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A prospective epidemiological study of comorbid conditions in psoriasis

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ABSTRACT

AIM

1. To determine the prevalence of diabetes, hypertension, obesity in psoriatic patients and controls.
2. To determine the abnormal lipid parameters and serum uric acid levels in psoriatic patients and in controls
3. To determine the prevalence of metabolic syndrome and cardiovascular disease in both psoriatic patients and control population.
4. To determine the association of psoriasis with diabetes, hypertension, lipid abnormalities, obesity, cardiovascular disease and metabolic syndrome.

MATERIALS

The study comprised 100 cases of psoriasis and 100 controls visiting the inpatient and outpatient Department of Dermatology at Rajah muthiah medical college & hospital. All clinically diagnosed cases of psoriasis of more than 18 yrs. Patients who are willing to undergo the laboratory investigations and those who give consent for the study. Patients taking systemic drugs for diabetes, hypertension & cardiovascular diseases for the past 3 months and those who are under control. Pregnant and lactating women

METHODOLOGY

A prospective clinical case control study, with 100 patients of psoriasis and 100 controls were undertaken to know the prevalence of diabetes and hypertension in cases and controls and the incidence of abnormal lipid parameters, metabolic syndrome and cardiovascular disease

CONCLUSION

Patients had increased prevalence of diabetes, hypertension, hypertriglyceridemia, metabolic syndrome when compared to controls. A correlation was found between the severity of the disease and diabetes mellitus, hypertension, hypertriglyceridemia and metabolic syndrome. However no correlation was found between psoriasis and serum uric acid levels, obesity and cardiovascular disease.

Key Words: Psoriasis, Diabetes mellitus, Hypertension, Hypertriglyceridemia, Metabolic syndrome

INTRODUCTION

Psoriasis is a chronic autoimmune disease that mainly affects the skin. Current studies indicate that the prevalence of psoriasis in the United States ranges between two and three percent where as in India it affects 1.02 to 2.3 percent of skin patients1. Various studies revealed strong linkage between psoriasis and other serious, chronic and life-threatening conditions,

including cardiovascular disease, diabetes, stroke and cancer. Unfortunately, psoriasis often is overlooked or dismissed because it is not typically a direct cause of death; it is commonly and incorrectly considered as "cosmetic" and "not medically necessary." New research has found that psoriasis is associated with numerous other serious, chronic, and life-threatening comorbid conditions like Diabetes, Hypertension and Metabolic syndrome2. Additionally, a recent analysis suggests that psoriasis patients with comorbidities are more likely to experience intensive care, greater rates of hospitalization, lifelong outpatient visits and also have greater economic burden than psoriasis without comorbidities. Recently, the association of psoriasis with metabolic syndrome (MS) has gained considerable attention. There are very few Indian studies to elucidate the role of Metabolic syndrome in psoriasis. Several lifestyle factors including alcohol, smoking, stress, psychological factors like anxiety, depression may worsen psoriasis. All those comorbities should be confirmed by appropriate study designs (cohort studies) which will help to elucidate their true associations with psoriasis and in various regions of India.

AIM

To determine the prevalence of diabetes, hypertension, obesity, abnormal serum uric acid levels & lipid parameters, metabolic syndrome and cardiovascular disease both psoriatic patients and controls. To determine the association of psoriasis with diabetes, hypertension, lipid abnormalities, obesity, cardiovascular disease and metabolic syndrome.

METHODOLOGY

The study comprised 100 cases of psoriasis and 100 controls visiting the inpatient and outpatient Department of Dermatology of Rajah muthiah medical college & hospital.

STUDY DESIGN

SAMPLE

A total number of approximately 200 patients attending the out-patient and inpatient department of Skin and STD of Rajah Muthiah Medical College and Hospital from November 2012 to October 2015 will be included in the study.

METHOD OF COLLECTION OF DATA

Patients with psoriasis and normal patients will be randomly selected for the study.

STUDY DURATION

THREE YEARS (September 2012- October 2015).

Selection criteria

INCLUSION CRITERIA

1. Age more than 18 years.
2. All clinically diagnosed cases of psoriasis.
3. Patients who are willing to undergo the laboratory investigations and those who give consent for the study.

EXCLUSION CRITERIA

1. Patients not willing to take part in the study or unwilling to give their written consent for the study.
2. Patients taking systemic drugs for diabetes, hypertension & cardiovascular diseases for the past 3 months and those who are under control.
3. Pregnant and lactating women.

METHODOLOGY

The data for the study was collected from all those who fulfilled the inclusion and the exclusion criterion on a purposive sampling using a pretested structured questionnaire basis by obtaining a written informed consent.

HISTORY AND EXAMINATION

The clinical data pertaining to all patients were recorded as per the proforma attached in the annexure. A detailed history was taken pertaining to the duration of psoriasis, treatment taken for psoriasis, family history of psoriasis, occupation, drug intake other than for psoriasis, personal history of diabetes, hypertension, cardiac events, smoking and alcohol intake. All the patients were graded according to Psoriasis Area Severity Index (PASI) and Body Surface Area (BSA) into 3 categories - Mild, Moderate and Severe. All the changes involving nails, scalp, genitalia were documented as per the proforma.

SCORES

The patients were classified based on Psoriasis Area Severity Index (PASI) and Body Surface Area (BSA).

PASI

Is a useful tool in monitoring the response of psoriasis to any therapeutic regimen. Four sites of affection - head (h), upper limbs (u), trunk (t) and lower limbs (l) are separately scored. Morphologic scoring of psoriasis plaques is done by evaluation of three parameters - erythema, induration and desquamation, each of which is graded on a severity scale of 0 to 4 where 0 = nil, 1 = mild, 2 = moderate, 3 = severe and 4 = very severe. The addition of these scores for each site is multiplied by the grading for area wise percentage involvement of that particular site in the

following manner: 1 = less than 10% area , 2 = 10-29% , 3 = 30-49% , 4 = 50-69% , 5 = 70-89% , 6= > 90%. Since the four body region (head, upper limbs, trunk and lower limbs) represent about 10%, 20%, 30% and 40% of body surface area respectively, they are given corresponding, weight-age in scoring by multiplying their scores, by 0.1, 0.2, 0.3 and 0.4 respectively.

Hence, the final formula for calculating PASI score is as follows;

PASI = 0.l (Eb +Ih+ Dh) A + 0.2(Eu + Iu + Du) A + 0.3(Et + It + Dt) A + 0.4 (El + Il +Dl)A

The score can vary between 0 and 72 in steps of 0.1, One limitation of the PASI score lies in its inter-observer variation which makes evaluation by the same evaluates necessary and the consensuses are arrived after 2 clinician's observations.

IN OUR STUDY

PASI <3 was graded as MILD;
3-10 was graded as MODERATE;
>10 was graded as SEVERE

RESULTS

In the present study, the prevalence of diabetes, Hypertension, psoriatic arthritis, obesity, serum lipids profile, metabolic syndrome and cardiovascular disease is studied in psoriatic patients and association with the severity of the disease. Frequency distribution was calculated for age, gender and for all selected study parameters. The comparison of measures between cases and controls is carried out by the independent sample non parametric test (man-Whitney 'U' test). The entire statistical work is analyzed by statistical packages for social sciences, (sp ss- 21) suitable packages for social sciences (Sp ss-21). Suitable graphical illustrations were also made.

TABLE 1: AGE DISTRIBUTION

AGE (in years)	CASES	CONTROL
	N (%)	N (%)
18-30	19	22
31-40	18	17
41-50	25	25
51-60	28	27
61-70	9	9
>70	1	-
TOTAL	100	100

AGE	MEAN	S.D
CASES	45.03	13.51
CONTROL	43.75	14.28

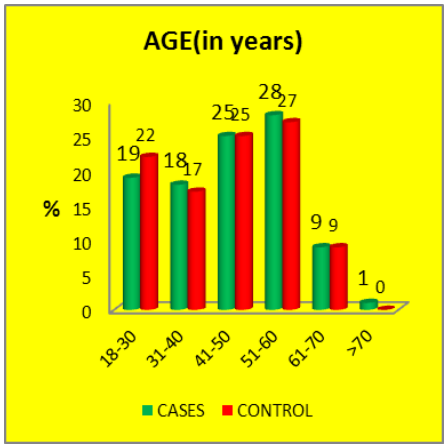


Table 1 represents age distribution of the study participants, 28% of cases and 27% of controls of maximum number are within the 51-60yr age group. 25% of cases and controls equally are within the age group of 41-50 yrs. The Mean age of cases was around 45.03yrs with a standard deviation of 13.51. The Mean age of controls was around 43.75yrs.

Table 2: Clinical Diagnosis of Case

CLINICAL DIAGNOSIS	No. (%)
PPP	30
PV	53
ERY.P	5
SEB.P	9
P.P	3
	100

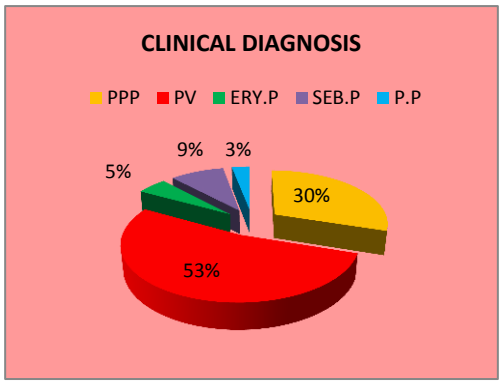
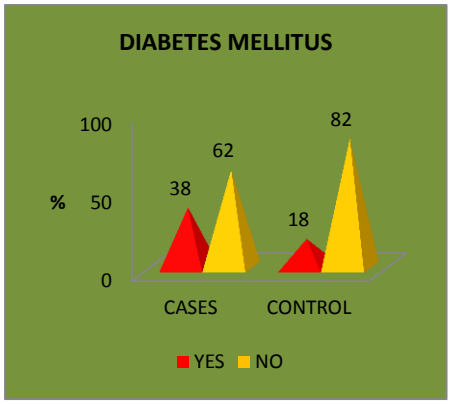


Table 2 represents different types of psoriasis in cases. The majority of patients presented with Psoriasis vulgaris (PV) are 53%. The next common presentation is Palmoplantar psoriasis (PPP) where 30% of them have been reported. Seborrhoeic psoriasis (SEB.P) accounted for 9%. Erythrodermic psoriasis (ERY.P) accounted for 5%. Only 3% are diagnosed with Pustular psoriasis (P.P).

Table 3: Prevalence of Diabetes Mellitus

DIABETES	Cases N (%)	Control N (%)
Yes	38	18
No	62	82
Total	100	100



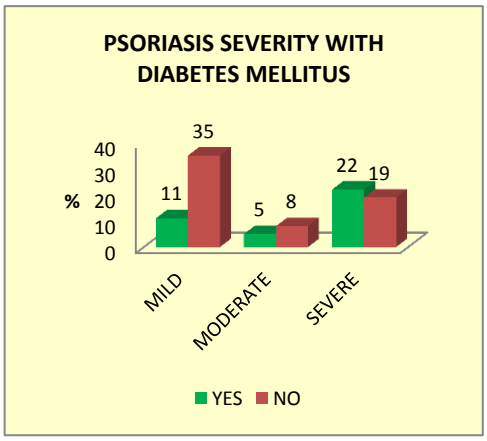
Independent Sample Test

Independent non parametric sample test	'Z' value	Significant ('p' value)
Mann-Whitney 'U' test	-3.14	.002

In table 3, prevalence of diabetes mellitus in cases and controls is reported. It is inferred that, the prevalence rate is 38% in cases and 18% in controls. The prevalence rate significantly differed between cases and controls. Mann Whitney 'U' test was used to study the difference. The "p" value was 0.002 which was <0.05, hence significant difference is observed. Therefore, diabetes is significantly associated with psoriatic patients when compared to control group.

Table 4: Psoriasis Severity with Diabetes Mellitus

	SEVERITY			
DIABETES MELLITUS	**MILD**	**MODERATE**	**SEVERE**	**Total**
YES	11	5	22	38
NO	35	8	19	62
TOTAL	46	13	41	100



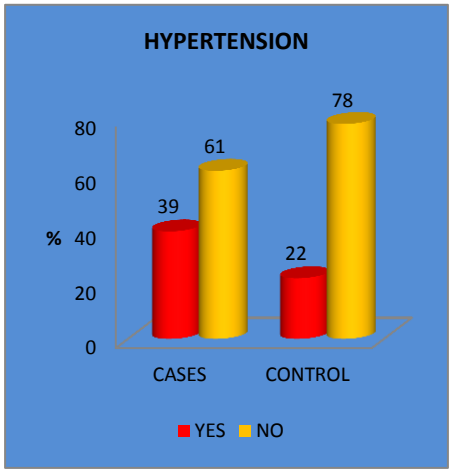
Name of test	Value	Significance 'p' value
PEARSONS CHISQUARE TEST	8.143	.017

CHI – SQUARE TEST

The distribution of diabetes in psoriasis patients according to the severity of disease was as follows: mild disease (11%), moderate disease (5%) and severe disease (22%). Henceforth, correlation of the prevalence of diabetes mellitus was found with the severity of disease (p value 0.017).

TABLE 5: PREVALENCE OF HYPERTENSION

HYPERTENSION	Cases	Control
	%	%
Yes	39	22
No	61	78
Total	100	100



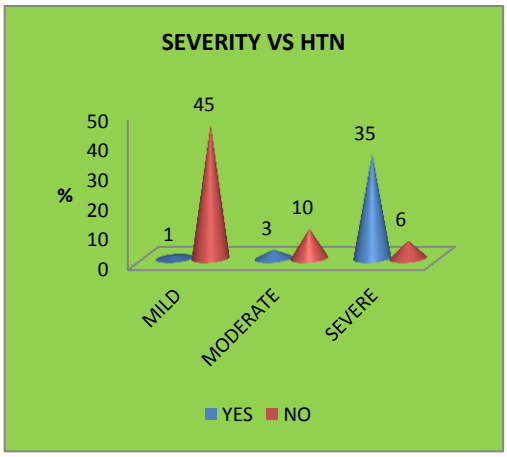
INDEPENDENT SAMPLE TEST

Name of test	'Z' value	Significant('p')value
Mann Whitney 'U' test	-2.604	.009

In table 5, prevalence of hypertension in cases and controls is studied. It is inferred that, the prevalence rate is 39% in cases and 22% in controls. The prevalence rate significantly differed between cases and controls. Mann Whitney 'U' test was used to study the difference. The "p" value was 0.009 which was statistically significant ($p<0.05$), hence significant difference is observed. Therefore, hypertension is significantly associated with psoriasis.

Table 6: PSORIASIS SEVERITY WITH HYPERTENSION

HYPERTENSION	SEVERITY			
	Mild	Moderate	Severe	Total
Yes	1	3	35	39
No	45	10	6	61
	46	13	41	100



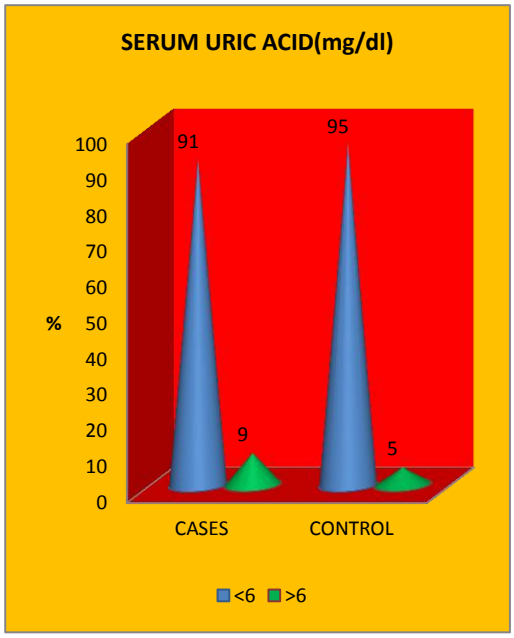
CHI – SQUARE TEST

Name of test	Value	Significance 'p' value
PEARSONS CHI – SQUARE TEST	64.66	.001

The distribution of hypertension in psoriasis patients according to the severity of disease was as follows: mild disease (1%), moderate disease (3%) and severe disease (35%). Henceforth, correlation of the prevalence of hypertension was found with the severity of disease (p value 0.001).

TABLE-7: SERUM URIC ACID

Serum uric acid (mg/dl)	Cases	Control
	Number (%)	Number (%)
<6	91	95
>6	9	5
Total	100	100



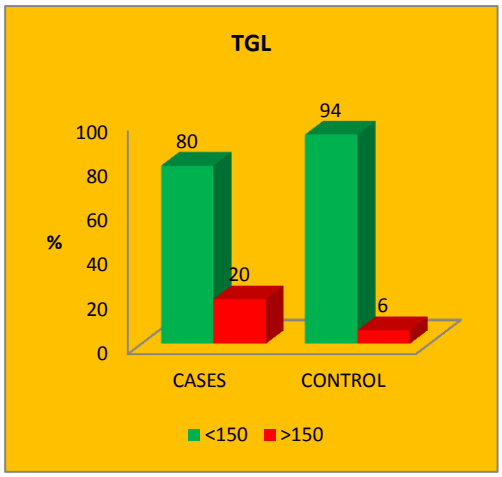
INDEPENDENT SAMPLE TEST

	'Z' value	Significant (p)value
Mann Whitney 'U' test	-1.106	.269

In table 7, serum uric acid levels in cases and controls are measured. 9% of cases have serum uric acid levels > 6 mg/dl and Mann Whitney 'U' test was used to study the difference. The "p" value was 0.269 which showed no statistical significance with any group. Therefore, both cases and controls had serum uric acid levels below the threshold level.

Table-8: TGL

TGL mgldl	Cases	Control
	N (%)	N (%)
≤150	80	94
>150	20	6
Total	100	100



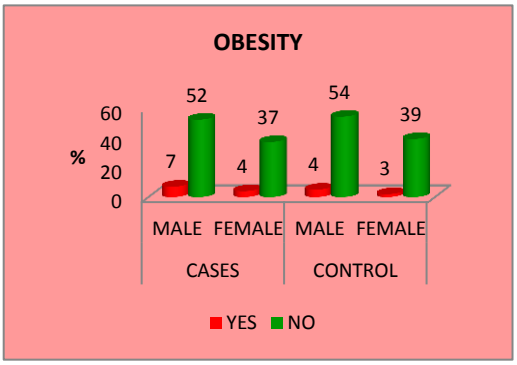
TGL	Minimum	Maximum	Mean	S.D
Cases	100	174	136.88	16.44
control	100	169	131.18	11.24

Name of the test	'Z' value	Significant ('p')value
Mann Whitney 'U' test	-.097	.034

In table 8, comparison of serum TGL between cases and controls is charted. It is inferred that, there are 20% of patients have TGL greater than 150 mg/dl, where only 6% in control group have greater than 150mg/dl. The mean TGL for cases is 136.88 ± 16.444 and for controls is 131.18 ± 11.24. Mann Whitney 'U' test was used to study the difference. The "p" value was 0.034 which was statistically significant ($p<0.05$), hence significant difference is observed. Therefore, there is significant elevation of TGL levels in patients with psoriasis.

Table-9: OBESITY

OBESITY	Cases		Control	
	Male	Female	Male	Female
Yes	7	4	4	3
No	52	37	54	39
	59	41	58	42



In table 9, the prevalence of obesity in both cases and controls is charted. It is observed that, 11% of cases are obese in which 7% are male and 4% are female when compared to 7% obesity in controls.

Table-10: Waist Circum Ference

	W.C (in cm)	Mean	S.D
CASES	Male	73.55	9.79
	Female	70.29	8.48
CONTROLS	Male	73.03	10.22
	Female	70.33	7.40

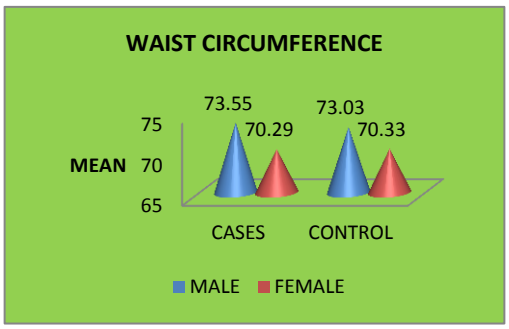
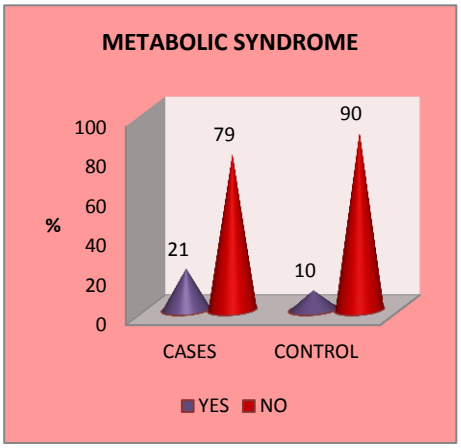


Table: 10, represents, comparison of waist circumference between groups, the mean waist circumference of male cases was 73.55 ± 9.79 cm, the mean circumference for female cases was 70.29 ± 8.4 cm. The mean circumference of control group were 73.03 ± 10.22 cm in male and 7.33 ± 7.40 cm in females. Therefore, there is no significant difference between cases and controls.

Table-11: Metabolic Syndrome

METABOLIC SYNDROME	Cases N (%)	Control N (%)
Yes	21	10
No	79	90
Total	100	100



INDEPENDENT SAMPLE TEST

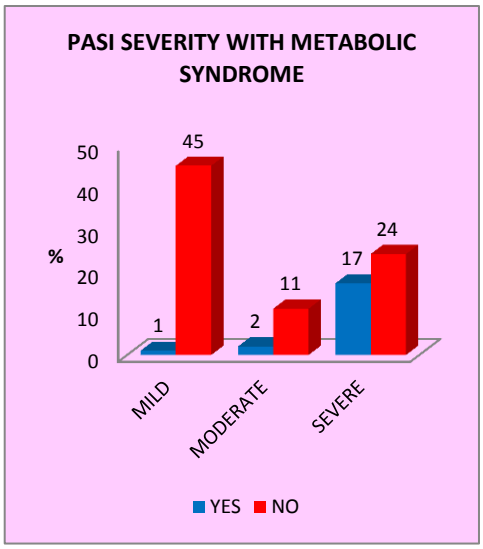
NAME OF TEST	'Z' value	Significance 'p'value
Mann Whitney 'U' Test	-.213	0.048

In table 11, prevalence of metabolic syndrome in cases and controls is charted. It is accounted that the prevalence rate is 21% in cases and 10% in controls. The prevalence rate significantly differed between cases and controls. Mann Whitney 'U' test was used to study the difference. The "p" value was 0.048 which was ($p<0.05$), hence significant difference is observed. Therefore, metabolic syndrome is significantly associated with psoriatic patients when compared to control group.

Table 12: Pasi Severity Vs Metabolic Syndrome

	'z' value	Significant
Mann Whitney 'U' test	21.114	0.001

Metabolic Syndrome	SEVERITY			
	Mild	Moderate	Severe	Total
Yes	1	2	17	20
No	45	11	24	80
	46	13	41	100



In table 12, the distribution of metabolic syndrome in psoriasis patients according to the severity of disease was as follows: mild disease (1%), moderate disease (2%) and severe disease (17). The 'p' value was 0.001 which was statistically significant ($p<0.05$), hence metabolic syndrome was observed in patients with severe psoriasitic patients.

DISCUSSION

Psoriasis is a paradigm of a chronic and relapsing inflammatory skin disease which so far was supposed to be restricted to the skin with the exception of psoriatic arthritis. There has been a lot of recent research on its consideration as a systemic disease with the researchers being of the view that the dermatological manifestations represent only a part of spectrum. The systemic inflammation present in psoriasis, various systemic treatments for psoriasis and an increased prevalence of unhealthy life style factors may all contribute to this unfavorable cardiovascular risk profile. This study was undertaken to study one such debatable association with abnormalities in the lipid profile, blood glucose levels and prevalence of hypertension, metabolic syndrome and cardiovascular abnormalities and other autoimmune diseases. Genetic studies demonstrate that psoriasis and cardiovascular disease share common pathogenic features in which, for example inflammatory cytokines like TNF-α and IL-1 play an important role. The chronic inflammation in psoriasis has an unfavorable effect on the cardiovascular risk profile. Multiple cardiovascular risk factors seem to be influenced; the blood pressure, oxidative stress, dyslipidemia, endothelial cell dysfunction, homocysteine levels and blood platelet adhesion. In our study 100 cases and 100 age, sex matched controls were recruited. Mean age of cases was 45.03 years while mean age of the controls was 43.75 years. The samples were thus age matched. Maximum number of patients (28%) of psoriasis belonged to age group of 51-60 years. Out of 100 cases, 59 were males and 41 were females. Male: female ratio was 1.4:1. A high male preponderance seen in our study correlates with other published studies. Inderjeet Kaur et al2 revealed a sex ratio of 2.3:1, whereas Mehta et al3 reported a sex ratio of 4:1 in their studies. Thus, the sex ratio in our study correlated with the above literature. The ratio in controls was 1.4:1. The samples were thus sex matched. In our study, PASI was used to grade the patients. As a definite literature regarding the classification of PASI into mild, moderate and severe is lacking, we classified the patients depending on the available studies. According to PASI, 46% had mild psoriasis (PASI <3), 13% of patients had psoriasis of moderate severity (PASI 3-10) whereas 41% had severe type (PASI >10). Thus, 59% of patients had PASI score less than 10, which correlates with other studies4, 5. The prevalence of diabetes mellitus in cases of psoriasis was 38% as compared to 18% in controls. Thus, there was significant increase in prevalence of diabetes in patients with psoriasis (P value: 0.002). This is also in agreement with the studies done by Neimann et al7, Sommer et al6, Shapiro et al8 and Cohen et al9 have all reported an increase in the prevalence of diabetes in patients with psoriasis. The results were contradictory with that of an Indian study by Alexander et al10 which revealed only a prevalence of diabetes in 13.1% of psoriasis patients. The distribution of diabetes in psoriasis patients according to the severity of disease was as follows: mild disease (11%), moderate disease (5%) and severe disease (22%). Henceforth, correlation of

the prevalence of diabetes mellitus was found with the severity of disease (p value 0.017). The prevalence of hypertension in cases of psoriasis was 39% as compared to 22% controls. Thus, there was significant increase in prevalence of hypertension in patients with psoriasis (P value: 0.009). The distribution of hypertension in psoriasis patients according to the severity of disease was as follows: mild disease (1%), moderate disease (3%) and severe disease (35%). Henceforth, correlation of the prevalence of hypertension was found with the severity of disease (p value 0.001). The results were consistent with that of Cohen et al71 Their study reported that the prevalence of hypertension was significantly higher in psoriasis patients than controls (38.8%, 29.1% respectively). Similar results were noted by Sommer et al6. In contrast, an Indian studies by Alexander et al10 which revealed a prevalence of hypertension in 8.1% of psoriasis patients. The serum triglyceride composition varied in cases and controls. The mean value in cases was 136.88 which were significantly higher than the mean value in controls which was 131.18 (p value: 0.034). Serum triglycerides have been significantly associated with psoriasis. Results were consistent with Rocha-Pereira11. The mean value of uric acid in patients with mild, moderate and severe disease was 4.7, 4.5 and 4.6 mg/dl respectively. In our study, no significant association was found between the severity of psoriasis and the levels of uric acid (p value 0.314). This was consistent with the study of 50 psoriatic patients by Ramesh Chand et al14, where they found that 7 patients had elevated serum uric acid levels without any relation to the extent of skin involvement. Another study by Brenner et al15 also concluded that there is no relationship between the frequency of hyperuricemia and the extent of psoriatic skin involvement. The prevalence of metabolic syndrome in cases of psoriasis was 21% as compared to 10% in controls. Thus, there was significant increase in prevalence of Metabolic syndrome in patients with psoriasis (p value: 0.048). These results are consistent with a study done by Ilkin Zindancı12 et al where the prevalence of metabolic syndrome in cases was 53% and in controls it was 39% with P value being 0.004. In a study conducted by Gisondi et al13, there was significant increase in prevalence of Metabolic syndrome in patients with psoriasis (p value: 0.005). The distribution of metabolic syndrome in psoriasis patients according to the severity of disease was as follows: mild disease (1%), moderate disease (3%) and severe disease (35%). Henceforth, correlation of the prevalence of hypertension was found with the severity of disease (p value 0.001).

CONCLUSION

Psoriasis is one of the most common dermatological conditions seen in the daily practice. There has been a lot of recent research on its consideration as a systemic disease with the researchers being of the view that the dermatological manifestations represent only a part of spectrum. Recent review of literature suggests that psoriasis is associated with metabolic syndrome. Strong associations with dyslipidemia, obesity, diabetes, hypertension, increased cardiovascular morbidities apart from common comorbidities like psoriatic arthritis .Psoriasis has a male preponderance in our study male : female ratio was 1.44:1.Maximum number of patients (28%) belonged to age group of 51-60 years.46% had mild psoriasis, 13% of the patients had moderate disease while 41% of the patients had severe disease. Psoriatic arthritis was noted in 8% of cases. 38% of the patients had concomitant diabetes along with psoriasis while 18% of the controls also had diabetes. Hence a correlation of occurrence of diabetes mellitus was found with the severity of psoriatic disease. Thus, we could conclude that diabetes is related to the severity of psoriasis and may be related to the systemic inflammation seen in these patients. 39% of the patients had coexistent hypertension and psoriasis as compared to 22% of controls. Hence a correlation of occurrence of hypertension was found with the severity of disease. 9% of the patients had an increase in serum uric acid levels as compared to 5% of controls. Therefore, no suggestive significance was found. However, no correlation was noted between the serum uric acid levels and the severity of the disease. Further serum uric acid levels were not found to be significantly elevated in patients with psoriatic arthritis. Thus, we concluded that occasional elevation in serum uric acid in psoriasis patients is also an independent finding and is not related to the disease process or to the severity of the disease. Amongst the various lipid parameters, significant elevation was found only in triglycerides while other parameters like HDL, LDL and Total Cholesterol did not show any significant association. Further there was no correlation of abnormality in lipid parameters with the severity of disease. Although there have plenty of studies from the west reporting an association of psoriasis with the metabolic syndrome, there are no large scale Indian studies evaluating Asian patients. The present study was an endeavour in this regard. In our study, suggested association of psoriasis with metabolic syndrome in Indian patients is clearly depicted. In addition, there is also higher prevalence of coexistent conditions like hypertension, diabetes, and

hyperlipedemia which may contribute to the morbidity and prevalence of metabolic syndrome. Looking at various studies around the world, which included population samples, aged from 20 to 45 and upwards, the prevalence of metabolic syndrome in healthy adults varied from different countries. Only 6% of psoriatic patients had evidence of cardiovascular disease, which is relatively of low prevalence. Hence, longterm follow up of these psoriatic patients is needed as they may be predisposed to cardiovascular disease in future. This has important implications for treating dermatologist, as it allows them to be more adventurous and aggressive in treating these patients while simultaneously doing necessary investigations that they may help to rule out underlying metabolic syndrome.

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