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ORIGINAL ARTICLE

Study of Cardiometabolic Markers Along with Lipid Indices in Psoriasis

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Abstract

Background: Psoriasis is one of the most common chronic inflammatory skin diseases which affects 2-4% of the general population. The results of epidemiological studies have demonstrated that the risk to develop cardiovascular disease (CVD) is higher in patients with severe psoriasis. The pathogenesis of atherosclerosis followed by CVD is inflammation dependent in psoriasis. **Material and Methods:** It is a cross sectional observation study conducted in a tertiary care hospital from January 2019 to January 2021. 110 patients with psoriasis were included in cases and 110 controls. Anthropometric markers viz. blood pressure (BP), abdominal circumference and cardiometabolic markers lipid profile, hs-CRP, uric acid, Lp(a) were estimated in both groups. The data obtained was subjected to appropriate statistical analysis. **Results:** Anthropometric markers BP (136.1 ± 14.0/ 81.4 ± 8.3; 125.0 ± 8.9/76.2± 5.5) and abdominal circumference (85.4±15.3; 44.7± 11.9), BMI (40.9±8.3;22.3±3.2) were statistically high in cases than controls. The cardiometabolic markers as Triglycerides (TG) (212.3 ± 39.5; 122.9 ± 43.2), Total cholesterol (241.0 ± 60.4; 155.0 ± 43.2), High Density Lipoprotein-Cholesterol (HDL-C) (34.9 ± 6.8; 43.5 ± 9.8), Low Density Lipoprotein-Cholesterol (LDL-C) (196.8 ± 43.1; 132.0 ± 10.0), uric acid (17.1 ± 7.2; 4.5 ± 1.0), hs-CRP (16.2 ± 7.7; 2.8 ± 1.3), Lipoprotein (a) [Lp(a)](41.3 ± 8.7; 25.1 ± 7.9) and lipid indices AIP (0.79 ± 0.12, 0.46 ± 0.11), CI-I (7.20 ± 2.43; 3.70 ± 1.13), CI-II (5.85 ± 1.70; 3.21 ± 0.83), AC (239.97 ± 60.44; 152.25 ± 35.05), LTI (6654.34 ± 39207.47; 92.29 ± 38.92) were significantly high in cases compared to controls. **Conclusion:** The present study found significant increase in cardiometabolic markers in psoriasis patients compared to controls. So, this study emphasizes the importance of screening of cardiometabolic markers and other metabolic co-morbidities in psoriasis patients to help in early detection and treatment in order to reduce cardiovascular events.

Key Words

Psoriasis, Anthropometric Markers, Lipid Profile, Cardiometabolic Markers, Lipid Indices

Introduction

Psoriasis is one of the most common chronic inflammatory skin diseases which affects 2-4% of the general population. However, variations between and within countries and causes a significant social and pharmaco economic burden. [1]

In recent years, various population-based epidemiological studies have shown that patients with psoriasis have an increased risk for various cardiovascular comorbidities such as hypertension, hyperlipidaemia, obesity, metabolic syndrome and cardiovascular diseases. [2] The results of epidemiological studies have also demonstrated that the risk to develop CVD is higher in patients with severe psoriasis [3] and that this risk persists even after adjusting for conventional cardiovascular risk factors. [4] Psoriasis is known to be an independent risk factor for CV disease

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where as age, BMI, metabolic syndrome, and smoking status have been found to increase the risk of psoriasis. [5] The pathogenesis of atherosclerosis followed by CVD is inflammation dependent. [6] Central obesity, a component of metabolic syndrome (MS), is frequently encountered in patients with psoriasis. [7]

The PASI score is the most commonly used system to assess the severity. However, this system is subjective and difficult to interpret due to nonlinear scaling, time-consuming, and having high intra and inter-ratter variability and also other comorbidities are not evaluated. [8]

Previous studies have shown that mortality rates are increased in psoriasis patients and the life expectancy of patients with moderate to severe psoriasis is decreased by approximately 5 years, mainly due to cardiovascular comorbidities. [9]

Hence the present study is undertaken to assess cardiovascular risk in psoriasis patients. Therefore the objectives of the study were to assess anthropometric markers like BP, abdominal circumference and cardiometabolic markers like lipid profile, uric acid, hs-CRP, Lp(a) and atherogenic lipid indices in both cases and controls. Further to correlate these cardiometabolic markers with lipid indices in these patients.

Material & Methods

This is a cross-sectional observation study conducted in tertiary care hospital attached to a medical college from January 2019 to August 2020. Total sample size was 220 in which 110 cases and 110 controls. Sample size was calculated according to study done by Sandhya M *et.al.*, [10] using Open Epi software Version 2.3.1 with confidence level: 95% and power of the study: 80%. Calculation results were 100 in each group.

Inclusion Criteria: The newly diagnosed patients with clinical features of psoriasis like erythema, itching, thickening and scaling of the skin were included for the study. The clinical severity was determined according to the Psoriasis Area and Severity Index (PASI) score .[11]

Exclusion Criteria: Patients with any chronic inflammatory disease, diabetes mellitus, renal disorders, IHD, hypothyroidism, hyperthyroidism, nephritic syndrome, obstructive liver disease, and any other skin disorders were excluded from the study. All the patients receiving systemic drug therapy like beta blockers, thiazides, retinoids, cyclosporine and lipid lowering agents in the recent 6 months were excluded from the study.

Approval was obtained from the institutional ethical committee. After taking informed consent, detailed history and clinical examination was done and patients were classified as mild, moderate and severe according to PASI score. Mild <7, Moderate 7-12, Severe >12. [11]

Under aseptic precautions around 5mL of blood was drawn in plain tube and EDTA was added and subjected to centrifugation at 3000 rpm for 20 minutes to separate the serum.

Separated serum was used for analyzing different biochemical parameters. Lipid profile in fully automated analyser by enzymatic method, hsCRP by ELISA, Uric acid in fully automated analyser by enzymatic method as per kit instructions, BP by using sphygmomanometer, abdominal circumference by using measuring tape, Lipid indices were calculated using formulas.

Statistical analysis

was done using SPSS software. For categorical data, the number and percentage were used in the data summaries and diagrammatic presentation. Chi-square test was used for association between two categorical variables. The difference of the means of analysis variables between two independent groups was tested by unpaired't' test. The difference of the means of analysis variables between more than two independent groups was tested by ANOVA and 'F' test of testing of equality of Variance.

Results

In the present study there were totally 220 subjects out of which 110 were cases and 110 controls. The subjects in the age group were between 20-60yrs. Table 1 shows demographic and anthropometric markers of subjects who attended skin out-patient department at tertiary care hospital and Research centre. *Fig1* shows distribution of gender in both cases and controls. *Table 2* shows the mean levels and standard error of mean and comparision of cardiometabolic parameters between cases and controls. We found significant increase cardiometabolic parameters in cases compared to controls. *Table 3* shows distribution of uric acid according to level of PASI score and controls. There was significant increase in uric acid level from mild to severe cases. Table 4 shows distribution of lipid indices between cases and controls. The lipid indices were statistical significant in cases compared to controls. *Fig 2* shows comparison of different lipid indices between study groups.

Table 5 shows correlation between lipid indices and cardiometabolic parameters among cases and controls. Among cardiometabolic markers Lp(a),TG, Cholesterol, HDL-C, LDL, and anthropometric marker Abdominal circumference showed statistical significant correlation with some lipid indices.

Discussion

In the present study, anthropometric markers like blood pressure, abdominal circumference, BMI were statistically significant increased in psoriasis patients compared to

Table 1. Demographic and Anthropometric markers between Cases and Controls

Demographic & Anthropometric	Cases (Mean± S.D)	Controls (Mean± S.D)	't' value	'p' value
Age (yrs)	40.8± 11.4	39.4± 11.1	0.935	0.351
Systolic-BP(mm/Hg)	136.1 ± 14.0	125.0 ± 8.9	7.004	<0.001*
Diastolic-BP (mm/Hg)	81.4 ± 8.3	76.2± 5.5	5.456	<0.001*
Abdominal circumference(cm)	85.4±15.3	44.7± 11.9	22.055	<0.001*
BMI (wt in kg/ht in m^2)	40.9±8.3	22.3±3.2	12.6	<0.001*

Note: p value significant at 5% level of significance (p<0.05)*

Table 2. Cardiometabolic markers between Cases and Controls

Parameters	Cases Mean ± SD	Controls Mean ± SD	't' value	'p' value
TG	212.3 ± 39.5	122.9 ± 14.6	22.257	<0.001*
Cholesterol	241.0 ± 60.4	155.0 ± 43.2	12.76	<0.001*
HDL-Cholesterol	34.9 ± 6.8	43.5 ± 9.8	-7.568	<0.001*
LDL-Cholesterol	196.8 ± 43.1	132.0 ± 10.0	15.368	<0.001*
Uric acid	17.1± 7.2	4.5 ± 1.0	18.2	<0.001*
Lp(a) mg/dl	41.3 ± 8.7	25.1 ± 7.9	14.515	<0.001*
hs-CRP	16.2 ± 7.3	2.8 ± 1.3	18.952	<0.001*

Note: p value significant at 5% level of significance (p<0.05)*

Table 3. Distribution of uric acid serum levels according to level of PASI Score and Controls

Parameters (Mean±SD)	Level of PASI Score			Controls	F value	p value
	Mild	Moderate	Severe			
Uric acid	16.3±9.2	16.7±6.2	17.4±7.2	4.5±1	110.033	<0.001*

Note: p value significant at 5% level of significance (p<0.05)*

Table 4. Distribution of Lipid Indices between Cases and Controls

	Cases		Controls		t value	p value
	Mean	SD	Mean	SD		
AIP[log(TG/HDL)]	0.79	0.12	0.46	0.11	20.507	<0.001*
CI-I[TC/HDL]	7.20	2.43	3.70	1.13	13.687	<0.001*
CI-II[LDL/HDL]	5.85	1.70	3.21	0.83	14.582	<0.001*
AC[TC-HDL/HDL]	239.97	60.44	152.25	35.05	13.168	<0.001*
LTI[TCxTgxLp(a)/HDL]	66541.34	39207.47	92.29	38.92	17.775	<0.001*

AIP-Atherogenic Index of Plasma; CI- Castelli Index; AC- Atherogenic coefficient; LTI – Lipid tetrad index

Note: p value significant at 5% level of significance (p<0.05)*

controls as depicted in *Table 1*. Several studies have shown psoriasis patients had uncontrolled hypertension and this risk correlated with disease severity. A cross sectional study done in Germany have shown that central obesity or waist circumference was statistically more in psoriasis patients than controls. They also showed significant correlation between degree of obesity and severity of psoriasis. [12]

A study has shown that in patients with psoriasis who were obese, and weight loss has been shown to increase the efficacy of anti-TNF-alpha biologic therapy.[13] A study done by Dickison *et. al.*, showed women with psoriasis have a risk of hypercholesterolemia and hypertension, and overweight women are more susceptible to type 2 diabetes than are women with normal weight. [14] This was not in accordance to our study.

The molecular mechanisms underlying the association between psoriasis and obesity are currently not clearly understood. Various studies have shown that the disordered production of adipokines from fat tissue in obese patients with psoriasis may lead to chronic skin and systemic inflammation and increased cardiovascular risk. [12]

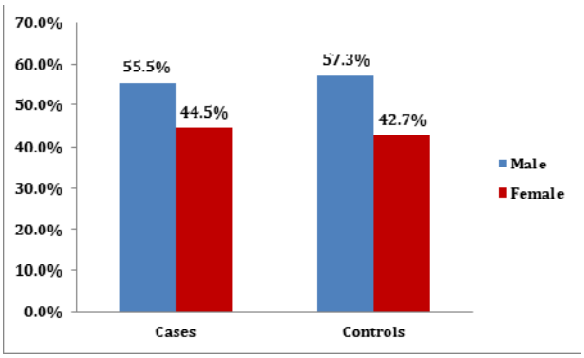
Among cardiometabolic markers uric acid was statistically significant from mild-moderate-severe (PASI score) in

Table 5. Correlation between lipid indices and cardiometabolic parameters among Controls / Cases

Parameter	AIP[log(TG/HDL)]		CI-I[TC/HDL]		CI-II[LDL/HDL]		AC[TC-HDL/HDL]		LTI[TCxTgxLp(a)/HDL]	
	r value	p value	r value	p value	r value	p value	r value	p value	r value	p value
LP(a) mg/dl	0.303	**0.044***	-0.037	0.899	0.011	0.971	-0.112	0.704	0.626	**0.017***
TG	0.72	**0.004***	-0.004	0.989	0.082	0.781	-0.038	0.897	0.587	**0.027***
Cholesterol	0.022	0.941	0.843	**<0.001***	0.23	0.429	1	**<0.001***	0.497	0.07
HDL	-0.793	**0.001***	-0.575	**0.032***	-0.7	**0.005***	-0.073	0.804	-0.455	0.102
LDL	0.144	0.624	0.242	0.405	0.755	**0.002***	0.246	0.397	0.14	0.632
Uric acid	-0.073	0.804	0.312	0.278	-0.076	0.795	0.219	0.451	0.003	0.991
Systolic-BP	-0.078	0.791	0.321	0.264	-0.082	0.78	0.195	0.503	-0.022	0.94
Diastolic-BP	0.059	0.84	-0.081	0.783	-0.447	0.109	0.008	0.978	-0.045	0.879
BMI	-0.034	0.908	-0.032	0.912	0.484	0.079	-0.276	0.34	-0.124	0.672
MS	-0.356	**0.044***	-0.045	0.88	-0.213	0.465	-0.007	0.981	-0.227	0.434
hs-CRP	-0.296	**0.044***	-0.084	0.775	-0.03	0.918	-0.164	0.576	-0.102	0.729

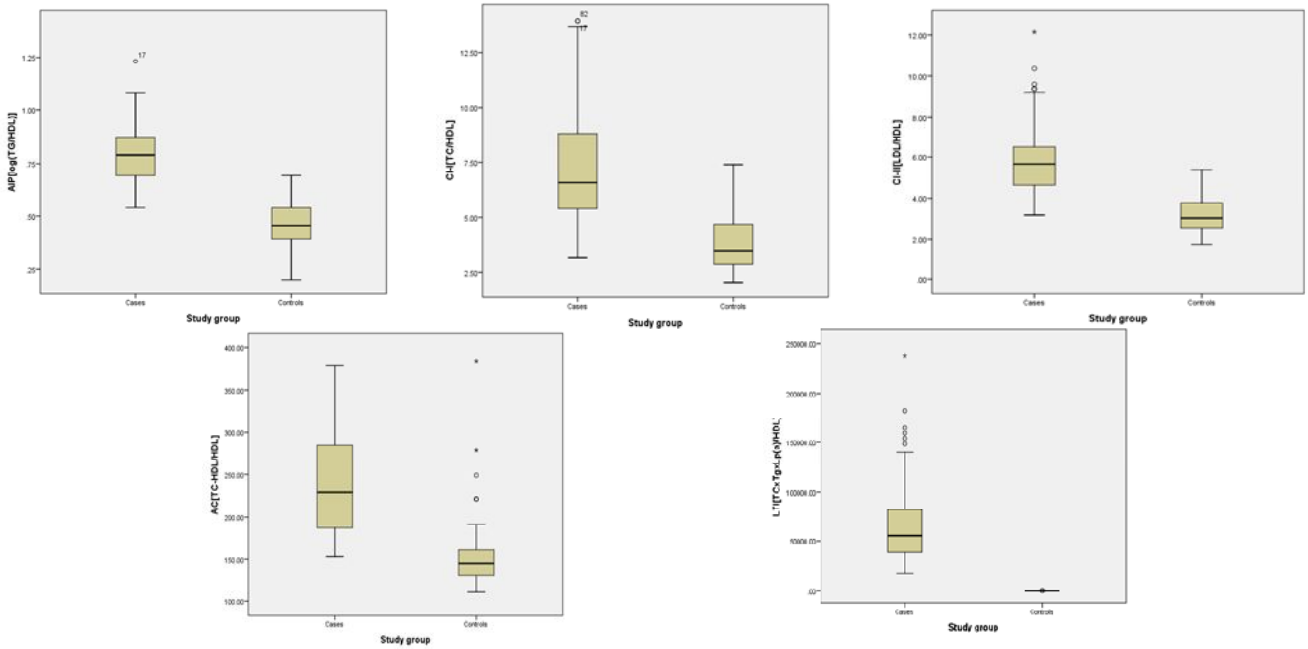
Note: p value significant at 5% level of significance (p<0.05)*

Fig 1. Distribution of Gender between Cases and Controls



cases shown in Table 3. Elevated uric acid levels are frequent finding in psoriasis. Study done by Ukonu and Ibekwe found a prevalence of 40.7% of hyperuricemia among psoriasis patients as compared to 7.0% of the control group (p=0.001) which showed strong association between serum uric acid level and psoriasis. [15] This study was in accordance to our study. The findings of our study have clinical implications as elevated serum uric acid levels causes gouty arthritis, which needs to be differentiated from psoriatic arthritis in clinical practice. The elevated serum uric acid is associated with increased carotid-artery intima-media thickness in patient with psoriatic arthritis, and independently predicts the development of cardiovascular events and mortality in

Fig 2. Showing comparison of different lipid indices between study groups



nonpsoriatic populations. [16] A study done by Xin-Yu Gu *et al.*, [17] showed increase in uric acid levels from mild to severe but with no statistical significance This was not in accordance to our study where along with increase uricd acid levels we got statistical significant correlation with severity.

All lipid indices showed statistical significant increase in cases compared to controls depicted in *Table 4*. These lipid indices were compared with cardiometabolic markers among cases and controls as depicted in *Table 5*. Among atherogenic markers Lp(a) and TG showed significant positive correlation with AIP and LTI where as cholesterol showed positive significant correlation with CI-I and AC lipid indices. A study done by Rocha-Pereira *et al* [18], reported increased serum total cholesterol, VLDL-cholesterol, LDL-cholesterol and a decrease HDL-cholesterol levels which was in accordance to our study. On the other hand, HDL good cholesterol showed negative significant correlation with AIP, CI-I, CI-II where as LDL being bad cholesterol showed positive correlation with CI-II. Both abdominal circumference and hsCRP showed negative correlation with AIP.

Along with lipid indices and anthropometric markers even hs-CRP, uric acid and Lp(a) also showed significant increase in psoriasis patients compared to controls. The increased levels of these markers in psoriasis patients have risk indicate that they are more susceptible for cardiovascular complications and require specific remedial steps which are necessary in considering the treatment. [12] A study by Ridker PM *et al* [19] have shown increased hs-CRP in psoriasis patients have been found to be associated with subclinical atherosclerosis and, therefore they have a predictive value for developing future cardiovascular events. These markers are over expressed in psoriasis, even in patients without overweight/obesity or other traditional CVD risk factors such as hypercholesterolemia, hypertension, and diabetes. [19]

A study generated from a German database of 42,461 dermatologic patients, in which 2,941 with psoriasis, reported that after controlling for age and sex, the rate of hypertension was twice as high in psoriatic patients compared with controls. However, two recent studies have failed to demonstrate a dose response relationship between hypertension and the psoriasis severity after controlling for confounders. [20]

Studies have shown that dyslipidaemia profile was present at the onset of psoriasis, suggesting that dyslipidaemia may precede the onset of psoriasis. [20] An increase in hs-CRP also reflects metabolic disorders, including insulin resistance and adiposity [21] , which are very common in patients with PS. As psoriasis is frequently associated with obesity, the excess adipose tissue might further contribute to atherogenic dyslipidemia. Hs-CRP, an acute phase reactant protein, is produced from hepatocyte within hours after being stimulated from inflammation, infection, tissue damage. [22] Kanelleas *et al*, found levels of hs-CRP was the only marker correlated with PASI score both before and after treating with etanercept and the more difference of hs-CRP level revealed the more treatment response. [23] Several studies have shown the common features of atherogenic dyslipidemia in psoriasis which include increased blood levels of total cholesterol, triglycerides, LDL, and apolipoprotein A and low HDL and apolipoprotein B levels in patients with psoriasis in patients with psoriasis, not only lipoprotein levels can be altered, but also their composition and function may be significantly different from controls. In the study done by, Mehta *et al*. showed that the HDL efflux capacity in psoriasis patients compared with controls was diminished beyond cardiovascular risk factors. [24]

Thus the pathogenetic mechanisms of cardiovascular disease in psoriasis patients appear to be of a complex nature. The pro-atherogenic lifestyle and cardiometabolic risk factor like diabetes, hypertension, hyperlipidaemia, obesity and metabolic syndrome, along with psychosocial and behavioral risk factors such as smoking, alcohol abuse, lack of exercise and depression will all increase the risk of cardiovascular disease in psoriasis patients. [25]

Limitations: The limitation of the present study is that psoriasis being inflammatory condition inflammatory markers could be included in the study. Further investigations are required to clarify the mechanisms underlying the association between psoriasis and cardiovascular comorbidities, and also to define optimal treatment regimens so as to reduce the risk of cardiovascular events in patients with psoriasis.

Conclusion

The present study found statistical significant increase in anthropometric markers BP, abdominal circumference & BMI in psoriasis patients compared to controls. Along with anthropometric markers, cardiometabolic markers also showed significant increase in psoriasis patients. Thus it is emphasized that the routine screening of cardiometabolic markers and other metabolic co-morbidities should be done which helps in early detection and treatment so as to reduce cardiovascular events in future. Physicians should be more aware of these cardiovascular risk while treating these patients.

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Conflicts of Interest
There are no conflicts of interest.

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