

## “Study of Cardiovascular Manifestations in Ankylosing Spondylitis”

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**Abstract:** Ankylosing spondylitis is a chronic inflammatory disorder primarily affecting the sacroiliac joints and vertebral column, often manifesting in young males than in females in the ratio of 3:1 in the second or third decade, also causing extraarticular manifestations involving Cardiac, ophthalmic, pulmonary, renal and neurological systems.

Cardiovascular manifestations remains one of the common cause of morbidity and mortality in patients with Ankylosing spondylitis .The aim and objective is to find the prevalence of cardiovascular manifestations in patients with ankylosing spondylitis and to find their association with age, sex, duration of the disease. 50 cases and 50 age and sex matched controls were selected for the study.

In the study, Cases had significant association with the cardiovascular abnormalities compared with the controls. 11(22%) out of 50 cases and 2(4%) out of 50 controls had cardiovascular manifestations. Among the cases Cardiac Conduction disturbances occurred in 10%, Valvular regurgitation in 10% and isolated aortic root dilatation in 2%.The prevalence of Cardiovascular abnormalities in Ankylosing spondylitis was found to be 22%. Increased age and longer duration of the disease was associated with increased incidence of the cardiovascular manifestations.

**Keywords:** Ankylosing spondylitis, cardiovascular abnormalities, conduction disturbances, valvular regurgitation.

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### I. Introduction

Ankylosing spondylitis is a chronic inflammatory disorder, principally a disease of axial and peripheral joints. The extraarticular manifestations of the disease affecting Cardiac, ophthalmic, pulmonary, renal and neurological systems are also common.

Ankylosing spondylitis has a worldwide prevalence of 0.1 to 1.4%. According to Yang et al, the prevalence of cardiac manifestations in ankylosing spondylitis patients were found to be 10% to 30%

Bulkley and Roberts were one of the first to put forward pathophysiologic description of valvular heart diseases in ankylosing spondylitis, when they studied autopsy findings in eight patients with ankylosing spondylitis. They demonstrated aortic root dilatation, with a cellular inflammatory process with fibroblast overactivity along with tissue thickening involving the aortic cusps, aortic annulus leading to aortic regurgitation and conduction abnormalities in patients with ankylosing spondylitis. The other associations were pericarditis, myocarditis, left ventricular diastolic dysfunction, mitral regurgitation.

The cardiac manifestations in ankylosing spondylitis can be symptomatic or asymptomatic. Hence the patients with ankylosing spondylitis should be screened for cardiac abnormalities by electrocardiography and echocardiography.

Many studies were carried out in relation to cardiovascular manifestations in ankylosing spondylitis and had found that the association of cardiac manifestations increased with increased duration of ankylosing spondylitis , increase in the age of the patient.

### II. Materials And Methods

**Source Of Data :** Patients approaching the outpatient department as well as the Inpatients of the Coimbatore Medical College Hospital, satisfying the ASAS criteria and age and sex matched controls, selected on a random basis.

**Study Area:** Coimbatore medical college hospital

**Design Of Study:** Cross sectional study

**Period Of Study:** One year, July 2014 - July 2015.

**Sample Size:** 50 cases and 50 age and sex matched controls

Selection Criteria

Inclusion Criteria

- Adult patients (both sex) between the age group of 18 to 60
- Patients satisfying Assessment of Ankylosing Spondylitis International Society (ASAS) criteria for Ankylosing Spondylitis

**Exclusion Criteria**

- Pregnant women
- Minors (below the age of consent)
- Persons suffering from congenital heart diseases
- Persons suffering from Psoriatic Arthritis
- Persons suffering from Rheumatic valvular heart diseases
- Persons not capable of giving consent (psychiatric patients)
- Persons unwilling to undergo the study (who refused to consent)

**All patients are evaluated with:**

Detailed history

Age, sex, duration of the disease, extra axial joint involvement, extraarticular manifestations, presence of other systemic diseases, response to anti inflammatory drugs, family history of ankylosing spondylitis were all documented.

Examination

Examination of all joints was done and cardiac examination was done to find for cardiomegaly, cardiac murmurs. Ophthalmic and other systemic examination was done.

**Investigations**

Routine investigations like Blood haemoglobin, Renal function test and blood sugar estimation were done. C Reactive Protein was estimated using latex agglutination kit. Erythrocyte sedimentation rate was measured.

**Radiography:**

X Ray B/L sacroiliac joint:

X Ray of peripheral joints were done.

Chest X Ray PA view was done to look for cardiomegaly

**Electrocardiogram:**

A 12 lead electrocardiogram was taken for all the cases and controls. Atrio ventricular blocks were found out by looking at the PR intervals and the proceeding QRS complexes, Bundle branch block and fascicular block were interpreted by looking at the QRS complexes in the specific leads. Chamber hypertrophies were also noted.

Echocardiogram:

With the patient in supine and left lateral position using a Hewlett Packard Sonos 2500 scanning machine, M mode, 2 dimensional and Doppler echocardiography were performed. Cardiac position, cardiac chambers, Atrial and ventricular septae, valves, pericardium, great vessels, ejection fraction, peak velocities across the valves, trans valvular mean gradient, grading of regurgitations and aortic root diameter were noted.

Grading of Aortic Regurgitation (AR) by echocardiography is done according to the following measures:

Parameters	Mild AR	Moderate AR	Severe AR
Jet width	<25% of LVOT	25 – 64% of LVOT	≥65% of LVOT
Vena contracta	<0.3 cm	0.3 – 0.6 cm	>0.6 cm
RVol	<30 ml/beat	30 – 59 ml/beat	≥60 ml/beat
RF	<30%	30% - 49%	≥50%
ERO	<0.10 sq.cm	0.10 – 0.29 sq.cm	≥0.3 sq.cm

Grading of Mitral Regurgitation (MR) by echocardiography is done by the following measures:

Parameters	Mild MR	Moderate MR	Severe MR
Central jet	<20% LA	20% - 40%	>40%
Vena contracta	<0.3cm	0.4 – 0.7cm	>0.7cm
RVol	-	<60 ml	≥60 ml
RF	-	<50%	≥50%
ERO	-	<0.40 sq.cm	≥0.40 sq.cm

Left ventricular diastolic dysfunction is assessed by Echocardiogram with peak Early (E) and Late (A) trans mitral filling velocities and their ratio (E/A).

### III. Statistical analysis

The data were reported depending on their distribution as Mean +/- Standard deviation or the median. Between groups, the differences in quantitative variables were assessed by means of the unpaired t test.

Comparison between groups was made by the Non parametric Mann - whitney test. Differences in categoric variables were assessed by Chi-square test between groups.

A p value of <0.05 using a two-tailed test was taken as being of significance for all statistical tests. All data were analysed with a statistical software package (SPSS, version 16.0 for windows).

### IV. Figures And Tables

Table 1: Mean age of cases and controls

Study Groups	Mean [Years]	SD	95% CI for Mean		Minimum	Maximum
			Lower	Upper		
Cases	38.1	3.1	37.2	39.0	33	44
Control	38.3	3.9	37.2	39.4	32	45
Total	38.2	3.5	37.5	38.9	32	45

In the study group the mean age group of patients with AS was 38.1 years with a standard deviation of 3.1 years and that of the control group was 38.3 years with standard deviation of 3.9 years. The youngest patient was 32 years and oldest was 45 years among the study groups.

Chart 1: Mean age of cases and controls

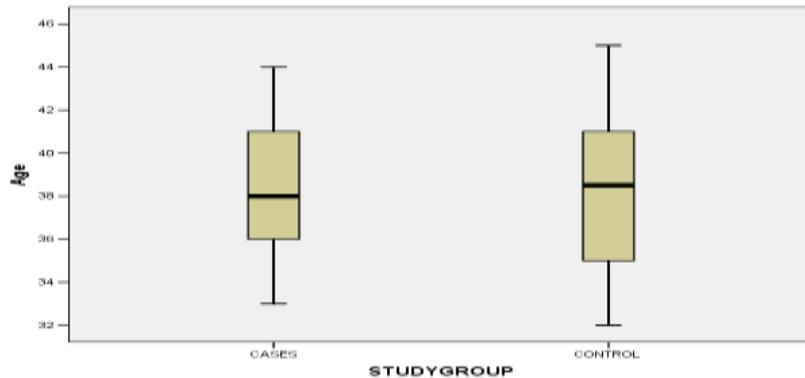
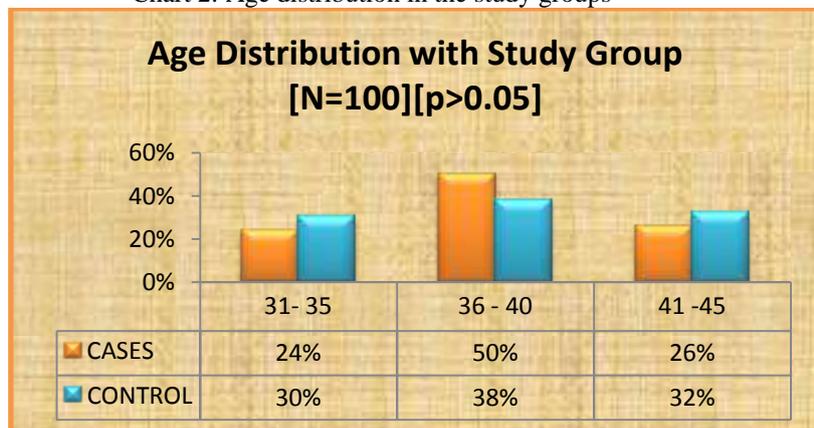


Table 2: Age distribution in study groups

AGE	STUDYGROUP		TOTAL	(%)
	CASES	CONTROL		
31- 35	12	15	27	27%
36 - 40	25	19	44	44%
41 -45	13	16	29	29%
TOTAL	50	50	100	

Chart 2: Age distribution in the study groups

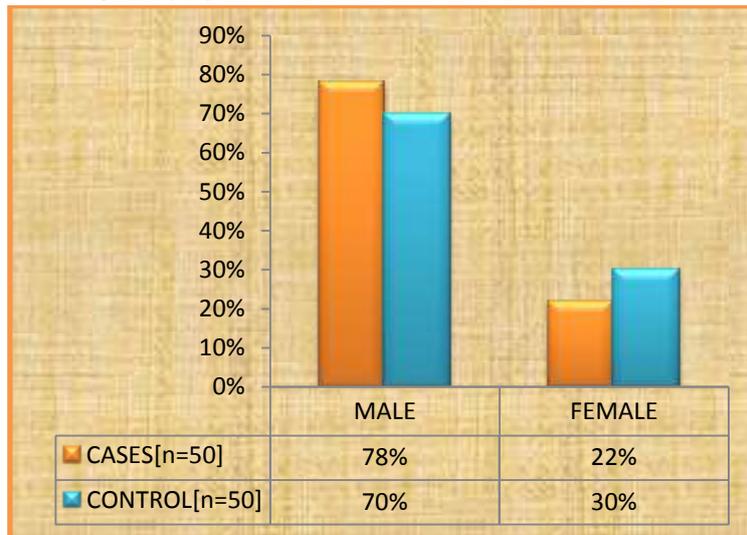


In both the cases and controls of the study groups, more number of people lie between the age group of 36 – 40 years. 50% of the cases and 38% of the controls lie in this age group. The remaining persons lie equally on either side in both the cases and the controls.

**Table 3:** Gender Distribution in the Study Groups

GENDER	STUDYGROUP		TOTAL	(%)
	CASES	CONTROL		
MALE	39	35	74	74%
FEMALE	11	15	26	26%
TOTAL	50	50	100	

**Chart 3:** Gender distribution in the cases and controls

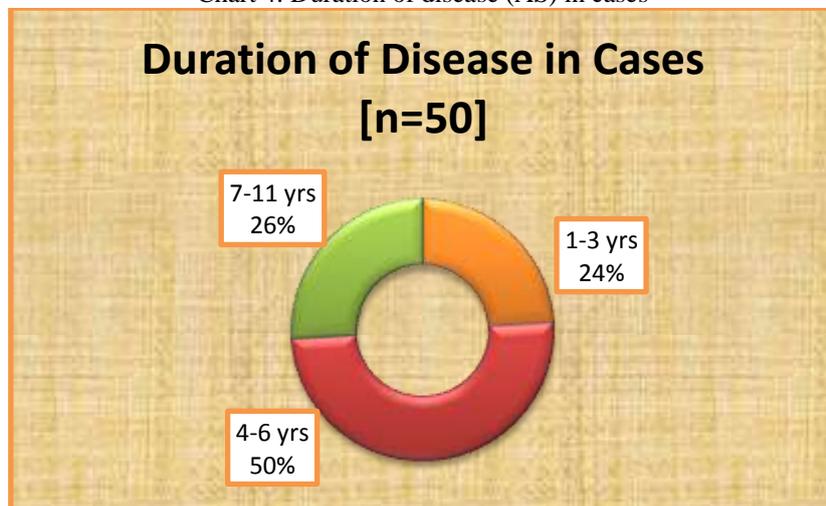


Males are more commonly affected with Ankylosing Spondylitis with 39 male cases (78%) and 11 female cases(22%). Control group also have a more number of males with 35 males and 15 females.

**Table 4:** Duration of disease(AS) in cases

Duration	n	(%)
1- 3 yrs	12	24%
4-6 yrs	25	50%
7-11 yrs	13	26%
Total	50	100%

Chart 4: Duration of disease (AS) in cases

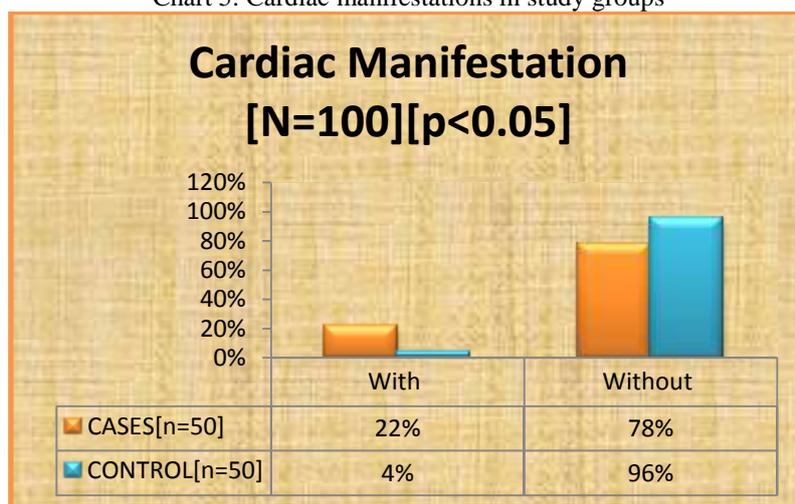


The duration of the disease varies between 1 and 11 years. Half of the cases lie within the duration of 4-6 years (50%). The remaining half is nearly equally shared by the duration of disease of 1-3 years(24%) and 7-11(26%) years.

**Table 5:** Cardiac manifestations in study groups

Cardiac Manifestation	STUDYGROUP		TOTAL	(%)
	CASES	CONTROL		
With	11	2	13	13%
Without	39	48	87	87%
TOTAL	50	50	100	

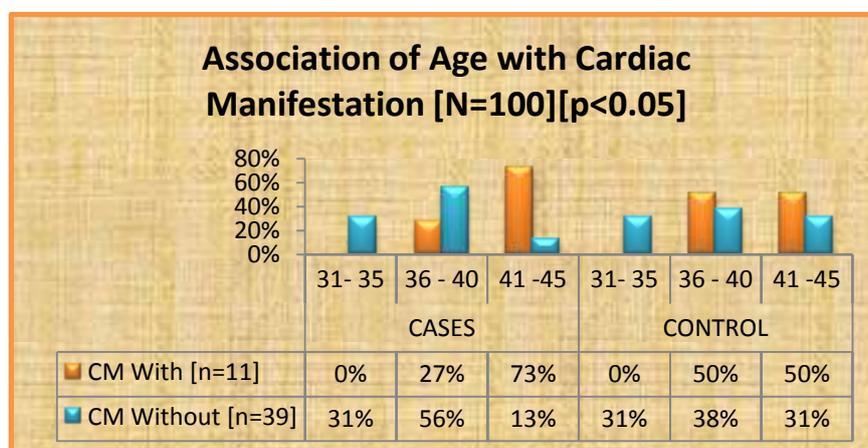
**Chart 5:** Cardiac manifestations in study groups



Cardiac manifestations in number of cases and controls revealed that the manifestations occurred in 11 (22%) out of 50 cases and 2 out of 50 controls (4%) in the study group.

**Table 6:** Age in relation to the cardiac manifestations in the study groups

STUDYGROUP	Age	Cardiac Manifestations			(%)	Sig
		With	Without	Total		
CASES	31 - 35	0	12	12	24%	<0.05
	36 - 40	3	22	25	50%	
	41 -45	8	5	13	26%	
	<b>Total</b>	<b>11</b>	<b>39</b>	<b>50</b>	<b>100%</b>	
CONTROLS	31 - 35	0	15	15	30%	>0.05
	36 - 40	1	18	19	38%	
	41 -45	1	15	16	32%	
	<b>Total</b>	<b>2</b>	<b>48</b>	<b>50</b>	<b>100%</b>	



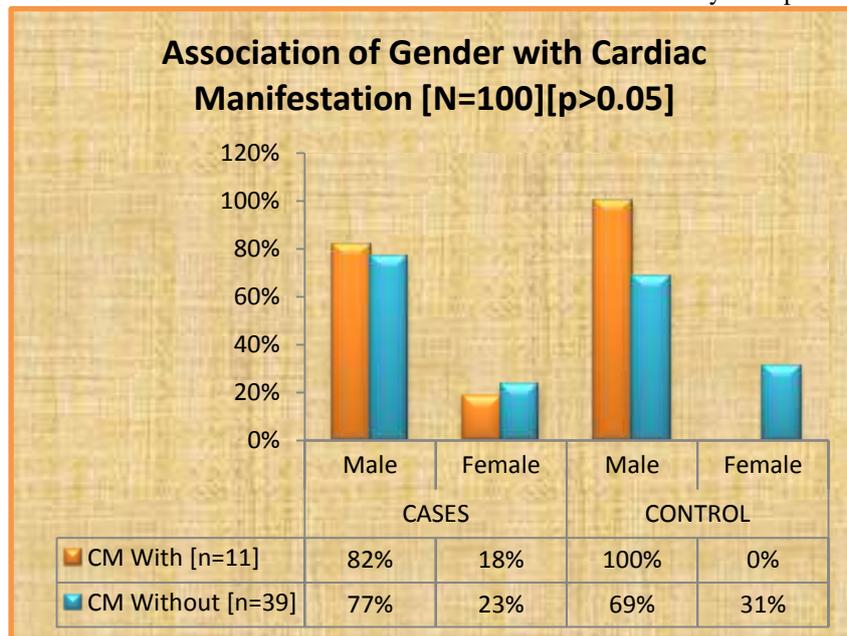
**Chart 6:** Age in relation to the cardiac manifestations in the study groups

When the occurrence of cardiac manifestations in AS were divided according to the age among the cases, it was found that 73% of cardiac manifestations were found in the age group of 41 – 45 years, 27% in the age group of 36 – 40 years and none in the age group of 31 -35 years. This showed that Cardiac manifestations occurs with increasing age with a statistical significance ( $P>0.05$ ) whereas it is not so in the control group.

**Table 7: Gender in relation to Cardiac Manifestations in study Groups**

STUDYGROUP	Gender	Cardiac Manifestations			Sig
		With	Without	Total	
CASES	Male	9	30	39	78%
	Female	2	9	11	22%
	<b>Total</b>	<b>11</b>	<b>39</b>	<b>50</b>	<b>100%</b>
CONTROL	Male	2	33	35	70%
	Female	0	15	15	30%
	<b>Total</b>	<b>2</b>	<b>48</b>	<b>50</b>	<b>100%</b>

**Chart 7: Gender in relation to Cardiac Manifestations in study Group**

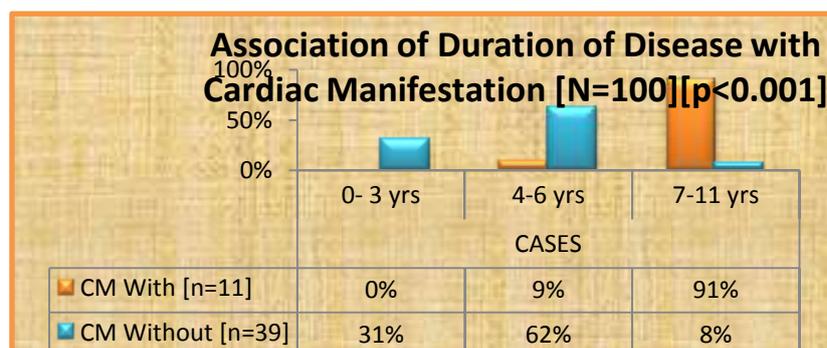


In the association of gender with cardiac manifestations it was found that males (82%) are more commonly involved than the females (18%) among the cases in the study group.

**Table 8. Duration of Disease(AS ) in relation to Cardiac Manifestations in study Groups**

STUDYGROUP	Duration	With	Without	Total	(%)	Sig
CASES	0- 3 yrs	0	12	12	24%	<0.001
	4-6 yrs	1	24	25	50%	
	7-11 yrs	10	3	13	26%	
	<b>Total</b>	<b>11</b>	<b>39</b>	<b>50</b>	<b>100%</b>	

**Chart 8: Duration of Disease(AS ) in relation to Cardiac Manifestations in study Groups**

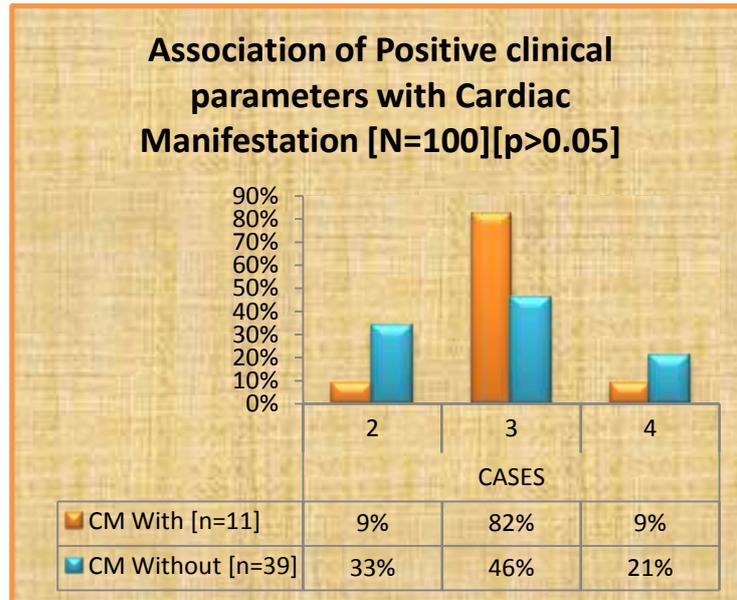


Longer duration of the disease was significantly associated with the occurrence of cardiac manifestations with 91% in those with the duration between 7-11 years, 9% in those between 4-6 years and none among those with duration of AS < 4 years which was statistically highly significant.

**Table 9:** Number of Positive Clinical Parameters in relation to Cardiac Manifestations in study Groups

STUDYGROUP	No of clinical	Cardiac Manifestations			Total	(%)	Sig		
		With	Without						
CASES	2	1	13	14	28%	>0.05			
	3	9	18	27	54%				
	4	1	8	9	18%				
	<b>Total</b>	<b>11</b>	<b>39</b>	<b>50</b>	<b>100%</b>				

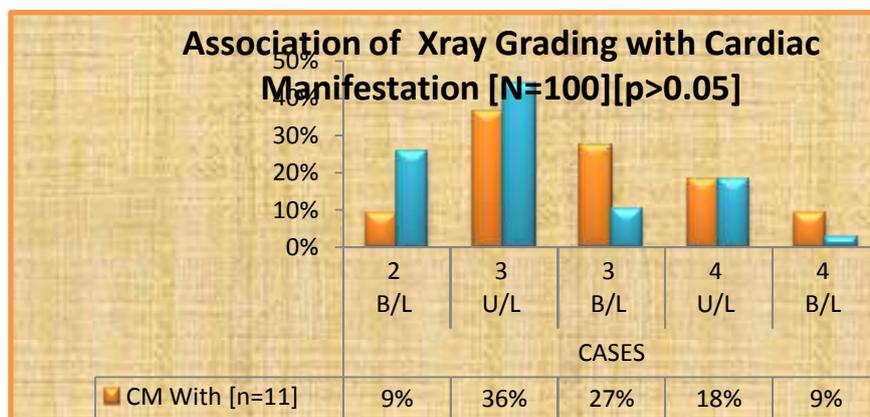
**Chart 9:** Number of Positive Clinical Parameters in relation to Cardiac Manifestations in study Groups



The number of clinically positive parameters of AS in cases with and without cardiac manifestations is not statistically significant.

**Table 10:** Grading by X ray imaging in relation to Cardiac Manifestations in study Groups

STUDYGROUP	X ray Grading	Cardiac Manifestations			Total	(%)	Sig		
		With	Without						
CASES	2 B/L	1	10	11	22%	>0.05			
	3 U/L	4	17	21	42%				
	3 B/L	3	4	7	14%				
	4 U/L	2	7	9	18%				
	4 B/L	1	1	2	4%				
	<b>Total</b>		<b>11</b>	<b>39</b>	<b>50</b>		<b>100%</b>		



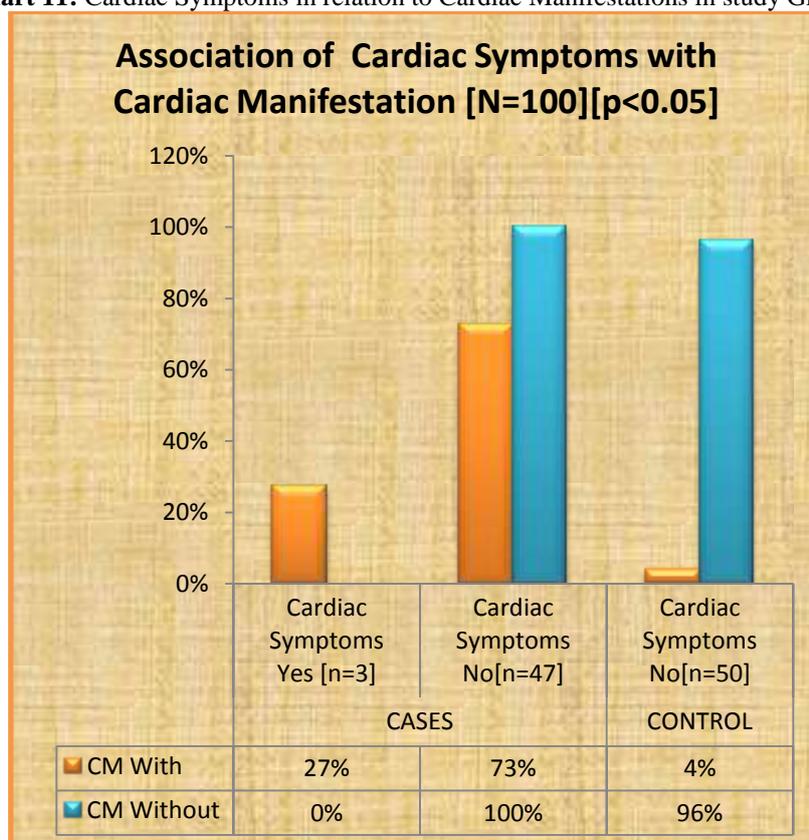
**Chart 10:** Grading by X ray imaging in relation to Cardiac Manifestations in study Groups

Cardiac manifestations in association with X Ray imaging by grading of sacroiliitis in AS is not found to be statistically significant. 36% of the cases with cardiac manifestations have 3 unilateral grading which is more than that of 3 bilateral, 4 unilateral and 4 bilateral.

**Table 11:** Cardiac Symptoms in relation to Cardiac Manifestations in study Groups

STUDYGROUP	Cardiac Symptoms	Cardiac Manifestations		Total	(%)			
		With	Without					
CASES	YES	3	0	3	6%			
	NO	8	39	47	94%			
	<b>Total</b>	<b>11</b>	<b>39</b>	<b>50</b>	<b>100%</b>			
CONTROL	NO	2	48	50	100%			
	<b>Total</b>	<b>2</b>	<b>48</b>	<b>50</b>	<b>100%</b>			

**Chart 11:** Cardiac Symptoms in relation to Cardiac Manifestations in study Groups

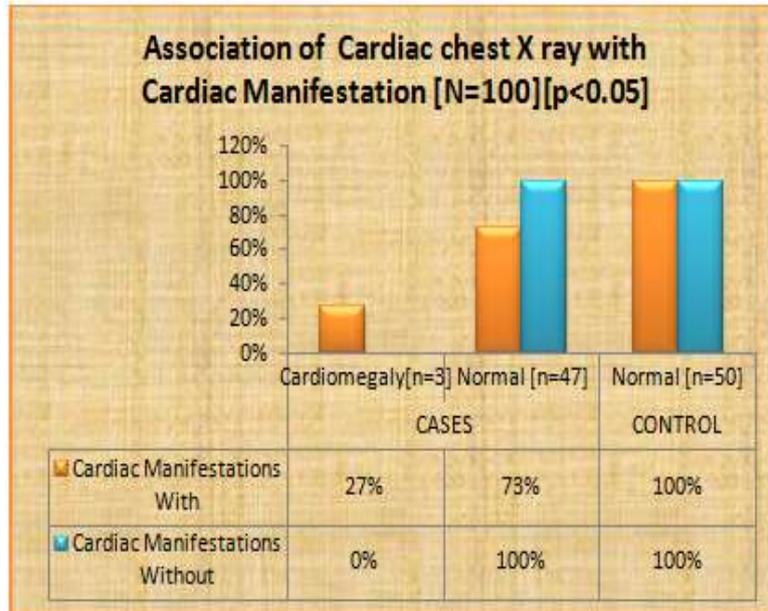


Cardiac symptoms were found in 27% of the cases with cardiac manifestations and not found in 73% of the cases with cardiac manifestations.

**Table 12:** Chest X ray in relation to Cardiac Manifestations in study Groups

STUDYGROUP	Chest X ray	Cardiac Manifestations		Total	(%)			
		With	Without					
CASES	Cardiomegaly	3	0	3	6%			
	Normal	8	39	47	94%			
	<b>Total</b>	<b>11</b>	<b>39</b>	<b>50</b>	<b>100%</b>			
CONTROLS	Normal	2	48	50	100%			
	<b>Total</b>	<b>2</b>	<b>48</b>	<b>50</b>	<b>100%</b>			

**Chart 12:** Chest X ray in relation to Cardiac Manifestations in study Groups

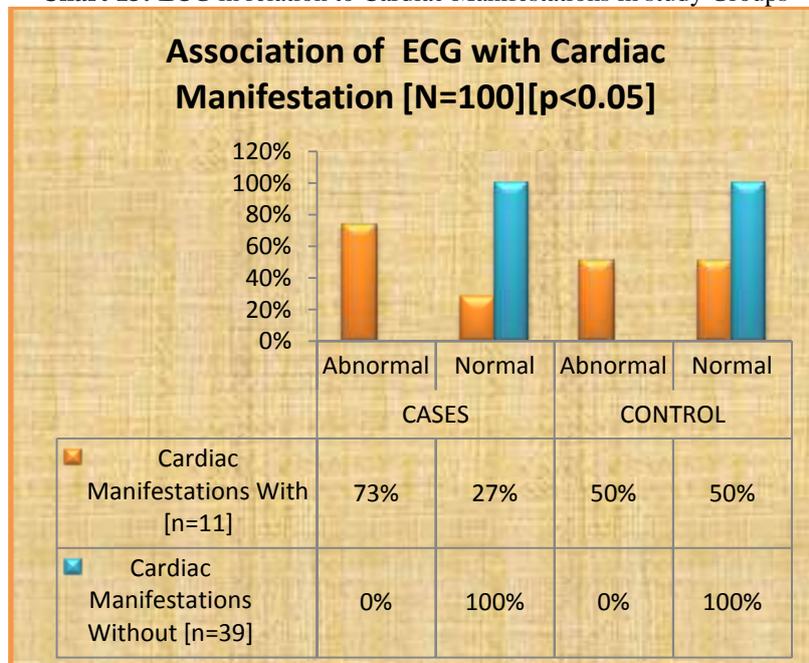


Chest X Ray showed cardiomegaly in 27% of the cases with cardiac manifestations and was normal in 73% of the cases with cardiac manifestations.

**Table 13:** ECG in relation to Cardiac Manifestations in study Groups

STUDYGROUP	ECG	Cardiac Manifestations			Total	(%)	Sig
		With	Without				
CASES	Abnormal	8	0		8	16%	<0.01
	Normal	3	39		42	84%	
	<b>Total</b>	<b>11</b>	<b>39</b>		<b>50</b>	<b>100%</b>	
CONTROL	Abnormal	1	0		1	2%	>0.05
	Normal	1	48		49	98%	
	<b>Total</b>	<b>2</b>	<b>48</b>		<b>50</b>	<b>100%</b>	

**Chart 13:** ECG in relation to Cardiac Manifestations in study Groups

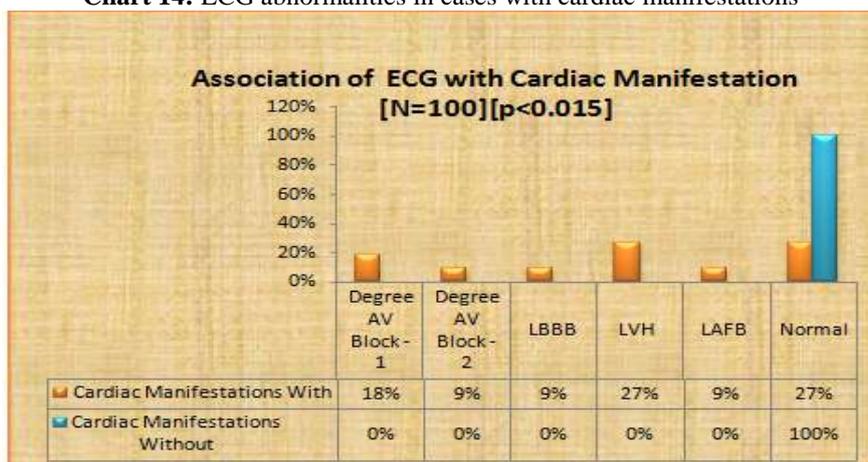


ECG was found to be abnormal in 8 out of 11 cases (73%) and normal in 3 out of 11 cases (27%) with cardiac manifestations whereas it was abnormal in 1 out of 2 controls with the cardiac manifestations which was statistically highly significant (P<0.01).

**Table 14: ECG abnormalities in cases with cardiac manifestations**

ECG	Cardiac Manifestations		Total	(%)	Sig
	With	Without			
Degree AV Block - 1	2	0	2	4%	
Degree AV Block - 2	1	0	1	2%	
LBBB	1	0	1	2%	
LVH	3	0	3	6%	<0.01
LAFB	1	0	1	2%	
Normal	3	39	42	84%	
<b>Total</b>	<b>11</b>	<b>39</b>	<b>50</b>	<b>100%</b>	

**Chart 14: ECG abnormalities in cases with cardiac manifestations**



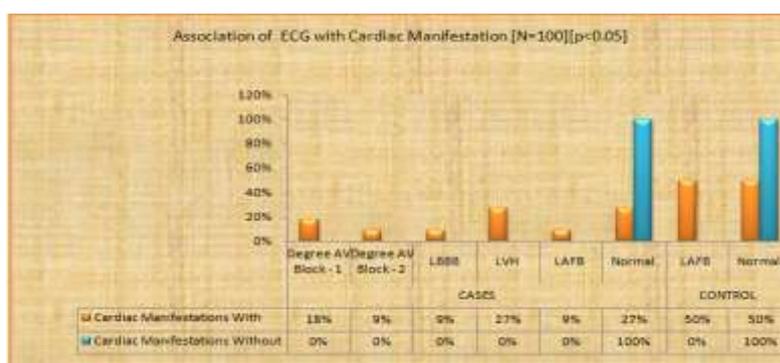
ECG among the cases with cardiac manifestations showed conduction disturbances (45%) and left ventricular hypertrophy (27%) and normal(27%). The conduction disturbances noted were first and second degree Atrio-ventricular block, left anterior fascicular block, left bundle branch block.

**Table 15: ECG abnormalities in cases and controls with cardiac manifestations**

STUDYGROUP	ECG	Cardiac Manifestations		Total	(%)	Sig
		With	Without			
CASES	Degree AV Block - 1	2	0	2	4%	
	Degree AV Block - 2	1	0	1	2%	
	LBBB	1	0	1	2%	
	LVH	3	0	3	6%	<0.01
	LAFB	1	0	1	2%	
	Normal	3	39	42	84%	
	<b>Total</b>	<b>11</b>	<b>39</b>	<b>50</b>	<b>100%</b>	
CONTROL	LAFB	1	0	1	2%	
	Normal	1	48	49	98%	>0.05
	<b>Total</b>	<b>2</b>	<b>48</b>	<b>50</b>	<b>100%</b>	

Various ECG changes among the cases with cardiac manifestations was compared with that among the controls which was statistically significant shown in the table above and the chart below.

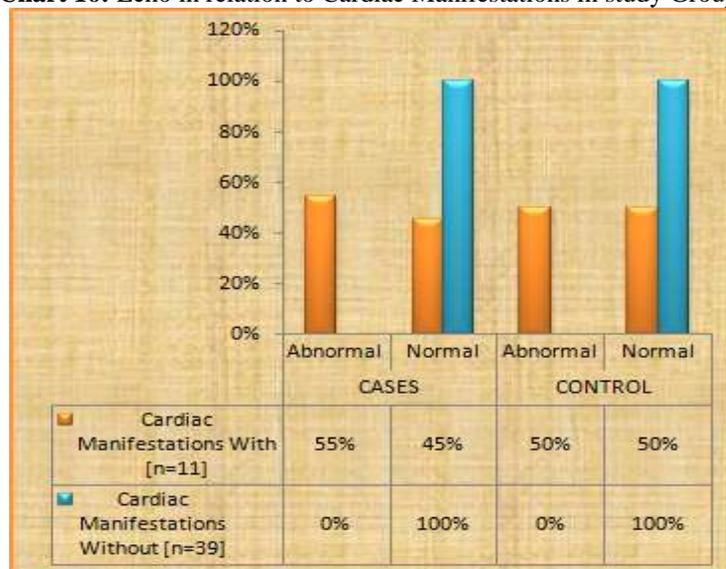
**Chart 15: ECG abnormalities in cases and controls with cardiac manifestations**



**Table 16: ECHO in relation to Cardiac Manifestations in study Groups**

STUDYGROUP	ECHO	Cardiac Manifestations			Sig
		With	Without	Total	
CASES	Abnormal	6	0	6	12%
	Normal	5	39	44	88%
	<b>Total</b>	<b>11</b>	<b>39</b>	<b>50</b>	<b>100%</b>
CONTROL	Abnormal	1	0	1	2%
	Normal	1	48	49	98%
	<b>Total</b>	<b>2</b>	<b>48</b>	<b>50</b>	<b>100%</b>

Chart 16: Echo in relation to Cardiac Manifestations in study Groups

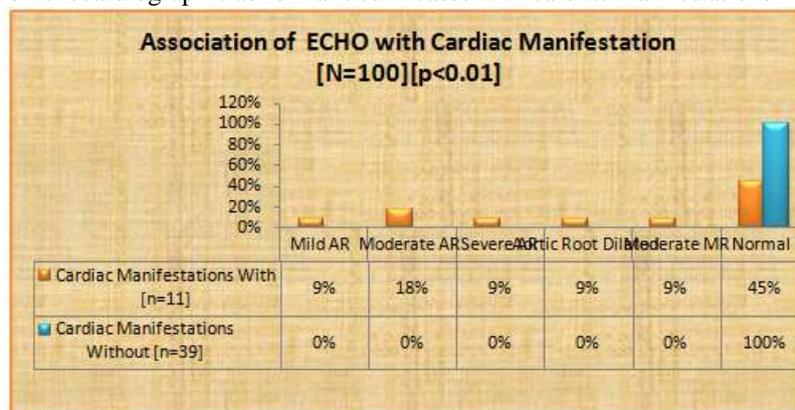


Echocardiographic was found to be abnormal in 6 out of 11 cases (55%) and normal in 5 out of 11 cases (45%) with cardiac manifestations whereas it was abnormal in 1 out of 2 controls with the cardiac manifestations. The association was statistically highly significant (P<0.01).

Table 17: Echocardiographic abnormalities in cases with Cardiac Manifestations

ECHO	Cardiac Manifestations			Sig
	With	Without	Total	
Mild AR	1	0	1	2%
Moderate AR	2	0	2	4%
Severe AR	1	0	1	2%
Aortic Root Dilated	1	0	1	2%
Moderate MR	1	0	1	2%
Normal	5	39	44	88%
<b>Total</b>	<b>11</b>	<b>39</b>	<b>50</b>	<b>100%</b>

Chart 17: Echocardiographic abnormalities in cases with cardiac manifestations



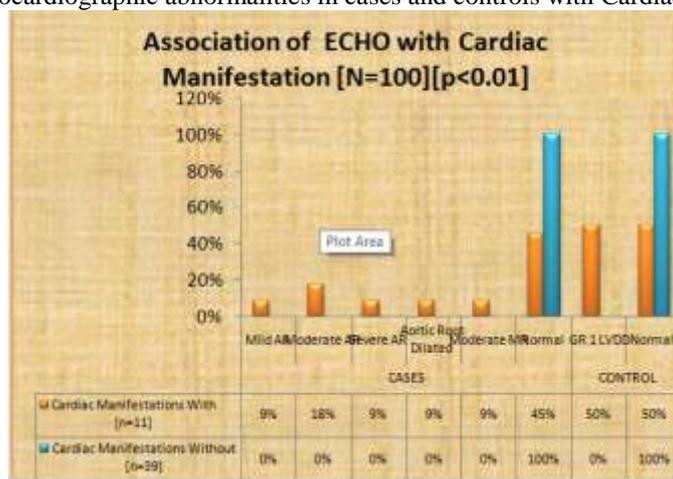
Echocardiographic findings among the cases with cardiac manifestations showed Aortic regurgitation (36%) and Isolated Aortic root dilatation (9%) and Mitral regurgitation (9%). Aortic regurgitation was mild in

9%, moderate in 18%, severe in 9% among the cases with cardiac manifestations. Aortic root dilatation was associated with aortic regurgitation in 2 of the cases.

**Table 18:** Echocardiographic abnormalities in cases and controls with Cardiac Manifestations

STUDYGROUP	Echo	Cardiac Manifestations			Total	(%)	Sig
		With	Without				
CASES	Mild AR	1	0	1	2%		
	Moderate AR	2	0	2	4%		
	Severe AR	1	0	1	2%		
	Aortic Root Dilated	1	0	1	2%	<0.01	
	Moderate MR	1	0	1	2%		
	Normal	5	39	44	88%		
	<b>Total</b>		<b>11</b>	<b>39</b>	<b>50</b>	<b>100%</b>	
CONTROL	GR 1 LVDD	1	0	1	2%		
	Normal	1	48	48	96%	>0.05	
	<b>Total</b>	<b>2</b>	<b>48</b>	<b>50</b>	<b>100%</b>		

**Chart 18:** Echocardiographic abnormalities in cases and controls with Cardiac Manifestations



Various Echocardiographic changes among the cases with cardiac manifestations was compared with that among the controls which was statistically significant. (P<0.05).

**Table 19:** Mean Clinical Variables in cases in relation to cardiac mmanifestations

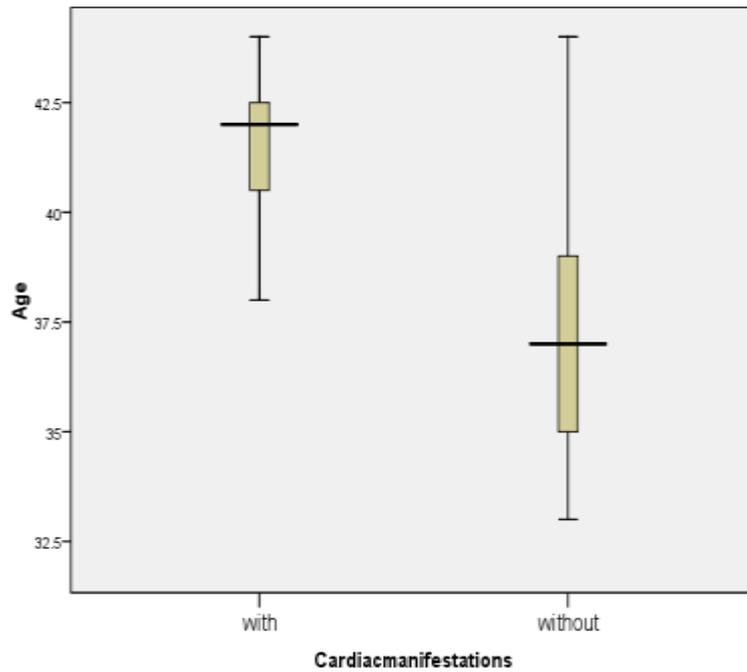
	Cardiac Manifestation	Mean	SD	95% CI for Mean		Minimum	Maximum	Sig
				Lower	Upper			
Age	WITH	41.45	1.695	40.32	42.59	38	44	
	WITHOUT	37.15	2.749	36.26	38.04	33	44	<0.001
	Total	38.1	3.112	37.22	38.98	33	44	
Duration	WITH	8.36	1.502	7.35	9.37	6	11	
	WITHOUT	4.33	1.675	3.79	4.88	1	8	<0.001
	Total	5.22	2.341	4.55	5.89	1	11	
CRP	WITH	13.36	5.784	9.48	17.25	8	28	
	WITHOUT	16.72	6.836	14.5	18.93	5	30	>0.05
	Total	15.98	6.711	14.07	17.89	5	30	

Mean of clinical variables

Age	41+/-1.7		37+/-2.7		<0.001
Duration of Disease	8.4+/-1.5		4.3+/-1.7		<0.001
CRP [mg/dl]	13.4+/-5.8	16.7+/-6.8			>0.05

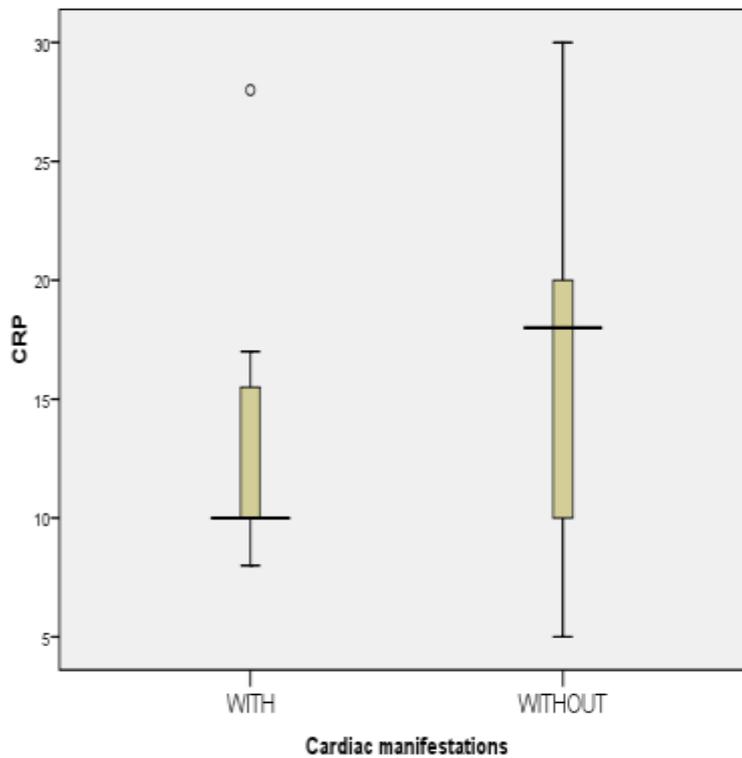
This table shows mean clinical variables – age of the cases, duration of the disease, CRP among the cases with and without cardiac manifestations and their statistical significance. Age and duration of the disease is statistically significant whereas CRP is not significant statistically in relation to cases with and without cardiac manifestations.

**Chart 19:** Mean age in cases with and without cardiac manifestations



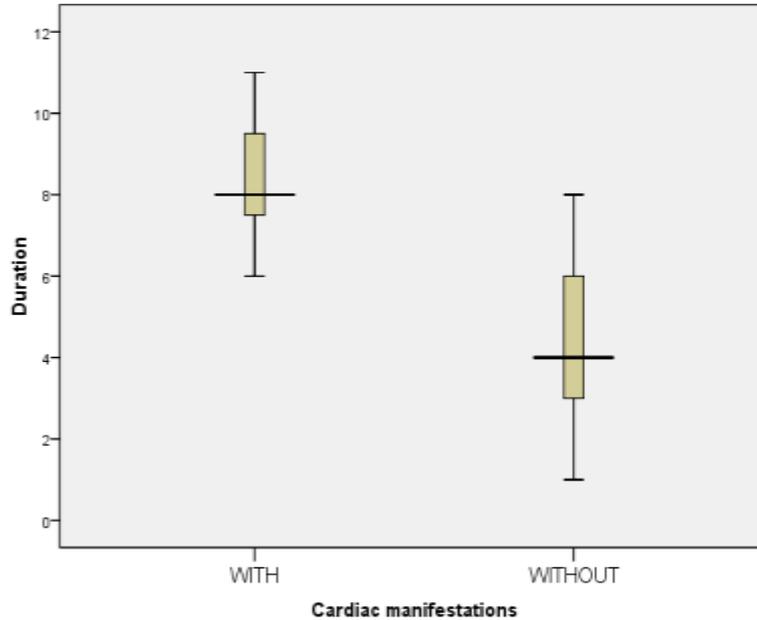
This box plot chart shows that the mean age of the cases with cardiac manifestations is 41.45 with a standard deviation (SD) of 1.695 (40.32 to 42.59) and range from 38 to 44 years and those without cardiac manifestations with mean of 37.15, SD of 2.749 (36.26 to 38.04) and range from 33 to 44 years. This shows statistical significance of  $P < 0.001$ .

**Chart 20:** Mean CRP value in cases with and without cardiac manifestations



This box plot chart shows that the CRP of the cases with cardiac manifestations has a mean value of 13.36 with a standard deviation (SD) of 5.784 (9.48 to 17.25) and range from 8 to 28 mg/dl and those without cardiac manifestations shows a mean of 16.72, SD of 6.836 (14.5 to 18.93) and range from 5 to 30 mg/dl. This association is not statistically significant ( $P>0.05$ ).

**Chart 21:** Mean duration of cases with and without cardiac manifestations



This box plot chart shows that the mean duration of the cases with cardiac manifestations is 8.36 years with a standard deviation (SD) of 1.502 (7.35 to 9.37) and range from 6 to 11 years and those without cardiac manifestations has a mean of 4.33, SD of 1.675(3.79 to 4.88) and range from 1 to 8 years. This shows statistical significance of  $P< 0.05$

**Summary data**

	Cardiac Manifestations		
	With [n=11]	Without [n=39]	
<b>Age</b>			
31- 35	0%	31%	
36 – 40	27%	56%	<0.05
41 -45	73%	13%	
<b>Gender</b>			
Male	82%	77%	
Female	18%	23%	>0.05
<b>Duration of Disease(AS) in years</b>			
0- 3 yrs	0%	31%	
4-6 yrs	9%	62%	<0.001
7-11 yrs	91%	8%	
<b>No.of positive clinical parameters</b>			
2	9%	33%	
3	82%	46%	>0.05
4	9%	21%	
<b>Grading of AS by X Ray imaging</b>			
2 B/L	9%	26%	
3 U/L	36%	44%	
3 B/L	27%	10%	>0.05
4 U/L	18%	18%	
4 B/L	9%	3%	
<b>ECG</b>			
Degree AV Block – 1	18%	0%	
Degree AV Block – 2	9%	0%	
LBBS	9%	0%	<0.01
LVH	27%	0%	
LAFB	9%	0%	
Normal	27%	100%	
<b>ECHO</b>			
Mild AR	9%	0%	
Moderate AR	18%	0%	
Severe AR	9%	0%	
Aortic Root Dilated	9%	0%	<0.05
Moderate MR	9%	0%	
Normal	45%	100%	

Thus when cases with and without cardiac manifestations were compared, a significant statistical correlation was found with Age, Duration of the disease, ECG findings and Echocardiography and not so with Sex, Number of positive clinical parameters present in relation to the disease, Grading of sacroiliitis in AS by X Ray imaging.

**Table 21:** ECG and ECHO abnormalities in cases and controls and their statistical significance

	STUDY GROUP				
	CASES [n=50]	CONTROL [n=50]			
<b>ECG</b>					
Abnormal	16%	2%			
Normal	84%	98%		<0.05	
<b>ECHO</b>					
Abnormal	12%	2%			
Normal	88%	98%		<0.05	

The association is statistically significant when the ECG and Echocardiographic findings are compared among the cases and controls.

### V. Discussion

O’Neill, T. W.et al<sup>1</sup>, (1992) found out that 29% of patients with ankylosing spondylitis were associated with cardiac abnormalities. The abnormalities were found in patients with ten or more than ten years duration. Cardiac abnormalities associated were aortic incompetence, pericardial effusion and conduction disturbances.

Park et al, depending on the disease duration, found out the early valvular involvement in young males with ankylosing Spondylitis using transoesophageal echocardiography. They measured the aortic valve thickness, mitral valve thickness, aortic root diameter.

Etiology of Ankylosing spondylitis is multifactorial, based on endogenous and exogenous causes. Endogenous factors involve the genetic component with increased prevalence of the disease in the population with HLA-B27 gene located in the chromosome 6 with increased familial recurrence.<sup>3</sup> Other genes that encode for the production of pro-inflammatory cytokines, like interleukin1. Exogenous factors involve certain bacterial infections.

The disease involves both axial and peripheral skeleton, though the axial skeleton gets involved at the earliest. Inflammation in the fibrocartilagenous enthesis is a characteristic lesion in Ankylosing spondylitis. This enthesitis is associated with prominent edema of the adjacent bone marrow and is often characterized by erosive lesions that eventually undergo ossification.

Sacroiliitis is often the earliest manifestation of AS. Synovitis, the earliest change will be followed by pannus and subchondral granulation tissue formation. This is followed by fibrocartilage regeneration of eroded joint margins and then by ossification. Enchondral ossification eventually bridging the adjacent vertebral bodies thus giving rise to a “Bamboo Spine”. The pathogenesis is immune-mediated with evidences suggesting more of an autoinflammatory process.

The disease activity is measured by BASDAI (Bath Ankylosing Spondylitis Disease Activity Index). It consists of a scale from 1 to 10, with respect to the increase in the severity of the problems. It consists of 6 questions with 5 major problems.

- Increase in tiredness
- Pain over the spine
- Swelling or pain over the joint
- Extra articular tenderness
- Duration of morning stiffness and
- Severity of morning stiffness.

Modified New York Criteria(1984)

1. Low back pain of atleast 3 months duration that improved by exercise and not relieved by rest
2. Limited lumbar spinal motion in sagittal and frontal planes
3. Chest expansion decreased relative to normal values for that sex and age
4. Bilateral sacroiliitis grade 1-2 or unilateral sacroiliitis grade 3 or 4

Ankylosing spondylitis is definite if criterion 4 and any one of the other criteria is satisfied.

Grading of Sacroiliitis by plain radiographs according to the modified New York Criteria:

- **Grade 0:** Normal
- **Grade 1:** Suspected changes
- **Grade 2:** Small areas with erosions or sclerosis without joint width alteration, minimal abnormality
- **Grade 3:** Advanced sacroiliitis with erosions, widening, sclerosis or partial ankylosis
- **Grade 4:** Total ankylosis

Diagnostic criteria:

- The Assessment of SpondyloArthritis International Society (ASAS) criteria:  
Patient with a >3 month history of back pain and aged <45 years at onset with either
- Sacroiliitis on imaging\* plus atleast one another SpA feature\*\*

Or

- HLA B27 positivity plus atleast two of the SpA features

Sacroiliitis on imaging\*

Active(acute) inflammation on MRI, highly suggestive of sacroiliitis associated with SpA or Definite radiographic sacroiliitis according to modified New York Criteria.

SpA features\*\*

Inflammatory back pain

Arthritis

Enthesitis

Uveitis

Dactylitis

Psoriasis

Crohns disease/colitis

Good response to Non steroidal anti- inflammatory drugs

Family history of SpA

HLA B27 positivity

Elevated C- Reactive protein level

HLA – Human Leukocyte Antigen; SpA – Spondyloarthritis; MRI – Magnetic Resonance Imaging

The characteristics of inflammatory back pain in AS are insidious onset of pain with onset in <40 years of age, which is improved with exercise and not so with rest, morning stiffness>30 minutes and pain more during night with alternating buttock pain.

### **Cardiac Manifestations:**

Cardiac involvement in Ankylosing spondylitis can occur in the form of

- a. aortic valve incompetence, aortitis of the ascending aorta
- b. conduction abnormalities.
- c. Mitral Regurgitation
- d. Myocardial involvement with Left ventricular dysfunction
- e. Cardiomyopathy and Pericarditis can also occur.

### **Conduction Disturbances:**

Inflammation and fibrosis of the membranous portion of the interventricular septum and that affecting the atrioventricular node leads to conduction disturbances<sup>2</sup>. The occurrence of conduction disturbances in patients with AS varies from 1-33%. It can result in any form of heart block. First degree heart block is very common among them. Sometimes patients may require pacemaker implantation in case of a complete heart block. Conduction disturbances increases with increased duration of the disease.

Aortic Regurgitation:

1 – 10% of patients with ankylosing spondylitis will have Aortic insufficiency. Age and duration of the disease increases the incidence of aortic insufficiency<sup>3,4</sup>. Inflammatory process affecting the aortic wall leading to fibrotic thickening and shortened aortic valve cusps and a dilatated aortic root resulting in aortic regurgitation<sup>5,6</sup>.

The aortic insufficiency results in volume overload to the left ventricle with eccentric hypertrophy and dilatation of the chamber. This results in increased end diastolic pressure in the left ventricle and ultimately resulting in heart failure in several years. The patient presents with chest pain and dyspnoea which often leads to Aortic valve replacement as the effective therapy<sup>7</sup>. The occurrence of mitral regurgitation, myocardial involvement with left ventricular dysfunction, cardiomyopathy and pericarditis in ankylosing spondylitis is rare.

In our study, the cases satisfying the ASAS criteria for Ankylosing spondylitis were selected and evaluated for cardiac manifestations with electrocardiography and echocardiography.

In this study cardiac abnormalities were seen in 11(22%) patients with ankylosing spondylitis. Among them cardiac conduction abnormalities were seen in 5 (10%), aortic regurgitation in 4(8%), Isolated aortic root dilatation in 1(2%), mitral regurgitation in 1(2%). Cardiac conduction abnormalities seen were first degree heart block (4%), second degree heart block (2%), left anterior fascicular block(2%), left bundle branch block(2%). Aortic regurgitation was mild in 2%, moderate in 4%, severe in 2%. 4% of AR were associated with aortic root dilatation.

Age and sex distribution:

The mean age of patients with ankylosing spondylitis was 38.1 years and that of the controls was 38.3 years. The age of the patients in the study group ranged from 31 – 45 years.

The maximum prevalence of cardiac manifestations was between 41 – 45 years among the cases. Mean age of cases with cardiac manifestations was 41.45 years. Association of age of the cases with and without cardiac manifestations is statistically significant ( $P<0.05$ )

The study has 50 cases and 50 controls among which 39 are male cases and 11 are female cases and 35 are male controls with 15 of female controls. The male to female ratio in the cases was 3.5:1, in which cardiac manifestations occurred in 9 male cases and 2 female cases. Cardiac abnormalities occurred in 2 male controls.

S.Sukenik et al<sup>8</sup>, made a study with 40 patients with a mean age of the cases being 44.6 years, with 37 male cases and 3 female cases. The mean age of these patients was slightly higher than in our study.

Duration of Ankylosing Spondylitis:

In this study there were significantly higher prevalence of cardiac involvement in patients with increased duration of ankylosing spondylitis. The duration of the disease in the cases varied from 1 – 11 years. Higher prevalence of cardiac manifestations occurred between the duration of 7 – 11 years(91%). The mean duration of disease in patients with cardiovascular manifestations was 8.36 years. This had statistically significant correlation when compared with patients with and without cardiac manifestations ( $P<0.001$ ).

O,Neill.T.W.et al<sup>1</sup>, conducted study in twenty four patients with a disease duration of more than or equal to ten years and found cardiac abnormalities in 29% of the cases.

Roldan et al<sup>9</sup>, conducted a study on cardiovascular manifestations in cases suffering from ankylosing spondylitis and found that the association was increased with increased duration of the disease.

Number of positive clinical parameters, severity of ankylosing spondylitis by X Ray grading, C-Reactive protein, all these parameters had no significant correlation with the occurrence of cardiac manifestations in patients with ankylosing spondylitis ( $P>0.05$ )

Roldan et al<sup>9</sup>, in the study had described that cardiac manifestations in patients with ankylosing spondylitis was unrelated to the disease activity, severity.

Electrocardiogram:

In the study, 16% of the cases had electrocardiographic changes among which 10% had conduction abnormalities in the form of first degree heart block, second degree heart block, left bundle branch block and left anterior fascicular block. 6% of the cases had left ventricular hypertrophy according to Romhilt Estes criteria. 2% of the controls had left anterior fascicular block. The association of electrocardiographic manifestations in the cases with and without cardiac manifestations was statistically significant ( $P<0.01$ ) and also that between the cases and controls ( $P<0.05$ )

Helena Forsblad-d'Elia et al<sup>10</sup>, in the study found that 10-33% of patients with ankylosing spondylitis had conduction disturbances, mostly of first degree atrioventricular block, complete bundle branch blocks.

S.Sukenik et al<sup>8</sup>, in the study conducted in forty patients found out that eight patients(20%), had conduction disturbances in the form of atrioventricular block and bundle branch block.

O,Neill et al<sup>1</sup>, in the study conducted in twenty four patients with ankylosing spondylitis found that significant 10% of the cases had conduction abnormalities.

Echocardiogram:

In the study 12% of the cases were with echocardiographic abnormalities among which 8% of the patients had aortic regurgitation, 2% had mitral regurgitation, 2% had isolated aortic root dilatation and 4% was associated with aortic regurgitation. This had statistically significant association in the cases with and without cardiac manifestations( $P<0.05$ ) and that between the cases and the controls( $P<0.05$ ).

O,Neill T.W. et al<sup>1</sup>, in the study of twenty four patients found that two patients had aortic regurgitation(8%).

Several studies had found the prevalence of aortic regurgitation to be high in patients with ankylosing spondylitis when the patients are subjected to trans oesophageal echocardiography rather than transthoracic echocardiography and also early valvular changes have been found with transoesophageal echocardiography, as done by Roldan et al<sup>9</sup>.

The prevalence of cardiovascular abnormalities in the present study would have been higher if transesophageal echocardiography has been done and if the duration of ankylosing spondylitis in the cases had been longer.

## VI. Conclusion

- Cardiovascular manifestations in ankylosing spondylitis were seen in 11 out of 50 cases. Maximum prevalence occurred in the age group of 41-45 years with a male to female ratio of 3.5:1. Mean age of the cases with cardiovascular abnormalities was found to be 41.45 years.
- Duration of ankylosing spondylitis among the cases in the study group varied between 1 – 11 years. The maximum prevalence of Cardiovascular manifestations in AS occurred in patients with increased duration of the disease. Mean duration of the disease associated with cardiovascular manifestations was found to be 8.36 years.
- No significant correlation was found in association with sex, increased number of positive clinical parameters to the occurrence of cardiovascular manifestations in ankylosing spondylitis.
- Increase in C-Reactive protein, grading of sacroiliitis by X Ray, cardiac symptoms in AS, Chest X Ray also were not found to be significantly associated with the cardiovascular manifestations.
- Three patients had cardiomegaly (6%) in the chest X Ray and those patients had cardiac symptoms like chest pain and breathlessness.
- The electrocardiogram revealed significant cardiac conduction abnormalities (10%) and left ventricular hypertrophy(6%) among the cases. Conduction abnormalities were first degree AV block (4%), second degree AV block(2%), left anterior fascicular block(2%), left bundle branch block (2%) whereas only 2% of control subjects had conduction abnormalities in ECG, left anterior fascicular block.
- The echocardiographic abnormalities were found in 12% of the cases which had significant association in patients with AS. Most common abnormality found among AS patients were aortic regurgitation (8%) [Mild – 2%, Moderate – 4%, severe – 2%]. One case had moderate mitral regurgitation (2%) and one another had aortic root dilatation(2%) with 4% aortic regurgitation associated with aortic root dilatation.
- Statistically significant association of the cardiovascular manifestations occurred with increase in the age, duration of the disease.
- The conduction disturbances in electrocardiography and valvular lesions and aortic root dilatation in echocardiography among the cases were statistically significant when compared with the controls.
- Since cardiovascular abnormalities are one of the most common cause of mortality in patients with ankylosing spondylitis, these should be detected early and thereby it will assess in the proper management of the patients with the disease at the appropriate time.
- Therefore it is mandatory that every patient with ankylosing spondylitis should undergo cardiac evaluation to help in early detection and treatment of cardiovascular abnormalities, to reduce the morbidity and mortality associated with the disease and to improve the quality of life of patients with ankylosing spondylitis.

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