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Medicine

Study of Carotid Intima Media Thickness in Relation with Severity and Duration of Rheumatoid Arthritis

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Abstract **Original Research Article**

Background: Increased cardiovascular morbidity and mortality has been observed in rheumatoid arthritis (RA) because of accelerated atherosclerosis. We measured carotid intima-media thickness (CIMT) as a surrogate marker of subclinical atherosclerosis in RA in this study. We aim to study the relationship between carotid intima media thickness and the severity and duration of rheumatoid arthritis. ***Methodology:*** Carotid intima media thickness (CIMT) was measured in 45 patients of RA divided into three groups based on duration of disease ,less than two years, two to five years, and more than five years). Both common carotid intima media thickness (CCIMT) and total carotid intima media thickness (TCIMT) i.e., mean of values of CCA, ICA, and ECA) measured and values DAS-28 activity score was calculated. ***Results:*** In RA patient Both CCIMT and TCIMT increased significantly with duration of disease but not with severity of disease which was calculated by DAS-28 score. ***Conclusion:*** In view of relation to duration of disease, the physicians should regularly screen the established RA patients, so as to identify the evidence of atherosclerosis and manage it earlier.
Keywords: cardiovascular, CIMT, CCIMT, RA

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory disorder involving the joints (non suppurative proliferative synovitis) along with other organ involvement including blood vessels and heart [1]. Cardiovascular mortality has been found to be increased in rheumatic diseases, which is attributed to accelerated atherosclerosis [2]. Dyslipidaemia has been attributed to cause accelerated atherosclerosis in RA. Single photon emission computed tomography (SPECT) studies have confirmed that myocardial perfusion abnormalities occur earlier in patients with RA [3]. Carotid intima media thickness (CIMT) which is indirect evidence of accelerated atherosclerosis in RA, is a simple, reliable, inexpensive, non-invasive marker that is increasingly being used to detect subclinical atherosclerosis and has been recommended by the American Heart Association (AHA), American Society of Echocardiography (ASE) and Society for vascular Medicine (SVM) as a screening test for heart disease in apparently healthy individuals [4]. Carotid ultrasonography allows the identification of CIMT and presence of plaques [5]. The importance of abnormally high CIMT and plaques as predictors of cardiovascular events in patients with RA has been emphasized [6].

Due to paucity of Indian data regarding atherosclerosis in RA, this study was designed to assess subclinical atherosclerosis in RA patient using CIMT as a surrogate marker of atherosclerosis and relationship between carotid intima media thickness and the severity and duration of rheumatoid arthritis

Aim and objectives

AIM: To study the relationship between carotid intima media thickness and the severity and duration of rheumatoid arthritis

Objectives

- To study the correlation between carotid intima media thickness and severity of rheumatoid arthritis.
- To study the correlation between carotid intima media thickness and duration of rheumatoid arthritis.

MATERIALS AND METHODS

This study was conducted on total of 45 pre-diagnosed or newly diagnosed cases of Rheumatoid Arthritis (based on ACR/EULAR 2010 criteria)[7].Written well-informed consents were obtained from all participants after approval from ethical committee.

Exclusion criteria are cases of chronic diseases, Dyslipidemia (patient on lipid lowering drugs, familial form of hypertriglyceridemia, pancreatitis metabolic disorder, pregnancy, OCP's and steroid therapy, H/O renal pathology),Obesity(BMI >30kg/m^2), Alcoholism and Patient age <18 yrs & >65 yrs.

45 cases divided in three groups (on basis of disease duration)
Group I – duration less than two years.
Group II – duration between two to five years.
Group III - duration more than five years.

All subjects included in study were evaluated for their disease activity score using DAS-28 score

DAS 28 = 0.56√TJC + 0.28√SJC + 0.70 (log ESR) + 0.014 GH where,

TJC is tender joint count
SJC is swollen joint count
GH is general health status as assessed by patient on visual analog scale (VAS).

Laboratory Evaluation

All routine investigations, lipid profile, ESR and rheumatoid factor were done.

CIMT Measurement

Bilateral assessment of the common carotid artery (CCA) wall thickness was made with duplex B ultrasound machines. 2 cm proximal to the carotid bulb, the distance between two echogenic lines was measured as carotid intima media thickness [8]. Average of CIMT of right and left common carotid arteries was used.

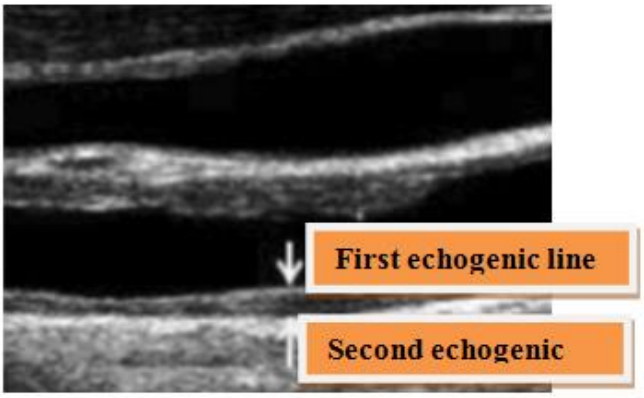

Fig-1: Ultra sonographic Image of a patient showing carotid intima media thickness

RESULTS

Table-1: Demographic profile

Study groups	Mean age (years)	Gender		Disease duration (years)
		Male	Female	
< 2 years	42.41	1	7	1.12
2-5 years	46.31	4	20	3.12
>5 years	50.21	5	8	7.21
Total	46.48	10	35	3.86

- Comparison of CIMT obtained in study group and CIMT calculated by Homa *et al.* formula- According to Homa *et al*, the intima media thickness of common carotid artery (measured at areas devoid of plaque) increases linearly with age from 0.48 mm at 40 years of age to 1.02 mm at 100 years of age (following a formula 0.009 x age + 0.116 mm)[9].

- The mean age of our study population was 46.48 years. So expected common carotid thickness was approximately 0.527 mm. In the present study, common carotid intima media thickness (CCIMT) in RA was higher, i.e., 0.889 ± 0.22 mm.
- Relationship of DAS 28score amongst disease duration groups. On applying ANOVA test there was no significant relation of DAS 28 score with the duration of disease (F=0.602, p=0.552).
- Correlation of DAS 28 score with TCIMT: On applying Pearson's correlation test, there is no statistically significant correlation between DAS 28 score and TCIMT. (p= 0.063)
- Distribution of plaque positive and plaque negative patient in study groups: We found total 4 cases are plaque positive in 45 subjects. In which 3 case (75%) in more than 5yrs disease duration and 1 case (25%) in 2-5 yrs disease duration.

Table-2: Comparison of mean TCIMT with disease duration

Age groups	N	Mean TCIMT	SD	ANOVA test	
				F	P Value
Less than 2 years	8	0.69	0.15		
2 to 5 years	24	0.81	0.18	9.447	0.000*
More than 5 years	13	1.03	0.19		
Total	45	0.85	0.21		

Table-3: Comparison of TCIMT amongst the groups by Tukey Post Hoc Tests

	RA Age Group	RA Age Groups	p value
Mean TCIMT	Less than 2 years	2 to 5 years	0.259
		More than 5 years	0.001*
	2 to 5 years	Less than 2 years	0.259
		More than 5 years	0.004*

Table-4: Correlation between Duration of disease and various variables of RA cases

Association of various variables with	Duration of RA (p-value)	DAS28 score (p-value)	TCIMT (p-value)
HDL	0.029*	0.09	0.169
LDL	0.031*	0.07	0.259
Triglycerides	0.002*	0.25	0.003*
Total Cholesterol	0.001*	0.084	0.139
FBS	0.284	0.361	0.341
PPBS	0.385	0.83	0.220
ESR	0.894	0.041*	0.974

*significant (p<0.05)

Karl Pearson correlation test applied

Table-5: Relation between duration of disease and lipid profile

Total cholesterol [mg/dl]	Less than 2 years	2 to 5 years	.965
		More than 5 years	.024
	2 to 5 years	Less than 2 years	.965
		More than 5 years	.006
Triglcerides [mg/dl]	Less than 2 years	2 to 5 years	.689
		More than 5 years	.037
	2 to 5 years	Less than 2 years	.689
		More than 5 years	.059
LDL [mg/dl]	Less than 2 years	2 to 5 years	.904
		More than 5 years	.192
	2 to 5 years	Less than 2 years	.904
		More than 5 years	.020
HDL [mg/dl]	Less than 2 years	2 to 5 years	.957
		More than 5 years	.262
	2 to 5 years	Less than 2 years	.957
		More than 5 years	.053

A Tukey post hoc test revealed that TCIMT is not statistically significantly more in 2 to 5 years duration (p=0.259) than <2 years duration, but TCIMT is statistically significantly more in >5 years of duration (p=0.001) of disease than <2 years duration.

There is also statistically significant difference between 2 to 5 years of disease duration and >5 years of disease duration (p=0.004)

DISCUSSION

Rheumatoid arthritis, a chronic inflammatory disease mainly involving joints has been found to have accelerated atherosclerosis.

Carotid IMT is a measurable index of subclinical atherosclerosis by Doppler ultrasound as a simple reading technique and a noninvasive screening test for early subclinical detection and management of atherosclerosis in rheumatoid arthritis patients. RA and atherosclerosis are associated with elevated levels of acute phase reactants- CRP, serum amyloid A, ESR, fibrinogen, and secondary phospholipase.

Since RA predominantly affects women, and is also an independent risk factor, a search for asymptomatic atherosclerosis especially among women with RA using CIMT will be fruitful.

In our study, CIMT was found higher than expected for age in RA patients. A similar observation has also been shown by Gonzalez *et al*. [10] and Alkabbi *et al*. [11] in their respective studies. In recent Indian studies, Balaraju G [12], Saigal R *et al*. [13] and Singh H *et al*. [14] have similar observations.

The mean Total CIMT increases as the disease duration increases, but the increase is more significant in patients with disease duration more than 5 years. Del Rincon *et al.* [15] also had similar observations. This may be due to more years of exposure to increased inflammation, and other factors like increased arterial stiffness and prothrombotic marker in RA patients.

DAS 28 score and duration of disease had no significant relationship in our study which is similar to study done by Balraju *et al.* [12] and Singh H *et al*. [14] as disease activity depends on acute inflammatory markers and not on duration of disease.

No significant correlation of CIMT and ESR or DAS 28 was found in our study. It might be due to the fact that DAS28 and ESR levels often fluctuate in chronic inflammatory diseases and their measurement at a single point only can show the inflammatory burden at that point of time and fails to reveal the inflammatory burden of the entire disease duration.

Lipid metabolism is a complex process, especially when associated with chronic inflammatory states; therefore in many autoimmune diseases lipid abnormalities are frequently seen. The involvement of common pro-inflammatory cytokines, such as interleukin-1 and 6 & tumor necrosis factor-alpha (TNF-α), play a role in the development and progression of both RA and atherosclerosis.

In our study on applying Pearson coefficient test, we found that the duration of disease showed a positive correlation with Total cholesterol, LDL and triglycerides, which was statistically significant, but on applying Tukey Post Hoc test for relationship of lipids within the individual group it was found that when the duration of disease was less than 2years and in between 2-5yrs there was no significant rise in the levels of lipids. However, when the duration of disease was more than 5yrs there was significant rise in the level of lipids.

In the study done by Athanasios N Georgiadis *et al*. [16], RA patients exhibited higher serum levels of total cholesterol, LDL and triglycerides, whereas their HDL levels were significantly lower compared to controls. As a consequence, the atherogenic ratio of TC/HDL as well as that of LDL/HDL was significantly higher in early RA patients compared to controls. Other study done by Rizzo *et al*. [17] showed higher triglycerides and lower levels of HDL when compared with controls.

In our study, we also found even though there was a significant rise in the level of lipids and TCIMT when the duration of disease was more than 5yrs, however, there was no relationship between lipids and TCIMT. They rise independently in the patients of RA and do not affect levels of each other.

In our study, the incidence of carotid plaque increases as the duration of RA increases. More plaque positive RA cases were found in more than 5 years disease duration group compared to the other two duration groups.

SUMMARY

This observational study was performed on RA patients had study population in fifth decade of age and showing female preponderance for rheumatoid arthritis.

The mean CIMT increases as duration of Rheumatoid arthritis increases and this increase is more significant after 5 years of disease duration.

In our study, lipid levels were statistically significant when the duration of disease was more than 5years suggesting Lipids increase with the duration of the disease.

There was no correlation of disease activity with duration of disease and with CCIMT. The incidence of carotid plaque was more in more than 5 years disease duration group compared to the other two duration groups.

CONCLUSION

Rheumatoid arthritis, a chronic inflammatory disease mainly involving joints has been found to have accelerated atherosclerosis. The aim of our study is to study the relationship between Carotid intima media thickness which is a surrogate marker of atherosclerosis and the severity and duration of Rheumatoid Arthritis. Shared immunological disease mechanisms in systemic autoimmune disorders and coronary vascular disease such as clonally expanded CD4+ and CD28 T-cells, systemic endothelial activation and circulating immune complex, may be involved in the development of cardiovascular comorbidities in RA patients.

In RA patients, CIMT values were found higher and it increases with duration of disease and hence increases the risks of Myocardial Infarction and Cerebrovascular accidents.

CIMT and lipid levels increase with increase in duration of RA and not with severity of RA. Hence, regular screening for CIMT and monitoring of lipids required in patients of RA with increasing disease duration.

We highly recommend measuring CIMT by Doppler USG, being a non-invasive and cost effective screening test which can be used for early detection and earlier management of atherosclerosis in RA patients. Our findings emphasize the need to raise awareness among healthcare professionals regarding the development of hyperlipidemia in RA patients. Statins should be started in patients with disease duration more than 5 years

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