrated to constitute a serious risk factor for coronary heart disease [63]. As for serum LDL-cholesterol our results are consistent with the alterations observed by the majority of researchers (the insignificant increase) [15,16,21,23,28]. It is noteworthy that a similar pattern, but with highly significant differences between the studied groups, has been reported by Offidani et al. [17], Rocha-Pereira et al. [3], Piskin et al. [25] and Kural et al. [26,27]. The cited literature data suggest that there may be relationship between psoriatic processes and serum LDL level. Increased serum LDL-cholesterol concentration observed in psoriatics may result from changes in production or abnormal function of LDL receptors on fibroblasts. Finally, our work seems to confirm the studies by Rocha-Pereira et al. [3] and Vahlquist et al. [4] regarding markedly increased serum VLDL-cholesterol. Other researchers

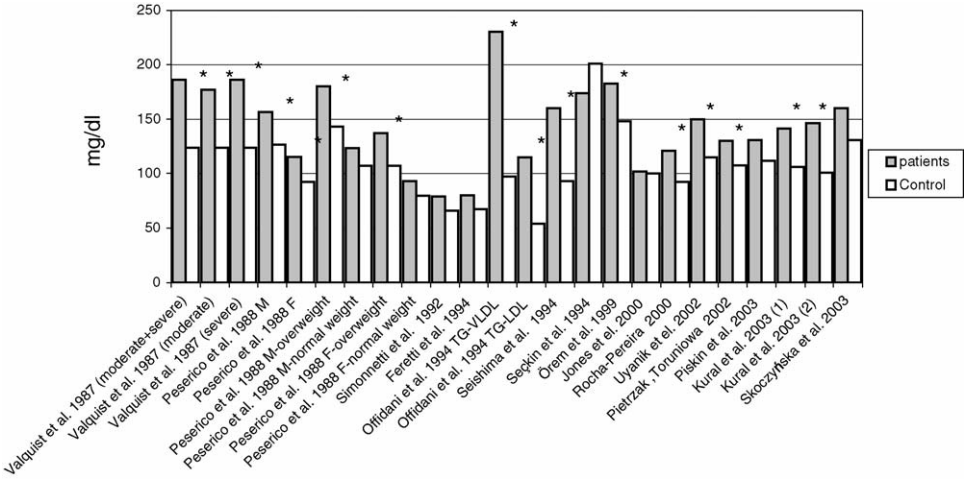

Fig. 4. Diagram illustrating mean HDL-cholesterol concentrations detected in previous studies analysing the lipid profile in patients suffering from psoriasis. The studies marked with asterisks noted significant differences between data from the psoriatic and control groups. If the values were expressed in mmol/l, they were converted into mg/dl according to the formula: mmol/l = g/l × 2.586 [75].

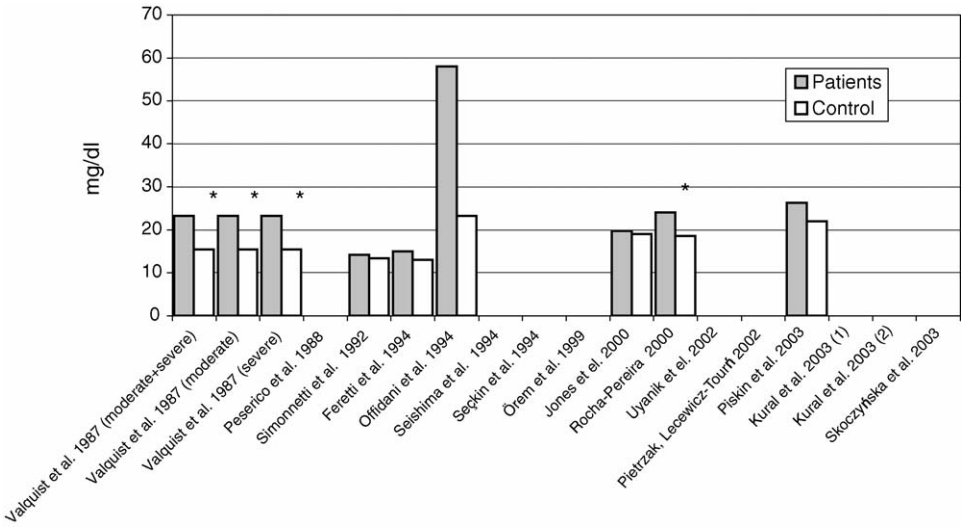

Fig. 5. Diagram illustrating mean VLDL-cholesterol concentrations detected in previous studies analysing the lipid profile in patients suffering from psoriasis. The studies marked with asterisks noted significant differences between data from the psoriatic and control groups. If the values were expressed in mmol/l, they were converted into mg/dl according to the formula: mmol/l = g/l × 2.586 [75].

assessing concentration of this cholesterol fraction noted only a slight tendency for it to increase (Fig. 5) [15–17,22,25]. Similarly to reasons for the abnormal serum LDL level, the increased serum VLDL level may be related to changes in production, namely increased or decreased synthesis, or alteration in the particle size. It should be highlighted that there is a direct relationship between serum VLDL and triglyceride levels, so that the higher VLDL concentration the higher triglyceride concentration.

In an attempt to establish links between observed lipid abnormalities and pancreas, the main organ implicated in lipid metabolism, serum pancreatic lipase activity was found to significantly correlate with serum triglyceride ($r = 0.42$; $p = 0.04721$) and serum VLDL-cholesterol concentration ($r = 0.42$; $p = 0.04721$) in psoriatic individuals (Fig. 6). There were no clear relationships between the enzyme activity and other lipid fractions. The reciprocal relation between serum pancreatic lipase activity and serum triglyceride level seems to confirm the hypothesis about abnormal lipid metabolism in the course of psoriasis. Moreover, serum pancreatic lipase seems to be another factor contributing to the changes in the serum lipid profile observed in psoriasis. The results of our previous investigation [30] indicated that lipoprotein lipase (EC 3.1.1.34) and hepatic lipase (EC 3.1.1.3) play the important role in abnormal lipid blood serum metabolism in the disease. Postheparin serum lipolytic activity, controlled mainly by these enzymes, was altered in psoriatic patients compared to healthy control group [30]. As the blood serum metabolism of lipids is immensely complicated and all of the mentioned enzymes seem to be involved, in future the current work will be extended to include changes in activity of lipoprotein lipase and hepatic lipase as well as other members of the lipase gene family in the course of psoriasis.

The second objective of this study was to explore the distribution of blood DC subsets in psoriasis and relation of separate DC subpopulations to the disease activity and abnormal lipid

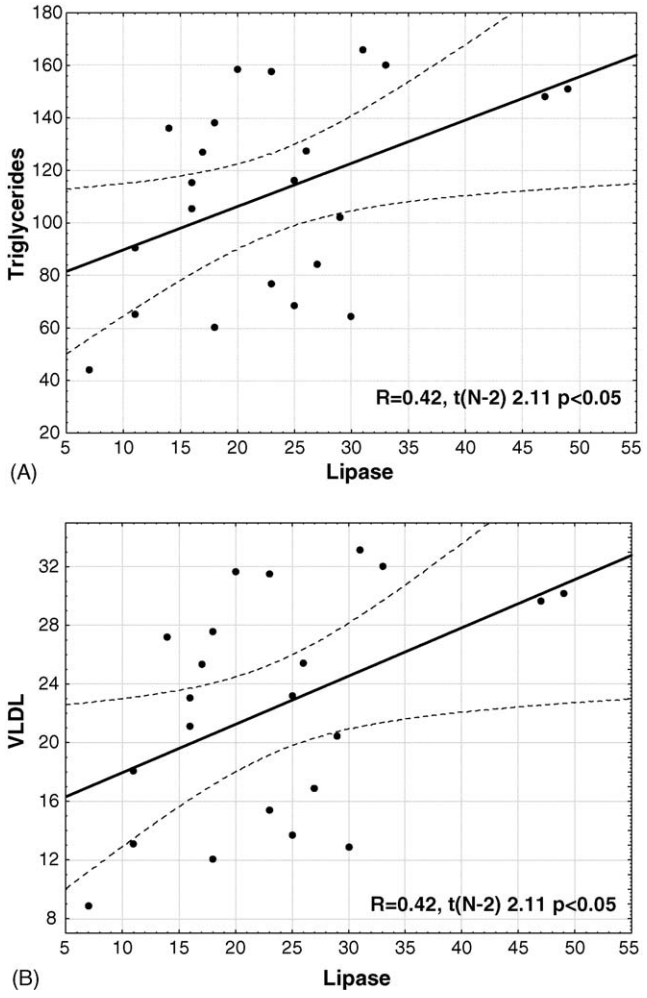

Fig. 6. Correlations of serum lipase activity (U/l) with: (A) triglyceride level (mg/dl) and (B) VLDL-cholesterol level (mg/dl) in serum of psoriatic patients.

Table 5
Immune cell counts in patients with psoriasis ($n = 22$) and control subjects ($n = 12$)

	Mean value ± S.D.	Minimum–maximum	p-Value
White blood cells (cell no. × 10^3 μl^{-1})			0.50497
Psoriasis	6.782 ± 1.58	4.330–9.360	
Control	6.325 ± 1.29	5.100–9.100	
Mononuclear cells (cell no. × 10^3 μl^{-1})			0.20720
Psoriasis	2.388 ± 0.64	1.303–4.600	
Control	2.518 ± 0.39	1.790–3.200	
Myeloid DCs (%)			0.54932
Psoriasis	0.417 ± 0.44	0.080–1.980	
Control	0.276 ± 0.14	0.083–0.490	
Lymphoid DCs (%)			0.14210
Psoriasis	0.359 ± 0.31	0.080–1.490	
Control	0.499 ± 0.30	0.070–0.930	
Myeloid DCs/lymphoid DCs			**0.03569***
Psoriasis	**1.579 ± 1.62**	**0.213–8.120**	
Control	**0.850 ± 0.76**	**0.355–3.000**	

* $p < 0.05$ was accepted as statistically significant.

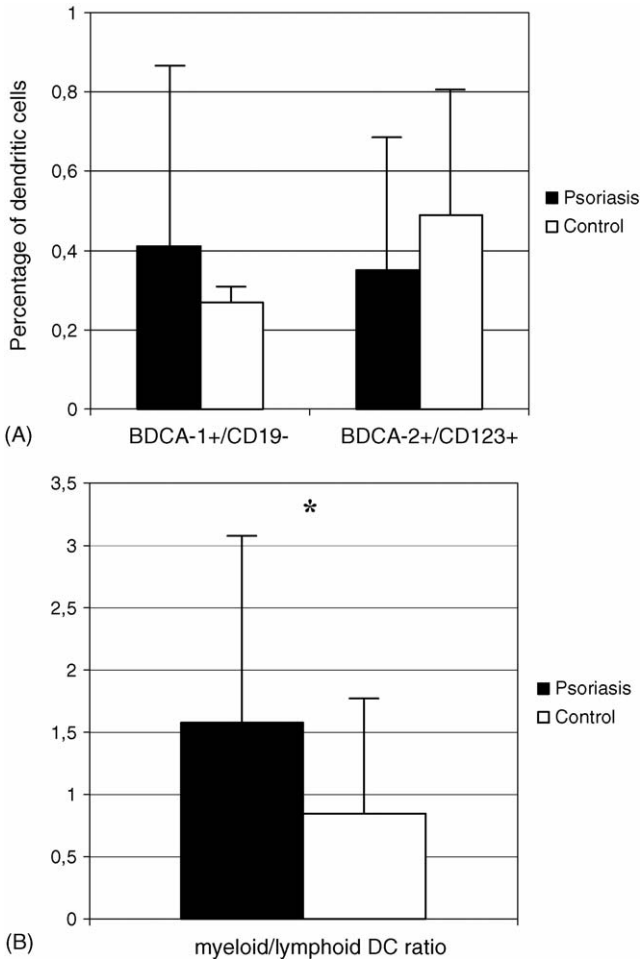

Fig. 7. (A) Percentages of myeloid (BDCA-1^+/$CD19^-$) and lymphoid (BDCA-2^+/$CD123^+$) dendritic cells in peripheral blood of psoriatic patients and healthy individuals. (B) Comparison between the myeloid/lymphoid DC ratios for psoriatic and control groups. Values are presented as mean ± standard deviation. * $p < 0.05$ was accepted as statistically significant.

metabolism. Numerical characteristics of peripheral blood DCs in patients suffering from psoriasis and healthy subjects are presented in Table 5 and simultaneously in Fig. 7. As indicated in Table 5, there were no significant differences in white blood cell and mononuclear cell counts between psoriatic and control groups, so that observed changes in the distribution of separate DC subpopulations cannot be attributed to the considerable discrepancy in total white blood cell count between groups. In the comparative analysis of the myeloid and lymphoid DC percentages, no significant differences between examined groups could be detected. However, in the course of psoriasis myeloid DCs show a slight inclination towards an increase and there is a tendency for lymphoid DCs to decrease (Table 5). These results differ somewhat from those previously reported. Experimental data concerning the role of blood DCs in psoriasis are scarce, but there are a few studies indicating that blood DCs may be biologically relevant to pathological psoriatic processes. Our recently published research paper has demonstrated the different distribution of these cell subpopulations in psoriatics compared to healthy individuals [65]. Furthermore, the study by Hashizume et al. [66] also noted a subtle difference in blood DC pattern between psoriatic patients and healthy subjects, though its main area of interest were compartmental shifts in DCs in atopic dermatitis and psoriatic patients were analysed only as a reference group (a Th1 disease model group). By contrast with the present study, in both mentioned reports a decrease in blood myeloid and lymphoid DCs in psoriatics compared to healthy individuals was observed; but except for lymphoid DCs in our previous study [65], the detected differences were not significant. It should be highlighted that a direct comparison between the cited studies and the present report cannot be made. The criteria for entry to the present study were expanded and included additional requirements regarding serum lipids (see Section 2.1). Thus, the different enrolment criteria, at least partially, may account for noted discrepancy. Exploring the underlying reasons for myeloid DCs to increase and lymphoid DCs to decrease, several factors should be taken into consideration. The most important ones include intrinsic DC properties, especially immune function and migratory properties, and interaction of DCs with environmental factors. According to literature data the number of peripheral blood DCs is probably determined by emigration of blood DCs to peripheral non-lymphoid tissues, the promotion of hemopoietic progenitor cell differentiation by different cytokines and growth factors and mobilisation of resultant DCs, or DC survival [45,67–69]. For example, de la Rosa et al. [69] have described a clear difference in the migration pattern between myeloid and lymphoid DCs; and whereas the former have an overall high migratory potency, the latter migrate across activated endothelium mainly in response to SDF-1 and especially RANTES, expression of which is strongly upregulated within psoriatic epidermis [70]. However, emigration of blood DCs into psoriatic skin is still controversial. Despite the presence of detectable subsets of lymphoid ($CD123^+$ cells) and myeloid ($CD11c^+$ cells) DCs in a pool of diverse DC populations within psoriatic lesions being reported [71], there are also communications that psoriatic plaques do not harbour blood DCs [66].

Interestingly, the present examination revealed significantly higher myeloid DC/lymphoid DC ratio in psoriatic group than in healthy controls (Table 5 and Fig. 7B). It is difficult to draw the definite conclusion from this observation, as alteration in the predominance of myeloid DCs over lymphoid DCs reflects relative shifts in separate blood DC subsets. Since the detected differences in myeloid and lymphoid DC percentages between patients with psoriasis and healthy individuals were not statistically significant, the considerably higher myeloid DC/lymphoid DC ratio in psoriatics may be attributed to relative increase in the myeloid DC number, relative decrease in the lymphoid DC number, as well as simultaneous increase in the myeloid DC number and decrease in the lymphoid DC number. Thus, these data seem to suggest that blood DCs may contribute to the pathological psoriatic processes; however, to explain the significance of separate DCs subpopulations for psoriasis pathogenesis, more detailed examination on considerably larger groups is required.

The present study, apart from careful examination of pancreatic lipase activity, lipid metabolism and immune system disturbance in psoriasis, was an attempt to combine biochemical disorders and the immune system abnormalities into one working hypothesis on the disease pathogenesis. Recently published data that dyslipidemia related to atherosclerotic disease affects DC function and kinetics [49,72], in context of complex alteration in serum lipids in psoriatic individuals, raised the question if there are any relations between peripheral blood DC subsets and changes in serum lipids in psoriasis. Our analysis failed to find the correlations between DC percentages and the pancreatic lipase activity or the serum lipid levels in psoriatics, and healthy individuals as well (data not shown). Although the study demonstrated changes in the lipid profile of psoriatic patients similar to those observed in the course of atherosclerotic disease (Table 1), it cannot confirm the modulating effect of increased LDL on DCs. However, LDL is known to be oxidised in vivo [73] and oxidised LDL was demonstrated to disturb DC function in vitro [50], so that changes in lipid profile modulating DC function and kinetics may be of qualitative not quantitative nature. Similar to other analysed parameters, more detailed examination is required.

In the present study, PASI score did not correlate with either biochemical or immune parameters. However, it is known that PASI score do not reflect the severity of the psoriasis correctly [74].

The mean percentage of lymphoid cells in blood of patients with psoriasis was $0.359 + 0.31$ and in control group $0.499 + 0.30$. The difference was not significant ($p > 0.1$). Similarly the mean percentage of myeloid cells in blood of patients with psoriasis was $0.417 + 0.44$, compared with control group $0.276 + 0.14$, which was not significant ($p > 0.05$). Although the data from literature suggests the relationship between dendritic cells blood level and lipid concentrations in serum, we did not find any dependence in our study. It should be mentioned, that we had analyzed normolipemic patients with psoriasis. We are about to start the study involving hyperlipemic individuals which could valuable considering such a relationship between dendritic cells and lipids.

4. Conclusions

The direct cause of the abnormal lipid profile in patients suffering from psoriasis, as well as its relationship with the immune system disturbances, remain unclear. However, the reciprocal relation between serum pancreatic lipase activity and serum triglyceride level appears to confirm the hypothesis about abnormal lipid metabolism in psoriasis. Furthermore, psoriatics seem to be especially predisposed to lipid metabolism aberrations, and thereby to dyslipidemia with changes in serum lipid composition similar to those observed in the course of occlusive vascular diseases. Alteration in serum lipids of atherogenic and prothrombotic character seems to considerably increase the risk for serious cardiovascular complications in the course of psoriasis. When deciding about the systemic management of psoriasis, choices of agents should be individualised to control the disease efficiently, reduce a risk for frequent relapses and prevent serious side effects, mainly those related to the abnormal serum lipid profile. Measurement of serum pancreatic lipase activity should be considered as a routine diagnostic procedure in psoriasis, especially in patients with excessive alcohol intake.

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