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Original Research Article

Carotid intima medial thickness as a marker of atherosclerosis in ankylosing spondylitis

Sarvagya Mishra[1], Abhishek Singhai[2]*, Prakash Joshi[1], Rajesh Kumar Jha[1]

[1]Department of Medicine, Sri Aurobindo Medical College and PGI, Indore, Madhya Pradesh, India
[2]Department of Medicine, All India Institute of Medical Sciences, Bhopal, Madhya Pradesh, India

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***Correspondence:**
Dr. Abhishek Singhai,
E-mail: drabhisheksinghai@gmail.com

ABSTRACT

Background: Ankylosing Spondylitis (AS) is an inflammatory disorder of unknown cause that primarily affects the axial skeleton; peripheral joints and extraarticular structures are also frequently involved. The present study was planned to generate more data on this subject with the aim of measuring the CIMT in AS, as these patients are more prone to develop early atherosclerosis and develop early macro vascular complications like CAD.
Methods: It was a cross-sectional study with a sample size of 60 patients. The study group included 30 patients with a known history or clinical features suggestive of AS. The control group included 30 normal adult subjects without any previous history. All subjects included in the study underwent detailed clinical history, analysis, physical examination and necessary investigations.
Results: CIMT in the control group was 0.54±0.19 mm and in the AS group was 0.65±0.21 mm. The difference was found to be statistically significant (P<0.05), showing a higher CIMT in the AS group in comparison to the control group. The mean age in the control group was 30.43±6.14 years and in the AS group was 29.3±10.1 years. The difference was found to be statistically not significant (p>0.05), showing comparable age between the two groups. The age to CIMT showed positive correlation which was statistically significant (r=0.405, p=0.026).
Conclusions: Results of this study showed that there is a higher prevalence of subclinical atherosclerosis (20%) in AS patients as compared to controls as evidenced by a higher CIMT. Every effort should be made in order to control inflammation and traditional risk factors in this population, to avoid the consequences of accelerated atherogenesis.

Keywords: Ankylosing spondylitis, Atherosclerosis, Cholesterol

INTRODUCTION

Ankylosing Spondylitis (AS) is an inflammatory disorder of unknown cause that primarily affects the axial skeleton; peripheral joints and extraarticular structures are also frequently involved. The disease usually begins in the second or third decade; male to female prevalence is between 2:1 and 3:1. The pathogenesis of AS is thought to be immune-mediated, but there is no direct evidence for autoimmunity. There is uncertainty regarding the primary site of disease initiation. A unifying concept is that the AS disease process begins at sites where articular cartilage, ligaments, and other structures attach to bone. The dramatic response of the disease to therapeutic blockade of tumor necrosis factor α indicates that this cytokine plays a central role in the immunopathogenesis of AS. The symptoms of the disease are usually first noticed in late adolescence or early adulthood; the median age in Western countries is 23. In 5% of patients, symptoms begin after age 40. The initial symptom is usually dull pain, insidious in onset, felt deep in the lower lumbar or gluteal region, accompanied by

low-back morning stiffness of up to a few hours' duration that improves with activity and returns following inactivity. The standardized mortality rates associated with AS are approximately 50% higher than in the general population.[1,2] Increased mortality is predominantly attributable to cardiovascular diseases (CV).[2] There is increased risk of ischemic heart disease (prevalence ratio 1.2), peripheral vascular disease (odds ratio 1.6), atherosclerosis (odds ratio 1.5), congestive heart failure (odds ratio 1.8) and more cardiovascular risk factors (prevalence ratios between 1.3 and 1.7) in AS patients compared to healthy controls.[3]

Imaging of peripheral arteries like carotid artery is a means of increasing predictive ability for coronary artery disease (CAD) beyond that of traditional risk factor models. B-mode ultrasound of the extracranial carotid arteries is a novel, valid and repeatable non-invasive method for quantifying the extent of atherosclerosis.[4-6] Ultrasound imaging of carotid vessels provides information on Carotid Intima Medial Thickness (CIMT), plaque presence and type, calcification, wall diameter. This procedure is used to examine pre-symptomatic lesions, assess atherosclerotic burden and assess the risk of cardiovascular events. This can potentially lead to early interventions.[7] CIMT is independently associated with CAD in Indian subjects.[8] There are very few Indian studies where CIMT has been measured in patients with AS. Therefore, the present study was planned to generate more data on this subject with the aim of measuring the CIMT in AS, as these patients are more prone to develop early atherosclerosis and develop early macro vascular complications like CAD.

METHODS

It was a cross-sectional study with a sample size of 60 patients. The study group included 30 patients with a known history or clinical features suggestive of AS. The control group included 30 normal adult subjects without any previous history. The AS study group and the control group subjects were selected from the patients presenting to the outpatient department of a tertiary care centre between September 2015 and February 2017.

Inclusion criteria

Patients fulfilling the assessment of spondyloarthritis international society criteria for diagnosis of ankylosing spondylitis.

Exclusion criteria

We excluded subjects who have been already diagnosed with diabetes mellitus, hypertension, hyperlipidemia, coronary artery disease, hypothyroidism, liver disorders, renal disease, known inherited disorders of lipids, secondary dyslipidemia due to pregnancy or drugs like beta-blockers, thiazides, steroids, hypolipidemic drugs, oral contraceptives, and anticoagulants.

Study protocol

All subjects included in the study underwent detailed clinical history, analysis, physical examination and necessary investigations. The study was approved by ethical committee and an informed written consent was obtained from every patient. After an overnight fasting of at least 8 hours venous blood sample was obtained for the measurement of serum concentrations of total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), Very low-density lipoprotein (VLDL), triglycerides and erythrocyte sedimentation rate (ESR). ESR was done using Wintrobe's method.

Bilateral assessment of the common carotid artery (CCA) wall thickness was made with duplex B ultrasound machines namely IU 22 and Vivid E9. CIMT was measured 2cm proximal to the carotid bulb as the distance from the leading edge of the first echogenic line to that of the second echogenic line. The first line represented the lumen-intima interface, and the second line, the collagen-containing upper layer of tunica adventitia. Average of CIMT of right and left common carotid arteries was used. Though there are no normal values of CIMT as such but according to some studies the upper limit of normal for the mean carotid intima-media thickness ranged from 0.59-0.95mm in men and from 0.52-0.93mm in women.[9] According to some other studies CIMT >1.0mm is considered abnormal, and >1.2mm as being high risk.[10]

Statistical analysis

The initial data was captured in the customized performa designed for the study. This data was entered into the Microsoft excel sheet and then online statistical software was used for analysis. Correlation was structured using Pearson's coefficient of correlation. The mean comparison between the two groups was done using unpaired t test.

RESULTS

The present observational study was carried out in Department of General Medicine of a tertiary care centre. 30 AS patients and 30 healthy controls matched for age, sex and smoking status were studied. In the control group there were 28 (93.3%) males and 2 (6.7%) females. In the ankylosing spondylitis group, there were 28 (93.3%) males and 2 (6.7%) females. There was a male preponderance in both the groups. The mean age of the AS patients was 29 years and 93% of them were males, consistent with the usual pattern of the disease.

Comparison of AS cases and controls

The age, sex and smoking status of the cases and controls were comparable (Table 1). The mean ESR in the control group was 12.33±5.19mm and in the AS group was 18.30±12.20mm. AS patients had significantly higher

ESR (p<0.017) consistent with the chronic underlying inflammatory process. In the study group, ESR was negatively correlated with CIMT with p value of 0.609 being non significant. The mean cholesterol in the control group was 146.4±29.7mg/dl and in the AS group was 153.6±38.9mg/dl. The difference was found to be statistically not significant (P>0.05), showing a comparable cholesterol level in both the groups. The mean triglycerides in the control group was 113.0±66.0mg/dl and in the AS group was 125.5±63.0mg/dl. The difference was found to be statistically not significant (P>0.05), showing a comparable triglycerides level in both the groups. The mean HDL in the control group was 45.3±10.3 mg/dl and in the AS group was 41.3±11.0mg/dl. The difference was found to be statistically not significant (P>0.05), showing a comparable HDL level in the two groups. The mean LDL in the control group was 94.9±26.1mg/dl and in the AS group was 98.9±44.3mg/dl. The difference was found to be statistically not significant (P>0.05), showing a comparable LDL level in the two groups. In our study, CIMT showed a positive correlation with cholesterol which was statistically significant (r=0.472, p=0.009). In our study, CIMT showed a positive correlation with LDL which was statistically significant (r=0.571, p=0.001). In our study, CIMT showed a negative correlation with HDL which was statistically significant (r=-0.474, p=0.008). In our study, CIMT showed a positive correlation with triglycerides which was statistically significant (r=0.569, p=0.001). CIMT in the control group was 0.54±0.19 mm and in the AS group was 0.65±0.21 mm. The difference was found to be statistically significant (P<0.05), showing a higher CIMT in the AS group in comparison to the control group. The mean age in the control group was 30.43±6.14 years and in the AS group was 29.3±10.1 years. The difference was found to be statistically not significant (p>0.05), showing comparable age between the two groups. The age to CIMT showed positive correlation which was statistically significant (r=0.405, p=0.026).

Table 1: Comparison of as cases and controls.

	AS cases (N=30)	Controls (N=30)	P value
Mean age	29.3±10.1	30.4±6.1	0.602
Males N, (%)	28 (93)	28 (93)	
ESR (MM/HR)	18.3±12.2	12.3±5.1	0.017
CIMT (mean in MM)	0.65±0.21	0.54±0.19	0.037
Total cholesterol	153.6±38.9	146.4±29.7	0.424
Triglycerides	125±63	113±66	0.456
LDL	98.3±44.3	94.9±26.1	0.669
HDL	41.3±11	45.3±10.3	0.156

DISCUSSION

Ankylosing spondylitis is a chronic inflammatory arthropathy which has been recently associated with atherosclerosis. When this already enhanced risk of atherosclerosis is added to the risk of chronic inflammatory state in AS the prevalence of atherosclerosis in them could rise further.

In our study, we included 60 subjects, out of which 30 cases were the patients with a known history or clinical features suggestive of AS. In our study, there was a statistically significant difference in the mean CIMT value between the study (0.65±0.21) and the control group (0.54±0.19), with a positive p value of 0.037. The result of our study was comparable with the studies that have been mentioned below. Sharma SK et al, in their study took 37 AS patients and 37 controls.[11] Mean age of the study groups was 29.43±9.00 years. A significantly increased CIMT was observed in cases as compared to control group (0.62±0.12 versus 0.54±0.04; <0.001). Skare TL et al, compared CIMT (measured using Doppler ultrasonography) of 36 SpA patients with controls. The mean CIMT in SpA patients was 0.72±0.21mm; in controls, 0.57±0.13mm (P = 0.0007).[12]

In our study, the mean cholesterol in the control group was 146.4±29.7mg/dl and in the ankylosing spondylitis group was 153.6±38.9mg/dl. The difference was found to be statistically not significant (P>0.05), showing a comparable cholesterol level in the two groups. In our study, CIMT showed a positive correlation with cholesterol, LDL and triglycerides which was statistically significant. In our study, CIMT showed a positive correlation with LDL which was statistically significant. (r=0.571, p=0.001). Yoshimitsu Y et al, concluded that total cholesterol was significantly related to progress of CIMT.[13]

CONCLUSION

The AS patients had a significantly higher CIMT indicating that the disease itself could be a risk factor for atherosclerosis. CIMT was positively correlated with cholesterol, LDL and triglycerides and negatively correlated with HDL. Results of this study showed that

there is a higher prevalence of subclinical atherosclerosis (20%) in AS patients as compared to controls as evidenced by a higher CIMT. Every effort should be made in order to control inflammation and traditional risk factors in this population, to avoid the consequences of accelerated atherogenesis.

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