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A study of correlation between psoriasis and metabolic syndrome

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Abstract
Psoriasis affects 1-3% of Indian, 2% of the U.S. population; about 11% of these patients have psoriatic arthritis. There were four clinical variants of psoriasis, but plaque type is the most common (80% of cases) observed in our study. Prevalence of Metabolic syndrome is 29.2%. Among the 89 patients studied, a majority of patients were male (67.38%). 28 (31.5%) study subjects had abnormal fasting blood glucose levels. About 26% (23) of the study subjects showed abnormal triglyceride levels. About 50% of the study subjects showed low HDL value. 36(40%) of the study subjects were normal, 20.2% were overweight and 26% (23) were grade I obese. Age is having correlation with waist circumference and FBS and this correlation is significant. Waist circumference is correlating with AGE, BMI, FBS and Triglycerides. FBS correlates with increased Age, BMI, waist circumference, and decreased HDL. Triglycerides correlated with BMI, waist, FBS, and HDL levels. 10% of study subjects are under weight, 40% are normal, 46% are overweight and belong to grade 1 obesity, 3.3% constitute above grade 2 obesity. 31.5% of study subjects are Diabetics. Increased FBS correlates with increased Age, BMI, waist circumference, and decreased HDL levels. Triglycerides correlated with BMI, waist circumference, FBS, and HDL levels. Decreased HDL is correlated with increased FBS, and increased TGL levels.

Keywords: Psoriasis, keratinocyte, hyperlipidemia, dyslipidaemia metabolism

Introduction
Psoriasis is a chronic inflammatory skin disorder affecting 1-3% of the population. It is important to recognize that psoriasis is a term that embraces a spectrum of diseases ranging from localized plaques to more severe generalized involvement, with or without psoriatic arthritis and associated manifestations of other autoimmune diseases. Genetic factors play a critical role in the pathogenesis of psoriasis.

The lesions of psoriasis consist of red scaly, sharply demarcated, in durated plaques present particularly over extensor surfaces and scalp. The disease is enormously variable in duration, periodicity Psoriasis tends to worsen during periods of stress, during adverse environmental conditions of cold weather and low humidity, with the administration of certain drugs and during course of certain infections. Ethnic factors also play an important role of flares and extent.

For most of our patients, the disease is more emotionally than physically disabling, as its impact on quality of life may be significant even if relatively less body surface area is involved. It is characterized by epidermal, hyperproliferation, abnormal keratinocyte differentiation, angiogenesis with blood vessel dilatation, and Th 1 and Th 17 inflammation [1]. Psoriasis may act as an external indicator of underlying immune and metabolic dysregulation [2]. The metabolic syndrome is a constellation of lipid and non-lipid cardiovascular risk factors of metabolic origin [1]. 1t is a cluster of risk factors including central obesity, atherogenic dyslipidaemia, hypertension and glucose intolerance, and is a strong predictor of cardiovascular diseases, diabetes and stroke. Increased insulin-like growth factor-II (IGF-II) promotes epidermal proliferation and is also implicated in promoting atherosclerosis, in modulating body fat mass and lipid metabolism in mice, and is linked to diabetes and hyperlipidemia in animal and human models [1].

Recent studies implicate IL-17, which is released by a subset of memory T helper cells (Th17 cells) that are stimulated by IL-23, as a mechanistic link between T-cell activation and inflammation. In contrast to normal skin, IL-17 is expressed in psoriatic skin lesions, and is

known to induce the key psoriatic cytokines of TNFα, and IL-1, IL-6, and IL-8, among a cascade of inflammatory mediators. IL-17 is also seen at higher levels, along with IL6, IL-8, and C-reactive protein, in the plasma of patients who have suffered unstable angina and acute MI [2].

Aim of the study

- To know the prevalence of metabolic syndrome in psoriasis.
- To assess the morbidity when psoriasis is associated with metabolic syndrome.

Materials and Methods

The present study was conducted in patients who attended the outpatient department of Dermatology, Venereology and Leprology, Fathima Institute of Medical Sciences, Kadapa, A.P. The study was conducted over 20 months in a total of 89 patients were included in the study.

Inclusion criteria: Patients with psoriasis attending OPD of dermatology, Fathima Institute of Medical Sciences, Kadapa, A.P. Aged-18 years of age and above.

Exclusion criteria: Patients receiving any systemic therapy like methotrexate, acitretin 1 month before enrolment.

Method

Patients attending outpatient department of DVL, Fathima Institute of Medical Sciences were screened for the presence of psoriasis identified clinically. General data regarding age, sex, symptoms, duration of disease, treatment history, smoking and alcohol, family history, history of cardiovascular and cerebrovascular diseases were collected. A detailed general physical examination was conducted. Waist circumference and BP was recorded. Type and distribution of lesions were noted. Severity of psoriasis was assessed according to Psoriasis Area and Severity Index [PASI] and Body Surface Area [BSA]. Histopathology was done whenever the diagnosis was doubtful. Cases were screened for the presence of metabolic syndrome as defined by National Cholesterol Education Program Adult Panel III 2001 as given below.

Waist circumference was determined by placing tape at upper most part of the Hip bone around abdomen, horizontally. Blood pressure was recorded as the average of two measurements after asking patients to sit for 5 minutes. Serum samples were taken after the subjects had fasted overnight at least for 8 hours. Serum HDL cholesterol and triglycerides were measured with enzymatic procedures. Plasma glucose was measured using glucose oxidase method.

All results will be recorded, tabulated and analyzed according to statistical proportions using Pearson chi-square test.

Results

89 patients of psoriasis who presented to the department of dermatology were studied. There was a wide variation in the age group of the patients. The age of the patients belong to 18 years and above. The majority of patients (66%) were in the 31 to 60 years age group. Among the 89 patients studied, a majority of patients were male (67.38%), while female patients accounted for 32.62%.

Individual components of metabolic syndrome

According to the NCEP ATP III definition, metabolic syndrome is present if three or more of the following five criteria are met: waist circumference over 40 inches (Men) or 35 inches (Women), blood pressure over 130/85 mmHg, fasting triglyceride (TG) level over 150 mg/dl, fasting high-density lipoprotein (HDL) cholesterol level less than 40 mg/dl (Men) or 50 mg/dl (Women) and fasting blood sugar over 100 mg/dl.

Abnormal waist circumference was seen in 41 out of the total 89.46.1% had central obesity and 53.9% were normal. 40% (36) of the study subjects were normal, 20.2% were overweight and 26% (23) were grade I obese.

There was no significant difference between males and females in relation to the various factors of metabolic syndrome, except for age group and alcohol which showed statistically significant difference.

Table 1: Distribution of basic variables

	Frequency	Percentage
Age Distribution (Years)		
<20	3	3.4%
21-30	8	9.0%
31-40	19	21.3%
41-50	20	22.5%
51-60	20	22.5%
61-70	15	16.9%
>70	4	4.5%
Sex		
Males	60	67.38%
Female	29	32.62%
Waist circumference (WC)		
Abnormal	41	46.1
Normal	48	53.9
Hypertension		
Present	20	22.5
Absent	69	77.5
Fasting Blood Sugar		
Abnormal (>100mg/dl)	28	31.5
Normal	61	68.5
Triglyceride Levels		
Abnormal	23	25.8
Normal	66	74.2
HDL Levels		
Abnormal	45	50.6
Normal	44	49.4
Metabolic syndrome		
Positive	26	29.2
Negative	63	70.8
BMI		
<18.5	9	10.1
18.5-22.99	36	40.4
23-24.99	18	20.2
25-29.99	23	25.8
30-34.99	1	1.1
≥ 35	2	2.2

Table 2: Association between various parameters

FBS	Male	Female	
Abnormal	20	8	$X^2 = 0.299$
Normal	40	21	P= 0.584
TGL	Male	Female	
Abnormal	15	8	$X^2 = 0.068$
Normal	45	21	p= 0.794
Metabolic syndrome	Male	Female	
Positive	16	10	$X^2 = 0.578$
Negative	44	19	p= 0.447
HDL	Male	Female	
Abnormal	30	15	X^2= 0.023
Normal	30	14	p= 0.879
Alcohol	Male	Female	
Positive	24	1	$X^2 = 12.931$
Negative	36	28	p<0.0001

Table 3: Group Statistics

	Sex	N	Mean	Std. Deviation	t value	P value
Age	Male	60	52.4833	13.56777		
	Female	29	38.4828	12.03750	4.727	0.000
BMI	Male	60	22.7963	3.93936		
	Female	29	24.0372	3.91151	-1.396	0.166
WC	Male	60	88.9167	11.85833		
	Female	29	85.0345	13.98081	1.364	0.176
FBS	Male	60	107.2333	34.08234		
	Female	29	105.7931	37.85817	0.180	0.857
TGL	Male	60	118.1167	39.18063		
	Female	29	118.5172	41.56632	0.044	0.965
HDL	Male	60	42.3500	13.53442		
	Female	29	49.1034	17.87126	2.000	0.05

Table 4: Correlation between variables

		Age	BMI	Waist	FBS	TGL	HDL
Age	Pearson Correlation	1	-0.017	0.356**	0.214*	0.130	-0.126
	Sig. (2-tailed)		0.872	0.001	0.044	0.224	0.238
	N	89	89	89	89	89	89
BMI	Pearson Correlation	-0.017	1	0.629**	0.394**	0.301**	-0.015
	Sig. (2-tailed)	0.872		0.000	0.000	0.004	0.889
	N	89	89	89	89	89	89
WC	Pearson Correlation	0.356**	0.629**	1	0.423**	0.351**	-0.140
	Sig. (2-tailed)	0.001	0.000		0.000	0.001	0.191
	N	89	89	89	89	89	89
FBS	Pearson Correlation	0.214*	0.394**	0.423**	1	0.490**	-0.339**
	Sig. (2-tailed)	0.044	0.000	0.000		0.000	0.001
	N	89	89	89	89	89	89
TGL	Pearson Correlation	0.130	0.301**	0.351**	0.490**	1	-0.393**
	Sig. (2-tailed)	0.224	0.004	0.001	0.000		0.000
	N	89	89	89	89	89	89
HDL	Pearson Correlation	-0.126	-0.015	-0.140	-0.339**	-0.393**	1
	Sig. (2-tailed)	0.238	0.889	0.191	0.001	0.000	
	N	89	89	89	89	89	89

**. Correlation is significant at the 0.01 level (2-tailed). *. Correlation is significant at the 0.05 level (2-tailed).

Age is having correlation with waist circumference and FBS and this correlation is significant. Waist circumference is correlating with AGE, BMI, FBS and Triglycerides. FBS correlates with increased Age, BMI, WC, and decreased HDL. Triglycerides correlated with BMI, WC, FBS, and HDL.

Discussion

Psoriasis is associated with the cardiometabolic risk factors of metabolic syndrome. According to the NCEP ATP III definition, metabolic syndrome is present if three or more of the following five criteria are met: waist circumference over 90 cm (Men) or 80 cm (Women), blood pressure over 130/85 mmHg, fasting triglyceride (TG) level over 150 mg/dl, fasting high-density lipoprotein (HDL) cholesterol level less than 40 mg/dl (Men) or 50 mg/dl (Women) and fasting blood sugar over 100 mg/dl.

This study was undertaken to study one such debatable association – association with abnormalities in the lipid profile, blood glucose levels and prevalence of hypertension, which collectively constitute the so-called metabolic syndrome.

Age distribution

In our study, maximum number of patients (66%) of psoriasis belonged to age group of 31-60 years. Comorbidities tend to increase with age [3]. 4.5% psoriasis patients aged over 70 years have comorbidities. Comorbidities also have significant impact by increasing the patients' physical limitations [4].

As the number of comorbidities increase, so does the healthcare utilization and health care costs.[5] It has been observed that, while the frequency of skin conditions such as acne, urticaria and atopic dermatitis are reduced in patients with psoriasis compared with expected frequencies in the general population, the frequency of some non-cutaneous, although related, conditions is significantly increased [6].

Sex distribution: In our study, out of 89 cases, 60 were males and 29 were males. Male percentage being 67.4% females being 32%, though there is a male preponderance in our study it is as high compared to the other published studies. Inderjeet Kaur *et al*. [7] revealed a sex ratio of 2.3:1, whereas Mehta *et al*. reported a sex ratio of 4:1 in their studies.

Common Type of Psoriasis: In the present study, the most common type of psoriasis seen was chronic plaque psoriasis (87%). This is in consistent with the literature, which says that chronic plaque psoriasis is seen in 90% of patients. Considering the pro inflammatory nature of both psoriasis and metabolic syndrome and high prevalence of these disorders in Indian population, there is possibility of psoriasis incurring an increased risk for metabolic syndrome and its components.

Components of metabolic syndrome: NCEP ATP III criteria were employed to diagnose metabolic syndrome. We found that 29.2% of the patients were affected by metabolic syndrome, out of which 61.5% were males, 38.5% were females.

Central obesity: Using NCEP ATP III criteria central obesity was seen in 46% of the patients 3.3% constitute above grade 2 obesity. The modified NCEP ATP III criteria were also used. NCEP criteria, abdominal obesity is a component of the syndrome but not a prerequisite for its diagnosis.

Fasting blood sugars: Fasting blood sugars were deranged in31.5% of the individuals, Impaired fasting glucose is considered a pre-diabetic state, associated with insulin resistance and increased risk of cardiovascular pathology, although of lesser risk than impaired glucose tolerance (IGT). IFG sometimes progresses to type 2 diabetes mellitus. There is a 50% risk over 10 years of progressing to overt diabetes. A recent study by Nicolas *et al.* cited the average time for progression as less than three years [6]. IFG is also a risk factor for mortality. Cohen *et al*. [9] have all reported an increase in the prevalence of diabetes in patients with psoriasis.

Hypertension: 21 patients had hypertension, affecting 14 males, 7 females constituting 22.52% psoriatic patients. The results were compared with that of a study by Cohen *et al.* who reported that the prevalence of hypertension was significantly higher in psoriasis patients than controls (38.8%, 29.1%). Jacob Drehier [10] and Dahl reported that hypertension was present in 37.5% of the cases versus 29% of the controls. Similar results were reported by Cohen et, (27.5% vs 14.4%).

Hypertriglyceridemia: Serum lipids levels were analyzed in cases. Impaired triglyceride levels were seen in 23 out of the total 89 patients. 15 of these patients were males constituting 65.2% and remaining 8 patients were females constituting 34.8%. This is similar to study of Jacob Drehier and Dahlia (57.1% vs 47.4% of controls).

Hypercholesterolemia: In our study, impaired levels were seen in 40% of patients. 18 of these patients were females constituting 20% and remaining 18 patients were males constituting 20%. Rocha-Pereira reported increased cholesterol values in 38 psoriasis patients [11].

Metabolic syndrome: In our study 26 out of the89 psoriatic patients had metabolic syndrome out of which 16 were males, 10 were female patients. Isabela Guimarães Ribeiro Baeta *et al.* reported that 80 patients (44.9%) met the criteria for the diagnosis of MS according to the NCEP-ATP III (42.6% of men and 47.2% of women [12].

Metabolic syndrome & psoriasis: The majority of T cells infiltrating in psoriasis was assumed to belong to the T-helper cell (Th)1 subset, producing interferon (IFN)-Y and TNF-α [13, 14]. The aberrant activation of dendritic cells in the skin has been found to play a critical role in the pathogenesis of psoriasis Activated dendritic cells affect Th17 cells which produce interleukin (IL)-17 and IL-22, and IL-22 induces keratinocyte proliferation. Psoriasis, a chronic inflammatory skin disorder, shows systemic involvement affecting joints in some patients. Systemic inflammation is associated with a number of adipocytokines such as TNF-α, adiponectin, leptin and plasminogen activator inhibitor-1 (PAI-1). Among the inflammatory cytokines, TNF-α plays a pivotal role in both psoriasis and metabolic syndrome.

Obesity: According to the data from Ministry of Health, Labor and Welfare in 2009, 30.4% of the male and 20.2% of the female adult population are overweight in Japan. However, only 3% of the adult Japanese are obese. In contrast, 66% and 32% of the adult population in the USA are overweight and obese, respectively. In the European population, 30–80% and 30% were diagnosed as overweight and obese, respectively. Substantial evidence indicates that psoriasis is closely associated with increased risk of obesity. However, it remains unknown whether obesity is a result or a cause of psoriasis. Herron *et al*. retrospectively examined bodyweight before the onset of psoriasis and concluded that obesity follows psoriasis.

Dyslipidemia: Several studies showed that psoriasis is associated with atherogenic dyslipidemia with increased blood levels of total cholesterol, triglycerides, LDL, very LDL and lipoprotein A, and low HDL and apolipoprotein B. Mallbris *et al.* reported that psoriasis patients with a duration of less than 1 year show significantly elevated LDL and apolipoprotein A-1 and altered cholesterol/triglyceride ratio compared with healthy controls. The study in Japan also revealed that dyslipidemia was significantly associated

with psoriasis with an OR of 2.73 (95% CI = 1.59–4.69. Because psoriasis is associated with obesity and the excess psoriatics showed an increased prevalence of DM.

Hypertension: Several reports indicate the prevalence of hypertension in psoriasis. Swedish psoriasis patients showed a significantly higher rate of hypertension (Observed/expected [O/E] ratio = 3.6; $p< 0.001$) compared with other dermatological patients. A similar tendency was observed in a German study (O/E ratio = 1.9; $p< 0.01$). Angiotensin II is produced by ACE following renin-dependent production of angiotensin I. Although hypertension might be prevalent in psoriatics, the mechanism of this association remains to be determined.

Cardiovascular Disorder (CVD): Cardiovascular disorders such as myocardial infarction and stroke are closely associated with psoriasis. Gelfand *et al*. [15] reported that mild or severe psoriatics show a significantly increased risk of myocardial infarction. The risk ratio of myocardial infarction was higher for young psoriasis patients (<30 years old) with hazard ratios (HR) of 1.29 and 3.10 for mild and severe psoriasis, respectively. In contrast, HR of mild and severe psoriasis in patients who were aged 60 years or older were 1.08 and 1.36, respectively.

Metabolic Syndrome and Adipocytokines: Recent studies have revealed that adipose tissue, especially visceral adipose tissue, functions as not only an energy store, but also as an endocrine organ contributing to the regulation of body functions such as glucose, lipid- and insulin-dependent metabolism, vascular tonus, coagulation and inflammation. Various adipocytokines involved in these process such as adiponectin, leptin, IL-6, TNF-α and PAI-1 are produced in the adipose tissue [16, 17]. Leptin is another adipocyte-specific secretary protein which acts primarily through a specific receptor in the hypothalamus. It decreases appetite and increases energy expenditure reflected in body fat mass. The leptin receptor is also expressed in various tissues including adipocytes endothelial cells, monocytes, and keratinocytes of injured skin. Elevation of leptin levels is known to affect arterial intima-media thickness and leptin is assumed to be an independent predictor of CVD and coronary heart disease. Johnston *et al*. showed a positive correlation between BMI and waist circumference with serum leptin levels. However, there exists no significant difference of leptin levels between psoriatics and matched healthy controls. Contrary to the results of Johnston *et al*., we and others demonstrated the increased leptin levels in psoriatics compared with other skin disease patients and matched healthy controls. The discrepancy might be due to the difference in the patient number of each study. Johnston's study was performed with only γ0 psoriasis patients, while the following studies were performed in 144 and 122 patients, respectively. *In vitro* study disclosed that leptin increases keratinocyte and lymphocyte proliferation. This is accompanied by increased secretion of TNF-α and IL- 6 from keratinocytes, and TNF-α, IL-6, IL-17, IL-22 and IFN-Y from T lymphocytes [18, 19].

Conclusion

Prevalence of metabolic syndrome is 29.2%. Most of the patients belonged to the age group of 31-60 years. 10% of study subjects are under weight, 40% are normal, 46% are overweight and belong to grade 1 obesity, 3.3% constitute above grade 2 obesity. 46% of study subjects have abnormal WC (Men above 90 cm & women above 80 cm). 31.5% of study subjects are Diabetics. 25.8% of subjects show elevated Triglyceride levels (>150 mg/dl). Almost half of study subjects low HDL values (Females less than 50, males less than 40. Prevalence of hypertension among study subjects 22.5%. Age is having correlation with waist circumference and FBS and this correlation is significant. WC is correlating with AGE, BMI, FBS and Triglycerides. Increased FBS correlates with increased Age, BMI, WAIST circumference, and decreased HDL. Triglycerides correlated with BMI, WC, FBS, and HDL levels. Decreased HDL is correlated with increased FBS, and increased TGL, Females shows 27.6% and 20% males are hypertensive.

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