

CARDIOVASCULAR CHANGES IN PSORIASIS

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ABSTRACT**BACKGROUND**

It is now widely accepted that patients with psoriasis have an increased likelihood of developing cardiovascular complications.

Aim of this study was to identify the possible increased incidence of cardiovascular risk factors and the prevalence of cardiovascular disorders in individuals with psoriasis.

MATERIALS AND METHODS

The study was conducted in the first 40 patients who attended the outpatient department between October 2010 and October 2011. The presence of cardiovascular risk factors and diseases was assessed based on the history, examination findings and relevant investigations. The data obtained were compared with that in the normal population using appropriate statistical measures.

RESULTS

More patients in the study group had statistically significant diabetes mellitus ($p=0.023$) and impaired fasting glucose ($p=0.017$) when compared to the normal population. The abdominal obesity in males was found to be statistically significant ($p=0.0009$) when compared to the normal population.

CONCLUSION

Early detection of cardiovascular involvement and appropriate intervention in psoriasis patients is recommended for a favourable outcome.

KEYWORDS

Psoriasis, Cardiovascular Changes.

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BACKGROUND

Psoriasis is a disorder associated with chronic inflammation. It can also be related to inflammatory states in other systems, particularly the cardiovascular system (CVS). In addition, studies indicate that there is an increased incidence of cardiovascular risk factors such as smoking, alcoholism, obesity, hypertension, hyperlipidaemia, diabetes mellitus and metabolic syndrome in patients with psoriasis,^[1] which aggravate the deleterious effects on the CVS. This study was done with the aim of evaluating the prevalence of cardiovascular disorders in psoriasis patients and the prevalence of cardiovascular risk factors in these patients.

MATERIALS AND METHODS

This was a cross sectional study performed after obtaining approval of the protocol from the institutional ethics committee. Forty consecutive patients suffering from psoriasis attending the Department of Dermatology and Venereology in

our tertiary care public hospital between October 2010 and October 2011 were studied. Patients with psoriatic erythroderma, or psoriasis limited to palms and soles, or cardiac disorders prior to the onset of psoriasis were excluded from the study.

Detailed medical histories were recorded with special reference to cardiovascular risk factors. Height and weight were recorded, and body mass index (BMI) calculated to determine the presence of obesity. A detailed assessment of the CVS was done under the guidance of a cardiologist. As studies have shown that patients with severe psoriasis are more at risk of developing cardiovascular disorders, the extent of cutaneous involvement was assessed by PASI score.

All patients were subjected to routine laboratory examination of blood and urine, fasting and postprandial blood sugar levels, (FBS and PPBS), fasting lipid profile, renal and liver function tests, electrocardiography and echocardiography. They were investigated for hypertension, diabetes mellitus, dyslipidaemia, obesity, abdominal obesity, metabolic syndrome, coronary artery disease (CAD), ECG and echo changes.

Hypertension was defined as blood pressure $\geq 140/90$ mm of mercury or a previously diagnosed case of hypertension on antihypertensives. Diabetes mellitus was defined as FBS ≥ 126 mg% or PPBS ≥ 200 mg% or previously diagnosed diabetes on treatment. Dyslipidaemia was defined as total cholesterol > 200 mg/dL or LDL > 130 mg/dL or triglycerides ≥ 150 mg/dL

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or VLDL > 40 mg/dL or HDL < 40 mg/dL in men or < 50 mg/dL in women.

Obesity was defined as BMI \geq 30, and abdominal obesity was defined as waist circumference \geq 90 cm in males and \geq 80 cm in females.

Metabolic Syndrome was Diagnosed if a Patient had at Least Three of the following Five Conditions

1. Fasting glucose \geq 100 mg/dL or receiving drug therapy for hyperglycaemia.
2. Blood pressure \geq 130/85 mm of mercury or receiving drug therapy for hypertension.
3. Triglycerides \geq 150 mg/dL or receiving drug therapy for hypertriglyceridaemia.
4. HDL-C <40 mg/dL in men or <50 mg/dL in women, or receiving drug therapy for reduced HDL-C.
5. Waist circumference \geq 102 cm in men or \geq 88 cm in women.

Statistical Analysis

The results of the study were expressed in proportions and percentages (mean \pm standard deviation). Cardiovascular changes in different grades of psoriasis were compared using Chi square test for trend (for qualitative variables) and ANOVA (for quantitative variables). Comparison of psoriatic patients with the normal population was done by using Chi square test (for qualitative variables) and 't' test (for quantitative variables). A 'p' value \leq 0.05 was considered statistically significant.

RESULTS

Of the 40 patients enrolled in the study, 33 were male and 7 were female. Their ages ranged from 15 to 79 years with a mean age of 48.95. The majority of the patients were in their fifth decade of life, with a second peak at the seventh decade. The duration of the disease ranged from one month to 30 years, with an average of 9.1 years. The age of onset of the disease ranged from 12 to 70 years, with a mean of 39.1 years. Associated arthralgia was present in 10 (25%) patients. A history of erythroderma was present in four patients (10%). Twenty six patients (65%) had received systemic treatment for psoriasis – 25 of them methotrexate and one was on systemic retinoids. The most common site of involvement was the trunk [Figure 1], and the least affected sites were the palms and soles. No mucosal involvement was seen in our patients. The most common type of skin lesion was the chronic plaque type. Nail changes were observed in 34 patients (85%). The PASI score ranged from 3.2 to 55.8, with a mean value of 25.34 [Table 1].

Cardiovascular Risk Factors

Smoking: Thirty five percent of the patients, all of them male, were smokers. This prevalence was not found to be statistically significant, as the prevalence rate of smoking in the male population of Kerala has been reported to be 30.6%.^[2]

Hypertension

Hypertension was present in 15 (37.5%) patients, 14 of them male. Of these, 11 (73.3%) were diagnosed after the onset of psoriasis. Only 4 (26.7%) had hypertension prior to the onset

of psoriasis. This prevalence was not found to be statistically significant, as the prevalence rate is 36.1% in the population.^[2]

There was no statistically significant correlation between PASI score and duration of the disease with the presence of hypertension.

Diabetes Mellitus

Eleven patients (27.5%) were diabetic, 9 of them male. This prevalence was statistically significant ($p = 0.023$).^[2] Of these, 6 (54.5%) were diagnosed after the onset of psoriasis, and 5 (45.5%) had diabetes prior to the onset of psoriasis. The presence of diabetes did not correlate significantly with the duration of the disease or the PASI score.

Six (15%) patients had impaired fasting glucose (IFG) (FBS 100-125 mg%), of which 5 were male and one female. The prevalence was statistically significant, ($p = 0.017$) compared with the prevalence of 5.1% in the population.^[2]

Obesity and excess weight: Obesity was found in only one female patient (2.5%), whereas 10 (25%) patients were overweight (BMI 25.1 – 29.9). This was not statistically significant compared to the prevalence of 51.1% in the population.^[2]

Abdominal obesity was found in 26 (65%). Of the 33 male patients, 20 (60.6%), and of the 7 female patients, 6 (85.7%) had abdominal obesity. The prevalence of abdominal obesity in males was statistically significant.^[3]

Dyslipidaemia

Elevated total cholesterol levels were seen in 12 (30%) of the male patients and 4 (10%) of the female patients. Triglyceride levels were elevated in 8 (20%) of the male patients but in none of the female patients. Raised LDL levels were seen in 12 (30%) of the male and 4 (10%) of the female patients. Reduced HDL values were noted in one (2.5%) male and 3 (7.5%) female patients. Raised VLDL levels were seen in 2 (5%) male and none of the female patients. The alterations in the lipid profile did not have any statistically significant correlation with the prevalence in the general population, the PASI score or the duration of the disease.

Metabolic Syndrome

This was observed in 13 (32%) patients, 10 male and 3 female. There was no statistically significant difference when compared to the general population.

Cardiovascular Disease

A history of myocardial infarction (MI) was present in 5 (12.5%) patients. All were male and had MI after the onset of psoriasis. All the 5 patients had hypertension, 4 had diabetes, 3 had dyslipidaemia and 2 were smokers.

One male patient had a history of stroke after the onset of psoriasis.

ECG Changes

T wave inversion was seen in 8 male and 3 female patients, ST depression in one, Q waves in 2, and left ventricular hypertrophy (LVH) in 4 male patients.

Echocardiography Findings

The ejection fraction was >50 in 37 (92.5%) patients, indicating good ventricular function, and between 45 and 50 in 3 (7.5%) patients, indicating mild ventricular dysfunction.

LVH was detected in 3 (7.5%), and mild left ventricular diastolic dysfunction in 2 (5%) male patients. Two male patients had regional wall motion abnormalities (RWMA), which indicated ischaemic changes.

In total, 15% of our patients had coronary artery disease (CAD), which was not found to be statistically significant [Table 2].

Our Study Revealed

1. A statistically significant association between psoriasis and abdominal obesity, diabetes and IFG values, when compared with the general population.
2. A high prevalence of cardiovascular risk factors such as smoking, hypertension, obesity, dyslipidaemia and metabolic syndrome in patients with psoriasis.
3. Occurrence of CAD in psoriatic patients with a prevalence as high as 15%.



Figure 1. Psoriasis on the Trunk

Patient Characteristics	
Total no. of patients	40
Mean age in years	48.95
Mean age at onset in years	39.1
Mean duration of psoriasis in years	9.1
Mean PASI score	25.34

Table 1. Patient Characteristics

*PASI: Psoriasis Area Severity Index

Cardiovascular Risk Factors	Males (n=33)	Females (n=7)	Total (n=40)
Smoking	14 (42.4)	-	14 (35)
Hypertension	14 (42.4)	1 (14.3)	15 (37.5)
Diabetes Mellitus	9 (27.3)	2 (28.6)	11 (27.5)
IFG*	5 (15.2)	1 (14.3)	6 (15.0)
Obesity	-	1 (14.3)	1 (2.5)
Overweight			10 (25.0)
Abdominal Obesity	20 (60.6)	6 (87.5)	26 (65.0)
Dyslipidaemia	12 (36.4)	4 (57.2)	16 (40.0)
Metabolic Syndrome	10 (30.3)	3 (42.9)	13 (32.0)
MI†	5 (15.2)	-	5 (12.5)
Stroke	1 (3.0)	-	1(2.5)
LVH‡	3 (9.1)	-	3 (7.5)
RWMA§	2 (6.1)	-	2 (5.0)
LV Dysfunction	4 (12.2)	-	4 (10.0)

Table 2. Prevalence of Cardiovascular Risk Factors in the Study Population

(Figures in the parentheses indicate column wise percentages)

*IFG: Impaired Fasting Glucose †MI: Myocardial Infarction ‡LVH: Left Ventricular Hypertrophy §RWMA: Regional Wall Motion Abnormality ||LV Dysfunction: Left Ventricular Dysfunction

DISCUSSION

The CV morbidity in psoriatic patients is dependent on the severity of the skin involvement, with deleterious effects reported mainly in severe psoriasis.^[1] These patients have an increased incidence of insulin resistance, obesity, hypertension, dyslipidaemia and metabolic syndrome.

Patients with severe psoriasis have an increased risk of atherothrombosis,^[4] stroke and atrial fibrillation,^[5] as well as arterial and venous vascular diseases such as thrombophlebitis, pulmonary embolisation,^[6] coronary artery calcification,^[7] and myocardial infarction.^[8]

Multiple common pathogenic features are involved in this link between psoriasis and cardiovascular morbidity. These include:

A predilection for insulin resistance is seen in patients with psoriasis due to many inter-linked factors. These include elevated levels of tumour necrosis factor- α ,^[9] inhibition of tyrosine kinase activity of the insulin receptor, and suppression of adiponectin secretion from adipocytes.^[10]

Patients with psoriasis have decreased peroxisome proliferator-activated receptor delta (PPAR δ), which is responsible for metabolic syndrome in these patients. Reduced PPAR δ is associated with diabetes, hypertension, insulin resistance and dyslipidaemia.^[11]

Obesity leads to secretion of multiple inflammatory cytokines by adipose tissue, especially leptin, which is associated with atherosclerosis and arterial thrombosis. Hyperleptinaemia has also been demonstrated in psoriasis.^[12] Hypertension: Psoriasis has been demonstrated to be associated with polymorphisms in inflammation genes such as the angiotensin converting enzyme (ACE) gene.^[13]

Elevated plasma renin activity^[14] and increased levels of endothelin-1^[15] have been reported in patients with psoriasis, leading to the development of hypertension. Endothelin-1 is produced by keratinocytes as an autocrine growth factor and is a potent vasoconstrictor.

Inflammatory cytokines in psoriasis such as interferon-gamma produced by Th1 cells and interferon-17 produced by Th17 cells cause inflammation involving interferon-gamma, tumour necrosis factor, and interleukins.^[16] These cytokines also are involved in the process of atherosclerosis and acute coronary syndrome.^[17]

Increased levels of cytokines such as IL-6 and TNF- α lead to increased levels of C-reactive protein (CRP) in psoriasis. Increased levels of CRP lead to an increased risk for adverse cardiac events such as acute myocardial infarction (AMI), unstable angina, hypertension, MI and stroke.^[18]

Intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) are upregulated in psoriasis, and are also involved in the formation of atherosclerotic plaques. Vascular endothelial growth factor (VEGF) is upregulated and leads to angiogenesis in both psoriasis and atherosclerosis.^[18]

Naïve T cells activated by antigen-presenting cells in the lymph nodes interact with dendritic cells, macrophages and keratinocytes in psoriasis, and with smooth muscle cells in atherosclerosis, leading to the development of psoriatic or atherosclerotic plaques.^[18]

Common genetic loci of susceptibility PSORS2, PSORS3 and PSORS4 have been demonstrated for psoriasis, metabolic syndrome, type 2 diabetes, familial hyperlipidaemia and cardiovascular disease.^[19] Individual genes such as CDKAL1 are associated with psoriasis and type 2 diabetes,^[20] and Apolipoprotein E with psoriasis and hyperlipidaemia.^[21,22] Increased serum levels of homocysteine in psoriasis and the associated dyslipidaemia lead to atherothrombosis in these patients.^[4]

High circulating levels of osteopontin occur in psoriasis, which is also associated with atherosclerosis.^[23]

Oxidative stress is greatly increased in psoriasis, in conjunction with an abnormal lipid profile, leading to increased risk of cardiovascular disease.^[24]

Systemic drugs used to treat psoriasis such as retinoids and cyclosporine can cause hyperlipidaemia and hypertension.

The increased priority given to treatment of psoriasis leads to decreased attention to the presence or development of CV risk factors.

Studies on patients with psoriasis have demonstrated statistically significant abnormal findings on electrocardiography, the most common being ST-T wave changes. The intima-media thickness of both common carotid arteries was found to be significantly higher in these patients indicating subclinical atherosclerosis.^[25] Psoriasis could also be a risk factor for hypertension and cardiovascular disease even in the absence of metabolic syndrome.^[26]

CONCLUSION

Based on the results of our study, we recommend regular monitoring of patients with psoriasis for the presence of comorbidities which have a definite adverse effect on both psoriasis and the CVS. Early detection and control of these risk factors is imperative to reduce the morbidity and mortality associated with these conditions, and to provide a better quality of life to these patients.

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