A study on lipid profile and apolipoprotein levels in psoriatic patients

Hiader Kadhim Alrubaye, MSc [1]
Khalil Ismail Alhamdi, PhD [2]
Jamal Ahmed Abdel Barry, PhD [3]
Majid Hameed Alabbood, MD [4,5*]

1. Basrah Health Directorate, Basrah, Iraq.
2. Department of Dermatology, College of Medicine, University of Basrah, Basrah, Iraq.
3. Department of Biochemistry, College of Medicine, University of Basrah, Basrah, Iraq.
4. Specialized Endocrine and Diabetes Center, Almawani Hospital,Basrah, Iraq
5. Alzahraa Medical College, University of Basrah, Basrah, Iraq

*Corresponding author:
Majid Alabbood, MD
Specialized Endocrine and Diabetes Center, Almawani Hospital, Basrah, Iraq
Email: dr_majid79@yahoo.com
Tel: +9647801046883

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Background: Psoriasis is a chronic, recurrent, inflammatory, and proliferative disease. Previous studies have demonstrated that patients with psoriasis may have an increased risk of developing coronary artery disease. High serum lipid levels have been suggested in the pathogenesis of this phenomenon. Accumulating evidence suggests that apolipoprotein B is superior to other lipid parameters in predicting atherosclerotic cardiovascular disease. This study aimed to examine the differences in the lipid profile and apolipoprotein A-I and apolipoprotein B levels between psoriatic patients and healthy subjects.

Methods: This was a case-control, cross-sectional study. A total of 93 psoriatic patients and 113 healthy individuals were enrolled. This study was conducted at the outpatient department of dermatology in Alsader Teaching Hospital, Basra, Iraq. The serum level of total cholesterol (TC), triglyceride (TG), very low-density lipoprotein cholesterol (VLDL-C), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), apolipoprotein A-I and apolipoprotein B were measured.

Results: The psoriatic patients had significantly higher levels of TC, TG, VLDL-C, LDL-C, and apolipoprotein B compared with the control group.

Conclusion: Lipid profile values were significantly higher among patients with psoriasis than normal controls. Early screening and treatment of hyperlipidemia in these patients are advisable to prevent atherosclerosis and its complications. Apolipoprotein B may serve as a marker for dyslipidemia and CVD in patients with psoriasis.

Keywords: psoriasis, apolipoprotein, hyperlipidemia

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INTRODUCTION

Psoriasis is a common, recurrent, genetically determined, inflammatory, and proliferative disease of the skin. The characteristic lesion is a chronic sharply demarcated, dull-red, scaly plaque, situated particularly on the extensor surfaces and scalp [1]. Patients with psoriasis face increased mortality and morbidity from cardiovascular events, particularly in severe and longstanding disease [2]. The link between cardiovascular disease (CVD) and psoriasis has been reported in several studies [3,4]. One of the factors that may explain the increased susceptibility of patients with psoriasis to CVD is an abnormal lipid profile [5]. Another factor is some of the pharmacological agents that are used in the treatment of psoriasis such as retinoids and cyclosporine, which may

induce hyperlipidemia [6,7]. Apolipoprotein B is the major structural protein in lipoproteins like low-density lipoprotein (LDL), intermediate-density lipoprotein (IDL), and very-low-density lipoprotein (VLDL) [8,9]. Each compound carries one molecule of apolipoprotein B. Therefore, the total value of apolipoprotein B represents the total level of atherogenic lipoproteins [10]. Studies have shown that apolipoprotein B is more accurate than LDL, especially in patients with hypertriglyceridemia, very low LDL values, or non-fasting samples [8]. Furthermore, accumulating evidence suggests that apolipoprotein B is superior to LDL in predicting atherosclerotic CVD. Additionally, an elevated apolipoprotein B level is more strongly associated with coronary heart disease incidence than a similar elevation in LDL cholesterol level [9]. Consequently, apolipoprotein B has been designated as a secondary target to monitor statin therapy in several guidelines [8]. This study aimed to approximate the lipid profile, apolipoprotein A-I, and apolipoprotein B levels in psoriatic patients in comparison with healthy subjects.

MATERIALS AND METHODS

This was a cross-sectional, case-control study conducted in Alsader Teaching Hospital in Basrah, Southern Iraq from 1st of May 2017 till 1st of May 2018. A total of 93 patients with plaque psoriasis were enrolled in this study. Psoriasis was diagnosed clinically by a consultant dermatologist and confirmed in borderline cases by histopathological examination of a skin biopsy taken by the same dermatologist. The control group (113 subjects) was comprised of apparently healthy paramedical staff and volunteers with similar age, gender, and body mass index (BMI) to that of the psoriatic patients.

Individuals with secondary causes of hyperlipidemia such as diabetes mellitus, hypothyroidism, nephrotic syndrome, chronic kidney disease, and cholestatic liver disease were excluded from the study, in addition to patients on medications such as beta-blockers, thiazides, oral contraceptive pills, corticosteroids, retinoids, and lipid-lowering agents in the preceding six months. Other exclusion criteria included pregnancy, active smoking, alcohol consumption, and obesity. The psoriatic patients were classified into three groups according to the Psoriasis Area and Severity Index (PASI) score (mild < 3, moderate 3-15, severe > 15) [11]. After fasting for 12-14 hours, blood samples were drawn for the measurement of total cholesterol (TC), triglyceride (TG), and high-density lipoprotein cholesterol (HDL-C) levels. Also, fasting blood glucose was measured to exclude diabetes mellitus besides serum creatinine to exclude chronic kidney disease. All the aforementioned tests were done by an auto-analyzer using the enzymatic colorimetric method. Furthermore, apolipoprotein A-I and B levels were measured from the same samples via the turbidimetric method. Serum very-low-density lipoprotein cholesterol (VLDL-C) was calculated using the equation: VLDL-C = TG/5. Low-density lipoprotein cholesterol (LDL-C) was calculated by applying Friedewald's equation [12]. A urine sample was analyzed for protein to exclude nephrotic syndrome. The BMI was calculated as weight (kg) divided by squared height (m^2).

The study was approved by the Ethical Committee of the College of Medicine, University of Basrah. Informed consent was taken from all the participants.

Statistical analysis was performed using SPSS Statistics Version 23 (IBM Corporation). Descriptive statistics were expressed as mean ± standard deviation (SD). The Chi-squared test was used to examine the significance of the difference of variables between cases and controls. Statistical significance was defined as a p-value of less than 0.05.

RESULTS

A total of 93 patients (48 females) with plaque psoriasis were enrolled in this study. Their age ranged from 15-45 years. The control group (113 healthy subjects) included 50 males and 63 females.

Regarding the studied biochemical parameters, serum levels of TC, TG, VLDL-C, LDL-C, and apolipoprotein B were significantly higher in the psoriatic group as compared with the control group. Conversely, the serum level of HDL-C was significantly lower in the psoriasis group. On the other hand, there was no significant difference between patients and controls in terms of the apolipoprotein A-I level, as shown in Table 1.

Regarding the effect of the severity of psoriasis on the lipid profiles of the patients, it was found that the values of the investigated parameters,

Table 1. Biochemical parameters of the participants.

Variable	Control group	Case group	*P*-value
	Mean ± SD (mg/dl)	Mean ± SD (mg/dl)	
Cholesterol	163.16 ± 19.74	196.44 ± 45.87	< 0.05
Triglyceride	135.15 ± 22	160.5 ± 26.77	< 0.05
VLDL-C	26.99 ± 6.9	32.22 ± 5.41	< 0.05
HDL-C	46.04 ± 5.49	41.03 ± 5.89	< 0.05
LDL-C	90.14 ± 19.33	128.79 ± 45.23	< 0.05
Apolipoprotein A-1	144.9 ± 11.22	143.57 ± 10.75	0.83
Apolipoprotein B	102.04 ± 21.85	129.51 ± 30.07	< 0.05

HDL-C: high-density lipoprotein cholesterol, LDL-C: low-density lipoprotein cholesterol, SD: standard deviation, VLDL-C: very-low-density lipoprotein cholesterol.

except for HDL-C, were significantly higher among patients with moderate and severe psoriasis relative to those with mild psoriasis (Table 2).

The effect of psoriasis severity on apolipoprotein A-I and apolipoprotein B levels is also shown in Table 2. There was a statistically significant higher level of apolipoprotein B among patients with moderate and severe psoriasis than those with mild psoriasis. However, there was no significant difference in the level of apolipoprotein A-I among the three groups.

DISCUSSION

This study aimed to approximate the lipid profile values and apolipoprotein A-I and apolipoprotein B levels in psoriatic patients in comparison with healthy subjects. The overall results of this study showed that the lipid profile was clearly disturbed among patients with psoriasis. Serum levels of TC, TG, VLDL-C, LDL-C, and apolipoprotein B were higher while HDL-C was lower among psoriatic patients in comparison with the control group. It is important to clarify whether these lipid abnormalities are secondary to psoriasis or whether the reverse is true, or if both are caused by a common genetic abnormality.

There are several possible explanations for the increased prevalence of CVD mortality and morbidity in patients with psoriasis. Firstly, patients with psoriasis could be considered as a group with increased atherosclerotic risk because of increased oxidant stress, decreased antioxidant capacity, abnormal lipid profiles, and increased lipoprotein content [8]. At the cellular level, even patients with mild psoriasis display disequilibrium between markers of oxidative stress and antioxidants. In addition, psoriasis may further promote oxidative stress through an association with decreased folic acid levels [9]. Secondly, recent evidence strongly suggests that chronic inflammation, a characteristic of psoriasis, plays a role in the initiation and progression of atherosclerosis [8]. Furthermore, elevated levels of high-sensitivity C-reactive protein (hs-CRP), a non-specific marker of inflammation, is one of the emerging risk factors for CVD, with increased hs-CRP levels being able to predict the long-term risk of developing CVD [10]. Thirdly, abnormalities in plasma lipids and lipoproteins are likely to play an important role in the increased risk of psoriatic patients for developing atherosclerosis and CVD [5]. Besides, there is evidence that established treatments of psoriasis such as retinoids and cyclosporine may induce hyperlipidemia that can promote the development of CVD [6,7]. The lipid abnormalities seen in psoriasis might facilitate and maintain the

Table 2. Relation between psoriasis severity and lipid profile parameters as well as apolipoprotein A-1 and B levels.

Parameters	Psoriasis severity		
	Mild Mean ± SD (mg/dl); n=26	Moderate Mean ± SD (mg/dl); n=37	Severe Mean ± SD (mg/dl); n=30
Cholesterol	162.44 ± 22.5	185.9 ± 34.7 a*	239.1 ± 41.1 ab*
Triglyceride	137.2 ± 25.1	163.4 ± 24.3 a*	177.6 ± 14.3 ab*
VLDL-C	27.4 ± 5	33 ± 4.96a*	35.9 ± 2.9 ab*
HDL-C	43 ± 5.4.3	42 ± 4.55	37 ± 6.6 ab*
LDL-C	94.6 ± 31.6	120.6 ± 32.8 a*	168.8 ± 38.9 ab*
Apolipoprotein A-I	140.7 ± 11.4	145.9 ± 11	143.8 ± 9
Apolipoprotein B	108.69 ± 29	131.8 ± 26 a*	145.5 ± 24.4 ab*

HDL-C: high-density lipoprotein cholesterol, LDL-C: low-density lipoprotein cholesterol, SD: standard deviation, VLDL-C: very-low-density lipoprotein cholesterol.
* Significant difference (P < 0.05)
a As compared with the mild group.
b As compared with the moderate group.

inflammatory reaction in the skin. Furthermore, the level of the antibodies against oxidized LDL is reported to correlate with disease severity [11].

Therapy with statins may benefit patients with psoriasis as these reduce LDL oxidation and may even have immune-modulatory activities that can improve the psoriatic skin and cause a shift from a pro-inflammatory state to an anti-inflammatory condition (9).

In psoriasis,the production of pro-inflammatory cytokines such as TNF-α and IL-6can modulate lipid metabolism and cause lipid abnormalities [13], possibly through the following mechanism: firstly, TNF-α alters the gene expression profile of adipocytes and hepatocytes, leading to increased release and production of free fatty acids (FFAs), cholesterol, and VLDL-C [2]. Moreover, intravenous administration of tumor necrosis factor-α (TNF-α) to normal rats was found to cause a rapid increase in hepatic FFA levels. Meanwhile, high levels of FFAs act on the liver to induce the production of TGs including VLDL-rich TG [2]. Secondly, elevated interleukin-6 (IL-6) levels are associated with decreased HDL-C content [2]. Thirdly, psoriasis is a chronic inflammatory disease that induces a decrease in HDL-C and impairs reverse cholesterol transport by inducing changes in HDL composition and metabolism. These changes include induction of acute phase lipase that catabolizes HDL phospholipids [14], increasing the HDL content of acute-phase amyloid A with the displacement of apolipoprotein A-I [15]. In addition, the inflammatory effect of psoriasis leads to decreased hepatic excretion of cholesterol [16] and inhibits TG clearance by reducing lipoprotein lipase activity and reducing the level of VLDL-associated apolipoprotein E [17].

On the other hand, the deregulation of lipid metabolism may influence the development of psoriasis [16]. Since HDL-C associated apolipoprotein A-I can inhibit the activation of monocytes/macrophages by interfering with their interaction with T cells, it can lead to a decrease in TNFα level [18]. Moreover, increased VLDL and LDL levels could also contribute to the pathogenesis of psoriasis [19].

Another study suggested that genetic alterations in the HDL-C and/or apolipoprotein A-I genes may be linked with psoriasis. This genetic hypothesis is supported by a study on lipid and lipoprotein profiles among Swedish patients with psoriasis, which revealed significant lipid abnormalities and supported the notion that this might be genetically determined rather than acquired [20].

From what has been mentioned, it is clearly seen that the relationship between psoriasis and dyslipidemia is a matter of controversy. Based on these controversial findings, no one can conclude which one of them causes the other or whether both of them are caused by a common genetic abnormality on a solid scientific base. However, we suggest that psoriasis possibly induces secondary hyperlipidemia, which places psoriatic patients at more risk of having CVD. However, we cannot rule out the other two possibilities. Therefore, a future advanced study is advisable to clarify this issue with certainty.

The power of this study lies in the measurement of lipoprotein levels in addition to the lipid profile among the studied participants. There are limitations in this study, which include the inability to ascertain the causation in the relationship between a disturbed lipid profile and psoriasis due to its design as well as the fact that it was conducted in a single center.

CONCLUSION

Obtaining a lipid profile is prudent among patients with psoriasis. This practice may help clinicians to detect dyslipidemia early and to consequently treat them with lipid-lowering agents that may primarily prevent CVD. Apolipoprotein B may be used as a marker to predict those patients with psoriasis who are at risk of dyslipidemia and probably CVD.

Conflict of Interest: None declared.

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