A Study of Cardio-Metabolic Risk Profile in Patients with Psoriasis

Ritu Karoli*, Jalees Fatima**, Vaibhav Shukla*, KS Dhillon***, Sachin Khanduri****, Sumit Maini†, Ashok Chandra‡

Abstract

Introduction/Background: Psoriasis is a chronic immune mediated inflammatory disorder of the skin and joints. Recent studies have shown increased prevalence of traditional cardiovascular risk factors such as diabetes mellitus, hypertension and metabolic syndrome. Since atherosclerosis and psoriasis share a common link of inflammation, different workers have shown psoriasis to be a risk factor for atherosclerosis. The aim of our study was assessment of cardiovascular risk factors and evidence of subclinical atherosclerosis in patients of psoriasis.

Methods: In a hospital based, cross-sectional study, 96 patients with psoriasis and 100 age, sex and weight matched controls were enrolled. Prevalence of diabetes, hypertension, metabolic syndrome was studied. They were also assessed for endothelial dysfunction by brachial artery flow mediated dilatation (FMD) and carotid intima media thickness (CIMT).

Results: There was higher prevalence of hypertension, hypertriglyceridaemia, diabetes mellitus and metabolic syndrome in patients with psoriasis than in controls. FMD was lower in patients with psoriasis than in controls (5.6 ± 2 vs 7.5 ± 2.8, P = 0.02). The mean CIMT was significantly increased (0.78 ± 0.12 vs 0.62 ± 0.08, P = 0.001) in patients with psoriasis compared with controls. In psoriasis patients, CIMT was associated with hypertension, hypertriglyceridaemia, diabetes, insulin resistance, increased severity and duration of psoriasis while in multivariate analysis insulin resistance (OR 2.8, 95% CI 1.92 - 6.34 P = 0.02) and increased duration of disease (OR 3.12, 95% CI 2.34-7.56) a were the independent risk factors associated with higher CIMT.

Conclusion: Patients of psoriasis have higher prevalence of metabolic syndrome, cardiovascular risk factors and subclinical atherosclerosis than general population. As a routine, individuals with moderate to severe psoriasis of long duration should be recognised as being at increased cardio vascular risk and thus encouraged for therapeutic interventions to reduce the modifiable risk factors.

Introduction

Psoriasis is a chronic immune mediated inflammatory disorder of the skin and joints that affects nearly 3-4% of the population worldwide.1,2 Patients of psoriasis have shorter life expectancy, mostly due to cardiovascular disease3 and studies have shown increased prevalence of traditional cardiovascular risk factors such as diabetes mellitus, hypertension, dyslipidaemia and obesity.4 Different workers have shown psoriasis to be a risk factor for atherosclerosis, myocardial infarction, stroke, endothelial dysfunction and cardiovascular mortality.5-8 Recent research has shown that systemic inflammation has played a role in atherosclerosis. Since atherosclerosis and psoriasis share a common link of inflammation, inflammatory cytokines may play a role in pathogenesis of both psoriasis and atherosclerosis or metabolic syndrome, but the exact mechanism is not yet elucidated.9,10

Emerging epidemic of obesity and metabolic syndrome are major public health problems.11-13 Traffic light system of nutrition labelling can play a role in public health initiatives to increase awareness and reduce obesity.14-16

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health concerns globally. There are not many studies on early cardiovascular risk markers in our patients with psoriasis who otherwise are also more prone to have metabolic syndrome. Better identification of asymptomatic individuals with high risk of future coronary artery disease, who should therefore receive aggressive risk reduction interventions is an important challenge.

In recent times certain surrogate markers of atherosclerosis such as endothelial dysfunction and carotid intima media thickness (CIMT) have been devised which can help to assess the cardiovascular risk noninvasively.

Endothelial dysfunction has been regarded as early feature of atherosclerosis. Assessment of endothelial dysfunction by measuring flow mediated dilatation (FMD) of the brachial artery is considered as potential tool for predicting coronary atherosclerosis and carotid intima media thickness (CIMT) and compared with controls. Homoeostasis model assessment (HOMA) method for insulin resistance was calculated by the formula: Fasting serum insulin (micro units/ml) x fasting serum glucose (mill moles per liters)/22.5.

Diagnosis of metabolic syndrome was based on most widely accepted criteria, issued by the adult treatment panel III which defines metabolic syndrome as the presence of at least three of the following conditions:

- Elevated waist circumference
  - Men ≥ 40 inches (102 cm)
  - Women ≥ 35 inches (88 cm)
- Elevated triglycerides ≥ 150 mg/dl
- Reduced HDL cholesterol
  - Men < 40 mg/dl
  - Women < 50 mg/dl
- Elevated blood pressure < 130/85 mmHg
- Elevated fasting glucose < 100 mg/dl or use of medication for hyperglycaemia

FMD and CIMT measurement: Endothelial function was measured noninvasively by ultrasonographic assessment of right brachial artery dimensions. The diameter of the right brachial was measured twice, first at rest then after inducing reactive hyperaemia with the help of pneumatic cuff. It was carried out by a blinded sonologist after an overnight fast in a cool, quiet room with B mode ultrasound scanner (Siemens, Germany) using 10MHz linear transducer. The diameter of right brachial artery was measured 2-8 cm above the antecubital space in the end diastolic phase from one media-adventitia interface to the other at the clearest part three times and an average was taken. After the detection of the right transducer position, skin was marked and arm kept in same position. The blood pressure cuff was tied on the upper arm and inflated to supra systolic levels kept inflated for 4 minutes. Sixty seconds after the cuff was released, brachial artery dimensions were again measured. The maximum diameter measurement was defined as the average of three consecutive diameters measurements. Carotid intima media thickness (CIMT) was measured by B mode ultrasound using linear probe at frequency of 10 MHz. The common carotid arteries were scanned at the level of bifurcation on either side and

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients with psoriasis(n=96)</th>
<th>Controls(n=100)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age(years)</td>
<td>46±14.6</td>
<td>47±16.3</td>
<td>0.7</td>
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<tr>
<td>Sex</td>
<td>56/40</td>
<td>54/43</td>
<td>0.2</td>
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<td>BMI</td>
<td>26.1±2.4</td>
<td>25.7±1.8</td>
<td>0.67</td>
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<tr>
<td>Waist circumference</td>
<td>41(43%)</td>
<td>32(32%)</td>
<td>0.04</td>
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<tr>
<td>HOMA-IR</td>
<td>8.2±3.45</td>
<td>4.43±2.67</td>
<td>0.02</td>
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</tbody>
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Material and Methods

In a prospective hospital based case control study patients of psoriasis were enrolled between August 2011 and July 2012 from department of dermatology at Era’s Lucknow Medical College hospital. We included those patients who were more than 20 years old, disease duration at least six months and were not receiving any systemic treatment for psoriasis at least one month before enrollment. We excluded patients who had any other autoimmune disorder such as rheumatoid arthritis or systemic lupus erythematosus. Age, sex and weight matched healthy controls were enrolled among patients attendants and hospital staff. All study participants gave written informed consent and study protocol was approved by Institutional Ethics committee. A detailed history,
mean value was used for analysis. The intima media thickness was measured in the far wall of the arteries at sites identified as diffuse and continuous projections with the greatest distance between the luminal intimal interface and media adventitial interface but without atherosclerotic plaques. Localised lesions > 2 mm thickness were considered to be atherosclerotic plaques. CIMT was assessed by single observer who was blinded for the diagnosis.

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS version 15.0) was used for statistical analysis. Results were expressed as mean ± SD. The characteristics of distribution were tested with Kolmogorov-Smirnov test. Highly skewed variables were analysed after logarithmic transformation. Spearman rank correlation were used for these variables. When variables showed persistent skewed deviation, Mann-Whitney ‘U’ test was used. Differences between means were analysed by Student’s unpaired ‘t’ test. P < 0.05 was considered statistically significant. Analysis of correlations between parameters was performed by using Pearson’s correlation coefficient and regression analysis was done to predict FMD and CIMT.

Results

The study included 96 patients with psoriasis and 100 age, sex and BMI matched controls. The mean age of patients in psoriasis group was 46 ± 14.6 years and 47 ± 16.3 years in controls (Table 1). Duration of the disease in cases ranged from six months to 26 years with mean of 7.58 ± 3.6 years. Sixty-four patients had mild psoriasis (PASI < 8), twenty patients had moderate psoriasis (PASI 8-12) and 13 patients had severe psoriasis (PASI > 12). Sixteen patients had psoriatic arthritis.

There was higher prevalence of hypertension, hypertriglyceridaemia, diabetes mellitus and metabolic syndrome in patients with psoriasis than in controls (Table 2). The prevalence of smoking was also higher but was not statistically significant. Significantly higher prevalence of metabolic syndrome was also observed in patients with psoriasis. Table 3 is showing the characteristics of patients of psoriasis with and without metabolic syndrome. The duration of psoriasis along with its severity was significantly associated with presence of metabolic syndrome. The mean CIMT was significantly higher in psoriatic patients with metabolic syndrome compared to those who did not have metabolic syndrome. FMD was also lower in this subset of patients but difference was not statistically significant.

Baseline brachial artery diameter was 3.8 ± 0.6 in psoriatic patients and 3.6 ± 0.5 in controls (p = 0.22). FMD (Table 4) was lower in patients with psoriasis than in controls (5.6 ± 2 vs 7.5 ± 2.8, P = 0.02). We found correlation between FMD and age, BMI, hypertension, hyper triglyceridaemia, diabetes and insulin resistance. In addition, the FMD impairment was related to the duration but not to the severity of psoriasis. In multiple regression analysis duration of psoriasis was the only independent variable related to FMD.

The mean CIMT was significantly increased (0.78 ± 0.12 vs 0.62 ± 0.08, P = 0.001) in patients with psoriasis compared with controls. CIMT was associated with male sex, hypertension, diabetes, insulin resistance and presence of psoriasis. In multiple regression analysis of whole group (patients and controls) male sex (OR 4.2, 95% CI 1.32 - 10.6, P = 0.01) and presence of psoriasis (OR 12.34, 95% CI 5.6 - 48.78, P = 0.001) were the independent predictors of higher CIMT. In psoriasis patients, CIMT was associated with hypertension, hypertriglyceridaemia, diabetes, ,insulin resistance, increased severity and duration of psoriasis while in multivariate analysis insulin resistance (OR 2.8, 95% CI 1.92 - 6.34 P = 0.02) and increased duration of disease(OR 3.12, 95% CI 2.34 - 7.56a) were the independent risk factors associated with higher CIMT.
Discussion

Psoriasis is now considered as a systemic inflammatory disorder. Recent research has demonstrated an association between the systemic inflammatory disease such as rheumatoid arthritis, systemic lupus erythematosus or psoriasis and the cardiovascular risk factors including metabolic syndrome. Inflammatory cytokines play an important role in the pathogenesis of both psoriasis and atherosclerosis; however, the mechanisms that mediate the process are still ill defined. Recent reports have shown an increased prevalence of diabetes mellitus, obesity, hypertension, dyslipidaemia, myocardial infarction and heart failure in patients of psoriasis. Cardiovascular disease is an important cause of morbidity and mortality in patients with psoriasis. Although controversy exists for psoriasis to be accepted as independent risk factor for cardiovascular disease. There is significantly higher prevalence of risk factors for cardiovascular disease in patients with psoriasis as compared to general population and so is the risk of atherosclerosis adversity. They appear to be highest for more severe disease and might be related to duration of the disease. While managing psoriatic plaques of these patients concerns should extend to the atherosclerotic plaques as well.

The prevalence of hypertension and diabetes has been reported higher in patients with psoriasis compared with that in the general population. Tam et al. compared cardiovascular risk factors in 102 patients with psoriatic arthritis and 82 healthy controls. After adjusted for body mass index patients with psoriatic arthritis were still more likely to have hypertension and diabetes mellitus. Insulin resistance, was also significantly increased in patients with psoriatic arthritis compared with that in controls. Similar to the results of other studies we also found higher prevalence of hypertension, hypertriglyceridaemia, type 2 diabetes and smoking in patients with psoriasis than age, sex and BMI matched controls.

The metabolic syndrome is a cluster of traditional risk factors that include abdominal obesity, atherogenic dyslipidaemia, hypertension, and insulin resistance. Raychaudhuri et al. reported an increased prevalence (58.1%) of the metabolic syndrome in 105 patients with psoriatic arthritis compared to the 35.2% reported from the general population. Similar to other workers the greater prevalence of metabolic syndrome was also observed in our study in cohort of psoriasis patients compared to controls. In our study presence of metabolic syndrome was significantly associated with severity and duration of psoriasis. Choi et al. also found similar association with severity of psoriasis while Mehta et al. in a large cohort study concluded that severe psoriasis confers an additional risk of major adverse cardiac events. Other Indian studies on prevalence of metabolic syndrome and cardiovascular risk factors in patients with psoriasis did not find association with severity of psoriasis however, Nisa et al. did find a significant association of metabolic syndrome with increased duration of psoriasis similar to our study.

Endothelial dysfunction is considered an early feature in atherogenesis and has been consistently associated with cardiovascular risk. It encompasses an imbalance between vasodilating and vasoconstricting substances, leading to an impaired ability of the artery to dilate in response to physical and chemical stimuli. Postocclusion flow-mediated vasodilatation (FMD%) of the brachial artery using ultrasonography is used to noninvasively evaluate endothelial function. However, not many studies have evaluated ED in psoriasis patients using FMD. In the study by Gonzalez-Juanatey et al. in 50 patients with psoriatic arthritis without cardiovascular risk factors or clinically evident CVD, FMD was found significantly lower in patients with psoriatic arthritis compared with 50 matched healthy controls, indicating endothelial dysfunction in psoriatic arthritis as a potential basis for the association with atherosclerosis. We found a significantly impaired mean FMD in psoriasis patients compared with healthy controls, in line with similar findings reported by Ulusoy et al. and Balci et al. and duration of psoriasis was the only independent variable related to FMD.

Carotid intima media thickness is a surrogate marker and indicator of subclinical atherosclerosis determined by carotid ultrasound can refine cardiovascular risk assessment in these patients with psoriasis. Many previous case-control studies, have demonstrated that patients with psoriasis have a higher prevalence of subclinical atherosclerosis. The largest increase (23%) in carotid IMT was found by Tam et al. in a study done in a Chinese cohort. The smallest increase in carotid IMT (8.7%) was found in the study by Gonzalez-Juanatey et al. in patients with psoriatic arthritis without cardiovascular risk factors or clinically evident CVD, significantly higher than that in matched healthy controls.

In our study, mean CIMT was higher in psoriatic patients and was associated with hypertension, hypertriglyceridaemia, diabetes, insulin resistance, increased severity and duration of psoriasis in univariate analysis while in multivariate analysis insulin resistance and increased duration of disease were the only independent risk factors associated with higher CIMT.

Overall, results of our study show that patients with psoriasis are often associated with co-morbid states.
and there is higher prevalence of metabolic syndrome and cardiovascular risk factors than general population. All patients with metabolic syndrome have a sufficiently high relative risk of cardiovascular events to justify for long term intervention and monitoring in the clinical setting. First step in curbing this epidemic of metabolic syndrome and subsequent cardiovascular risk would be to identify high risk individuals at an early stage so as to implement preventive measures for further development of metabolic complications. As a routine part of general medical care, otherwise healthy individuals with moderate to severe psoriasis of long duration should be recognised as being at increased cardiovascular risk and thus encouraged for therapeutic interventions to reduce the modifiable risk factors.

Conclusion

Patients of psoriasis have higher prevalence of metabolic syndrome and cardiovascular risk factors than general population. All patients with metabolic syndrome have a sufficiently high relative risk of cardiovascular events to justify for long term intervention and monitoring in the clinical setting. First step in curbing this epidemic of metabolic syndrome and subsequent cardiovascular risk would be to identify high risk individuals at an early stage so as to implement preventive measures for further development of metabolic complications. As a routine part of general medical care, otherwise healthy individuals with moderate to severe psoriasis of long duration should be recognised as being at increased cardiovascular risk and thus encouraged for therapeutic interventions to reduce the modifiable risk factors.

References


