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Original Article

Carotid artery intima-media thickness in psoriatic patients and its relation to severity and duration of the disease

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Abstract

Objective The study was conducted to find out the relation between the severity and duration of psoriasis with carotid artery intima-media thickness in psoriatic patients.

Methods This descriptive type of cross-sectional study was conducted during the period of April 2016 to August 2017. Fifty psoriatic patients were enrolled through purposive sampling. History was taken, physical examination and necessary laboratory tests were done for each of the participants. Disease severity of each and every patient was measured by Psoriasis Area Severity Index (PASI). High-resolution B-mode ultrasonography with a linear array transducer and ultrasound frequencies 5–15 MHz was used to measure CIMT. All the data were recorded using predesigned questionnaire. Continuous data were expressed as the mean ± standard deviation (SD). Pearson correlation coefficient test was used to correlate between mean carotid intima-media thickness with continuous variable.

Results The mean age of the patients was 33.0±10.5 years and 74.0% patients were male. The mean duration of disease was 44.1±54.4 months, onset of disease was at the age of 28.4±10.6 years, the PASI was 14.4±10.1 and overall 10.0% of the patients had ≥0.9 mm (abnormal) CIMT. There was significant association between mean CIMT values and duration of disease ($r= +0.587$, $p<0.001$) and also significant positive correlation between mean CIMT with age ($r= +0.460$, $p<0.001$) but insignificant positive correlation between mean CIMT and PASI score ($r = +0.045$, $p=0.756$).

Conclusion Psoriatic patients had a relationship between increasing mean carotid artery intima-media thickness and duration of disease that may predict a higher risk of cardiovascular diseases. So, all psoriatic patients should be advised to avoid traditional cardiovascular risk factors to reduce cardiovascular morbidity and mortality.

Key words
Carotid Artery Intima-Media Thickness, psoriasis, severity, duration of the disease.

Introduction

Psoriasis is a common chronic inflammatory skin disease characterized by erythematous plaques with silvery scale that affects people of all ages, and in all countries. The reported prevalence of psoriasis in countries ranges between 0.09% and 11.43%, making psoriasis a serious global problem with at least 100 million individuals affected worldwide.[1] The pathogenesis of psoriasis results from interaction among specific environmental factors and

immune mechanisms. T cells, dendritic antigen-presenting cells, and cytokine networks are recognized as playing a major role in the pathogenesis of psoriasis.[2,3] T cells and cytokines (TNF–α, IFN-ϒ, IL–17, and IL–22) play pivotal roles in the pathophysiology of psoriasis. These cytokines contribute to change that enhance and perpetuate psoriasis.[4-6] The continuous inflammation proceeds step-by-step inducing systemic inflammatory cascade. However, there has been increasing awareness of the link between psoriasis and cardiovascular risk factors like hypertension, type 2 diabetes, dyslipidemia, metabolic syndrome, and cardiovascular disease. Psoriatic patients had an increased risk of stroke, atherosclerosis, myocardial infarction (MI), coronary artery disease (CAD) and endothelial dysfunction when cardiovascular risk factors were adjusted.[7] Smoking habits, obesity, hypertension, diabetes mellitus, and dyslipidemia are contributing to the development of atherosclerosis in patients with psoriasis.[8]

Psoriasis and atherosclerosis share a common pattern of Th1 and Th17 cytokine upregulation, T–cell activation, local and systemic expression of adhesion molecules and endothelins. Activated T-cells in areas of inflammation produce type1 cytokines such as IFN–α, IL–2, and TNF–α. TNF–α is an inflammatory cytokine that is involved in the pathogenesis of both psoriasis and atherosclerosis.[9,10] Another mechanism of atherosclerosis associated with psoriasis is the production of vascular endothelial growth factor (VEGF) produced by keratinocytes, which is increased in psoriasis.[11] Atherosclerosis is a chronic, progressive, inflammatory disease with a long asymptomatic phase. Disease progression can lead eventually to the occurrence of acute cardiovascular events such as myocardial infarction, unstable angina pectoris, sudden cardiac death, and stroke.[12] In this study, we want to find out the relationship of severity and duration of psoriasis with CIMT as well as measurement of CIMT, assess the co-relation between severity of psoriasis and mean CIMT and the co-relation between duration of psoriasis and mean CIMT in psoriatic patients.

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Material and Methods

This descriptive type of cross-sectional study was conducted in the Department of Dermatology and Venereology and the Department of Vascular Surgery, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka during the period of April 2016 to August 2017.

A total of 50 patients suffering from psoriasis vulgaris were enrolled through purposive sampling. The patients who were diagnosed clinically as psoriasis by dermatologist with/ without supported by histopathology report; age less than 45 years for male and 55 years for female; who were non-hypertensive, non-diabetic; had no history of smoking and alcohol intake; no family history of heart disease at early ages; no personal history of myocardial infarction, angina pectoris, stroke or peripheral arterial disease; BMI <23 kg/m²; normal fasting blood lipid profile (total cholesterol <200 mg/dl, LDL <130 mg/dl, HDL >40 mg/dl, Triglyceride <150 mg/dl) and patients with normal renal function were included in the study. Patients with history of diseases mentioned in inclusion criteria, history of taking drugs those affect carotid artery intima-media thickness e.g. anti-hypertensives, nitrates, antiplatelet and lipid-lowering drugs and participants who were not willing to participate were excluded.

Written informed consent was obtained from each of the participants. Then we interviewed them, did physical examinations and necessary laboratory tests. Duration of disease was measured in month. Disease severity of each and every patient was measured by Psoriasis Area Severity Index (PASI). The score of PASI varies between 0 and 72. PASI score of less than or equal to 10 is classified as mild disease, whilst a score of greater than 10 was considered to be moderate to severe. High-resolution B-mode ultrasonography with a linear array transducer and ultrasound frequencies 5–15 MHz was used to measure CIMT. Carotid artery was scanned in supine position with the neck extended and head position 45–50° to right or left. Then intima-media thickness was measured within the 1cm segment proximal to its bifurcation. The measurement was repeated three times on each side of common carotid artery and the mean of each side measurement was defined as right or left CIMT. Then mean CIMT was calculated as the arithmetical mean of all six measurements of both CIMT. CIMT of 0.9 mm or more is abnormal which is a marker of subclinical atherosclerosis (asymptomatic organ damage) while >1.2 mm is indicative of atherosclerotic plaque.

The study was approved by the Ethical review committee of BSMMU, Dhaka. STROBE statement guidelines were followed.[13]

Psoriasis Area Severity Index (PASI) A PASI score is a tool used to measure the severity and extent of psoriasis. According to PASI score, the body is divided into four sections head (H) (10% of a person's skin), upper extremities (A) (20%), trunk (T) (30%), lower extremities (L) (40%). Each of these areas is scored by itself, and then the four scores are combined into the final PASI. For each section, the percent of the area involved is estimated and then transformed into a grade from 0 to 6. Grade 0: 0% of involved area, grade 1: <10% of involved area, grade 2: 10–29% of involved area, grade 3: 30–49% of involved area, grade 4: 50–69% of involved area, grade 5: 70–89% of involved area, grade 6: 90–100% of involved area. Within each area, the severity was estimated by three clinical signs: erythema (redness), induration (thickness) and desquamation (scaling). Severity parameters were measured on a scale of 0 to 4, from none to the maximum. The sum of all three severity parameters was then calculated for each section of skin, multiplied by the area score for that area and multiplied by the weight of respective section (0.1 for the head, 0.2 for upper extremities, 0.3 for trunk and 0.4 for lower extremities). The score was given as a number from 0 (not affected) to 72 (severely affected). A PASI score of less than or equal to 10 is classed as a mild disease, whilst a score of greater than 10 is considered to be moderate to severe.[14]

Carotid intima-media thickness (CIMT) CIMT is defined as a double-line pattern of the common carotid artery (CCA) in a longitudinal view, two parallel lines (leading edges of two anatomical boundaries) form it by lumen-intima and media-adventitia interfaces. High-resolution B-mode ultrasonography equipped with a linear array transducer and ultrasound frequencies 5-15 MHz (better 10 MHz) is used to measure CIMT. Carotid artery is scanned in supine position with the neck extended and head position 45°-50° to right or left. Then intima-media thickness is measured within the 1cm segment proximal to its bifurcation.[15]

Variables of interest Age (year), Height (meter), Weight (kg), BMI (kg/m²), age of onset of disease (year), duration of disease (month), Psoriasis Area Severity Index (PASI) (score), fasting blood sugar (FBS) level (mmol/l), fasting total cholesterol (FTC) level (mg/dl), fasting triglyceride (FTG) level (mg/dl), fasting low-density lipoprotein (FLDL) level (mg/dl), fasting

Table 1 Distribution of the study participants.

	Frequency (%)	*Mean ± SD*
Age group (in years)		
<10	2 (4.0%)	
11-20	4 (8.0%)	
21-30	14 (28.0%)	33.0 ± 10.5
31-40	16 (32.0%)	
41-50	12 (24.0%)	
51-60	2 (4.0%)	
Sex		
Male	37 (74.0%)	
Female	13 (26.0%)	
Duration of disease (months)		
6-11	18 (36.0%)	
12-24	12 (24.0%)	
25-36	6 (12.0%)	44.1 ± 54.4
49-60	5 (10.0%)	
> 60	9 (18.0%)	
PASI (Psoriasis Area Severity Index) score		14.4 ± 10.1
Mild	18 (36.0%)	
Moderate to severe	32 (64.0%)	
CIMT (mm) value in right or left carotid artery		
<0.9 mm (normal)	45 (90.0%)	
≥0.9 mm (abnormal)	5 (10.0%)	
Presence of plaque (>1.2 mm) in right or left carotid artery		
Yes	2 (4.0%)	
No	48 (96.0%)	
Systolic Blood Pressure(mmHg)		117.3±9.8
Diastolic Blood Pressure (mmHg)		75.6±7.3
Fasting Blood Sugar (mmol/l)		4.9±0.61
Body mass index (BMI) (kg/m^2)		21.7±1.2
Total Cholesterol (mg/dl)		162.1±27.8
Triglycerides (mg/dl)		108.0±31.7
HDL (mg/dl)		48.7±7.1
LDL (mg/dl)		107.9±20.6
Right CIMT (mm)		0.59±0.31
Left CIMT (mm)		0.55±0.18
Mean CIMT (mm)		0.59±0.24

high-density lipoprotein (FHDL) level (mg/dl), right carotid artery intima-media thickness (CIMT) (mm), left carotid artery intima-media thickness (mm), mean carotid artery intima-media thickness (mm).

Data analysis Statistical analysis was carried out by using the Statistical Package for the Social Sciences (SPSS) software version 23.0 for windows (SPSS Inc., Chicago, Illinois, USA). Continuous data were expressed as the mean±standard deviation (SD) and categorical variables were expressed as percentages. Pearson correlation coefficient test was used to correlate between mean carotid intima-media thickness with a continuous variable. Multivariate regression analysis was done to identify the factors associated with mean CIMT. For all statistical tests, the p-value is < 0.05 was considered as statistically significant.

Results

A total 50 patients were examined and among them the mean age of the patients was 33.0±10.5 years and 74.0% patients were male. The mean duration of disease was 44.1±54.4 months, onset of disease onset was 28.4±10.6 years, the PASI was 14.4±10.1 and overall, 10.0% patients had ≥0.9mm (abnormal) CIMT where 2 (4.0%) patients had more than Mean CIMT 1.2 mm **(Table 1)**. Moreover, the mean SBP (mmHg) was 117.3±9.8, DBP (mmHg) 75.6±7.3, FBS (mmol/l) 4.9±0.61, BMI 21.7±1.2, FTC (mg/dl) 162.1±27.8, FTG (mg/dl) 108.0±31.7, HDL (mg/dl) 48.7±7.1, LDL (mg/dl) 107.9±20.6, Right CIMT (mm) 0.59±0.31, Left CIMT (mm) 0.55±0.18 and mean CIMT (mm) was 0.59±0.24 **(Table 1)**.

Moreover, Pearson's correlation coefficient (r) test was performed to compare the relationship between mean CIMT (mm) with atherogenic parameters and to compare the relationship between mean CIMT (mm) with the duration of disease (months) and PASI. The accepted level of significance considered $P<0.05$.

We found a significant positive correlation between mean CIMT with age, SBP, DBP and FBS where Correlation–Coefficient or 'r' was +0.04 ($P<0.001$) for age, +0.41 ($P=0.003$) for SBP, +0.34 ($P=0.014$) for DBP and +0.38 ($P=0.006$) was for FBS. There was no

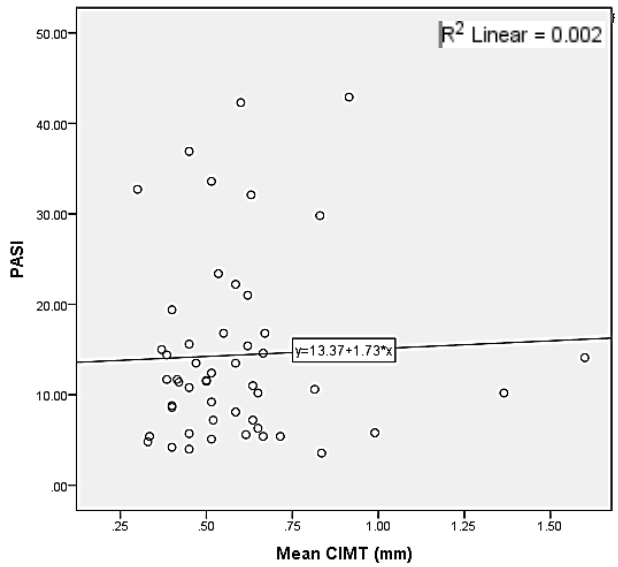

Figure 1 Scatter diagram showing no correlation with mean CIMT (mm) and PASI score.

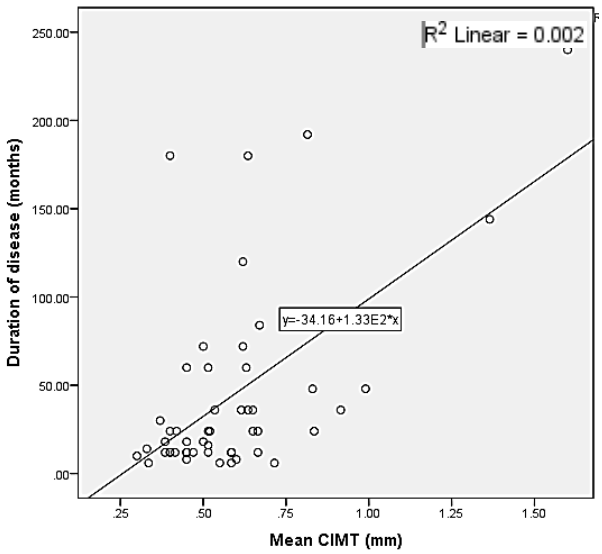

Figure 2 Scatter diagram showing the correlation with mean CIMT (mm) and duration of disease (months).

Table 2 Correlation between the mean CIMT with duration of disease (months), psoriasis area severity index (PASI) and atherogenic parameters (n=50).

Mean CIMT	*Pearson's correlation*	
Parameters	*r*	*P**
Age (years)	+ 0.460	0.001*
Systolic Blood Pressure (mmHg)	+ 0.415	0.003*
Diastolic Blood Pressure (mmHg)	+ 0.344	0.014*
Fasting Blood Sugar (mmol/l)	+ 0.385	0.006*
Body mass index (BMI) (kg/m^2)	+0.036	0.806
Total Cholesterol (mg/dl)	+ 0.220	0.124
Triglycerides (mg/dl)	+ 0.078	0.592
HDL (mg/dl)	- 0.084	0.561
LDL (mg/dl)	+ 0.246	0.085
Age of onset of disease (years)	+0.207	0.149
Duration of disease	+ 0.587	<0.001*
PASI	+ 0.045	0.756

correlation between mean CIMT with BMI (r=0.036, *P*=0.806), FTC (r=0.22,*P*=0.124), FTG (r=0.07,*P*=0.592), LDL (r=0.24,*P*=0.085), age of onset of disease (r=0.20,*P*=0.149) and for HDL (r=–0.08,*P*=0.561) **(Table 2)**. The level of significance was *P*<0.05.

However, there was no correlation between mean CIMT (mm) and PASI score **(Figure 1)** but significant positive correlation with duration of disease (months) where Correlation-Coefficient or 'r' was +0.045 (*P*=0.756) for PASI score and duration of disease was +0.587 (*P*<0.001) **(Table 2)**. This means there was a strong positive correlation between mean CIMT (mm) with the duration of disease (months) **(Figure 2)** and it's statistically significant. The duration of disease was significantly associated with mean CIMT (*P*=0.001), while patients age (*P*=0.078), FBS (*P*=0.075), SBP (*P*=0.376) and DBP (*P*=0.858) were not **(Table 3)**. The standardized coefficients (β) were 0.434 for duration of disease (months), 0.233 for age

Table 3: Summary of multiple linear regression analysis to identify the factors associated with the mean carotid intima-media thickness (mm).

Variables	*Unstandardized Coefficients*		*Standardized Coefficients*	
	B	*Std. Error*	*Beta*	*P **
Age (Years)	0.005	0.003	0.233	0.078
Duration of disease (months)	0.002	0.001	0.434	0.001*
Fasting Plasma Sugar (mmol/dl)	0.081	0.045	0.209	0.075
Systolic Blood Pressure (mmHg)	0.003	0.004	0.140	0.376
Diastolic Blood Pressure (mmHg)	-0.001	0.005	-0.027	0.858

(years), 0.209 for FBS (mmol/L), 0.140 for SBP (mmHg) and –0.027 for DBP (mmHg).

Discussion

This cross-sectional study is carried out to measure the CIMT in psoriatic patients who do not have any association with known cardiovascular diseases or any important cardiovascular risk factors and find out its relationship along with severity and duration of the disease.

Out of 50 patients, the male is predominant (74%) and in a similar study Shahidi-Daras M *et al*. reported 55% patients were men.[16] In that study, mean CIMT of psoriatic patients was significantly correlated with both PASI score and disease duration where Correlation-Coefficient or 'r' value was +0.98 (*P*<0.001) for PASI and +0.46 (*P*<0.001) for duration of disease. In our study, mean CIMT of psoriatic patients is significantly correlated with disease duration but there is no significant correlation between mean CIMT and PASI where Correlation-Coefficient or 'r' is +0.587 (*P*<0.001) for duration of disease and +0.045 (*P*=0.756) for PASI **(Table 2)**. The mean duration of the disease is 44.1±54.4 months and PASI Score of psoriatic patients with a mean of 14.4±10 and 64.0% patients have moderate to severe PASI. Enany BEl *et al*. in a study reported that an increased mean CIMT had the positive correlation with psoriasis severity (r=0.78, *P*<0.001) and disease duration (r=0.33, *P*<0.05).[17] They also found that the duration of disease with a mean 78±35.4 months and PASI score of psoriatic patients with a mean of 20.99±16.67.

A positive correlation was found between CIMT in psoriatic patients and their ages at the time of the study (r=0.46, *P*<0.001) and with the duration of disease (r=0.58, *P*<0.001) but no correlation is found between mean CIMT and PASI **(Table 2)**. S El-Mongy *et al*. in a study also found a positive correlation between CIMT in psoriatic patients and their ages at the time of the study (r=0.60, *P*<0.001), duration of the disease (r=0.40, *P*<0.001) and PASI score (r=0.50, *P*<0.001).[18] Another study reported presence of atherosclerosis in psoriatic patients associated with PASI score (*P*=0.001) and duration of disease (*P*=0.0001).[19]

In our study, we found the correlation between mean CIMT and atherogenic parameters after excluding patients with traditional cardiovascular risk factors. We found a significant correlation between mean CIMT with age (*P*=0.001), SBP (*P*=0.003), DBP (*P*=0.014) and FBS (*P*=0.006) but there was no correlation between mean CIMT with FTC (*P*=0.124), FTG (*P*=0.592), LDL (*P*=0.085), age of onset of disease (*P*=0.149) and HDL (*P*=0.561) **(Table 2)**. A study reported that the greater CIMT values were significantly associated with age of patient, age of onset of disease (*P*<0.001), SBP, DBP (*P*<0.05), but there was no correlation found between CIMT and disease duration, severity of the disease in the patients of psoriasis.[20]

In our study, we observed that among all the independent variables, duration of the disease was significantly associated with mean CIMT (*P*=0.001) and the standardized coefficient (β) is 0.434 for the duration of disease (months) **(Table 3)**. A study reported the opposite scenario in their study. They found PASI and age were significantly associated with the mean CIMT (*P*<0.001) but the duration of disease did not have any significant association with mean CIMT (*P*=0.070).[16] The standardized coefficients (β) were 0.623 for PASI, 0.273 for age and 0.122 for the duration of disease.

The main limitation of our single-center study is

the relatively small sample size. The disease severity is mild to moderate in most patients; therefore, the disease subgroups are too small to allow statistical evaluation. Moreover, Dietary habits and the level of physical activity may modify the prevalence of cardiovascular disease risk factors in patients with psoriasis, but these factors are not assessed in the present study.

Conclusion

Psoriasis is a chronic inflammatory disease that contributes to the development of atherosclerosis. Atherosclerosis may lead eventually to the occurrence of cardiovascular events. Subclinical atherosclerosis remains undiagnosed in patients of psoriasis who usually lack the established risk factors for cardiovascular disease. This study showed a significant positive correlation between mean CIMT and duration of disease of psoriatic patients, but no correlation between mean CIMT and PASI. Psoriatic patients had a relationship between increasing mean carotid artery intima-media thickness and duration of disease that may predict a higher risk of cardiovascular diseases. So, all psoriatic patients should be advised to avoid traditional cardiovascular risk factors to reduce cardiovascular morbidity and mortality.

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