ORIGINAL RESEARCH PAPER

Biochemistry

STUDY ON EVALUATION OF CARDIOVASCULAR RISK BIOMARKERS IN SUBJECTS WITH PSORIASIS

KEY WORDS: Psoriasis vulgaris, hs-CRP, fasting lipid profile, fasting blood sugar & cardiovascular risk

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ABSTRACT

Background: Psoriasis vulgaris is a T-cell mediated, chronic inflammatory, genetically determined autoimmune disorder of skin. Number of studies has mentioned higher levels of total cholesterol, triglycerides, low density lipoprotein cholesterol, and decreased levels of HDL cholesterol in patients with psoriasis. Several studies have observed a more atherogenic lipoprotein profile and decreased HDL efflux capacity in psoriasis patients compared to controls beyond CVD risk factors. The abnormal lipoprotein particle composition and HDL efflux capacity in psoriasis may provide a link between psoriasis and CVD. **Objectives of the study:** To estimate and compare lipid profile parameters and hS-CRP levels in subjects with psoriasis and healthy controls & To find out association if any of Lp (a) and hs-CRP in subjects with psoriasis. **Materials and Methods:** A specimen of blood was obtained aseptically from the antecubital fossa in each patient for measurement of lipid profile parameters, hs-CRP and fasting blood sugar. Student-t test was performed to evaluate the difference between the continuous variables of both psoriasis and controls. Mann-Whitney U test was performed to evaluate the statistical significance for hs-CRP. Results were expressed as mean ± SD. **Results & Conclusion:** The present study demonstrated higher prevalence of psoriasis in males. Hypercholesterolemia, lipoprotein (a) and hs-CRP are associated with psoriasis. The proportion of cardiovascular risk factors such as dyslipidemia, hypertension and diabetes were increased in psoriasis subjects. These risk factors not only affect the physical health but also patient's health related quality of life. The link between psoriasis and cardiovascular disease is still a matter of debate.

INTRODUCTION

Psoriasis vulgaris is a T- cell mediated, chronic inflammatory, genetically determined autoimmune disorder of skin.[1,2] The word psoriasis was used by the Greek physician Hippocrates (460-377 BC), in Greek the word "Psora", meaning "to itch".[3] It is characterized by the presence of raised, well demarcated erythematous plaques covered by silvery white scales which occurs due to hyper-proliferation and premature maturation of epidermal keratinocytes.[4] Psoriasis vulgaris skin plaques are often symmetrical and involve scalp, elbows, knees, buttocks and sites of local trauma.[5]

Number of studies has mentioned higher levels of total cholesterol, triglycerides, low density lipoprotein cholesterol, and decreased levels of HDL cholesterol in patients with psoriasis.[6] Mehta et al in 2011 observed a more atherogenic lipoprotein profile and decreased HDL efflux capacity in psoriasis patients compared to controls beyond CVD risk factors. The abnormal lipoprotein particle composition and HDL efflux capacity in psoriasis may provide a link between psoriasis and CVD.[8]

In psoriasis, there is cutaneous and systemic over expression of various pro-inflammatory cytokines and acute phase reactants which are strongly associated with the risk and outcomes of coronary events and hs-CRP is one of them.[9] Several reports have shown that hs- CRP enhances the expression of local endothelial cell surface adhesion molecules, monocyte chemo attractant protein1, endothelin 1 and endothelial plasminogen activator inhibitor 1. It also reduces endothelial nitric oxide bioactivity, increases the induction of tissue factor in monocytes and LDL uptake by macrophages and co localize with the complement membrane attack complex within atherosclerotic lesions.[10]

OBJECTIVES OF THE STUDY

1. To estimate and compare lipid profile parameters and hS-CRP levels in subjects with psoriasis and healthy controls.
2. To find out association if any of Lp (a) and hs-CRP in subjects with psoriasis

MATERIALS AND METHODS

Source of data: The present study was carried out for a period of one year from 2014 -2016. The patients will be selected from Pt. J.N.M Medical College, Raipur, and Chhattisgarh in collaboration with Department of Dermatology Pt. J.N.M Medical College, Raipur, and Chhattisgarh. The study was carried out in psoriasis patients and age and sex matched healthy controls. Both cases and controls were interviewed to obtain relevant data.

Inclusion Criteria:

The cases were patients attending the dermatology clinic. The controls were healthy subjects selected from general population.

Cases: 34 proven cases of psoriasis (27 males and 7 females) in age group of 20 - 40 years.

Controls: 30 cases of age and sex matched healthy controls (21 males and 9 females) will be compared.

Exclusion criteria: Subjects on medications altering the lipid metabolism or diseases in which alter the lipid levels such as Type 2 Diabetes mellitus, Pregnancy, Lactating mothers, Chronic smokers, Atherosclerosis, Hypertension, Hepatic, Renal and Endocrinal disorders were excluded.

Method of data collection: A specimen of blood was obtained aseptically from the antecubital fossa in each patient for measurement of total cholesterol and fasting blood sugar. Study subjects who did not observe the requisite fast were instructed to observe overnight fasts (10-12 hours) before specimens were collected and presented the following day.

About 6ml of venous blood was drawn aseptically from the antecubital fossa. Out of 6ml, 2ml sample will be taken in sodium fluoride vacutainer, 3ml in EDTA vacutainer, rest in plain vacutainer.

- Sodium Fluoride Vacutainer for Fasting Blood Sugar Estimation
- PLAIN Vacutainer for Lipid profile & Apo lipoprotein estimation
- Apo lipoprotein and hs-CRP by Nephelometry

Statistical analysis:
Student-t test was performed to evaluate the difference between the continuous variables of both psoriasis and controls. Mann- Whitney U test was performed to evaluate the statistical significance for hs-CRP. Results were expressed as mean ± SD.

RESULTS:
We evaluated a total of 34 proven cases of psoriasis (27 males and 7 females) and 30 age and sex matched healthy controls (21 males and 9 females) in age group of 20 - 40 years were compared.

Table 1: Shows the comparison of Cardiovascular Risk Biomarkers between Cases and Controls

Variables	Controls	Cases	P value
AGE (years)	49.07±14.017	42.85±11.758	0.058
BMI	25.580±2.2492	24.803±4.5713	0.402
Pulse	74.00±7.168	76.74±10.712	0.241
SBP (mm of Hg)	126.93±8.233	133.44±9.777	0.006
DBP (mm of Hg)	88.13±10.224	92.21±11.294	0.138
FBS (mg/dl)	81.57±12.599	91.53±24.387	0.049
CHOLESTROL (mg/dl)	159.30±21.587	188.35±37.620	<0.001
TRIGLYCERIDE (mg/dl)	121.63±50.209	164.65±88.541	0.022
HDL (mg/dl)	38.40±5.367	45.53±13.372	0.008
LDL (mg/dl)	98.10±18.052	108.65±31.686	0.113
VLDL (mg/dl)	23.30±7.585	32.65±17.708	0.009
LDLC: HDLC	2.590±.5416	2.588±1.1398	0.994
C:HDL	4.210±.6830	4.444±1.4304	0.417
hsCRP (mg/L)	6.29±17.80	5.7±5.97	0.003
Lp(a)(mg/dl)	16.07±12.690	35.32±26.364	0.001

From the Table 1, it is evident form the table that, the age difference between psoriasis and control groups was not statistically significant (P=0.058). The distribution of male and female subjects between psoriasis and control groups also is not significant (0.28). No significant difference was found for BMI (p=0.402). Psoriasis subjects were found to be having significantly higher Systolic blood pressure (p=0.006). Though pulse rate and DBP were found to be higher in cases compared to controls, the difference failed to reach statistical significance (p=0.241 and p=0.138 respectively). Fasting blood sugar levels were significantly different between psoriasis and controls (p=0.049). Differences in baseline lipid profile between psoriasis and controls demonstrated that the S. Cholesterol, S. TG, HDL, VLDL were statistically significant between groups. Whereas LDL, LDLC: HDLC ratio, C: HDL ratio is not significantly different between psoriasis and controls. The levels of high sensitive C reactive protein were found to be higher in psoriasis than in control group with statistically significant difference observed (p=0.003). Significantly higher levels of lipoprotein(a) was found in psoriasis group compared to controls.

Table 2: Shows the association of Lp(a) and hs-CRP with psoriasis

VARIABLES	Cut-off Values	CONTROL	PSORIASIS	OR (95%CI)	P value
Lp(a)	<30mg/dl	25	13	Reference	
	>30mg/dl	5	21	8.0(2.47-26.37)	0.001
hs-CRP	<3mg/l	22	12	Reference	
	>3mg/l	8	22	5.04(1.73-14.73)	0.003

Table 2: It is evident from the table 2 that, the Lp(a) and hs-CRP increased the risk of psoriasis. Strong association of Lp(a) was observed with psoriasis (OR:8.0; 95% CI: 2.47-26.37; p=0.001). Significantly increased risk (5.04 fold) was observed for hs-CRP is (OR: 5.04; 95% CI: 1.73-14.73; p=0.003).

DISCUSSION:
Analysis of biochemical profile of cardiovascular morbidity in 34 psoriasis patients and 30 healthy controls of Chhattisgarh revealed that the systolic blood pressure, FBS, Serum cholesterol, serum triglyceride, serum VLDL, Lipoprotein(a), and hs-CRP levels were significantly higher in Psoriasis patients compared to control group. No significant difference between psoriasis and control group was noted for BMI, diastolic blood pressure, LDL, LDL: HDL and C: HDL.

Our study revealed higher levels of fasting blood glucose levels in psoriatic subjects as compared to controls. The possible mechanism for development of diabetes mellitus in psoriasis may be largely due to insulin resistance and one of the study revealed that TNF-alpha acts as an important mediator of insulin resistance by its ability to decrease tyrosine kinase activity of insulin receptor and this mechanism is true for both obesity and diabetes mellitus.[11] Patients with psoriasis have more insulin resistance than healthy subjects.[12]

One of the causes of cardiovascular morbidity in psoriasis patients may be altered lipid profile and inflammatory mediators. In the present study, we found significantly higher levels of total cholesterol, serum triglyceride and serum VLDL levels in the psoriatic patients. This was in context with the study of Javidi Z et al who observed a significantly higher TC, TG and LDL values in patients compared to controls.[13] Serum LDL in our cases was also found to be higher than the control group though p value was not significant. A large population based study conducted by Mallbris et al on-lipid profile at the onset of psoriasis showed significantly higher VLDL and high HDL fractions.[14] Another case control study by Mehndi et al had similar results as present study. It included 50 psoriasis and 50 healthy controls matched for age and sex and a significant higher plasma levels of lipids were observed.[15] The cause of dyslipidemia in psoriasis may be multifactorial; the immune mechanisms involving IL-6 and tumor necrosis factor, C-reactive protein, and cellular oxidative stress may be responsible for altered lipid metabolism.[16]

Among the non-conventional risk factors, we found a significant higher level of lipoprotein (a) in psoriasis patients after comparing with control group with a significant association between lipoprotein (a) and psoriasis. Our study got the similar results as study by Rocha-Pereira et al.[17] They found in their study that the mean LP(a) concentration was 63.7 mg/dl in psoriatic subjects and 31.7 mg/dl in controls. The mean value for Lp(a) In the present study was 35.32 mg/dl in cases and 16.07 mg/dl in controls. Cimsit et al suggested that higher lipoprotein (a) levels in active period of psoriasis may lead increased risk of developing atherothrombotic events. Lp(a) has been thought to play a role as an inflammatory mediator that augments the formation of atherosclerotic plaque by inducing the expression of adhesion molecules on endothelial cells, chemotaxis of monocytes and proliferation of smooth muscle cells. Study by J. Fan et al showed that Lp(a) augments the production of cytokines by vascular cells and increase the rate of lesion progression. Similar results like our study was also observed by Pietrzak et al which concluded that Lp(a) may be a factor contributing to an increased risk of cardiovascular disease in psoriasis. The findings from our study also provide the support for role of lipids and Lp(a) in mechanisms linking psoriasis and cardiovascular disease pathogenesis.

Another non-conventional risk factor considered in study was high sensitive C-reactive protein (hs-CRP). It has been found that hs-CRP, a systemic inflammatory marker has been regarded as an independent risk factor for CVD. Ridker et al suggested that hs-CRP concentration can predict the vascular

risk even when cholesterol concentrations are low.[18] Patients with low LDL- cholesterol and high hs-CRP were found to be at a higher risk of future coronary events. Rocha-Pereira and Speidl et al have also attributed CRP as a prognostic disease marker in psoriasis.[17] In a study by Savitha jagganath, significant higher levels of hs-CRP were observed in psoriatic subjects when compared with controls. Also Cholesterol, TG, and LDL levels were found to be increased.[19] The present study was in agreement with above mentioned studies. We observed a higher level of hs-CRP in psoriasis patients than in control group. Logistic regression analysis also revealed a significant association between hs-CRP and psoriasis.

CONCLUSION:

The present study demonstrated higher prevalence of psoriasis in males. Hypercholesterolemia, lipoprotein (a) and hs-CRP are associated with psoriasis. The proportion of cardiovascular risk factors such as dyslipidemia, hypertension and diabetes were increased in psoriasis subjects. Clinical studies have confirmed the association of psoriasis with unfavorable cardiovascular risk profile. These risk factors not only affect the physical health but also patient's health related quality of life. The link between psoriasis and cardiovascular disease is still a matter of debate.

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