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Original Research Article

Subclinical atherosclerosis and serum lipid levels in relation to ultrasonographic enthesopathy in psoriasis patients, a single-center and comparative cross-sectional study

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ABSTRACT

Background: Psoriasis is a chronic autoimmune skin disorder characterised by persistent oxidative stress and elevated serum lipid levels, which are risk factors for atherosclerosis. Carotid intima-media thickness (CIMT) is a validated measure of subclinical atherosclerosis, while chronic inflammation in psoriasis may contribute to both entheseal and vascular pathology. Hence, this study was aimed to evaluate subclinical atherosclerosis using CIMT, serum lipid levels and their correlation with ultrasonographic enthesopathy in psoriasis patients without musculoskeletal symptoms.

Methods: A single-centred, comparative cross-sectional study was conducted, including 80 psoriasis patients without musculoskeletal symptoms or comorbidities and 80 age- and sex-matched healthy controls. Demographic parameters, Psoriasis Area and Severity Index (PASI), body mass index (BMI), and serum lipid profiles (total cholesterol, LDL, HDL, VLDL, triglycerides) were assessed. Ultrasonographic CIMT and entheseal sites were evaluated using OMERACT ultrasound consensus criteria. Entheseal scores were correlated with CIMT, BMI, and lipid levels, and results were compared between groups using the standard t-test.

Results: Psoriasis patients (mean age: 41.56 years; mean disease duration: 5.85 years) showed significantly higher mean CIMT, LDL, VLDL, and total entheseal scores compared to controls ($p<0.05$). Ultrasonographic entheseal inflammation scores significantly correlated with serum triglycerides, LDL, VLDL, and CIMT, while entheseal structural scores correlated with LDL, VLDL, and CIMT ($p<0.05$).

Conclusions: Subclinical atherosclerosis, serum lipid levels, and ultrasonographic entheseal abnormalities in psoriasis patients are significantly associated, reflecting a heightened inflammatory burden that links vascular and entheseal pathologies. These findings emphasise the need for integrated cardiovascular and musculoskeletal monitoring in psoriasis management.

Keywords: Carotid intima media thickness, Cardiovascular risk, Enthesitis, Dyslipidemias, Psoriatic arthritis

INTRODUCTION

Psoriasis is a chronic, systemic autoimmune illness that affects 2-3% of the global population and 0.4 to 2.8% of the Indian population.[1] Psoriasis extends its disease from skin to systemic complications, such as psoriatic arthritis (PsA), cardiovascular (CV) disease, and metabolic diseases like diabetes mellitus, hypertension, obesity, and dyslipidemias.

The accelerated atherosclerosis in psoriasis results from endothelial cell dysfunction, dyslipidemia and the intricate interplay of immune cells, including activated Th17 and Th1 cells, macrophages, and cytokines such as IL-17, IL-1, IL-6, and TNF-α.[2] This leads to heightened CV risk, evidenced by elevated rates of myocardial infarction and a reduced life expectancy of 4-5 years.[3]

Psoriasis is complicated by PsA, which manifests as arthritis, enthesitis, dactylitis, and spondylitis in about one-third of cases. The risk factors for psoriatic arthritis in patients with psoriasis include prolonged disease duration, severe disease symptoms, nail involvement, obesity, a familial history, unexplained arthralgias, and subclinical enthesitis or synovitis.[4] Enthesitis often serves as an early inflammatory hallmark detectable in subclinical stages via imaging.[5]

Carotid intima-media thickness (CIMT) is a validated method for detecting subclinical atherosclerosis.[6] IL-17 A levels are highly expressed in atherosclerotic plaques of psoriasis patients, which is also a major cytokine responsible for entheseal inflammation.[7] Chronic inflammation in psoriasis can affect both entheseal sites and vascular inflammation, predisposing individuals to atherosclerosis and an increased CV risk. Subclinical entheseal inflammation can be assessed through ultrasonography in psoriasis patients even without musculoskeletal manifestations.[8]

In this study, we examined the relation between subclinical atherosclerosis using CIMT, serum lipid levels and ultrasonographic enthesopathy in psoriasis patients without musculoskeletal symptoms or comorbidities, compared to age- and sex-matched healthy controls.

METHODS

This is a single-centred, cross-sectional study conducted at ESIC Medical College and Superspeciality Hospital in South India, from June 2023 to December 2023, following approval by the ethics committee. A total of 160 participants, including 80 psoriasis cases and 80 healthy controls, were enrolled, and the sample size was calculated according to the study by Ben et al.[9] Patients with psoriasis, aged 18-60 years, were recruited from the dermatology department's outpatient and inpatient clinics, with diagnoses confirmed clinically by dermatologists. Patients without any musculoskeletal symptoms or comorbidities were included. All psoriasis patients completed the Psoriasis Epidemiology Screening Tool (PEST) questionnaire, and those who scored lower than three were included in the study.[10]

Age- and sex-matched controls without a personal or family history of psoriasis or inflammatory arthritis were included in the study, after obtaining written informed consent. Controls are the attendees of outpatients and inpatients visiting the Rheumatology department.

Musculoskeletal manifestations, such as arthritis, enthesitis, dactylitis, and spondylitis, as well as other inflammatory arthritis and spondyloarthritis features like Inflammatory bowel disease, uveitis, and sacroiliitis, were excluded clinically. Presence of comorbidities like diabetes mellitus, hypertension, hypothyroidism, coronary artery diseases, cardiovascular accidents, smokers, and alcoholics was excluded from both the cases and controls groups.

At baseline, all the demographic data, including age, sex, and Body mass index (BMI), were recorded. The type of psoriasis, disease duration, and psoriasis severity were assessed using Psoriasis Area Severity Index (PASI) scores. Fasting serum samples were collected from both the cases and controls to measure serum lipid levels, including total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), very-low-density lipoprotein (VLDL), and triglycerides.

Ultrasonographic assessment

A single radiologist with experience in musculoskeletal ultrasound performed sonography using a Phillips Affinity 50G machine with a 5-12 MHz linear probe, evaluating six entheseal sites (bilateral lateral elbow epicondyle, medial femoral condyle, Achilles tendon insertion) according to OMERACT US consensus criteria.[11] Inflammatory (Doppler signal, hypoechogenicity, thickening) and structural (calcification, erosions, enthesophytes) changes were scored (1 for presence, 0 for absence), yielding a maximum score of 36 per participant (80 participants × 36=2880 total scores). The total scores and the individual (6x80=480) inflammatory and structural scores were compared between the psoriasis patients and the controls.

After assessing the entheseal sites using the same ultrasound machine and linear probe, the radiologist examined the bilateral common carotid arteries with the patient lying supine, with their head directed away from the side of interest, and their neck in slight extension. The transducer was manipulated so that the walls of the carotid artery were parallel to the transducer footprint. A region of 1 cm proximal to the carotid bifurcation was identified, and the distance between the lumen-intima interface and the media-adventitia interface was used to calculate the IMT. The IMT measurement was obtained from the four contiguous sites at 1 mm intervals, and the average of these four measurements was taken for the CIMT of the corresponding carotid artery.

Statistical analysis

The chi-square test was used to analyse categorical data, and the independent Student's t-test was used to analyse the mean difference between the two groups. Microsoft Excel 2007 was used to enter the data, and SPSS version 26 trial was used for analysis. P values less than 0.05 were considered statistically significant.

RESULTS

The average age of the psoriasis cases is 41.56 years (SD=15.4), compared to 38.01 years (SD=13.5) for the controls. The male-to-female ratio is 1.28:1, with no statistical difference compared to the controls. The cases were heavier compared to the controls (mean 69.01 kg vs. 63.4 kg; p=0.01). However, for BMI, there is no statistical difference between the two groups (Table 1).

Table 1: Baseline characteristics among the cases and controls.

Baseline characteristics	Psoriasis cases (n=80)	Controls (n=80)	P value
Males (%)	45 (56.2)	43 (53.7)	0.74
Females (%)	35 (43.7)	37 (46.2)	0.74
Mean age	41.56years (SD=15.4)	38.01years (SD =13.5)	0.74
Height	165.5cms (SD = 11.9)	164.4 cms (SD = 8.2)	0.63
Weight	69.01 kgs (SD = 13.4)	63.4 kgs (SD = 13.1)	0.01
BMI	25.3 (SD=5.5)	24.2 (SD=5.1)	0.16

BMI: Body mass index

The average duration of the disease in cases was 5.85 years, with a mean PASI score of 8.91. Plaque psoriasis is predominant type of psoriasis in our cohort and constitutes 72.5% of cases (n=58), followed by guttate psoriasis (11.25%; n=9), palmo-plantar psoriasis (11.25%; n=9), pustular psoriasis (3.75%; n=3) and erythrodermic psoriasis (1.25%; n=1).

Table 2: Comparison of lipid profile among the cases and controls.

Lipid profile	Study population	Mean	Standard deviation	P value
Total cholesterol	Cases	161.3	46.9	0.47
	Controls	157.4	20.6	
Triglyceride	Cases	142.6	64.9	0.10
	Controls	126.2	65.7	
HDL	Cases	47.4	9.4	0.14
	Controls	52.2	27.3	
LDL	Cases	94.2	28.7	0.00*
	Controls	74.5	23.4	
VLDL	Cases	25.1	11.3	0.001*
	controls	20.6	7.4	

HDL: High density lipoprotein, LDL: Low density lipoprotein, VLDL: Very low density lipoprotein, *p<0.05

Patients with psoriasis had significantly higher LDL (p<0.05), VLDL (p<0.05), and CIMT (0.64 mm vs. 0.59 mm; p=0.01) compared to controls, with no differences in total cholesterol, triglycerides, or HDL (Table 2). There was no statistically significant correlation between CIMT, Lipid profile in relation to the type of psoriasis, disease duration, and PASI in patients with psoriasis (Table 3).

Table 3: Comparison of CIMT score among the cases and controls.

Variable	Study group	Mean	Standard deviation	P value
CIMT score	Cases	0.64	0.13	0.01*
CIMT score	Controls	0.59	0.12	

CIMT: Carotid intima media thickness, *p<0.05

Ultrasonographic entheseal changes were significantly higher in psoriasis patients (69/2880 scores) than controls (20/2880; p<0.001), with 16.25% of cases showing inflammatory changes (vs. 0% in controls) and 38.75% showing structural changes (vs. 15% in controls). Among inflammatory changes, the most pronounced changes were observed in thickening, followed by hypoechogenicity and Doppler signal, whereas the majority of structural changes included calcifications, followed by enthesophytes and erosions. Maximum changes were observed at the Achilles tendon insertion, followed by the lateral elbow epicondyle and the medial femoral condyle among psoriasis patients, with both inflammatory and structural changes. Among the controls, structural changes were mainly observed in the Achilles tendon insertion, followed by the Lateral elbow epicondyle. There was no statistically significant correlation observed between the type of psoriasis, disease duration, and PASI scores with entheseal involvement in psoriasis patients.

Table 4: Comparison of lipid profile, CIMT, PASI and disease duration with ultrasonographic entheseal inflammation score among the psoriasis cases.

Lipid profile	Ultrasonographic entheseal inflammation score		Pearson correlation	P value
	Mean	SD		
	0.28	0.76		
Total cholesterol	161.6	46.9	0.10	0.34
Triglycerides	142.9	64.9	0.27	0.04*
HDL	47.4	9.4	0.06	0.59
LDL	74.5	23.4	0.28	0.01*
VLDL	20.6	7.4	0.109	0.03*
CIMT score	0.91	1.17	0.10	0.15
PASI	8.9	9.8	0.05	0.60
Disease duration	5.8	5.9	0.13	0.23

Standard deviation, HDL: High density lipoprotein, LDL: Low density lipoprotein, VLDL: Very low density lipoprotein, CIMT: Carotid intima media thickness, PASI: Psoriasis Area Severity Index scores, *p<0.05

On comparing ultrasonographic entheseal scores with lipid profile and CIMT, Inflammatory entheseal scores correlated with higher triglycerides, LDL, and VLDL

(p<0.05) (Table 4), while structural scores correlated with LDL, VLDL, and CIMT (p<0.05) (Table 5).

Table 5: Comparison of lipid profile CIMT, PASI and disease duration with ultrasonographic entheseal structural score among the psoriasis cases.

Lipid profile	Ultrasonographic entheseal structural score		Pearson correlation	P value
	Mean	SD		
	0.91	1.17		
Total cholesterol	161.6	46.9	0.10	0.33
Triglyderide	142.9	64.9	0.12	0.28
HDL	47.4	9.4	-0.03	0.76
LDL	74.5	23.4	0.32	0.03*
VLDL	20.6	7.4	0.26	0.04*
CIMT score	0.91	1.17	0.22	0.05*
PASI	8.9	9.8	0.15	0.17
Disease duration	5.8	5.9	0.16	0.15

Standard deviation, HDL: High density lipoprotein, LDL: Low density lipoprotein, VLDL: Very low-density lipoprotein, CIMT: Carotid intima media thickness, PASI: Psoriasis Area Severity Index scores, *p<0.05

Compared to controls, patients with psoriasis had statistically significant higher CIMT, LDL, VLDL, and ultrasonographic entheseal scores. Triglycerides, LDL, and VLDL have a substantial correlation with ultrasonographic inflammation scores, and LDL, VLDL, and CIMT scores have a statistically significant correlation with ultrasonographic structural scores in patients with psoriasis.

DISCUSSION

In this study, psoriasis patients without comorbidities have statistically significant higher CIMT, LDL, and VLDL levels compared to healthy controls, indicating an elevated cardiovascular risk and subclinical atherosclerosis. However, CIMT showed no correlation with psoriasis type, duration, or severity, suggesting that CV risk may be inherent to the disease itself. These findings align with prior research demonstrating increased subclinical atherosclerosis in psoriasis patients, as measured by CIMT.[12-16]

Numerous studies on psoriasis have consistently reported elevated LDL levels, aligning with our findings.[17-20] A reduction in HDL levels was noted in certain studies.[18,5] Total cholesterol levels were found to be elevated in several studies, but remained within normal ranges in others.[17-20] Similarly, triglyceride levels were elevated in some studies, while they were normal in others.[18,20,5,17]

Nakhwa et al found that lower HDL levels were associated with increased psoriasis severity and prolonged disease duration (over 5 years).[21] However, our study detected no such correlation with either disease severity or duration, possibly due to the intermediate disease duration in our cohort (mean of 5.85 years).

This study had significantly elevated ultrasonographic entheseal scores, with 38.75% of psoriasis patients exhibiting entheseal changes. This finding is consistent with prior research, which reports prevalence rates of 12-62% in psoriasis patients versus 0-20% in healthy controls.[22-24] We utilised the clinical Leeds Enthesitis Index sites for ultrasonographic assessment, differing from the Madrid Sonography Enthesitis Index (MASEI) and Glasgow Ultrasound Enthesitis Scoring System (GUESS) employed by Vyas et al and Gisondi et al, respectively.[22,23] No correlation was observed between entheseal scores and psoriasis type, disease duration, nail involvement, or PASI scores, aligning with earlier findings.[22-24]

The ultrasonographic entheseal inflammation scores correlated positively with triglyceride, LDL, and VLDL levels, while structural entheseal scores correlated with mean CIMT, LDL, and VLDL, suggesting a shared pathophysiological mechanism between entheseal and vascular inflammation. This is further supported by Huong NT et al, who demonstrated elevated IL-17A and TNF-α levels in subclinical atherosclerosis, and Elsayed et al, who identified increased IL-17 levels in psoriasis patients with subclinical enthesopathy, as assessed by ultrasonographic MASEI scores.[25,26] The higher serum lipid levels and CIMT, along with the positive correlation with the ultrasonographic entheseal scores, strengthen the evidence for this interconnected mechanism.

Limitations

This study has limitations, including a relatively small sample size and a single-centre design, which may limit its generalizability across diverse populations. Measuring cytokine levels, such as IL-17 and TNF-α, could help in elucidating the immunopathological associations between entheseal and vascular inflammation. Future research targeting these cytokines may provide therapeutic strategies to mitigate the risks of atherosclerosis and enthesitis in patients with psoriasis.

CONCLUSION

Patients with psoriasis who did not exhibit any musculoskeletal symptoms or comorbidities showed higher subclinical atherosclerosis and ultrasonographic entheseal abnormalities compared to healthy controls, with a significant positive correlation between these markers. This association underscores a heightened inflammatory burden in psoriasis, linking vascular and entheseal pathologies. These findings highlight the importance of comprehensive cardiovascular and musculoskeletal monitoring in the management of psoriasis to mitigate associated risks.

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