Correlation of Carotid Intima Media Thickness with Disease Activity in Ankylosing Spondylitis

Prasanta Dihingia[1], Nayanmoni Dutta[2], Pronami Borah[3], Sanjeeb Kakati[4], Anshu Kumar Jha[5]

ABSTRACT

Introduction: Ankylosing spondylitis (AS) is a chronic inflammatory disease involving the axial joints. It has association with HLA- B27. Measurement of intima media thickness (IMT) of common carotid artery has got a direct co-relation with atherosclerosis and increased cardiovascular mortality. In AS patients there is high chance of developing atherosclerosis because of it's chronic inflammatory nature. Thus the study tried to see the co-relation of IMT of common carotid artery with disease activity of AS and other functional index. Current research aimed to study the carotid IMT (CIMT) in AS patients and see the co-relation of CIMT with disease activity.

Material and methods: 53 patients satisfying Modified New York criteria 1984 were included in study. History, physical examination and necessary investigations were done. BASDAI and BASFI was calculated. Graphs were plotted showing the BASDAI and BASFI co-relation with the CIMT.

Results: Male:Female ratio was 3.4:1. Mean BASDAI score was 4.14±0.92 and mean BASFI was 4.27±2.02. Mean CIMT (average of right and left carotid) of all the patients was 0.63±0.19 mm. There was significant co-relation found between CIMT and BASFI (r=+0.6411, p,0.001) though no such co-relation was found with BASDAI (r=-0.2462, p=0.075). There was a significant negative co-relation between CIMT and ESR (r=-0.3602, p=0.008) though no such significant co-relation was seen with C-RP.

Conclusion: Our study concludes that the patients with longer duration of disease have increased CIMT and decreased functional index. This suggests that if disease is present for longer duration, there may be increased risk of atherosclerosis.

Keywords: Carotid Intima, Ankylosing Spondylitis, Carotid Intima Media Thickness

INTRODUCTION

Ankylosing spondylitis (AS) is a chronic inflammatory disease which is characterized by bilateral sacroiliitis, inflammatory axial joint arthritis, and several extra-articular manifestations and is associated with human leukocyte antigen B27, which is a prototype of spondyloarthropathies.[1] Ankylosing spondylitis (AS) belongs to the group of diseases known as the *spondyloarthropathies* or, better, *spondyloarthritides*. AS occurs globally, but some researchers have found that ethnic or geographic differences exist in terms of the prevalence and clinical expression of the disease.[2,3]

The predominant clinical features of AS are inflammatory back pain which is due to sacroiliitis and inflammation at other sites in the axial skeleton. Inflamation of entheseal sites is also occours. The hip joint and shoulder joints involves in about 20% of patients with AS. The peripheral arthritis is usually monoarticular or oligoarticular,and affects primarily but not exclusively the lower limbs.[4] Along with the articular manifestation, patient with AS may also have symptom of extraarticular manifestation which include constitutional symptom like fatigue low grade fever, symptom of other organ involvement which include Acute anterior uveitis, GIT manifestation, cardiac manifestation like cardiac conduction abnormality, valvular involvement mostly AR, pulmonary involvement like apical lobe fibrosis, ILD and renal involvement like renal amyloidosis, IgA nephropathy etc.

Mortality rates in patient with AS approximately 1.5-1.9 Times more than that of the general population.[5] Most of this excess mortality is mainly due to cardiovascular causes (20-40%),[6] but the predominant cardiac manifestations of AS (like aortic regurgitation, heart block, etc.) alone cannot explain this phenomenon. Recent studies results shown that the chronic inflammation associated with AS may produce many significant changes in all the organ systems throughout the body including the cardiovascular system, and these changes may be responsible for increased mortality and morbidity associated with it.[7]

Systemic inflammatory response which lead to accelerated atherosclerosis is an important risk factor for increased cardiovascular risk for autoimmune diseases such as rheumatoid arthritis (RA), psoriatic arthritis (PsA) and systemic lupus erythematosus (SLE).[8]

Measurement of the intima media thickness (IMT) of the common carotid artery has been a useful index to identify premature atherosclerosis, and it is strongly correlated with the presence of coronary artery diseases. Currently, a few studies have shown that patients with AS had greater carotid

[1]Associate professor, Department of Medicine, [2]Postgraduate, Department of Medicine, [3]Associate professor, Department of Radiology, [4]Professor and Head, Department of Medicine, [5]Postgraduate, Department of Medicine, Assam Medical College and Hospital, Dibrugarh, Assam, India

Corresponding author: Dr. Anshu Kumar Jha, Room No. 47, PG Boy's Hostel No. 8, Assam Medical College, Dibrugarh, Assam 786002, India

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artery intima–media thickness (CIMT) values than controls with other chronic inflammatory diseases, such as RA and SLE.[9-12]

There is lack of study and lack of data on ankylosing spondylitis from the North-Eastern part of India. For this reason this study was done. In the present study we assessed carotid intima media thickness in AS patient to see the correlation of ankylosing spondylitis with disease activity, atherosclerosis and to see the clinical profile of ankylosing spondylitis in patient of this part of India.

The present study was carried out in the Department of Medicine, Assam Medical College & Hospital, Dibrugarh, with the aims and objectives to study carotid intima media thickness in ankylosing spondylitis patient and to correlate carotid intima media thickness with disease activity in ankylosing spondylitis patient.

MATERIAL AND METHODS

The Present Study was a hospital based observational study carried out on patients of Ankylosing Spondylitis, who were admitted or attended various Out Patient Departments of Assam Medical College and Hospital, Dibrugarh, during a period of one year from July 2018 to June 2019. Patients aged more than 13 years who fulfil modified new York criteria (1984) were included in the study and patients who refused to give consent were excluded from the study. Patients with following feature are also excluded from study.

- Diabetes mellitus.
- Chronic kidney disease patient.
- Coronary artery disease patient.
- Hypertensive patient.
- Family history of premature symptomatic coronary heart disease (<55 years for male and <65 years for female).
- Tobacco chewing and smoking.
- Obesity.
- Dyslipidemia.
- Other spondylo-arthropathy.

After fulfilling the inclusion and exclusion criteria, and after obtaining formal informed conscent, 53 cases of Ankylosing Spondylitis, diagnosed on the basis of Modified New York (1984) criteria were included in the study.

All the patients are evaluate with proper history, physical examination and test for spinal mobility and laboratory investigations. For disease activity BASDAI (Bath Ankylosing Spondylitis Disease Activity Index),[13] and for functional ability BASFAI (Bath Ankylosing Spondylitis Functionnal Index)[14] is used. Haemoglobin, ESR, Renal Function Tests, Lipid profile, x-ray SI joint, HLA B-27, Chest x-ray, HRCT Thorax, Electrocardiogram and Echocardiography were done in all patients. MRI SI Joint was done in some cases as per requirement.

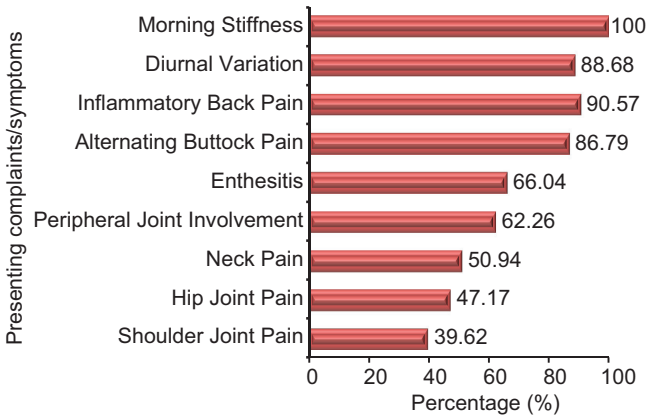
In the present study, carotid intima-media thickness was estimated with the help of SAMSUNG RS 80A ultrasound system with probe having frequency of 3 to 12 MHz. The CIMT assessment was done following a protocol standardised by The American Society of Echocardiography (ASE) in a consensus statement.[15,16]

STATISTICAL ANALYSIS

Statistical analysis of data was performed by using the computer program, Statistical Package for social sciences (SPSS for Windows, version 20.0.Chicago, SPSS Inc.) and Microsoft Excel 2010. Continuous data was expressed as mean ± standard deviation (SD) and categorical variables as proportion and percentages. Pearson's correlation coefficient was used to see correlation. Student t test was used to calculate p value. *p* value of <0.05 was considered statistically significant in this study.

RESULTS

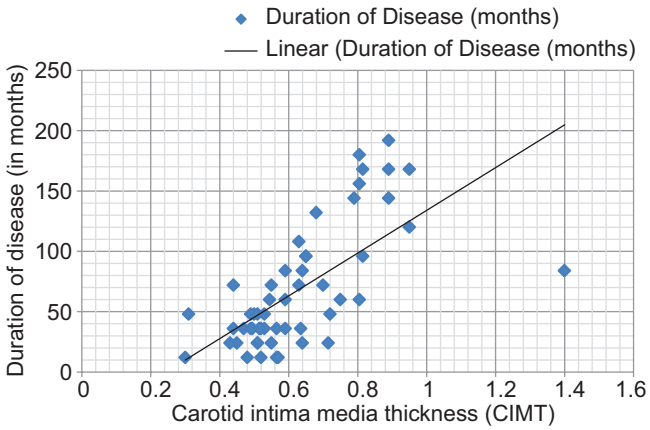
The mean age of presentation was 29.25±8.86 years.



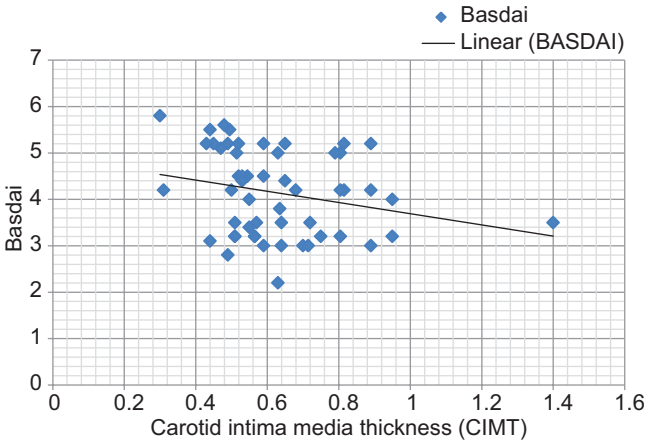
Figure–1: Presenting complaints/symptoms

Variable	r value	p value
Duration of Disease (months)	0.6644	<0.001
BASDAI	-0.2462	0.075
BASFI	0.6411	<0.001
ESR (mmAEFH)	-0.3602	0.008
CRP (mg/dL)	-0.0344	0.806
Total Cholesterol	0.0124	0.929
Serum Triglyceride	0.1513	0.279
HDL-c (mg/dL)	0.0262	0.852
LDL-c (mg/dL)	0.1336	0.340
Lumbar Flexion	-0.4927	<0.001
Lateral Flexion	-0.4729	<0.001
Chest Expansion	-0.5535	<0.001

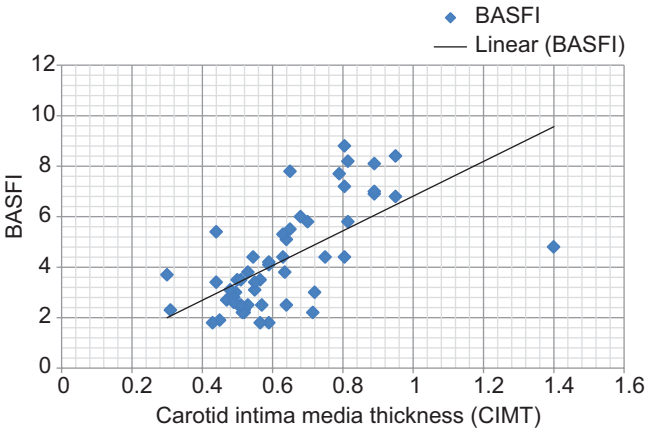
Figure-2: Correlation of cimt with other parameters



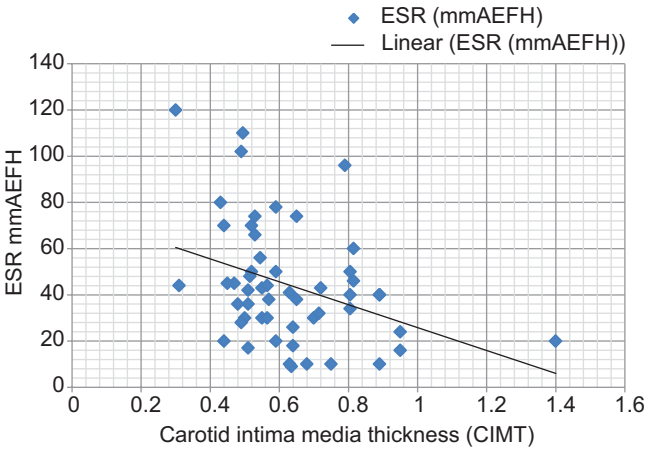
Figure–3: Correlation between CIMT and duration of disease



Figure–4: Correlation between CIMT and basdai



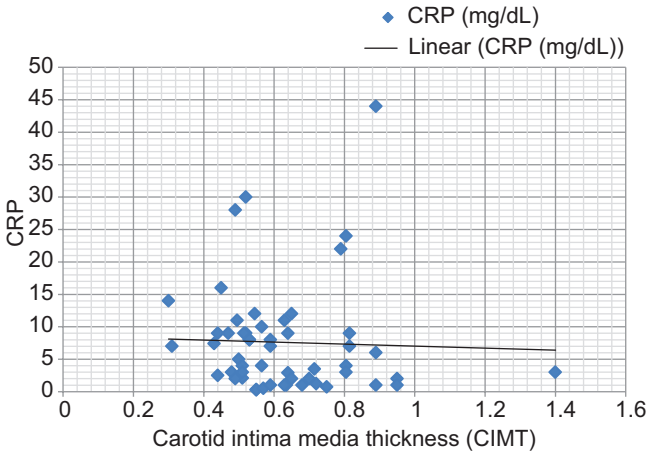
Figure–5: Correlation between CIMT and BASFI



Figure–6: Correlation between CIMT and ESR

And male to female ratio was 3.4:1. The mean age at onset was 23.55±6.92 years. The mean duration of disease was 68.38±50.18 months. Figure -1 shows the presenting complains or sympots observed in the study.

On laboratory evaluation the mean ESR was 44.13±25.89 and the mean CRP was 7.61±8.52. Mean total cholesterol (mg/dl) was 167.57±24.03, serum triglyceride (mg/dl) 94.43±37.04, HDL-C (mg/dl) 45.70±5.66 and LDL-c was 82.55±16.54. Mean CIMT (average of right and left carotid) of all the patients was 0.63±0.19 mm. The mean BASDAI was 4.14±.92 and mean BASFI was 4.27±2.02.



Figure–7: Correlation between CIMT and CRP

Correlation of CIMT with different parameters was observed as shown in figure 2,3,4,5,6 and 7.

DISCUSSION

In our study mean age of onset of disease was 23.55±6.92 years, maximum patients have age at onset in age group of 20-29 years (47.17%) followed by <20 years (32.08%). The mean age of presentation was 29.25±8.86 years, with 33.96% of patients in age group 20-29 years and 32.08% in the age group 30-39 years. Naveen gupta et al[17] found the mean age of presentation of ankylosing spondylitis was 29.43±9 years and mean age at onset was 24.01±8.36 years.Mishra et al[18] found the mean age of presentation was 29.3±10.1 years. In our study mean duration of disease in ankylosing spondylitis was 68.38±50 months.Naveen et al[17] found the duration of disease was 65.62±54.92 months.

In our study we found that the predominant presenting symptom was Inflamatory low back pain, seen in 90.57% of patients. Morning stiffness was seen in all patients. Also in present study we found that 88.68% have nocturnal or early morning back pain. Alternate buttock pain was seen in 86.79%.This finding was similar to what seen in study by Agarwal R. et al.[19] Of extra articular manifestations, in our study constitutional symptoms were present in 67.92% of cases. Fatigue was the most common constitutional symptom. Acute anterior uveitis is seen in 22.64% cases. Uveitis was seen in 25.7% in study by Agarwal R et al.[19] Montilla C. et al[20] found it in 23.5% cases.

In our study the mean BASDAI and BASFI was found to be 4.14±0.92and 4.20±2.02 respectively. Study done Naveen Gupta et al[17] found BASDAI 4.11±1.99 and BASFI 4.13±2.09.Shefali et al[21] found BASDAI and BASFI,4.3±1.8 and 3.9±2.2 respectively.

In our study the mean carotid intima media thickness (CIMT) of average of both right and left side was 0.63±0.19mm which was almost similar to study done by Bodnar et al[22] (0.65± 0.15) Naveen Gupta et al[17] (0.62 ± 0.12). In our study there is no any significant correlation found between CIMT and disease activity index (BASDAI) (r=-0.246, p value= 0.075).Significant correlation was also not found in study done by Naveen gupta et al[17] (r=-0.160, p>0.05),Sari et al[23] (r=-0.03, p=0.79). But significant correlation was found in

study done by Wafa Hamdi et al[24] 164 (r=0.412, p=0.002), Subhabrata Das et al[25] (r=0.46, p<0.001).In the present study we found significant negative correlation of CIMT with ESR (r=-0.360, p=0.008).Significant correlation of CIMT with ESR was also found in study done by Naveen Gupta et al[17] (r=-0.295, p<0.05),Wafa Hamdi et al[24] 164 (p=0.047). We did not find any significant correlation of CIMT with CRP.Significant correlation was also not found in study done by Naveen Gupta et al[17] but Wafa Hamdi et al[24] found significant correlation of CIMT with CRP (p=0.012). In our study we also correlate CIMT with other important parameters.We found significant positive correlation of CIMT with disease duration and BASFI (r=0.664, p<0.001 and r=0.641, p<0.001 respectively).We found significant negative correlation of CIMT with Lumbar flexion,Lateral flexion and Chest expansion (r=-0.492, p<0.001; r=-0.472, p<0.001; -0.553, p<0.001 respectively).We did not find any significant correlation of CIMT with total cholesterol, serum triglyceride,HDL cholesterol,and LDL cholesterol (r=0.0124, p=0.929; r=0.151, p=0.279; r=0.026, p=0.852; r=0.133, p=0.340 respectively). Study done by Naveen Gupta et al[17] found that the CIMT in the cases positively correlated with duration of disease (□=+0.549; □ < 0.01), and BASMI (□=+0.337; □ < 0.05). CIMT negatively correlated with lateral flexion (LF) (□=−0.344; □ < 0.05) and lumbar flexion (□=−0.313; □ < 0.05). No significant correlation was observed between CIMT and BASDAI, BASFI,HDL-C, LDL-C, and TG levels. Wafa Hamdi et al[24] found significant correlation of CIMT with Bath AS Disease Activity Index (p=0.002), Bath AS Functional Index (p=0.008), Schober index (p=0.039), Bath AS Metrology Index (p=0.028). Bodnar et al[22] found correlation of CIMT with disease duration (r=0.559; p=0.013), BASFI (r=0.691; p=0.003), decreased lumbar spine mobility (r=–0.656; p=0.006), and chest expansion (r=–0.502; p=0.047). The result of our study was in parallel to some study and against to some study. In our study we find significant positive correlation of CIMT with disease duration and BASFI and on the other hand we also found that BASFI was positively correlated with disease duration. So from this finding we can interpret that patient of ankylosing spondylitis for longer duration have both increased carotid artery intima media thickness and more functional inactivity .So it reflect that that there may be high chance of atherosclerosis, (as because increased CIMT is an indicator of atherosclerosis), and increased morbidity in patient of ankylosing spondylitis if the disease is present for longer duration.

CONCLUSION

While conducting this study the area of special interest was to measure the CIMT in Ankylosing spondylitis patients. CIMT in our study was almost similar to study done by other author,who in their study found increased CIMT in AS patients in comparision to control.In our study CIMT was not correlated with BASDAI and CRP,but negatively correlated with ESR.In our study CIMT was positively correlated with duration of disease, BASFI and negatively correlated with lumbar flexion,lateral flexion and chest expansion.So our study observation reflect that patients with longer duration of disease have increased CIMT and of decreased spinal mobility.Which suggest that if the disease is present for longer duration then there may be increasd risk of atherosclerosis and decrease spinal mobility.As there is increased risk of atherosclerosis there may high chance of cardiovascular and cerebrovascular disease in ankylosing spondylitis patients.Thus awareness of high chance of cardiovascular and cerebrovascular diseased is important not only among physicians but also among patients,so that appropriate preventive measures can be taken accordingly before the occourence of life threatening events. However, this study was a hospital based observational study.Small sample size was an important limitation of the study. Large population based prospective studies may be more informative on this regard.

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