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RELATION OF ELEVATED SERUM LIPIDS AND LIPOPROTEIN (A) TO OXIDATIVE STRESS IN PSORIASIS.

Dr. Dipankar Kundu*	Associate Professor, Department of Biochemistry, Medical College, Kolkata. *Corresponding Author
Dr. Aniket Paul	Senior Resident, Murshidabad Medical College.
Dr. Satyaki Basu	Resident, Medical College, Kolkata.

ABSTRACT **Background:** Psoriasis is a chronic inflammatory disease with multisystem involvement. Psoriasis is an immune mediated skin disease characterized by hyperproliferation of keratinocytes9 which is initiated and maintained by inflammatory mediators.

Objective: To determine the serum lipid disturbances in psoriasis. To assess the significance of lipoprotein (a) levels in psoriasis.

Materials And Methods: 30 Number of cases of patients suffering from Psoriasis in the age group of 15-75 was included in the study.30 age and sex matched healthy volunteers served as controls.

Results: Significant elevation in levels of fasting glucose, creatinine, total cholesterol.triglycrides, VLDL, LDL, Lipoprotein (a), and Malondialdehyde (MDA) was observed in cases compared with controls.

Conclusions: It is important to measure serum lipid level particularly cholesterol, LDL and TG in psoriatic patients for early screening of hyperlipidemia to evaluate risk to atherosclerosis and vascular obstructive disorders and its complications.

KEYWORDS : Psoriasis, Lipid Profile, Lipoprotein (a), Malondialdehyde

INTRODUCTION

Psoriasis is a chronic inflammatory disease with multisystem involvement. Psoriasis is an immune mediated skin disease characterized by hyperproliferation of keratinocytes which is initiated and maintained by inflammatory mediators.[1] It may be due to abnormalities in eicosanoid metabolism, essential fatty acid metabolism, lipid peroxidation, free radical generation, and lymphokine secretion. Psoriasis, which was primarily considered a cutaneous disease, is recently being identified as an associate of systemic inflammation. There is a complex network of inflammatory and immune cells, cytokines, chemokines and growth factors, all of which interact with one another to initiate a cascade of inflammatory events resulting in T-cell infiltration in the epidermis and dermis.[2, 3]. Recent studies have shown a rise in plasma lipid and lipoprotein levels with an increase in the levels of cholesterol, triglycerides and LDL in subjects with psoriasis, compared to controls[4]. It has been observed that patients with psoriasis have a disturbance in lipid metabolism and a predisposition for atherosclerosis.[5,6]. This alteration in lipid profile is due to the inflammatory milie]u maintained by the cytokines,[6,8]although there are some reports which show a normal lipid profile in psoriasis[7]. Low-density lipoprotein, on oxidation, induces monocyte infiltration and smooth muscle proliferation and favors atherosclerotic plaque formation.[8]. Similarly; it is thought that oxidative stress plays a major role in enhancing the inflammatory process of psoriasis.

There is an imbalance between the generation and removal of reactive oxygen species due to increased free radical generation and de[fective scavenging mechanisms [9]. This contributes to increased oxidant load and thus, increased cell damage by causing lipid peroxidation of cell membranes[10]. Malondialdehyde, which is a product of lipid peroxidation, is considered a marker of oxidative stress and lipid peroxidation[11]. Some previous studies in a North Indian population have shown raised malondialdehyde levels in psoriatic patients with co-morbidities like hypertension and diabetes.[12]. Another important marker for cardiovascular risk in the atherosclerosis-prone is lipoprotein (a), a form of low density lipoprotein with apolipoprotein B100 and apolipoprotein (a) attached by a disulfide bond which is also susceptible to lipid peroxidation.

Lipoprotein (a) has a structural homology with plasminogen, and also regulates synthesis of plasminogen activator inhibitor-1. It has a dual role in being thrombogenic and atherogenic, and thus increases cardiovascular risk, previous study also suggested that lipoprotein (a)is an important marker of cardiovascular disease[13].

The present study was undertaken to corroborate the correlation of serum lipids and compare the malondialdehyde and lipoprotein (a) values, in patients with psoriasis, and in controls.

MATERIALAND METHODS

The study comprised of cases of psoriasis visiting the inpatient and outpatient department of Biochemistry of Medical College and Hospital, Kolkata. Duration of the study was for one year.30 Number of cases of patients suffering from Psoriasis in the age group of 15-75 was included in the study.30 age and sex matched healthy volunteers served as controls. Patients suffering from Diabetes, hypertension, obesity, renal and liver failure, endocrine disorders and with family history of hyperlipidemia, taking systemic drugs especially lipid lowering agents, smokers and alcohol users were excluded from the study.

Blood and urine samples were collected after an informed written consent.

Statistical Analysis

The data collected will be analyzed statistically by computing descriptive statistics namely mean, standard deviation, range, chi-square test and any significant difference between the mean values of study group and control group will be tested using independent sample student t- test.

Specimen collection:

Blood:

5 ml plain venous blood sample after overnight fasting will be obtained by venepuncture. This will be followed by centrifugation and then sample will be processed immediately after collection. Overnight fasting urine sample will be collected in a clean dry container and will be tested immediately.

Plasma glucose (Glucose Oxidase), creatinine (Jaffe's Alkaline Picrate) was assayed.

Serum Total cholesterol (enzymatic method), Triglycerides (enzymatic method), HDL- Chlolesterol (phosphotungstate method), VLDL-Cholesterol is calculated according to the formula: VLDL=TG / 5, LDL- Cholesterol is calculated Friedwald's equation. Total Ch/ HDL and LDL-C/HDL-C ratio will be determined. Lipoprotein (a) (turbidimetric immunoassay).Oxidative stress was evaluated by measuring. Malondialdehyde (Thiobarbituric acid reaction).

RESULTS

Table 1: Basic Characteristics Of Study Population

Characteristics	Cases	Controls
Age(years)	38±7.76	35±8.69
Male: Female	18:12	17:13
BMI(Kg/Sq.m)	23.95±1.72	22.13±1.47

Table 1 depicts that this study included a total of 60 participants; Case group included 30 patients; 18 males and 12 females. Their ages ranged from 15 to 75 years with a mean of 38±7.76.Control group included 30 individuals; 17 males and 13 females their ages ranged from 17 to 75 years with a mean of 35±8.69 years and there was no significant difference in sex between the psoriasis and control groups (p= 0.84).

Table 2.Comparission of Glucose, Creatinine, Serum Lipid Profile, Lp (a) and MDA (Oxidative Stress) in Cases and Controls

Parameter	Cases	Controls	p Value
Glucose(mg/dl)	121±4.5	103±6.0	<0.005
Creatinine(mg/dl)	2.01±0.41	1.04±0.19	<0.001
Total Cholesterol(mg/dl)	212.91±36.48	159.22±23.81	<0.0001
Triglycerides(mg/dl)	231.06±32.59	138.75±20.43	<0.0001
VLDL(mg/dl)	46.4±6.88	29.1±4.34	<0.0001
HDL(mg/dl)	41.98±6.06	49.10±8.04	0.0001
LDL(mg/dl)	129.88±27.4	79.13±15.88	<0.0001
Lipoprotein(a) (mg/dl)	27.98±9.02	20.01±7.07	<0.001
MDA (µmol/ml)	13.47±3.40	7.49±1.39	<0.001

Table 2 depicts elevated levels of fasting glucose in cases (121±4.5mg/dl) as compared with controls (103±6.0mg/dl) and was statistically significant.

Elevated levels of serum creatinine were found in cases (2.01±0.41/dl) as compared with controls (1.04±0.19/dl) and was statistically significant.

Higher levels of cholesterol, triglycerides, VLDL and LDL levels in patients with psoriasis as compared to the healthy controls were also observed. HDL levels although were grossly diminished. Hypercholesterolemia was quite evident in the patients with psoriasis, with the study group exhibiting a mean of 212.91±36.48mg% which was substantially higher than the control group standing at159.22±23.81mg%.Serum triglyceride levels were also found elevated in psoriasis patients with mean serum triglyceride levels in the study group being 231.06±32.59.The control group on the other hand exhibited a mean serum triglyceride levels of 138.75±20.43.Mean VLDL and LDL levels were 46.4±6.88and 129.88±27.4mg% respectively in the psoriasis patients. This was substantially more as compared to that of the controls who exhibited a mean VLDL level of 29.1±4.34mg% and mean LDL level of 79.13±15.88mg%.

Mean HDL levels in the study group though was found to be less 41.98±6.06 as compared to that of the controls 49.10±8.04. There was a statistically significant association of abnormality in TG, TC, HDL and LDL.

Levels of lipoprotein (a) were elevated.i.e 27.98±9.02 mg/dl in cases as compared with controls 20.01±7.07 mg/dl and were statistically highly significant. Levels of MDA were also elevated i.e 13.47±3.40 (µmol/ml) in cases as compared with controls 7.49±1.39 (µmol/ml) and were statistically highly significant.

DISCUSSION

Fasting blood glucose level was significantly higher in the cases in our study. A previous study also observed significant impaired fasting plasma glucose level [1, 14, 15]. Patients with psoriasis, a chronic immunological skin inflammation, often develop diabetes. However, it is not clear to date how psoriasis leads to, or is correlated with, glucose intolerance. Psoriatic inflammation is not restricted to the skin and accounts for systemic inflammation such as systemic cytokine production and association with metabolic syndromes Thus, systemic psoriatic inflammation itself may play a key] role in glucose metabolism. However, it is not clear whether psoriasis causes diabetes or vice versa.

Serum Creatinine level was significantly higher in the cases in our study. There is some emerging evidence that immunologic mechanism such as chronic T-cell activation and increased levels of immune complexes and cytokines cause glomerular injury in psoriasis[16,17].However, other studies have demonstrated that direct tubular injury resulting from hypuricaemia could be probable mechanism[18].

These findings of elevated Lipid profile of ours are similar to a previous study[14].However some studies have also reported conflicting findings which do not corroborate with our findings[5,6] Although the various changes in lipid metabolism in psoriasis is not well understood but some researchers have proposed a few hypothesis which might be the best explanation for the possible derangement in lipid metabolism. Probably structural and functional abnormalities in nearly all segments of the gastrointestinal tract lead to an abnormal decomposition, modification and synthesis of lipids which eventually contribute to the defective metabolism as has been suggested by a previous study[7]. Lipid abnormalities have a profound effect on the immune system and inflammatory response in patients with psoriasis due to T cell cytokines which is characteristics of T helper cell response[8] .The changes in lipid composition are whether primary or secondary is still a matter of controversy. The lipid abnormalities in psoriasis are prevalent from the very onset of the disease, progressing thereby to altered metabolism of lipids and a consequent increased cardiovascular morbidity. Autoantibodies that recognize oxidized LDL has been reported and their titer correlates with the disease severity[10].

Thus a gross dyslipidemic status was quite evident in patients with psoriasis which itself is an independent risk factor for development of ischemic heart disease. Our results also undoubtedly depicted the significant lowering of HDL-C in cases with both the lifestyle factors studied in psoriasis. We also noted elevated levels of lipoprotein (a) and malondialdehyde in psoriatics as compared with controls. A previous study also observed a significant increase in the malondialdehyde levels in psoriasis patients as compared with healthy controls[14]. An interesting study by other researchers showing lower plasma malondialdehyde levels in psoriasis patients in remission than during the active phase also supports the view that oxidative damage plays an important role in etiopathogenesis of psoriasis. However, a study on 30 patients with psoriasis observed no significant difference in malondialdehyde levels between cases and controls. The malondialdehyde levels did not correlate with the severity of psoriasis in their study[10].Modifications of plasma lipids and an increase in the levels of biochemical markers of lipid peroxidation have been reported in psoriasis, suggesting a relationship between the disease, lipoproteins and oxidative damage[7, 18]. It has also been demonstrated that lipoprotein (a) is susceptible to lipid peroxidation and could be involved in atherogenesis through accumulation in the vessel wall leading to the recruitment of macrophages and finally, the development of atherosclerotic plaques[13] .

In our study, we observed significantly higher levels of lipoprotein (a) in patients with psoriasis when compared to controls and these levels correlated positively with the disease severity. In agreement with our studies, previous studies showed that serum lipoprotein (a) and triglycerides were significantly higher in psoriatic patients[7]. Similarly, previous study on 23 patients with psoriasis observed a positive correlation between lipoprotein (a) levels[19].

There are certain limitations of this study firstly, that it did not look into the gender differences in lipid profile parameters and also did not compare the lipid profile parameters in subgroup of psoriasis on the basis of severity. Secondly, a relatively smaller sample size, involving only 30 study subjects, was used in the study. A larger sample size would have validated our results further. Finally, different morphological types of psoriasis were not included and follow-up after treatment was not undertaken.

CONCLUSION

It is important to measure serum lipid level particularly cholesterol, LDL and TG in psoriatic patients for early screening of hyperlipidemia to evaluate risk to atherosclerosis and vascular obstructive disorders and its complications. Further research is needed to assess the impact of traditional cardiovascular risk factors, comorbidities, psoriasis disease severity, and the choice of lipid-lowering therapy on the lipids in patients with psoriasis. Administrating lipid-lowering medicines for patients particularly cases with severe disease may be beneficial in prognosis especially that hyperlipidemia is relatively easy to treat. Lifestyle modifications like diet low in fat and physical exercise must be advised to patients to prevent cardiovascular disease.

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