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Original Research Article

A comparative cross-sectional study on evaluation of carotid artery intima-media thickness in patients of psoriasis vulgaris: an early predictor of subclinical atherosclerosis

Rajkumar Kannan[1], Samuel J. Daniel[1], Mohideen Ashraf A.[2], Ramesh A.[1], Parimalam Kumar[1], Yuva Priya B.[1]*

[1]Department of Dermatology, [2]Institute of Radiodiagnosis, Madras Medical College, Chennai, Tamil Nadu, India

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***Correspondence:**
Dr. Yuva Priya B.,
E-mail: yuvapriya271@gmail.com

ABSTRACT

Background: Psoriasis is associated with atherosclerosis and increased cardiovascular risk. Carotid artery intima-media thickness (CIMT) is used as a non-invasive marker in the assessment of subclinical atherosclerosis. In this study, by using a doppler ultra-sonogram, subclinical atherosclerosis in patients with psoriasis was evaluated in need of special follow-up to reduce cardiovascular morbidity. It was aimed to evaluate the mean CIMT, determine the prevalence of subclinical atherosclerosis and to evaluate the association between the severity, duration of psoriasis and CIMT.
Methods: A hospital-based cross-sectional study was done on 25 patients with psoriasis and age, gender, and body mass index (BMI) matched 25 healthy controls over 2 months. CIMT was measured using a doppler ultra-sonogram.
Results: Compared to the controls, patients had higher CIMT. 24% of patients had subclinical atherosclerosis compared to 12% of controls. Chronic smokers with psoriasis had a significant association with subclinical atherosclerosis. Because of the COVID-19 pandemic, it was unable to determine the severity and prognosis of subclinical atherosclerosis through follow up.
Conclusions: This study provides an insight into the higher prevalence of subclinical atherosclerosis in psoriasis patients, smokers in particular. CIMT can serve as an important noninvasive marker to assess cardiovascular risk.

Keywords: Psoriasis, Subclinical atherosclerosis, Carotid artery intima-media thickness, Cardiovascular risk

INTRODUCTION

Psoriasis is a chronic inflammatory, a non-communicable disease that predominantly involves skin, nails and joints and is associated with systemic manifestations in many organs.[1] The World Health Organization noted that the reported prevalence of psoriasis ranges from 0.09% to 11.43% worldwide, which makes psoriasis a serious global problem with at least 100 million individuals affected all over the world.[2,3] Psoriatic patients are at higher risk of developing metabolic syndrome including obesity, dyslipidemia, diabetes, hypertension and more recently atherosclerosis.

Persistent skin inflammation in psoriasis patients may contribute to the development of premature atherosclerosis.[4] Atherosclerosis is a systemic and chronic inflammatory disease, which may cause cardiovascular disease, the most frequent cause of death in the world.[5]

The infiltration of low-density lipoprotein (LDL)-cholesterol through the endothelium of intima following oxidative and enzymatic processes lead to the intima-media atherogenic complex of arterial walls which can be quantified by carotid artery intima-media thickness (CIMT)-measurement.[6]

Intima-media thickness of the carotid artery is measured in B-mode ultrasound images and it is best visible in the measurement segment of the distal common carotid artery with the lowest measurement variability.[7] B-mode sonogram of the carotid artery is a safe, cheap, quick painless examination, free of radiation exposure and enables a detailed evaluation of different regions of the carotid artery.[8]

Several markers of inflammation like fasting lipid profile or C reactive protein are useful for the prediction of subclinical atherosclerosis. However, CIMT easily detects subclinical atherosclerosis, is a readily available tool for clinical purposes and is used as a non-invasive marker in the assessment of subclinical atherosclerosis.[9,10]

In this study, by using a carotid ultrasonogram, subclinical atherosclerosis in patients with psoriasis will be evaluated in need of special follow up to reduce cardiovascular morbidity and mortality.

METHODS

Study design

It was a comparative cross-sectional study.

Study period

The duration of the study was for 2 months (February 2021–March 2021).

Study center

The study was conducted at the Department of Dermatology, Rajiv Gandhi Government General Hospital, Chennai, Tamil Nadu, India.

Methodology

The study was approved by the institutional ethics committee. The diagnosis of psoriasis was done based on clinical findings. A total of 25 patients with psoriasis vulgaris, who were attending the outpatient clinic were consecutively enrolled after obtaining informed consent. Additionally, 25 healthy controls - with non- inflammatory dermatological conditions other than psoriasis (nevi, seborrheic keratosis or dermatosis papulosa nigra), having a similar age, sex and BMI range with them, were included. Survey study has a response rate of 100%. Detailed clinical history including basic demographic details were taken. General examination including height, weight, blood pressure, systemic examination and dermatological examination were done. BMI was calculated by the Quetelet index. In the patient's group, estimation of disease severity and psoriasis area involvement was calculated according to the psoriasis area and severity index (PASI) score.

Ultrasound measurement of the mean intima-media wall thickness of common carotid artery

The study population was subjected to an evaluation of CIMT. Patients were lying in a supine position during the examination and common carotid arteries were scanned longitudinally. A magnified image was recorded from the angle showing the greatest distance between the interface of lumen-intima, media and adventitia. From this, at least three measurements of the common carotid artery wall were taken approximately 10 mm proximal to the bifurcation (the arterial segment 1 cm proximal to the carotid bulb) to derive the mean intima-media wall thickness of the common carotid artery. Ultrasound scanning was performed using carotid duplex high-resolution B-mode equipment with a 7-12 MHz linear array transducer. The final intima-media wall thickness value represents an average from three different points on the common carotid artery wall thickness. The plaque was assumed as a localized thickening >1.2 mm that did not uniformly involve the whole artery. A CIMT value >0.80 mm was considered an index of subclinical atherosclerosis.

Inclusion criteria

Patients of age >18 years attending the Dermatology Outpatient Department (OPD) during the study period with chronic plaque psoriasis for at least 6 months, involving >10% of body surface area (BSA) at the time of screening; and those who gave consent to participate in the study were included in the study.

Exclusion criteria

Psoriasis patients with <10% BSA involvement; patients with systemic treatment like steroids, immunosuppressive drugs, lipid-lowering therapy, antihypertensive or antiplatelet drugs for at least 3 months before the study; patients with a history of renal failure, hepatic impairment, cardiovascular, cerebrovascular disease or connective tissue disease; pustular/erythrodermic psoriasis; age <18 years and pregnant women were excluded.

Statistical analysis

The collected data were entered in the Microsoft excel sheets and analyzed using statistical package for the social sciences (SPSS) software version 21.0. Continuous variables were represented in mean, median, mode and standard deviation. Categorical variables were represented in frequencies and percentages.

The Chi-square test was used to determine the significance of the difference between the two proportions. Fisher's exact test was used when more than 20% of the cell values have an expected cell value of less than 5. The student 't' test was used to determine the significance of the difference between the two means. P values less than 0.05 were considered as statistically significant.

RESULTS

A total of 25 patients with psoriasis and 25 healthy control subjects matched for age, gender and BMI were included in this study. The mean age of the study population was 51.9 (SD±12.6) years. There were 17 males and 8 females in each group. The average duration of the disease was 6.1±5.4 years. Overall, 12% of the patients were obese and 24% were overweight with BMI, with no statistically significant difference between these groups. The mean PASI score of the patients' group was 8.38±7.5. Greater than 90% of participating patients had psoriasis vulgaris and the remaining patients with either palmoplantar or inverse psoriasis (Figure 1). Topical therapy (n=13, 52%) was the most frequently utilized treatment. The frequency of systemic treatment was 32% (n=8).

The mean CIMT was higher in psoriasis patients (0.67) than in controls (0.64) (Figure 2). A total of 6 patients (24%) and 3 controls (12%) had subclinical atherosclerosis (CIMT >0.8 mm) with of p value of 0.162 and among that, one psoriatic patient had a carotid plaque (Figure 3). A significant difference was detected between psoriasis patients and healthy controls regarding smoking habits (p<0.005). There was no significant difference between diabetic-non diabetic, hypertensive-non hypertensive, psoriasis disease duration and CIMT (p>0.05) (Table 1).

Table 1: Demographics and disease characteristics of the study population.

Factors	Group (%)		P value
	Case	Control	
Smoking			
No	16 (64)	24 (96)	0.005
Yes	9 (36)	1 (4)	
Alcohol			
No	23 (92)	25 (100)	0.245
Yes	2 (8)	0 (0)	
Diabetes			
No	20 (80)	18 (72)	0.21
Yes	5 (20)	7 (28)	
Hypertension			
No	20 (80)	19 (76)	0.252
Yes	5 (20)	6 (24)	
Arthritis			
Present	23 (92)	25 (100)	
Absent	2 (8)	0 (0)	
PASI score	8.384±7.50	(0)	
Scalp			
No	17 (68)	0 (0)	
Yes	8 (32)	0 (0)	
Nails			
No	15 (60)	0 (0)	
Yes	10 (40)	0 (0)	
Palms and soles			
No	20 (80)	0 (0)	
Yes	5 (20)	0 (0)	

Among the patient's group, it was observed that subclinical atherosclerosis risk increased with increasing age. In this study, psoriatic patients had higher cardiovascular risk at younger mean age than controls although without statistical significance (Table 2). The unadjusted odds ratio of subclinical atherosclerosis was 2.3 times higher in psoriasis patients than in controls (95% CI: 0.51-10.5, p=0.162). The association was considerably more pronounced after adjusting the age (adjusted odds ratio 5, 95% CI: 0.44-56.6) likely due to more atherosclerosis in younger psoriasis age group of 55-60 years old comparing 60-70 years old. 71% of psoriasis patients had subclinical atherosclerosis versus 14% of controls in the same age group.

Table 2: Prevalence of subclinical atherosclerosis (CIMT >0.8 mm) in cases and controls.

CIMT (mean)	Group (%)		P value
	Case (n=25)	Control (n=25)	
CIMT	0.6728±0.17	0.644±0.13	0.515
<0.8 mm	19 (76)	22 (88)	0.162
>0.8 mm	6 (24)	3 (12)	

CIMT – Carotid artery intima-media thickness

Figure 1: Chronic plaque psoriasis involving the trunk.

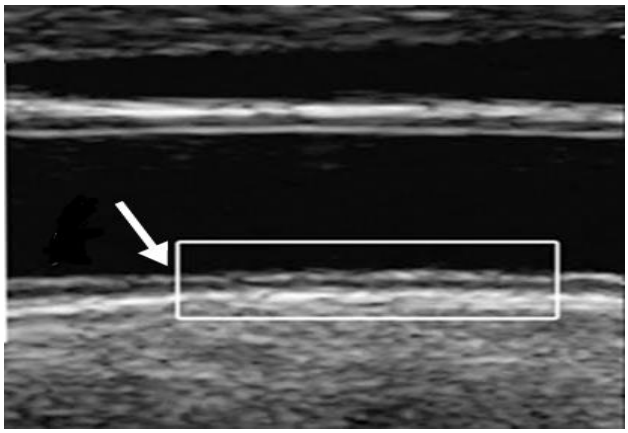

Figure 2: Psoriasis patient's - ultrasound image showing increased carotid artery intima-media thickness.

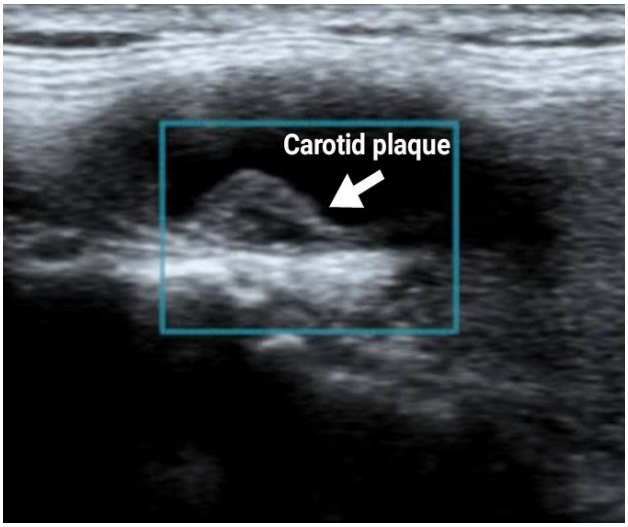

Figure 3: Psoriasis patient's - ultrasound image showing carotid plaque.

An analysis of psoriasis patients only using PASI or BSA failed to establish an association with subclinical atherosclerosis. Two patients had psoriatic arthritis and while performing analysis after the removal of these psoriatic arthritis patients, the results were unchanged. Subjects with or without psoriasis didn't differ statistically regarding alcohol consumption, diabetes and hypertension.

DISCUSSION

In this study increased prevalence of subclinical atherosclerosis was observed even at the stage of mild to moderate psoriasis. The inflammatory response in psoriasis leads to insulin resistance, oxidative stress, endothelial dysfunction and the development of atherosclerosis that culminates with acute myocardial infarction or stroke. Therefore, psoriasis may be considered an independent risk factor for cardiovascular events.[11] Atherogenesis is caused by chronic low-grade inflammation that results from an interaction between immune mechanisms and metabolic abnormalities within the vessel wall.[12,13] In the initial phase, there is up regulation of intercellular adhesion molecule-1 (ICAM-1) and T-helper-1 (Th-1) cell activity leading to an increase in cytokines which leads to the capture of leukocytes on the surface and their translocation from the blood through the endothelial layer into the intima, plaque formation and adverse outcomes like plaque rupture and thrombus formation.[14,15] This process can occur due to irritative stimuli, such as lipid abnormalities or systemic inflammation, as in psoriatic disease.[16,17]

Interleukin 17 (IL-17), a key cytokine that drives psoriasis, has been linked with reactive oxygen species formation and with endothelial dysfunction, providing a potential link between psoriatic disease and the initial phases of atherogenesis.[18] In this study, by using a Doppler ultrasonogram CIMT was measured in psoriasis patients and controls to identify the cardiovascular atherosclerotic risk. In our study, even patients with mild psoriasis and low PASI scores are at an increased risk of cardiovascular diseases with high CIMT. Wu et al demonstrated in their retrospective analysis of more than 10 thousand patients with mild psoriasis and more than 50 thousand healthy controls, with a significantly higher risk of heart attack in a group with psoriasis.[19] On the other hand, Katarzyna et al showed that even patients with mild to moderate psoriasis and low PASI values are at an increased risk of cardiovascular diseases.[20] This may confirm the hypothesis that one of the causes of the increased risk and development of premature atherosclerosis in psoriasis patients is a common inflammatory pathway of both diseases. TNF α, IFN γ, IL 6, IL 17, and IL 8 are the cytokines, that share the common inflammatory pathways of psoriasis and atherosclerosis. Th1, Th17 and T regulatory cells have a crucial role to play. Chronic smokers with psoriasis had a significant risk to develop cardiovascular disease while comparing with healthy controls ($p<0.005$). Cigarette smoke contains nicotine which may increase IL-12 production through dendritic cells.[21] In addition to that, dioxin, which results from the burning of tobacco, binds the aryl hydrocarbon receptor excreted by the Th17 and Th22 cells. This receptor can act as a transcription factor for IL-17 and IL-22. As a result, cigarette smoking could play a role in both the development of psoriasis and in the exacerbation of the disease, by increasing the production of free radicals, stimulating inflammatory pathways such as NFkB and by increasing pro-inflammatory mediators.[22,23]

Balci et al demonstrated increased CIMT in patients with psoriasis, compared to the control group. Moreover, CIMT was significantly associated with the PASI score ($r=0.5$; $p<0.01$).[24] On the other hand, Kimhi et al in their study did not show any correlation between CIMT and PASI.[25] Inconclusive findings may result from the course of the disease. Psoriasis has periods of remission and exacerbation with variable PASI score. In genetically prone individuals to develop pustular psoriasis, Immunohistochemistry of deep palmar biopsy specimens show, altered staining pattern of nicotinic receptors to acetylcholine and thus there exists a strong association between smoking, palmo-plantar pustulosis and atherosclerosis.

The evaluation of atherogenic damages caused by inflammatory diseases like psoriasis and the identification of subclinical atherosclerosis should be made by all the treating physicians and should alert the patient towards the risks of cardiovascular disease and if necessary, refer them to the specialist for follow-up and management of comorbidities. The use of Doppler ultrasonogram in Dermatology is still uncommon, but it is a non-invasive, cost-effective and widely accessible tool for the visualization of atherosclerotic changes in the vessel wall caused by the chronic inflammatory activity that occurs in some dermatological diseases, like psoriasis.

Limitations

Because of the COVID-19 pandemic, it was unable to determine the severity and progression of subclinical atherosclerosis through follow-up.

CONCLUSION

In our cross-sectional study, a higher prevalence of subclinical atherosclerosis was observed in psoriasis patients, smokers in particular, hence at high cardiovascular risk. This was in concurrence with previous studies done about systemic inflammation and cardiovascular risk in psoriasis. CIMT easily detects subclinical atherosclerosis and serves as a cost-effective, non-invasive marker in the assessment of subclinical atherosclerosis. Educating the patient about such a risk will help them to make lifestyle modifications to decrease morbidity. It is of utmost importance for the dermatologists to be aware of the systemic nature of skin diseases and insist on their primary and secondary prevention for patients.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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