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CASE-CONTROL STUDY OF LIPOPROTEIN (A) AND URIC ACID IN PATIENTS OF PSORIASIS AT RISK OF DEVELOPING CARDIOVASCULAR DISEASES

TYPE: ORIGINAL RESEARCH ARTICLE

CORRESPONDING &1ST AUTHOR: DR. AMITA GUPTA

Affiliation : Assistant professor, MGM Medical College & MY Hospital , Indore
Address: 6, Nandgaon, Nandvihar, Near Girdhar Nagar, Indore, MP, 452001
EMAIL ID: AMITA.GUPTAGMC@GMAIL.COM
Mobile no. 8223068877

2ND AUTHOR: DR. RAJEEV LOHOKARE

Affiliation: Associate professor, MGM Medical College & MY Hospital , Indore

3RD AUTHOR: DR. P. D. SARKAR

Affiliation: Professor, MGM Medical College & MY Hospital , Indore

4TH AUTHOR: DR. SHIVAM DIXIT

Affiliation: Assistant professor, MGM Medical College & MY Hospital , Indore

Abstract

Objectives: To evaluate and compare lipoprotein A and uric ucid in patients of psoriasis and its correlation with severity of the disease and associated cardiovascular disease risk. **Methods**: Present study conducted in the dept. of biochemistry M.Y.H. Our study included 80 subjects which were divided into two groups, group A comprising 40 apparently healthy controls and group B comprising 40 patients of psoriasis, which is again divided into subgroups, group C comprising of 25 mild cases of psoriasis and group D comprising of 15 moderate/ severe cases of psoriasis. Subjects were enrolled in the study as per the inclusion criteria. Severity of the disease was assessed by PASI(Psoriasis Area and Severity Index) score. Fasting blood samples were collected and evaluated for Lipid profile, lipoprotein 'a' and uric acid , risk ratio was calculated. **Results**: Mean level of Lp(a) was higher in cases as compared to control but the difference was not significant statistically. Difference between control and moderate/severe psoriasis were highly significant .Differences between mild and moderate/severe psoriasis patients were significant. Difference in serum uric acid between all the groups except between control and mild cases of psoriasis were highly significant statistically. Difference in risk ratios between group A and group B were significant and difference in risk ratios between group A and group D and in between group C and D were highly significant statistically.**Conclusion**: Patients of psoriasis must be considered as a group at high risk for cardiovascular diseases. Lipid derangements correlate with the severity of disease and also act as a good prognostic sign. We conclude that psoriatic patients should be evaluated and followed up for the risk of dyslipidemia and cardiovascular morbidity.
Key words: - Psoriasis, PASI, lipoprotein 'a', uric acid, dyslipidemia.

INTRODUCTION:

The hypothesis that the atherosclerotic and the psoriatic plaques are the two offshoots of same root is a focus of current research. Few recent advances in the understanding of

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atherosclerosis, psoriasis and metabolic syndrome should bring the consideration of exploring a common etiopathogenetic pathway for the diseases.

Atherosclerosis represents an ongoing low-grade systemic inflammatory state.[1] Psoriatic patients have higher prevalence of metabolic syndrome.[2] Psoriasis confers an independent risk for adverse cardiovascular events.[3] Psoriasis is an auto-immune disorder characterized by erythematous scaly plaques over extensor aspects of the body.[4] It affects about 2-3% of world population.

About 125 million people all over the world suffer from this disease (*National Psoriasis Foundation*), is common in Caucasians and affects equally men and women. Researchers from Copenhagen University Hospital in Denmark found that people with severe psoriasis were 54% more likely to suffer a stroke, 21% more likely to have a heart attack, and 53% more likely to die over a 10-year period than people without the skin disorder. They were also more likely to need a procedure such as angioplasty to open up clogged heart arteries.

Prevalence of psoriasis varies in India from 0.44 to 2.8%, it is twice more common in males compared to females, and most of the patients are in their third or fourth decade at the time of presentation *(Sunil Dogra & Savita Yadav 2010)* [5]

Etiology of the psoriasis is unknown, but genetic, metabolic and immunologic mechanisms have been proposed. Clinical manifestations of the disease include inflammation.

Patients with psoriasis appear to have an increased morbidity and mortality from cardiovascular events, especially those with a severe and long duration of psoriasis. Multiple factors including increased oxidative stress, decreased antioxidant capacity and other established risk factors such as hypertension, obesity and diabetes mellitus have been associated with psoriasis. However, the pathogenesis of atherothrombotic events in psoriatic patients is yet to be identified.

Lp (a), a genetically determined lipoprotein, is most powerful and most prevalent independent risk factor for coronary heart disease. Lp (a) is an essential component for tissue repair, whose primary function is to deliver large amounts of cholesterol to peripheral cells and to promote regeneration following inflammation.

Uric acid emerging as a new marker for CVD, the urate redox shuttle: Uric acid act as an antioxidant as well as a pro-oxidant. Uric acid stimulates vascular smooth muscle cell proliferation & induces endothelial dysfunction .Uric acid stimulates the production of cytokines from leukocytes & chemokines from vascular smooth muscle cells (TNF, IL-1, IL -6). In the pro–oxidative environment, the antioxidant properties of Uric acid paradoxically become prooxidant. This contributes to the oxidation of lipoproteins within atherosclerotic plaques.

Hyperuricemia has been associated with cardiovascular diseases and metabolic syndrome. Specifically, the prevalence of CVD has been linked with higher levels of uric acid (UA).In addition; hyperuricemia has been reported to cause adverse cardiovascular outcomes, especially sudden cardiac death.

Information is largely not available on lipid abnormalities as well as on uric acid status in psoriatic patients; hence the present study is an attempt to assess the lipid abnormalities as well as uric acid status in patients of psoriasis which are independent risk factors for atherothrombotic events to occur.

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MATERIALS AND METHODS

The present study was conducted in the Departments of Biochemistry and Dermatology of the Mahatma Gandhi Memorial Medical College, Indore, Madhya Pradesh, after it was approved and permitted by the institutional scientific and ethical committee. The period of study extended from March 2015 to March 2016.

The present study included 40 cases of psoriasis aged between 18 to 50 years attending dermatology clinics of Maharaja Yashwant Rao Hospital, Indore and 40 apparently healthy controls matched for age and sex. Informed written consent was taken from all the subjects. Total 80 study subjects were divided into two groups, group A comprising 40 apparently healthy controls and group B comprising 40 patients of psoriasis, which is again divided into subgroups on the basis of severity of the disease, group C included mild cases of psoriasis and group D of moderate/ severe cases of psoriasis.

Excluded from the study were subjects with Secondary hyperlipidemia, hypothyroidism ,nephritic syndrome, diabetes mellitus,on medications like anti hypertensive, corticosteroids, lipid lowering agents, patient of psoriasis on treatment for more than 1 month, smokers and alcoholics, pregnant females, obstructive liver diseases, patients of gout.

Subjects were examined and severity of the disease was assessed by PASI(Psoriasis Area and Severity Index) score and cases were graded accordingly.

Collection of Samples:-

After overnight fasting 5 ml of venous blood sample was drawn by venepuncture from a peripheral vein with all aseptic precautions in a disposable syringe. The blood thus collected in clean dry glass tubes was allowed to stand for 30 minutes at room temperature for the retraction of clot. Then it was centrifuged at 3000 r.p.m. for 10 minutes to separate the serum. The serum sample was stored at -20^0C in the refrigerator for analysis. Care was taken to avoid haemolysis of the sample.

Then serum was analyzed for lipid profile and uric acid with the help of Transasia XL-640 Automated analyzer lipoprotein (a) .

Lipoprotein (a) estimation was done on Bio system BA 400 Automated Analyzer with reagent kit.

STATISTICAL ANALYSIS:

At the end of the study all the data was transferred on to a master chart and inference was drawn. Results on continuous measurements were presented as Mean ± SD. P value < 0.05(95% confidence interval) was considered significant and p value < 0.001 considered as highly significant. Unpaired student t test was applied to find the significance of study parameters on continuous scale between two groups (control and total cases).

ANOVA and POST HOC tests were applied for comparisons within multiple groups (control with mild cases, control with moderate/severe cases and between mild and severe cases).

TABLE NO.1

Characteristics	Cases (N=40) (Mean±S.D)	Controls (N=40) (Mean±S.D)
Age (yrs)	36.55±9.075	34.05±7.81

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Height (cm)	154.27±4.16	154.82±3.83
Weight (kg)	60.12±7.33	58.82±5.91
BMI (kg/m sq.)	25.43±3.53	24.51±2.07

Basic Characteristics of Study Population

TABLE NO. 2

Sex	Control (N=40)	Case(N=40)
Male	19(47.5%)	21(52.5%)
Female	21(52.5%)	19(47.5%)
Total	40(100%)	40(100%)

Gender based Distribution of the Subjects

TABLE NO. 3

S.No.	Subjects	Size
1.	Control (Group A)	40
2.	Cases (Group B)	40
	Mild cases (Group C)	25
	Moderate/Severe cases (Group D)	15
3.	Total	80

Distribution of study subjects

TABLE NO. 4

Comparison of biochemical parameters between Control and Psoriasis Patients

Parameters (mg/dl)	Controls (N=40) (Mean±S.D)	Psoriasis Cases (N=40) (Mean±S.D)	P -Value
Total Cholesterol	167.8±31.89	192.1±42.67	*< 0.001*
Triglycerides	145.85±51.90	168.97±72.26	>0.05
LDL-C	92.21±27.16	111.26±36.60	*< 0.05*
HDL-C	45.06±4.83	45.58±8.30	>0.05
TC/HDL-C	3.68±0.95	4.39±1.41	*< 0.05*

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LDL-C/HDL-C	2.08±0.73	2.58±1.11	*< 0.05*
Lipoprotein (a)	23.33±17.09	32.01±25.45	>0.05
Uric acid	5.14±0.67	5.90±1.03	*< 0.001*

Unpaired 't' test applied. P value < 0.05 was taken as statistically significant.

P value < 0.001 was taken as statistically highly significant.

TABLE NO. 5

Comparison of Lipoprotein (A) in Multiple Groups

S. No.	Group	Lipoprotein(A) (mg/dl)	P value
1	Control (group A) (N=40)	23.33±17.09	>0.05
	Psoriasis Case (group B) (N=40)	32.01±25.45	
2	Control (N=40)	23.33±17.09	>0.05
	Mild Psoriasis (group C) (N=25)	25.16±24.65	
3	Control (N=40)	23.33±17.09	*< 0.001*
	Moderate/Severe Psoriasis(N=15) (group D)	43.43±23.22	
4	Mild Psoriasis (N=25)	25.16±24.65	*< 0.05*
	Moderate/Severe Psoriasis (N=15)	43.43±23.22	

ANOVA and then POST HOC tests for multiple comparisons were applied,p-value< 0.05 was taken as statistically significant. P value < 0.001 was taken as statistically highly significant.

TABLE NO. 6

Comparison of Uric acid in Multiple Groups

S. No.	Group	Uric acid(mg/dl)	P value
1	Control (group A) (N=40)	5.14 ± 0.67	*< 0.001*
	Psoriasis Case(group B) (N=40)	5.90 ± 1.03	
2	Controls (N=40)	5.14 ± 0.67	>0.05
	Mild Psoriasis (group C) (N=25)	5.40 ± 0.79	
3	Controls (N=40)	5.14 ± 0.67	*< 0.001*
	Moderate/Severe Psoriasis (group D) (N=15)	6.72 ± 0.85	
4	Mild Psoriasis (N=25)	5.40 ± 0.79	*< 0.001*
	Moderate/Severe Psoriasis (N=15)	6.72 ± 0.85	

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ANOVA and then POST HOC tests for multiple comparisons were applied,p-value< 0.05 was taken as statistically significant. P value < 0.001 was taken as statistically highly significant.

Discussion

Psoriasis has been traditionally viewed as an inflammatory skin disorder of unknown aetiology. Recent advances in our understanding of the immunopathogenesis and genetics of the disease have shifted the focus from a single organ disease confined to dermal structures to a systemic inflammatory condition. Patients with psoriasis are prone to cardiovascular disease. The biologic mechanisms that putatively contribute to accelerated atherosclerosis and increased risk of cardiovascular events in psoriasis are largely unknown but are likely to be multifactorial. Dyslipidemia is one of the important risk factors for cardiovascular disease. In the present study we evaluated lipid profile in patients of psoriasis.

Uric acid emerging as a new marker for CVD, the urate redox shuttle: Uric acid act as an antioxidant as well as a pro-oxidant. In the present study we also evaluated the serum uric acid concentration of the psoriatic patients.

In our study the mean age of the patients was 36.55 ± 9.07 years(table 2) while in the study of Bajaj et al[6]. the mean age of patients was 37 ± 7.96 years and in the study of Akhyani et al.[7] the mean age was 41.18 ± 17.37 years.

Family history of psoriasis was present in three (7.5%) patients. Bedi et al[8] reported positive family history of psoriasis in 14% of their patients. A study by Kaur et al[9] comprising of 1220 outpatient in which they found a positive family history in only 2% of patients. Our study was accordance with various western studies in which the familial incidence varied from 4.6% to 6.4%. (Hellgren L.,1967 ,Farber EM et al., 1974)[10]

In our study, mean BMI of psoriasis patients was found to be 25.43 ± 3.53 and that in control was 24.51 ± 2.07, the difference being non significant (p>0.05)(table 2). Where as in the study of Gisondi et al[11], the mean BMI in psoriasis patients was 26.9 ± 4.2 versus 26.4 ± 3.2 in controls (p=0.68) and had not demonstrated correlation between two parameters. However in a study of 17388 psoriatic patients, Herron et al.[12] documented BMI to be significantly higher in patients as compared to control.

LIPOPROTEIN (A)

Mechanism of pathogenicity of Lp(a) excess include destabilization of plaque, increased smooth muscle cell proliferation and migration, inhibition of transforming growth factor β, formation of occlusive thrombus, impaired formation of collateral vessels, enhanced oxidation uptake and retention of LDL-C and up regulation of expression of the plasminogen activator inhibitor (PAII) [Rajasekhar D et al., 2004][13], It is reported that macrophages activated by engulfing low density lipoprotein (LDL) immune complexes release large quantities of tumor necrosis factor (TNF) -alpha and IL-1β. Cytokine driven inflammation and tissue destruction is a common theme of chronic inflammatory diseases such as psoriasis and atherosclerosis.The striking homology of apo(a) with plasminogen causes impaired fibrinolysis by competing with plasminogen and enhances thrombogenesis. So Lp (a) modulates thrombosis and fibrinolysis.In the present study there was elevated levels of Lp(a) in Psoriatic patients compared to controls but difference between the multiple groups varies ;difference between the control and severe cases of psoriasis were highly significant(p value<0.001)and difference between mild and severe cases were also significant(p

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value<0.05)(table 7) but difference between control and cases as a whole were non significant statistically(p value >0.05). In a study by Uyanik et al[14], Lp (a) level was significantly higher in patients with psoriasis than in controls (p <0.01). Pietrzak[15] in his study on 34 psoriasis cases showed significantly higher serum levels of Lp (a) relative to controls. Lp (a) may be a factor contributing to an increased cardiovascular risk in patients with psoriasis. A pathogenetic link may exist between this lipoprotein and psoriatic pathophysiology. Lp(a) are involved in the immuno-inflammatory and oxidative stress process in psoriasis, the present study has explored the possible usefulness of this parameters as markers of risk factor for development of cardiovascular disease in patients of severe psoriasis.

URIC ACID

In the present study serum uric acid concentration of cases were highly significant as compared to control (p value< 0.001). Present study also shows a highly significant (p valve< 0.001) raised levels of uric acid in severe cases of psoriasis as compared to the mild cases of psoriasis(table 8). Our study is in agreement with study by Maryam Ghiasi Amir Houshang et al[16] suggested that mean serum uric acid levels were in normal range but value significantly higher in patient with more severe form of psoriasis and uric acid level exacerbate by increases in the severity and duration of psoriasis. Our study supported by the study of Paolo Gisondi[17] who found that the prevalence of asymptomatic hyperuricemia was approximately 3-fold higher in psoriatic patients than in matched control subjects (19% vs 7%). Interestingly, and more importantly, the multivariable regression analysis showed that psoriasis was the strongest predictor of hyperuricemia after adjusting for potential confounders, such as age, sex, BMI, and other features of metabolic syndrome.[17] Kwon et al [18] recently proposed that an increased epidermal cell turnover could be an important cause of raised SUA levels among psoriatic patients. Paolo Gosondi also found significant, graded relationship between SUA levels and PASI score.

Serum lipid changes showed a parallel accompaniment with the severity of the disease. Abnormalities of plasma lipids are likely to play an important role in the increased risk of atherosclerosis, as patients with psoriasis seem to have an increased morbidity and mortality from cardiovascular events . Therefore, the severity of the disease needs to be considered as an increased risk for cardiovascular disease.

CONCLUSION

It is concluded from our study that patients with psoriasis had a higher risk of dyslipidemia and the risk of dyslipidemia increases as the severity of the disease increases as we found 66.66% of cases with moderate/severe psoriasis has altered lipid profile. Psoriatic patients are predisposed to high Lp(a) levels, this may increase the risk of occlusive vascular disorders in patients with psoriasis .

Patients of psoriasis are at increased risk of developing hyperuricemia and increased serum uric acid levels shows positive correlation with the severity of disease. Since lipids, Lp(a) and uric acid are involved in the immuno-inflammatory and oxidative stress process, our study has explored the possible association of these parameters as markers of risk factor for development of cardiovascular disease in patients of psoriasis.

We suggest early screening with serum lipid profile and uric acid assay in psoriatic patients at the time of presentation and follow-up for evaluating risk and treatment

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of hyperlipidemia and hyperuricemia to modify and prevent the risk of cardiovascular diseases.

Conflict of interest : No

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