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Original Research Article

A cross-sectional study to assess correlation of electrocardiographic abnormalities and echocardiographic findings in rheumatoid arthritis patients in Western Rajasthan

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Abstract

Background: Rheumatoid arthritis (RA) is a chronic multi system disease of unknown cause. The most frequent site of cardiac involvement in RA is the pericardium. Cardiac disease is clinically silent and is rarely a life-threatening complication in RA. Cardiac failure is the result of either systolic or diastolic dysfunction, or both. Hence this study was conducted to study correlation of electrocardiographic abnormalities and echocardiographic findings in rheumatoid arthritis patients without clinically evident cardiovascular manifestations with the duration of disease.
Methodology: The Hospital based cross sectional observational study was conducted on 50 patients, above 20 years attending the medicine outpatient department of Dr. S.N. Medical College and Mathura Das Mathur Hospital Jodhpur with an established diagnosis of RA, as defined by the ACR/EULAR criteria for Rheumatoid arthritis. A questionnaire was prepared and investigations were performed.
Results: Cardiovascular manifestations are common in Rheumatoid arthritis patients. This study highlights the need for systematic electrocardiogram in patients with rheumatoid arthritis, even in the early stages of the disease when cardiovascular involvement is clinically silent because electrocardiographic abnormalities are real and should alarm the physician and lead to the initiation of appropriate therapy that may help reduce the incidence of cardiovascular death in RA patients. The relation between transmitral flow alteration and disease duration suggests a sub-clinical myocardial involvement with disease progression and may be related to the high incidence of cardiovascular deaths in patients with RA.

Keywords: rheumatoid arthritis, ECG abnormalities, echo findings

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Introduction

Rheumatoid arthritis (RA) is the most common inflammatory arthritis and hence an important cause of potentially presenting disability. RA affects ~0.5-1% of the adult population worldwide. The prevalence of RA in India (0.75%) is quite similar to that reported from the developed countries [3].

Rheumatoid arthritis is a chronic multi system disease of unknown cause. Although there are a variety of systemic manifestations, the characteristic feature of Rheumatoid arthritis is a persistent inflammatory synovitis, usually involving peripheral joints in a symmetric distribution. Extraarticular manifestations may develop during the clinical course of RA in up to 40% of patients, even prior to the onset of arthritis. Recent studies have shown a decrease in the incidence and severity of at least some extraarticular manifestations, particularly Felty's syndrome and vasculitis [2]. The most frequent site of cardiac involvement in RA is the pericardium. However, clinical manifestations of pericarditis occur in <10% of patients with RA despite the fact that pericardial involvement is detectable in nearly one-half of cases by echocardiogram or autopsy studies. Cardiomyopathy, another clinically important manifestation of RA, may result from necrotizing or granulomatous myocarditis, coronary artery disease or diastolic dysfunction. This involvement too may be subclinical and only identified by echocardiography or cardiac magnetic resonance imaging (MRI). Rarely, the heart muscle may contain rheumatoid nodules or be infiltrated with amyloid. Mitral regurgitation is the most common valvular abnormality in RA, occurring at a higher frequency than the general population [3, 4, 5]. However, cardiac disease is clinically silent and is rarely a life-threatening complication in RA. Cardiac failure is the result of either systolic or diastolic dysfunction, or both. Left ventricular diastolic dysfunction is usually attributable to common structural abnormalities such as hypertrophy or interstitial fibrosis and impaired myocyte relaxation resulting from ischemia [6].

Material and Methods: The Hospital based observational study was conducted in Department of Medicine, Mathura Das Mathur Hospital Dr. S.N. Medical College, Jodhpur. This hospital caters all section of societies of Western Rajasthan and thus sample drawn from this hospital can be considered true representation of Western Rajasthan.

Study design: Cross sectional study.

Study subjects: The current study was performed in selected patients attending outdoor and indoor of Department of Medicine M.D.M. Hospital, Dr. S.N. Medical College, Jodhpur. Case selection was based on patients in attending outdoor and indoor of medicine department with history of rheumatoid arthritis as per ACR/EULAR Criteria.

Inclusion criteria

Patients aged above 20 years attending the medicine outpatient department of Dr. S.N. Medical College and Mathura Das Mathur Hospital Jodhpur with an established diagnosis of RA, as defined by the ACR/EULAR criteria for Rheumatoid arthritis. The duration of disease should be more than 2 years.

Exclusion criteria

1) Patients with history of cardiac disease, hypertension, diabetes mellitus, chronic obstructive pulmonary disease, interstitial lung disease diagnosed in the past (not as a systemic complication of rheumatoid arthritis), pulmonary tuberculosis or pulmonary

thromboembolism as assessed by history and physical examination. Patients with moderate mitral regurgitation, mitral stenosis or a left ventricular ejection fraction below 64% was considered to have a cardiac cause for their PASP and so was excluded.

2) In view of the radiation exposure involved in the study, patients excluded if they was pregnant.
3) Patients of juvenile rheumatoid arthritis.

Data collection

A questionnaire was prepared noting the duration of RA, extra-articular complications, the use of current and previous disease-modifying drugs, corticosteroid use, and early morning joint stiffness. Questions was asked relating to previous chest disease, cough, dyspnea, sputum production, chest pain, weight loss and risk factors for respiratory disease, including smoking, medications, domestic pets and occupation. Cigarette consumption was evaluated in pack years (1 pack yr = 20 cigarettes/day for 1 yr). A detailed clinical examination was performed.

Investigations

Patients were subjected to following investigations.

- Complete Blood Count (Sysmex 5-part differential hematology analyzer).
- C-reactive protein, ESR.
- Blood Urea, Serum Creatinine, Serum Uric Acid (By RemiR 80 machine).
- SGOT, SGPT, Serum Total Bilurubin, Serum Albumin, Serum Globulin, Prothrombin Time (By RemiR 80 machine).
- RA factor.
- Anti CCP antibodies.
- Chest x ray.
- Electrocardiogram (Cp200/BPL/Scheler Machine available in MDM hospital).
- Echocardiograph (VIVID 3, General Electric).

Sample size calculation

Sample size was calculated at 95% confidence interval to verify an expected 88% prevalence of positive findings such as pulmonary hypertension, cor pulmonale left ventricular diastolic dysfunction (as per reference article) at absolute allowable error of 10%. Sample size was calculated using the formula for sample size for estimation of proportion-

$$N = \frac{Z_{\alpha/2}{}^2 P(1-P)}{E^2}$$

$$\frac{1.96x1.96x88/100x12/100}{10/100x10/100}$$

Where,

$Z_{\alpha/2}$ = Standard normal deviate for 95% confidence interval (taken as 1.96)

P = Expected prevalence of positive findings such as pulmonary hypertension, cor pulmonale left ventricular diastolic dysfunction (88% as per reference article).

E = Allowable error (taken as absolute 10%).

Sample size was calculated to be to be minimum 41 subjects. For study purpose sample size was enhanced and rounded off to 50 subjects.

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Statistical analysis

Continuous data were described as mean and standard deviation (mean +/- SD) and categorical variables as numbers. To analyze categorical data we performed the chi square test. Pearson correlation was used to correlate the continuous variables like disease duration and pulmonary artery pressure and parameters diastolic dysfunction.

Observations and Results

Table 1: Age and gender wise distribution of study population

Age (in years)	Number	Percentage	Male	Female
20 - 30	14	28.00	04 (40.0%)	10 (25.0%)
31 - 40	22	44.00	03 (30.0%)	19 (47.50%)
41 - 50	14	28.00	03 (30%)	11 (27.50%)
Total	50	100%	10 (20.0%)	40 (80.0%)
Mean age (in years)	35.50±6.67		34.70±6.49	35.70±6.77

The main demographic, clinical and laboratory features of the 50 patients with RA without clinical evidence of cardiovascular disease are shown in Table 1. Women outnumbered men. The mean age at the time of diagnosis was 35.50 + 6.67 years. During the course of the disease, extra-articular manifestations were observed in almost 58% (29) of the patients. Rheumatoid nodules were found in 10 patients, all of whom were rheumatoid factor positive.

Table 2: Duration of disease in Rheumatoid arthritis patients

Duration (in years)	Number	Percentage
2 - 5	31	62.00
5 - 10	13	26.00
>10	06	12.00
Total	50	100%
Mean duration of disease (in years)	5.58±3.63	

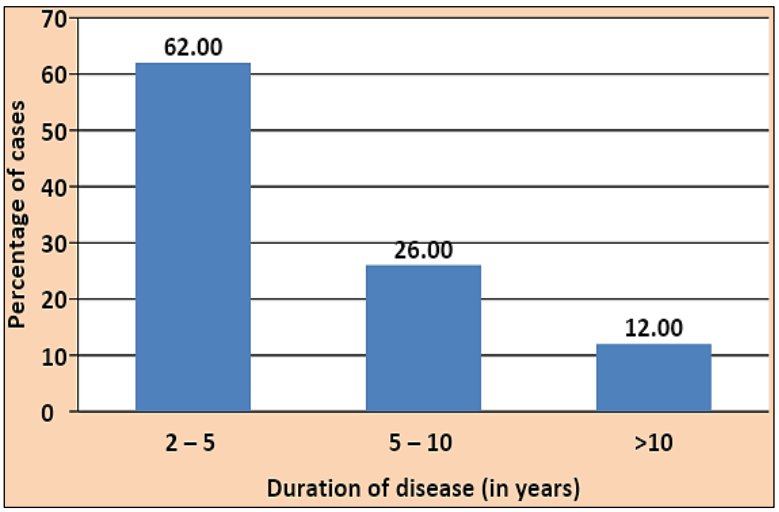

Fig 1: Duration of disease in Rheumatoid arthritis patients

Distribution of patients according to duration of disease showed that mean duration of RA was 5.58±3.63 yrs. Majority of patients i.e. 62% had RA since 2-5 years, followed by 26% patients who had disease since 5-10 years, while only 12% patients had disease since >10 years.

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Table 3: EGC Findings in study population of RA cases

ECG Findings		Number	Range
Heart Rate		81.38±14.20	56.00-112.00
PR Interval		154.34±25.61	100.0-240.0
(LVH)Left Ventricular Hypertrophy		18 (36.0%)	
QRS Duration		86.16±20.75	49.0-156.0
QT Interval		401.20±31.85	346.0-500.0
Complete or incomplete RBBB		03 (6.0%)	
Complete or incomplete LBBB		02 (4.0%)	
Presence of atrial premature beat (APC)		04 (8.0%)	
Ventricular premature complexes [VPC]		06 (12.0%)	
AVB: Atrioventricular block			
1. First degree		2(4%)	
2. Second degree		0	
3. Third degree		0	
Myocardic ischemia ST-T changes		16(32%)	
Anomaly of heart's axis	Right	2(4%)	
	Left	14(28%)	

Fifty patients with asymptomatic cardiovascular RA, meeting the definition of ACR criteria 1987 were enrolled. Main electrocardiographic data are reported in Table 10. There is a significant number of left ventricular hypertrophy in 18 patients (36%) and myocardial ischemia 16 patients (32% ST-T Changes). From the analysis, it appeared that the existence of these abnormalities was correlated with age. Left axis deviation was found in 8 patients (16%). RBBB found in 3patients (6%) LBBB in 2 patients (4%) there is also present of APC (Atrial premature beat) in 4 patients (8%), ventricular premature complex in 6 patients (12%), first degree block in 2 patients (4%).

Table 4: Structural abnormalities found on Echocardiography of patients with RA

Finding on Echocardiogram	Number	Percentage
Aortic stenosis	03	6.00
Aortic regurgitation	07	14.00
Mitral regurgitation	13	26.00
Pericardial effusion	02	4.00
Tricuspid regurgitation	36	72.00
Aortic root dilatation	12	24.00
Multiple valvular involvement	13	26.00

We found Structural abnormalities found on Echocardiography of patients with RA 36 patients (72.0%) tricuspid regurgitation, mitral regurgitations 13patients 26%), aortic regurgitation 7 patient (14%), aortic root dilatation 12 patients (24%), aortic stenosis 3 patients (6%) and pericardial effusion 2 patients (4%) Tricuspid regurgitation visible for their pulmonary artery pressure to be assessed by Doppler echocardiography. There was also found multivalvular abnormalities in () patients, only 2 patient with RA had mild pericardial effusion. The structural findings in for the RA patients are listed in table 4.

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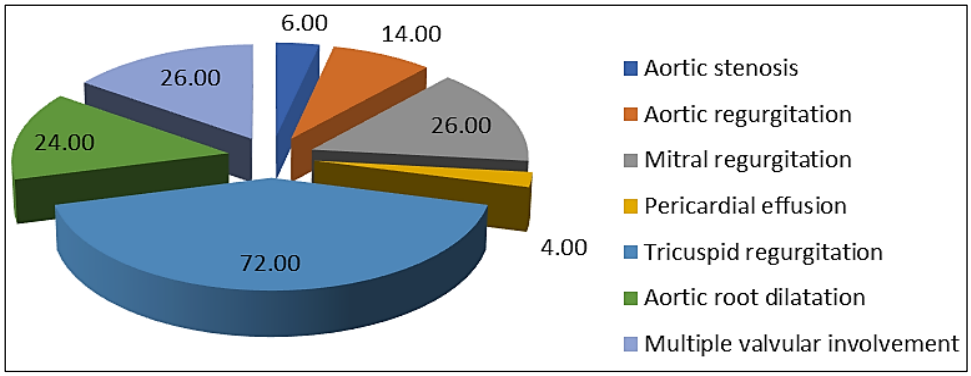

Fig 2: Structural findings found on echocardiography

Table 5: Echocardiogram and Doppler Variables in Patients in Study Population

ECHO Findings	Mean ± SD	Median	Range
Left Atrium Diameter (mm)	27.78±2.17	28.00	21-32
Aorta Diameter (mm)	30.20±1.34	30.00	26-33
Left Ventricular end diastolic dimension (mm)	46.99±2.01	47.00	43.2-51.2
Left Ventricular end systolic Dimension (mm)	29.88±2.61	29.40	24.2-39.4
Ejection Fraction (%)	66.16±2.32	69.00	60-75
Fractional Shortening (%)	39.08±1.71	39.50	33.3-42.7
Early Diastolic flow velocity E (cm/s)	76.50±7.21	78.80	60.2-90.7
Late Diastolic flow velocity A (cm/s)	71.07±6.72	70.10	60.1-87.8
E/A	1.08±0.16	1.09	0.75-1.46
Isovolumic Relaxation Time (ms)	74.28±6.50	70.65	65.6-88.8
Pulmonary Artery Pressure (mmHg)	28.42±12.80	28.00	20-52

Echocardiographic and Doppler finding in patients with RA

The echocardiographic and Doppler findings in this series of patients with RA without clinical evidence of cardiovascular disease are summarized in Table 5. The mean values of diameters in the left cavities were within the normal ranges. Similarly, it was normal for the mean left ventricular ejection fraction (Table 5).

Nodules were present in the aortic valve in 5 patients (10%). Mild aortic regurgitation was found in 7 (14%) of 50 patients (Table 4). 13 (26.0%) of the patients exhibited left ventricular diastolic dysfunction (E/A <1) due to impaired relaxation

In Echo findings left atrium diameter mean 27.78 mm(SD2.17), Aorta diameter mean 30.20mm (SD1.34), Left ventricular end diastolic dimension mean 46.mm (SD2.01), Left ventricular end systolic dimension mean 29.88mm (SD2.61), Ejection fraction % mean 66.16 (SD2.32), Fractional shortening % mean 39.08 (SD1.71), Early diastolic flow velocity E(cm/s) mean 76.50 (SD7.21), Late diastolic flow velocity A(cm/s) mean 71.07 (SD6.72), E/A 1.08 (SD0.16), Isovolumic relaxation time mean 74.28 msec (SD6.50), Pulmonary artery pressure mean 28.42mmHg (SD12.80).

Table 6: Echocardiographic and doppler variables in patients

ECHO Findings	E/A [<1] (n=13)	E/A [>1] (n=37)	t value	P value
Left Atrium Diameter (mm)	27.30±2.75	27.94±1.95	0.907	0.368
Aorta Diameter (mm)	30.30±1.88	30.16±1.11	0.333	0.740
Left Ventricular end diastolic dimension (mm)	47.96±1.84	46.64±1.98	2.101	0.040
Left Ventricular end systolic Dimension (mm)	31.90±2.32	29.12±2.32	3.702	0.0006
Ejection Fraction (%)	68.76±2.20	69.29±2.37	0.701	0.486

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Fractional Shortening (%)	38.03±2.01	39.45±1.45	0.275	0.008
Early Diastolic flow velocity E (cm/s)	68.83±6.94	79.08±5.12	5.609	<0.0001
Late Diastolic flow velocity A (cm/s)	78.80±4.71	68.36±5.00	6.556	<0.0001
E/A	0.86±0.07	1.16±0.10	9.321	<0.0001
Isovolumic Relaxation Time (ms)	79.52±5.07	72.44±5.97	3.810	0.0004
Pulmonary Artery Pressure (mmHg)	34.53±14.07	26.27±11.78	2.068	0.040
RF (Present)	0.87±0.07	1.13±0.10	7.801	<0.0001
RF (Absent)	0.78±0.00	1.18±0.10	--	NA

Echocardiographic differences between patients with ra with left ventricular diastolic dysfunction (E/A<1), without left ventricular diastolic dysfunction (E/A>1)

To further investigate the implication of the left ventricular diastolic dysfunction in patients with RA without clinically evident cardiovascular disease, we assessed whether patients with RA who had left ventricular diastolic dysfunction had some clinical or investigational peculiarities that might help identify these patients.

Rheumatoid factor was positive in patients with RA with left ventricular diastolic dysfunction (87.0% versus 1.1%; P<0.0001). However, no statistically significant differences in sex, presence of extra articular manifestations, cumulative prednisone dose were found. Also, there was a significant difference in the estimated pulmonary artery systolic pressure between patients with and without left ventricular diastolic dysfunction (34.53+ /-14.07 vs. 26.27+/-11.78 p=0.04).

Table 7: Correlation between duration of disease with echo findings

Variables	r value	p value
E/A	0.45	0.0001
Intraventricular relaxation time	0.55	<0.0001
Mitral filling velocity (cm/s)	0.52	<0.0001
PAP (mmHg)	0.71	<0.0001

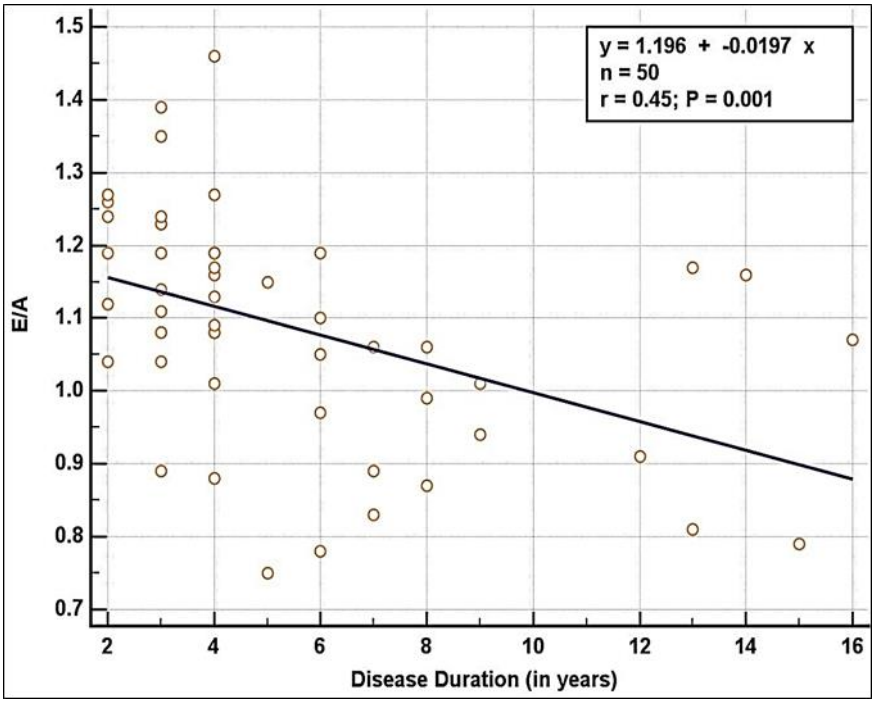

Fig 3: Correlation between E/A and disease duration of RA cases in study population

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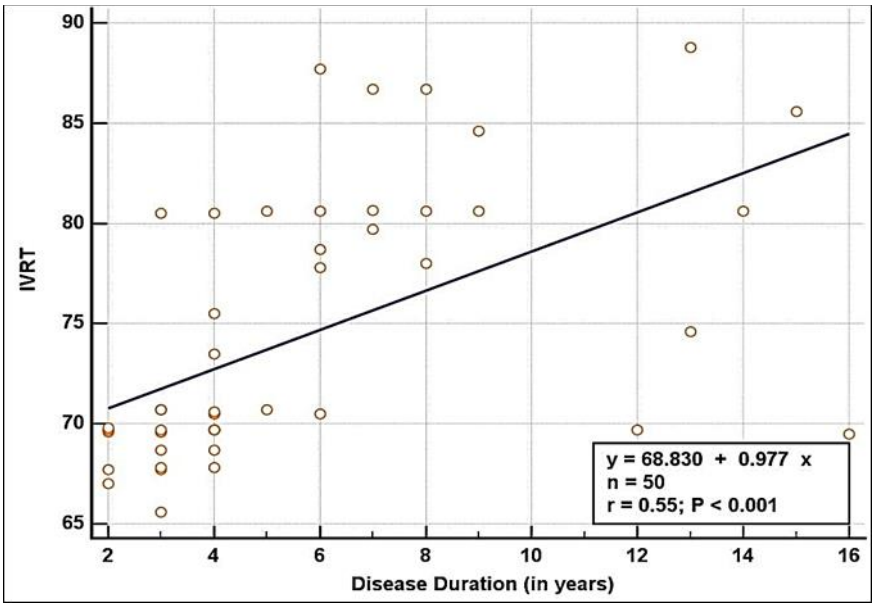

Fig 4: Correlation between intraventricular relaxation time [IVRT] and disease duration

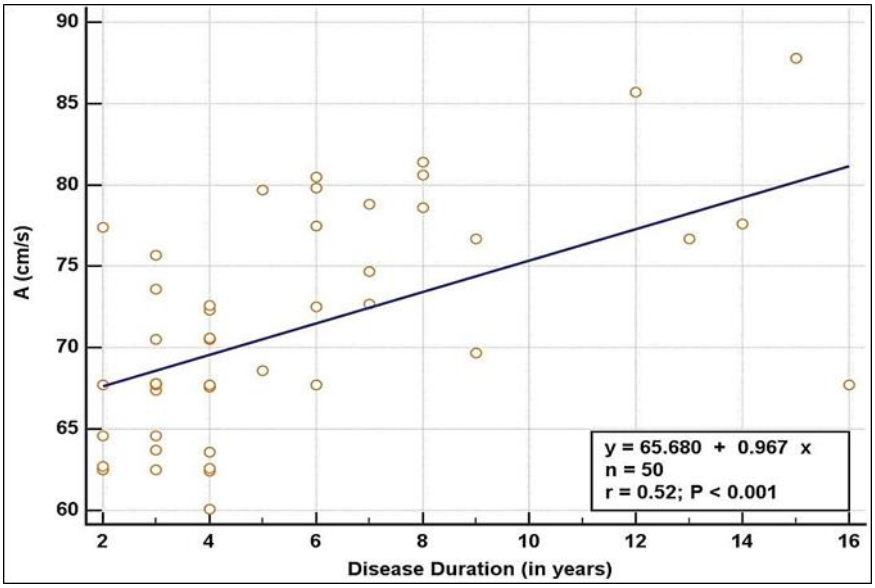

Fig 5: Correlation between mitral filling velocity (A) and disease duration

Discussion

The clinical importance of cardiovascular risk [7] and the value of routine electrocardiography in RA [8] and different electrocardiographic abnormalities have been observed. In our study, the electrocardiographic parameters are dominated by left ventricular hypertrophy (36%), where nearly one in three patients presented with this finding. The explanation could be related to the natural history of arthritis which is considered our day as a cardiovascular risk factor [9] but mainly from the combination of other co morbidities including diabetes, hypertension and age [10]. The disorder association of the minor conduction (1st degree AV block 4%) is encountered in our study, as pointed out by Goulenok [8].

Inflammation in the disease results in myocardial hyper-excitability our study APCs are found in 8% and VPCs were present in 12% of the patients and in turn causes premature beats to occur. In the study conducted by Dodo-Siddo *et al.* [13], APCs were present in 2.74% and VPCs were found in 8.45%. These results were almost synchronous with those present in our study. Similarly Seferovic [11], in a study of arrhythmias and conduction disorders in

rheumatic autoimmune diseases origins, noted that the presence of these abnormalities were more frequent in patients with active RA. In our study LBBB was present in 4% whereas RBBB was observed in 6% of the patients which is comparable to 2.75% LBBB and 4.11% found in the study of Villeco [12] in the series, found a different result with a high frequency of branch block particular rights (35%). This type of anomaly is a common phenomenon in rheumatoid arthritis and may be due to infiltration of the conduction tissue induced by the inflammatory process.

The average length of measured QT intervals in RF positive and RF negative patients respectively were 404.90+/-31.83ms and 395.15+/-31.80ms. The QT interval of 403.20 ± 3.66ms was found in study by Dodo-Siddo *et al*. [13] The calculated QT interval was normal in 72% of cases in our study. The prevalence of QTc interval was 28.77% were those of the negative T wave (32%), different from that observed by Barry (14.3%) [14]. In the French study on the value of routine electrocardiography in the detection of cardiac involvement in rheumatoid arthritis, abnormalities most frequently found repolarization were also negative T waves (21%) [7]. Myocardial ischemia related ST-T changes were present in 32% of the patients in our study which is similar to study by Dudo-Siddo *et al*. [13]. where 36.98% patients had ST-T changes.

In our study of patients with RA from Western Rajasthan, India without cardiovascular risk factors or clinically evident cardiac disease, a significant number of electro- and echo-cardiographic abnormalities were observed. Besides valvular involvement left ventricular diastolic dysfunction was found in 13 (26%) patients. Diastolic dysfunction is defined as the deterioration of the ventricular filling capacity without any compensatory increase in the left atrial pressure [13]. Another definition is the abnormal ventricular filling defect causing cardiac output inadequacy [14]. In a study of Egypt by Ghaleb *et al*. [15]. Left ventricular diastolic dysfunction was found in 28 (37.3%) of 75 RA patients whereas in the present study it was 13 (26%), thus both the studies can be considered comparable.

Thus, our results confirm diastolic abnormalities in RA patients and also point out that these abnormalities also concern left ventricular filling detected by echo Doppler examination of transmitral flow. In our study, we found a statistically significant correlation between disease duration and alteration of diastolic function expressed as late diastolic mitral filling velocity (A) and isovolumic relaxation time (IVRT). The relation between transmitral flow alteration and disease duration suggests a sub-clinical myocardial involvement with disease progression. This observation could be of a therapeutic benefit in sensitizing the doctors about the benefits of controlling the disease progression and periodic screening by echocardiography of RA patients. In Selçuk Coskon *et al*. study, that is similar to our study in terms of type of study, of the 100 patients, 67 subjects had disorders in echocardiography including pericardial involvement in 15%, diastolic dysfunction in 57%, mitral valve involvement in 24%, and aortic valve involvement in 7% of subjects [15].

In present study, of the 50 patients, 38 subjects had disorders in echocardiography including pericardial involvement in 4%, diastolic dysfunction in 26%, mitral valve involvement in 26%, and aortic valve involvement in 20% of subjects. In a study by Guedes *et al*., Mitral regurgitation (MR) was evidenced in 24 cases (80%). Aortic regurgitation was found in 10 cases (33%), seven cases (23%) had tricuspid valve abnormalities. Pericarditis was found in 4 cases (13%) [15].

In present study, Mitral regurgitation (MR) was evidenced in 13 cases (26%). Aortic regurgitation was found in 7 cases (14%), thirty-six cases (72%) had tricuspid valve abnormalities. Pericardial effusion was found in 2 cases (4%). The above comparison shows similarity between these and the present study.

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Conclusion

The aim of study was find out cardiovascular system involvement by electrocardiography and echocardiography in rheumatoid arthritis patients and its relation with disease duration. We studied 50 cases of age between group 20-50 years were known case of rheumatoid arthritis according to ACR/EULAR criteria. 40 female and 10 male whose disease duration more than 2 years. The mean age at the time of diagnosis was 35.50±6.67 years. Mean duration of disease 5.58±3.63 years. We found in 36 patients out of 50 cardiovascular abnormalities by electrocardiography and echocardiography.

Out of them significant electrocardiographic finding was 18 (36%) patients had left ventricular hypertrophy and 16(32%) had ST-T changes showing myocardiac ischemia.

In echocardiographic finding 36 (72%) patients found to have tricuspid regurgitation and multivalvular involvement was seen in 13 (26%) patients.

In echocardiography we found left ventricular diastolic dysfunction in 13(26%) patients. Significant correlation found between left ventricular diastolic dysfunction, intraventricular relaxation time and mitral filling velocity (cm/s) with duration of disease.

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