Original Article

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Dermatology Section

Association of Metabolic Syndrome in Chronic Plaque Psoriasis Patients and their Correlation with Disease Severity, Duration and Age: A Case Control Study from Western Maharashtra

AARTI SUDAM SALUNKE[1], MAHENDRA VINAYAK NAGARGOJE[2], VASUDHA ABHIJIT BELGAUMKAR[3], SUNIL NARAYAN TOLAT[4], RAVINDRANATH BRAHMADEV CHAVAN[5]

ABSTRACT

Introduction: Psoriasis is a chronic systemic inflammatory disease where the skin and the joints are the primary targets. Despite the fact that psoriasis carries minimal risk of mortality, it is associated with significant morbidity which may have a significant impact on quality of life of patients. Globally, psoriasis has been reported to be associated with Metabolic Syndrome (MS) including obesity, dyslipidemia, diabetes and hypertension. Association of MS and its various components with psoriasis has been consistently reported in various studies, but there is a paucity of data on this association from the Indian subcontinent.

Aim: To compare the prevalence of MS in patients with psoriasis and controls and to determine association of MS with age of patient, severity and duration of psoriasis.

Materials and Methods: A hospital based case control study on 95 psoriasis patients and 95 age and sex matched controls.MS was diagnosed by the presence of three or more of the South Asian Modified National Cholesterol Education Program's Adult Panel III SAM-NCEP criteria. Clinical, biometric and necessary laboratory evaluations were performed. Statistical analysis was performed by using Statistical Package for the Social Sciences (SPSS version 16.0). Data was compared between cases and controls using unpaired t-test and chi-square test and odds ratio with 95% confidence interval.

Results: MS was significantly more common in psoriatic patients than in controls (38.9%vs 21.05%, odds ratio 2.39, 95% confidence interval, 1.26-4.55; p-value=0.007). Psoriatic patients had higher prevalence of hypertriglyceridemia (45.2%vs.11.5%), decreased HDL cholesterol (27.3%vs.4.2%), abdominal obesity (32.6% vs.15.7%) and elevated blood pressure (18.9%vs.5.2%) whereas no association observed for elevated blood sugar level (12.6%vs.5.2%). MS was present in psoriasis cohort irrespective of severity and duration of psoriasis. (p-value 0.123, 0.596 respectively). MS was more prevalent in elderly individuals with psoriasis (51.1%vs.28% p-value=0.008; Odds ratio 3.12, 95% confidence interval 1.32-7.35).

Conclusion: Significant association between psoriasis and MS was noted and it was independent of disease duration and severity. Elderly psoriatic patients were more prone for developing MS. We suggest that all patients of psoriasis, irrespective of disease, duration and severity, should be screened for MS to prevent significant morbidity and mortality associated with it.

Keywords: Comorbidities, Diabetes, Dyslipidemia, Hypertension, Obesity

INTRODUCTION

Psoriasis is a chronic, T helper 1 cell mediated disease affecting 1-3% of the population worldwide [1]. The chronic inflammatory nature of psoriasis predisposes patients to other diseases with an inflammatory component, the most notable being cardiovascular and metabolic disorders. This concept is supported by studies showing that psoriasis is associated with cardiovascular risk factors such as diabetes, obesity, hypertension, dyslipidemia, smoking, and diseases including Myocardial Infarction (MI) [2,3].

The association between psoriasis and hypertension was thought to be due to increased levels of angiotensin converting enzyme, endothelial-1 and renin in psoriasis patients [4,5].

The role of obesity in Th1 mediated pathology where adipocytes are shown to secrete both hormones and cytokines. They increase plasma levels of TNF-α and alter levels of a number of other substances (e.g., adiponectin, resistin). TNF-α causes production of inflammatory cytokines which in turn trigger cell signaling by interaction with a TNF α receptor leading to insulin resistance [6].

Recently few studies has appeared showing an increased frequency of MS and its individual components amongst the psoriasis patients [7,8]. It is necessary to determine the role of psoriasis in disorders such as obesity, diabetes mellitus, dyslipidemia, hypertension; the role of severity and duration of psoriasis in modifying comorbidities and the role of psoriasis treatment in altering the risk of developing these serious comorbidities. However, both the condition will show variation in different geographic areas and people of different ethnic origin so this study was undertaken to determine the prevalence of MS in psoriasis and to evaluate the co-relation between MS and age, severity and duration of psoriasis in patients at Tertiary Care Centre in Maharashtra, India.

MATERIALS AND METHODS

This was a hospital based case control study involving 95 psoriatic patients and 95 controls attending the dermatologic clinics and inpatient department in a government teaching institute, from July 2010 to August 2012. Study was approved by Institutional Ethical Committee. A written as well as vernacular informed consent in participants local language was obtained from all the participants.

Sample size calculated by using formula n= $(Z_{\alpha} + Z_{1-\beta})^{2*} (p_1q_1+p_2q_2)/d^2$ where Z_{α} = 1.96, $Z_{1-\beta}$ = 0.84, p1 and p2 are prevalence of the two groups of MS and q1 and q2 is 100-p1 and 100- p2 respectively. To determine sample size for the present study, we assumed an expected level of prevalence of 25% in controls [9] from the available previous hospital data which came as minimum sample size of 93 per group. Ninty-five age and sex-matched controls were enrolled among patients of other dermatological conditions (scabies and tinea infections) from the Dermatology Outpatient Department. Patients with pre-existing coronary artery disease, liver disease, renal disease, diabetes mellitus, hypertension and receiving systemic treatment for psoriasis (acitretin, ciclosporin, methotrexate, phototherapy or biologics) for at least six weeks before enrolment were excluded from the study.

All subjects were registered for demographic, biometric and the other relevant data on a case proforma. All patients were observed by a dermatologist and a complete history was taken including occupation, duration of disease, course of disease, treatment history, concomitant illnesses, personal habits such as smoking, alcohol, family history of psoriasis, diabetes, and cardiovascular disease. All patients were thoroughly examined and the extent and severity of disease, presence of nail, joint involvement noted. Severity of psoriasis was assessed according to Psoriasis Area and Severity Index (PASI), and Body Surface Area (BSA) measurement. PASI score of<7, 7-12 and >12 was taken as mild, moderate and severe disease respectively [10]. BSA involvement of < 20% was taken as mild psoriasis and > 20% as severe psoriasis [11]. BMI was calculated as weight (kg)/height (m^2) [12]. Waist circumference was measured as the midpoint between lowest rib and iliac crest in the standing position [13]. Blood pressure was recorded as the average of two measurements after subjects had been sitting for five minutes. MS was diagnosed using the SAM-NCEP criteria [14] If three or more of the following were present, the patient was diagnosed as having MS:

1) Abdominal obesity (definition of abdominal obesity was modified using Asia Pacific WHO guidelines as waist circumference ≥90 cm for males and ≥80 cm for females);
2) Blood pressure >130/85 mmHg;
3) Fasting blood glucose ≥100 mg/dl;
4) Hypertriglyceridemia >150 mg/dl; or
5) Low HDL cholesterol (<40 mg/dl for males and <50 mg/dl for females).

Venous samples were taken at the enrolment visit of the subjects after 12 hours of overnight fasting. The fasting blood sugar, fasting lipid {HDL cholesterol and triglycerides} levels, postprandial blood sugar were measured.

Serum cholesterol and triglycerides were measured with enzymatic procedures. HDL cholesterol by spectro enzymatic assay with cholesterol esterase and oxidase; triglycerides by molecular absorption spectroscopy. Plasma glucose was measured using glucose oxidase method [15].

STATISTICAL ANALYSIS

Statistical analysis was done using Statistical Package for the Social Sciences (SPSSversion 16.0). Differences between means were analysed by Student's unpaired t-test. $p < 0.05$ was considered statistically significant. The comparison of the groups was performed by way of a bivariate analysis, taking the chi-square test for qualitative variables and Student's t-test for quantitative variables. Adjusted Odds ratio and their 95% confidence intervals were used to measure quantitative association of comparative groups. Odds ratio calculated with 95% confidence interval and values greater than one was taken as significant association.

RESULTS

The study included 95 psoriatic patients and 95 age and sex matched controls. The mean age of patients in psoriasis group and control group was 36.88±13.37 years and 36.30±13.07 years (mean±SD) respectively [Table/Fig-1]. Psoriatic patients were between 4-70 years of age with maximum number of patients (n=34) in 3rd decade. Duration of disease was classified as less than 10 years and more than 10 years. At the time of enrolment of cases, 52 patients had duration of psoriasis less than 10 years and 43 had long standing disease of more than 10 years. Patients had PASI score ranging from 0.6 to 35. Eleven (11.6%) had mild psoriasis (PASI < 7), 42 (44.2%) had moderate psoriasis (PASI 7-12) and 42 (44.2%) had severe psoriasis (PASI >12). For statistical analysis of data, PASI score was divided in two groups. PASI Mild to moderate group (n=53) and PASI severe group (n=42).

Scalp and nail involvement was seen in 25 and 21 cases respectively. Occupation of cases was classified as housewives (34%), labourers (32%), farmers (24%), and others like retired employees, drivers, conductors, carpenters, teachers, shop keepers (10%). In control group, it was classified as farmers (30%), housewives (30%), retired employees (25%), construction workers (10%), others like conductors, teachers, labourers (5%). There were 40 (42.1%) smokers in psoriasis group compared to 32 (33.68%) in controls. Though, smokers in psoriasis group outnumbered those of control group, the difference was not statistically significant.

Components of MS and Psoriasis

In psoriasis group 37(38.95%) patients had MS, while in control group, 20 (21.05%) had MS. (odds ratio 2.39, 95% confidence interval, 1.26- 4.55; p-value=0.007). Odds ratio greater than one was suggestive of stronger association of psoriasis group with MS.

There was significant association of presence of hypertriglyceridemia, abdominal obesity, decreased HDL, cholesterol and increased blood pressure in psoriasis group compared to controls. (p-value 0.001,0.007,0.001,0.004 respectively). There was negative correlation between impaired fasting glucose and psoriasis [Table/Fig-2].

MS and Severity of Psoriasis

Out of 53 patients who had mild to moderate disease, 17(32.08%) had MS and out of 42 who had severe disease 20(47.62%) had MS (p-value 0.123), indicating that MS was not associated with severity of disease. We observed no association of severity of psoriasis and individual components of MS, except for increased triglycerides and decreased HDL cholesterol level which was more prevalent in severe psoriasis group. (p-value 0.036 and 0.003 respectively) [Table/Fig-3]

MS and Duration of Psoriasis

In our study, no significant difference observed for occurrence of MS with respect to longer or shorter duration of disease (p-value 0.596). Amongst the individual components of MS, decreased HDL cholesterol and increased blood pressure were significantly associated with longer duration of psoriasis [Table/Fig-4].

MS and Age of Psoriasis Patients

We have studied prevalence of MS in younger and older age of psoriasis patients. MS was more prevalent in > 40 years age of psoriasis patients compared to younger age (p-value 0.008; odds ratio 3.12, 95% confidence interval 1.32-7.35). Individual components of MS were also more prevalent in elderly, except for increased fasting glucose levels with respect to p value.[Table/Fig-5].

DISCUSSION

Due to chronic nature and associated comorbidities psoriasis is now considered as a systemic disease. Severe psoriasis particularly

Baseline parameters	Cases (n-95)	Controls (n-95)	p-value
Sex (M/F)	71/24	73/22	0.735
Age (mean+ SD)	36.88±13.37	36.30±13.07	0.216
Smokers	40 (42.10%)	32 (33.68%)	0.232
h/o alcohol intake	24 (25.26%)	28 (29.47%)	0.515

[Table/Fig-1]: Comparison of baseline characteristics between cases and controls.
On applying chi-square test and sample t-test, the difference was not statistically significant

Parameters	Cases (%)	Control (%)	p-value	Odds ratio	Lower C.I.	Upper C.I
MS	37 (38.95)	20(21.05)	0.007	2.39	1.26	4.55
Increased Waist circumference	31(32.63)	15(15.79)	0.007	2.58	1.28	5.20
Deranged TG	43 (45.26)	11(11.58)	< 0.001	6.31	2.99	13.33
Reduced HDL	26(27.37)	4(4.21)	< 0.001	8.57	2.86	25.71
Elevated BP	18(18.95)	5(5.26)	0.004	4.21	1.49	11.86
Deranged BSL(F)	12(12.63)	5(5.26)	0.075	2.60	0.88	7.70

[Table/Fig-2]: Comparison of different components of MS among cases and control.
MS-Metabolic Syndrome, TG-Triglycerides, BP-Blood Pressure, BSL(F)-Fasting Blood Sugar Level. Statistically significant difference (highlighted in bold, p-value <0.05 statistically significant) calculated by chi square test. Odds ratio and lower confidence interval, both values >1 is considered statistically significant

Parameters	PASI mild to moderate (n-53) (%)	PASI severe (n-42)(%)	p-value	Odds ratio	Lower C.I.	Upper C.I.
MS	17(32.08)	20(47.62)	0.123	1.93	0.83	4.44
Increased Waist circumference	18(33.96)	13(30.95)	0.756	0.87	0.37	2.07
Deranged TG	19(35.85)	24(57.14)	0.036	2.39	1.04	5.47
Reduced HDL	8(15.09)	18(42.86)	0.003	4.22	1.60	11.12
Elevated BP	9(16.98)	9(21.43)	0.583	1.33	0.48	3.73
Deranged BSL(F)	5(9.43)	7(16.67)	0.292	1.92	0.56	6.55

[Table/Fig-3]: Comparison (of percentage) of psoriatic cases with respect to disease severity with MS and parameters of MS. Psoriatic cases divided into PASI mild to moderate group (n- 53) and PASI severe group (n-42).
Statistically significant difference (highlighted in bold) calculated by chi-square test.

Parameters	<10years (n- 52) (%)	>10years (n- 43)(%)	p-value	Odds ratio	Lower C.I.	Upper C.I.
MS	19(36.54)	18(41.86)	0.596	1.25	0.55	2.86
Increased Waist Circumference	14(26.92)	17(39.53)	0.192	1.77	0.75	4.22
Elevated TG	22(42.31)	21(48.84)	0.525	1.30	0.58	2.93
Reduced HDL	10(19.23)	16(37.21)	0.049	2.49	0.99	6.28
Elevated BP	5(9.62)	15(34.88)	0.003	5.04	1.65	15.36
Deranged BSL(F)	5(9.62)	7(16.28)	0.33	1.83	0.54	6.23

[Table/Fig-4]: Comparison of duration of psoriatic cases with MS and parameters of MS. Percentages of psoriatic cases with duration of psoriasis < 10 years (n-52) and > 10 years (n-43) were compared with chi square test.
Chi-square test was used

in young patients perpetuates an independent risk factor for developing MI and stroke. Patients with psoriasis are at increased risk of developing diabetes, hypertension and obesity which are known cardiovascular risk factors [16,17].

A direct correlation between severity of psoriasis and prevalence of obesity, dyslipidemia and hyperhomocysteinemia has been reported in psoriatic patients, suggesting that (inflammatory) skin changes caused by psoriasis have a direct role in determining these risk factors [18,19].

Parameters	Age >40 (n-45)(%)	Age <40 (n-50) (%)	p-value	Odds ratio	Lower C.I.	Upper C.I.
MS	23(51.11)	14(28)	0.008	3.12	1.32	7.35
Increased Waist Circumference	21(46.67)	10(20)	0.002	4.01	1.61	9.99
Increased TG	26(57.78)	17(34)	0.007	3.15	1.36	7.31
Reduced HDL	17(37.78)	9(18)	0.016	3.12	1.22	8.02
Elevated BP	13(28.89)	5(10)	0.011	4.07	1.32	12.59
Deranged BSL(F)	8(17.78)	4(8)	0.111	2.74	0.77	9.83

[Table/Fig-5]: Comparison between age of psoriatic patients with MS and its different parameters (younger vs. older). Percentages of psoriatic cases of age < 40 years and > 40 years were compared.
Chi-square test was used

Other autoimmune diseases such as rheumatoid arthritis and systemic lupus erythematosus, which are also T helper 1 mediated, associated with higher cardiovascular morbidity and mortality rates [20,21].

The common immunological mechanism shared by MS and psoriasis is the important factor for evaluation of this association. It is now clear that intra-abdominal fat is not merely an inert mass but an active metabolic organ with adipocytokines promoting inflammation and affecting glucose metabolism and vascular endothelial biology. Primary cytokine produced by adipocytes includes IL-6, TNF- α, Plasminogen Activator Inhibitor type 1(PAI-1), leptin and adiponectin, each of which plays multiple roles in inflammation, metabolism and endothelial cell function [22,23]. Besides, adipocytes bear Toll- like receptors that behave as component of innate immunity and allow an immediate response to foreign pathogen and releases cytokines. This drives the process of systemic inflammation with consequence of MS.

Our study similar to other studies performed in India and western part of the world showed that MS is more prevalent in patients of psoriasis (38.9%) as compared to age and gender matched controls (21.05%). A South Indian study by Madanagobalane S et al., observed 44% of the patients with psoriasis had MS which was higher as compared to our study [24]. One Indian study from Rajasthan and Kashmir showed this prevalence as 28% [7,25]. On the contrary, studies by Laxmi S et al., and Praveenkumar U et al., observed absence of significant association between psoriasis and MS. These studies attributed this negative association with small sample size [26,27].

Prevalence of MS and prevalence of individual components of MS varies in different populations. Factors like population age, sex, genetic background, level of physical activity, body habits all influence the prevalence of MS, also the different diagnostic criteria used for prevalence of MS varies with population. The overall prevalence of MS is about 30-40% in Indian population as compared to 25% in US adults [28]. Individual components of MS have variable correlation with psoriasis. In this study, we observed statistically significant association of abdominal obesity, increased blood pressure and dyslipidemia with psoriasis. We have observed, hypertriglyceridemia and abdominal obesity were more prevalent in psoriatic patients as compared to other components of MS. Some of the studies supports this, indicating direct correlation between psoriasis and prevalence of obesity and dyslipidemia [18,19]. We found no association of impaired fasting glucose level with psoriasis. Gisondi P et al., and Khungar N et al., also found that levels of hyperglycemia were not significantly associated with psoriasis [28,29]. Contrary to this, some studies showed higher prevalence of DM in psoriatic patients as compared to controls. Pereira R et al., also reported significantly higher prevalence of impaired glucose level in psoriatics but no association with dyslipidemia [30]. Madanagobalane S et al., reported higher prevalence of individual components of MS in psoriasis [24].

We observed that MS is present irrespective of severity of psoriasis, which was similar to some of the previous studies [7,24,26,28]. However, individual components of MS like reduced HDL cholesterol are more prevalent in severe psoriasis. In the literature, there are varying reports regarding relationship of MS and severity of disease. A study from Korea showed that MS is significantly prevalent in patients with moderate to severe disease [31]. Sommer DM et al., concluded that individual components of MS were more likely to be seen in patients with severe psoriasis [3].

In our study, occurrence of MS was unaffected by duration of psoriasis, except for Hypertension (HTN) which was more prevalent in patients with longer duration of disease. Our results were consistent with the study from South Indian population [24]. Similarly Sommer DM et al., concluded that risk of developing DM, HTN and hyperlipidemia was not associated with duration of disease [3]. A study by Malbris L et al., observed increased total cholesterol and HDL in recent onset psoriatics [32].

We found that MS was more prevalent in psoriatic individuals of older age. Individual components of MS were also more prevalent in elderly individuals. Nisa N et al., noted higher prevalence of MS in younger age (18-30 years) while Gisondi P et al., observed in older age (> 40 years) similar to our observation [25,28].

Even after matching for confounding factors like smoking and alcohol consumption there was a statistically significant association between psoriasis and MS indicating that psoriasis is not an innocent bystander. Occupation history in both subjects and controls was not suggestive of sedentary life style, though head to head comparison was not done.

LIMITATION

Our study was cross-sectional and therefore directionality of the association between psoriasis and MS could not be determined. Hence association alone was documented, causality could not be assessed. Controls which were enrolled should be from general population, we have taken hospital based controls so there could be chance for selection bias.

CONCLUSION

This is the first comprehensive study from West zone of India, which observed association of duration, severity and age of psoriasis patients with MS. Our study showed positive association of psoriasis with hypertriglyceridemia, abdominal obesity, reduced HDL cholesterol and increased blood pressure. Amongst all, hypertriglyceridemia was most common association. Levels of increased fasting glucose were not associated with psoriasis.

MS was associated with psoriasis irrespective of disease duration and area of involvement. Though elderly individuals with psoriasis are at increased risk of developing MS, younger patients should also be evaluated to prevent development of MS.

Thus, we propose that psoriasis should be considered as chronic inflammatory systemic disease and enhanced screening approach may be important while treating it.

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PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of Skin and V.D., B.J.G.M.C. and Sassoon General Hospital, Pune, Maharashtra, India.
2. Assistant Professor, Department of Skin and V.D., B.K.L. Walawalkar Rural Medical College, Dervan, Maharashtra, India.
3. Associate Professor, Department of Skin and V.D., B.J.G.M.C. and Sassoon General Hospital, Pune, Maharashtra, India.
4. Associate Professor, Department of Skin and V.D., B.J.G.M.C. and Sassoon General Hospital, Pune, Maharashtra, India.
5. Professor, Department of Skin and V.D, B.J.G.M.C. and Sassoon General Hospital, Pune, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Aarti Sudam Salunke,
Department of Skin and V.D, B.J.G.M.C. and Sassoon General Hospital, Pune-411001, Maharashtra, India.
E-mail: aarti24apr@gmail.com

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