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Original Article

Dermatology Section

Metabolic Syndrome in Psoriasis among Urban South Indians: A Case Control Study Using SAM-NCEP Criteria

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ABSTRACT

Introduction: Psoriasis is a chronic inflammatory disease of the skin associated with increased cardiovascular morbidity. Metabolic syndrome is a significant forecaster of cardiovascular events.

Aim: To assess the association of metabolic syndrome and its components in patients with psoriasis and to compare it with the age and sex matched control group.

Materials and Methods: We conducted a hospital based case-control study on 156 adult patients with chronic plaque psoriasis and 156 patients with skin diseases other than psoriasis. Height, weight, BMI, blood pressure and waist circumference were documented in all the subjects. Fasting levels of serum glucose, serum triglycerides and serum HDL were estimated by automated clinical chemistry analyzer. The South Asian modified NCEP ATP criterion was used for the diagnosis of metabolic syndrome. Statistical analysis of the data was done using statistical processing software (SPSS-17).

Results: Metabolic syndrome was significantly more common in psoriatic patients than in controls (28.8% vs 16.7%, p=0.01). Hypertriglyceridemia was significantly more prevalent in cases than in controls (34% vs 20.5%, p=0.008). The reduced HDL levels also showed a significantly high occurrence among cases (27.6% vs 13.5%, p=0.002). Moderate increase of blood pressure was seen among cases as compared to controls but the difference was not statistically significant (p=0.1). Impaired blood glucose and abdominal obesity were similar in both groups. Smoking and alcoholism did not influence the association of metabolic syndrome with psoriasis. There was no correlation of metabolic syndrome with severity and duration of psoriasis.

Conclusion: Our findings suggest that metabolic syndrome as well as dyslipidemia is common in psoriasis patients among urban South Indians. This study highlights the need for screening at diagnosis and regular follow up of the metabolic aspects of the disease along with the skin lesions.

Keywords: High density lipid, Smoking, Triglycerides

INTRODUCTION

Psoriasis is a chronic, inflammatory condition affecting approximately 1% to 3% of the population. It is a disease that can have a major impact on the patient as it is associated with several co-morbidities [1,2]. Over the past one decade there is accumulating evidence of psoriasis patients having an increased prevalence of cardiovascular risk factors and resultant adverse outcomes, metabolic syndrome, Chronic Obstructive Pulmonary Disease (COPD), inflammatory bowel disease, depression and osteoporosis [2,3]. Metabolic syndrome is a cluster of risk factors including obesity, dyslipidemia, hypertension and glucose intolerance. Insulin resistance and altered adipocyte function is thought to be the cause for metabolic syndrome [2]. The occurrence of metabolic syndrome is 15-25% in the general population and 30-50% among psoriasis patients [3,4]. Metabolic syndrome poses a cardiovascular risk which is greater than that conferred by its individual components [1].

Metabolic syndrome and psoriasis have certain common immunological mechanisms. The levels of Th-1 cytokines (TNF-α), adhesion molecules (ICAM and Eselectin) and angiogenic factors such as the Vascular Endothelial Growth Factors (VEG-F) are found to be high in psoriasis, obesity and coronary artery disease [5].

The metabolic features of chronic inflammation, angiogenesis and epidermal hyperproliferation in psoriasis have the likelihood to impact conditions like diabetes, atherosclerosis and thrombosis. Conversely, obesity, diabetes and atherosclerosis have a cocktail of inflammatory molecules and hormones which may influence the pathogenesis of psoriasis. Recent studies have demonstrated the role of IL-20 and IL-17 in the pathogenesis of psoriasis [5]. Finally, these diseases also share several common genetic loci. Several well-structured studies have demonstrated that the psoriasis susceptibility loci PSORS 2, PSORS 3 and PSORS 4 are associated with loci of susceptibility for metabolic syndrome, type II diabetes, familial hyperlipidemia and cardiovascular disease [6]. Campalani E et al., in their study found an increased prevalence of Apo E4, a gene with recognized function in cardiovascular disease, among psoriasis patients [7].

The diagnostic criteria for metabolic syndrome has been proposed by various organizations such as the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) and the International Diabetes Foundation [8-10]. The south Asian Modified National Cholesterol Education Program adult treatment panel III criteria (SAM-NCEP criteria) is a modification of the NCEP ATP III that is tailored to suit the South Asian population [11]. Studies have shown that higher body fat is seen in south Asians than Caucasians at similar BMI. South Asia comprises the sub-Himalayan countries, a major portion of which consist of the inhabitants of the Indian sub continent [12]. In this study we aim to assess the prevalence of the metabolic syndrome and its associated components among individuals with psoriasis, using the SAM-NCEP criteria, and to compare them with individuals without psoriasis in the south Indian urban population. To the best of our knowledge, our study has the largest sample size among similar studies published from India.

MATERIALS AND METHODS

This was a hospital based comparative study conducted over a period of one year from June 2013 to May 2014 at the Department of Dermatology of KS Hegde Charitable Hospital. One hundred fifty six adult patients with a clinical diagnosis of chronic plaque psoriasis who consented for the study were included. Patients who

have received systemic therapy (especially cyclosporine or/and systemic retinoids) during the previous six months were excluded. Pustular psoriasis and erythrodermic psoriasis were also excluded from the study.

One hundred fifty six age and sex matched controls were selected from patients attending the dermatology outpatient department with skin diseases other than psoriasis.

The study was initiated after obtaining the ethical clearance and the informed consent from the patients. Relevant data such as age, sex, occupation, weight, height, Body Mass Index (BMI), waist circumference, Blood Pressure (BP), smoking habit, alcohol intake, type and severity of psoriasis, exacerbations, remissions, duration and concomitant medication were collected and entered in a pre-structured proforma. BMI was calculated as weight (kg)/(height in m^2). Waist circumference was measured using a measuring tape placed snugly but not too tightly around the abdomen at the uppermost level of the pelvic bone. Severity of psoriasis was assessed using PASI score [13]. Mild psoriasis was classified as a PASI of <5, moderate between 5 and 10 and severe >10.

Blood samples for serum cholesterol, triglycerides, HDL and plasma glucose were collected after overnight fasting for at least 8 hours.

Fully automated clinical chemistry analyzer was used to analyze the samples. Serum glucose, serum triglycerides and serum HDL-cholesterol were estimated using the hexokinase method and the enzymatic colorimetric methods respectively.

The SAM-NCEP criterion was used to diagnose metabolic syndrome [11]. The following points were taken into consideration: Abdominal obesity using the waist circumference of ≥90 cm for males and ≥80 cm for females, fasting blood glucose of ≥100 mg/dl, blood pressure >130/85 mmHg, hypertriglyceridemia >150 mg/dl, or low HDL cholesterol <40 mg/dl for males and <50 mg/dl for females. Metabolic syndrome was diagnosed when ≥3 of the above mentioned criteria were present. Data was analyzed using SPSS software version 17.0 (SPSS Inc. Chicago, Illinois, USA). The values were reported as mean±standard deviation and percentage. Statistical significance was attributed if p<0.05. Pearson's chi-square test was used for nominal data. Student's unpaired t-test for numerical variables. Odd's ratio and confidence interval was calculated for the prevalence of metabolic syndrome.

RESULTS

The study population had a male preponderance (236 men and 76 women). The descriptive statistics are shown in [Table/Fig-1]. Patients had mild to severe psoriasis with the PASI score ranging from 0.9 to 32.2 with a median of 3.9. A total of 61.5% patients had a PASI of <5, 21.2% patients had PASI score of 5-10 and 17.3% had >10. Psoriatic arthritis was present in 4.5%. The prevalence of dermatologic diagnosis in the control group were as follows, 46.2% has eczemas, 26.8% infective skin disorders, 14.3% had acne vulgaris, 9.6% had melasma and 3.1% had vitiligo.

The mean disease duration was 7.9 years. The duration of the disease was classified as short (< 1year), intermediate (1-5 years) and long (> 5 years). A 19.2% had short duration of the disease, 30.8% had intermediate duration and 50% of the patients had the disease for long duration. Psoriatic patients were more frequently smokers and alcohol consumers as compared to the controls, however the differences were not statistically significant (p=0.2) [Table/Fig-1].

We found a significantly higher prevalence of metabolic syndrome in psoriasis patients than in the controls (28.8% vs 16.7%, p=0.01). A higher prevalence of metabolic syndrome in cases and controls was seen above the age of 55 years. The prevalence of metabolic syndrome did not correlate with the disease severity (p=0.27) and the disease duration (p-value=0.25).

	Cases (n=156)	Controls (n=156)	p-value
Sex M/F	118/38	118/38	1.0
Age at enrolment (months) mean±SD‡	45.5±12.6	45.4±12.5	0.9
Body mass index, mean±SD‡	24±4.8	25.2±2.2	0.1
Alcohol intake, n (%)	70 (44.9)	57(36.5)	0.2
Smoking, n (%)	65 (41.7)	53 (34)	0.2
Metabolic syndrome, n (%)	45 (28.8)	26(16.7)	0.01†
Triglyceridemia >150 mg/dl, n (%)	53 (34)	32 (20.5)	0.008†
HDL* cholesterol, <40 mg/dl (M), <50 mg/dl (F), n (%)	43 (27.6)	21 (13.5)	0.002†
Blood pressure ≥130/85 mmHg, n (%)	37 (23)	26 (16.7)	0.1
Waist circumference ≥90 cm (M), ≥80 cm (F)	73 (46.8)	71 (45.5)	0.5
Fasting plasma glucose ≥100 mg/dl	38 (24.4)	39 (25)	0.9

[Table/Fig-1]: Descriptive characteristic of cases and controls.
*HDL-high density lipoprotein
†Statistically significant (p-value <0.05)
‡p-value was calculated using student's unpaired t- test.
For all parameters except age and body mass index, p-value was calculated using Pearson's Chi-square test.

Hypertriglyceridemia was significantly more prevalent in cases than in controls (34% vs 20.5%, p=0.008). The reduced HDL levels was more frequent among cases and was statistically significant (27.6% vs 13.5%, p=0.002). Moderate increase of blood pressure was seen among cases as compared to controls but the difference was not statistically significant (p=0.1). Impaired blood glucose and abdominal obesity were similar in both groups [Table/Fig-1].

The mean values of the parameters of metabolic syndrome in cases and controls are given in [Table/Fig-2]. The mean values of triglycerides, HDL and waist circumference were significantly different in cases than in controls.

Parameters	Cases Mean± Standard Deviation	Controls Mean ±Standard Deviation	p-value
Triglycerides (mg/dl)	138.49±38.98	129.78±31.26	0.03†
HDL (mg/dl)*	44.42±9.02	46.53±7.7	0.027†
Systolic blood pressure (mm of Hg)	124.26±13.17	124.76±13.27	0.732
Diastolic blood pressure (mm of Hg)	81.48±6.77	80.62±7.34	0.287
Waist circumference (cm)	86.27±13.14	87.35±31.26	0.03†
Fasting plasma glucose (mg/dl)	97.07±14.70	97.01±15.78	0.973

[Table/Fig-2]: Comparison of the parameters of metabolic syndrome in cases and controls.
*High density lipid
†Statistically significant (p-value of < 0.05).
p-value of all the parameters were calculated using student's unpaired t-test

Comparison of descriptive characteristics of psoriatic patients with metabolic syndrome and without metabolic syndrome are shown in [Table/Fig-3].

DISCUSSION

Gerald Reaven, an endocrinologist, 1st described the metabolic syndrome in 1988 [14]. The WHO, the NCEP ATP III and the European group on insulin resistance agree to the same set of components however differ regarding the values for each [8,15,16].

Mallbris L et al., discussed the metabolic disorders in patients with psoriasis and psoriatic arthritis and in the same year Sommer DM et al., showed that metabolic syndrome was more prevalent in psoriasis patients [17,18].

The prevalence of metabolic syndrome in psoriatic patients was 28.8% in the present study. This is supported by previous observations by International and Indian studies. [Table/Fig-4,5]

	Psoriatic patients with metabolic syndrome (n= 45)	Psoriatic patients without metabolic syndrome (n= 111)	p-value
Sex M/F	38/7	80/31	0.103
Age at enrolment (years), mean±SD	51.7±12.3	43±11.9	<0.001‡
Alcohol intake (n)§	24	45	0.21
Smoking (n)§	26	38	0.01†
BMI (kg/m^2)	26.6±3.4	22.9±3.5	<0.001‡
Waist circumference (cm)	92.6±11.9	83.7±12.8	<0.001‡
HDL(mg/dl)*	37.46±9.55	47.23±7.12	<0.001‡
Systolic (mm of Hg)	131.78±14.46	121.20±11.33	<0.001‡
Diastolic (mm of Hg)	85.29±7.21	79.94±5.95	<0.001‡
Fasting plasma glucose (mg/dl)	104.38±19.28	94.10±11.19	<0.001‡
Triglycerides (mg/dl)	157.96±41.56	130.60±35.10	<0.001‡
Disease duration (years)	8.9±8.3	7.5±8	0.353
PASI	6.2±4.1	5.6±5.4	0.525

[Table/Fig-3]: Descriptive characteristic of psoriasis patients with and without metabolic syndrome.
*HDL-high density lipoprotein
†Statistically significant (p-value <0.05).
‡Very highly significant
§p-value was calculated using Pearson's chi-square test
For parameters other than smoking and alcohol intake p-value was calculated using student's unpaired t-test

depicts data from studies done internationally [1,4,18-21] and in India respectively. Several studies from India have reported a prevalence of metabolic syndrome in psoriasis ranging from 18% to 60%, with the studies from the Southern India showing a higher prevalence [22-27] [Table/Fig-5]. This pattern of prevalence reflects the prevalence of metabolic syndrome in the general Indian population, which is 9.3% in Central India and 29.7% in South India [12]. This diversity may also be due to the variations in sample size, the differences in the criteria used in these studies, life style and eating habits.

Metabolic syndrome in psoriasis in the Western population ranges from 14%-40% [Table/Fig-4]. The overall prevalence of metabolic syndrome in the general population corresponds to 30-40% among Asian Indians, 15-20% among Europeans and 35-40% in Americans [11]. These variations might have contributed to the final outcomes of the studies.

We found the prevalence of metabolic syndrome increased sharply above the age of 55 and this is consistent with other studies [1,9]. In our study, the disease severity did not have a correlation with metabolic syndrome (p=0.27). Disease duration and metabolic syndrome also showed no statistically significant association (p=0.25). Several other studies quote similar findings [24,27,28]. Recently a hospital based study from Pondicherry, India found a high prevalence of metabolic syndrome in psoriasis (60% vs 40%) however, the difference was not statistically significant and also the low sample size was a limiting factor in this study [27].

Analyzing the individual components of metabolic syndrome there is a wide variation among the Indian studies. The increased waist circumference was found in 46.8% of cases and 45.5% of controls. This difference was not statistically significant. Studies from North India by Nisa N et al., Pereira R et al., and a study from Pondicherry by Lakshmi S et al., are in agreement with our finding [22,23,26]. On the other hand Madanagobalane S et al., Khunger N et al., and Kathirvel D et al., found significant increase in abdominal obesity in psoriasis patients with metabolic syndrome [24,25,29]. This discrepancy may be due to the utilisation of the south Asian modified waist circumferences in our study.

Elevated blood pressure was found in 23% and 16.7% in cases and controls respectively but was not statistically significant. This is distinct from the studies done in India where systolic and diastolic blood pressures were found to be significantly higher in psoriasis patients compared to controls [22,25]. However, several other studies did not show such an association [24,26,27,29]. In our study we attribute this finding to the moderately high prevalence of high blood pressure in the control population as they were hospital derived.

Significant hypertriglyceridemia was found in cases compared to the control group. Madanagobalane S et al., and Nisa N et al., shared similar findings [22,24]. Contradictory to this, there were studies which did not show significant hypertriglyceridemia [23,26,27,29].

Study	Study Period	Geographic Area	Cases/Controls	Criteria for MS	No. Psoriasis Patients with MS* (%)	No. Controls with MS* (%)	Measure of Association (OR* and Confidence Interval)
Sommer DM et al., [18]	1996-2002	Germany	581/1044	WHO* criteria	25 (4.3)	11(1.1)	4.22(2.06-8.65)
Gisondi P et al., [1]	NR*	Italy	338/334	NCEP-ATP III*	102 (30.1)	69 (20.6)	1.65 (1.16-2.35)
Chen YJ et al., [19]	2006-2007	Taiwan	71/81	Clinical assesment	10 (14.1)	13 (16.3)	0.84 (0.31-2.26)
Chen YJ et al., [20]	2006-2007	Taiwan	40/37	Clinical assesment	9 (22.5)	4 (10.8)	2.40 (0.67-8.58)
Augustin M et al., [21]	2005	Germany	33,981/1,310,090	ICD-10*	61 (0.2)	786 (0.1)	2.86 (2.21-3.71)
Love T et al., [4]	2003-2006	USA	71/2385	NCEP-ATP III*	28 (39.9)	560 (23.5)	2.16 (1.16-4.03)
Present study	2013-2014	India	156/156	SAM NCEP*	45 (28.8)	26 (16.7)	0.49 (0.29-0.85)

[Table/Fig-4]: Comparison of International study results with the present study [1,4,18-21].
*MS, Metabolic syndrome; WHO, World health organisation; NCEP ATP III, National cholesterol education programme adult treatment panel III; ICD, International Classification of Diseases (ICD)-IO codes marking psoriasis; nr- not reported, OR- Odds Ratio.
†The odd's ratio and confidence interval was calculated using Pearson's chi-square test.

Study	Study Period	Geographic Area	Study Size Cases/Controls	Criteria For MS	No. Psoriasis Patients With MS* (%)	No. Controls With MS* (%)	p-value
Nisa N and Qazi MA [22]	2008-2009	Srinagar	150/150	NCEP-ATP-III*	42(28)	9(6)	0.00000004†
Pereira P et al., [23]	2007-2008	Mumbai	77/92	NCEP-ATP-III	14(18.2)	16(17.4)	0.893
Madanagobalane S and Anandan S [24]	2008- 2010	Chennai	118/120	SAM-NCEP	52(44)	36(30)	0.025†
Khunger N et al., [25]	NR	New Delhi	50/50	SAM-NCEP*	15(30)	4(8)	<0.05†
Lakshmi S et al., [26]	2012	Pondicherry	40/40	NCEP-ATP III	13(32.5)	12(30)	0.80
Praveen kumar U et al., [27]	2016	Pondicherry	30/30	SAM-NCEP	18(60)	12(40)	0.12
Present study	2013-2014	Mangalore	156/156	SAM-NCEP	45(28.8)	26(16.7)	0.01†

[Table/Fig-5]: Comparison of Indian study results with the present study [22-27].
*MS, Metabolic syndrome; NCEP ATP III, National cholesterol education programme adult treatment panel III; SAM-NCEP, South Asian modified national cholesterol education programme, nr, not reported
†Statistically significant (p-value of < 0.05).
‡p-values for the above studies were calculated using Pearson's chi-square test.

With regards to the reduced levels of HDL, our study reports a finding which is inconsistent to most of the published data [22-25]. The prevalence of low HDL levels were significantly higher in psoriasis patients in comparison with the controls (27.6% vs 13.5%, p=0.002) p-value. A study published recently by Praveenkumar U et al., and Cohen AD et al., reported a similar finding [27,30]. It is a known fact that psoriasis sufferers have high levels of depression and this may perhaps lead to a more sedentary lifestyle, lack of exercise, lower health seeking habits and as a consequence low HDL levels [30,31]. Increased alcoholism and smoking among psoriasis patients in our study supports this view.

In our study, the number of patients with impaired blood glucose levels were not significantly high among the psoriasis patients than in controls (24.4% vs 25 %, p=0.9). In studies done by Gisondi P et al., Love T et al., and Albareda M et al., metabolic syndrome was associated with significant dyslipidemia where as diabetes was not significantly high [1,4,32]. These findings were consistent with our studies. In contrast, slightly contradictory results have been reported by Nisa N et al., Pereira R et al., and Madanagobalane S et al., with regard to impaired blood glucose and metabolic syndrome [22-24].

LIMITATION

The subjects in the control group were derived from patients visiting the hospital for other skin complaints and thus may not be representative of the general population. Being a tertiary care hospital, the control group patients may be biased toward having metabolic system abnormalities which may have affected the study outcome. Being a cross-sectional study, the directionality of association between psoriasis and metabolic syndrome could not be determined.

CONCLUSION

We found a higher prevalence of metabolic syndrome in patients with psoriasis in the South Indian population. Hypertriglyceridemia and reduced HDL were commonly found in psoriatic patients with metabolic syndrome. Our study showed no significant association of psoriasis with abdominal obesity, hypertension and impaired blood glucose. Therefore, in order to avert the serious cardiovascular complications associated with metabolic syndrome our concerns should extend beyond the treatment of psoriatic plaques to the correction of modifiable cardiovascular risk factors.

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