ISSN: 2581 – 3633
PubMed - National Library of Medicine - ID: 101745081

International Journal of Medical Science and Advanced Clinical Research (IJMACR)

Available Online at:www.ijmacr.com

Volume – 6, Issue – 3, June - 2023, Page No. : 300 - 310

Study of cardiac valvular manifestations in patients with rheumatoid arthritis

[1]Dr. Abhay, Junior Resident, Department of Medicine, Patna Medical College and Hospital, Patna.

[2]Dr. Prof. Kaushal Kishore, Professor and Head, Department of Medicine, Patna Medical College and Hospital, Patna.

[3]Dr. Abhay Kumar Sinha, Associate Professor and Head, Department of Geriatrics, Patna Medical College and Hospital, Patna.

[4]Dr. Devendra Kumar Sinha, Associate Professor and Head, Department of Medicine, Patna Medical College and Hospital, Patna.

[5]Dr. Rahul Shekhar, Senior Resident, Department of Medicine, Patna Medical College and Hospital, Patna.

[6]Dr. Amit Kumar Tiwari, Senior Resident, Department of Medicine, Patna Medical College and Hospital, Patna.

Corresponding Author: Dr. Abhay, Junior Resident, Department of Medicine, Patna Medical College and Hospital, Patna.

How to citation this article: Dr. Abhay, Dr. Prof. Kaushal Kishore, Dr. Abhay Kumar Sinha, Dr. Devendra Kumar Sinha, Dr. Rahul Shekhar, Dr. Amit Kumar Tiwari, "Study of cardiac valvular manifestations in patients with rheumatoid arthritis", IJMACR- June - 2023, Volume – 6, Issue - 3, P. No. 300 – 310.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Introduction: Rheumatoid arthritis is a chronic systemic disease of unknown etiology. It is characterized by peripheral symmetrical polyarthritis. It has a progressive course with exacerbations and remissions being part of its natural history. Its onset could be at any age, although it usually starts in the fourth decade of life. Overall, there is a 3:1 female preponderance, but this excess is greater in young people and the age-related incidence is approximately equal in elderly people.[1]

Aims: To document the incidence of cardiac valvular involvement in patients suffering from rheumatoid arthritis

Materials and method: The study was performed on rheumatoid arthritis patients attending OPD in PMCH, Patna Bihar. A total of 30 rheumatoid arthritis patients were enrolled and were compared with 15 age and sex matched control subjects.

This is a cross-sectional observational study. The study was done in Department of Medicine at PMCH, Patna. This study was conducted from April 2021 to November 2022.

Result: Structural findings on echocardiography of RA patients revealed mitral regurgitation in 4 patients, Aortic regurgitation in 1 patient, Aortic + Mitral regurgitation, pericardial effusion in 2 patients, peri

cardial thickening in one patient, tricuspid regur gitation and pulmonary hypertension in one, and left ventricular diastolic dysfunction in 5 patients. In the control group echocardiographic normal in all patients.

Conclusion: Cardiac manifestations were seen in 15 patients (50%), 7 patients with cardiac valve abnormality, 5 patients with diastolic dysfunction, 3 patients with pericardial involvement, out of 30 cases studied the maximum incidence of the disease was seen in the 30-50 years age group and the male to female ratio was 1:3.8.

The mean duration of the disease was found to be 4.32 years in the entire study group and 6.93 years in patients presenting with cardiac valve abnormalities.

There was positive correlation of patients with cardiac abnormalities to tender joint counts, and mean duration of disease. However, there was no significant correlation between cardiac abnormalities and swollen joint counts, subcutaneous nodules, ESR, seropositivity and functional class

With cardiac valve there was positive correlation of patients only with mean duration of disease. However, there was no significant correlation between cardiac valve abnormalities and swollen joint counts, tender joint count, subcutaneous nodules, ESR, seropositivity and functional class.

The most common cardiac abnormality seen in this study was left ventricular diastolic dysfunction in 16.67%; followed by mitral regurgitation 13.33%; pericardial disease in 10 %; and pulmonary hypertension with tricuspid regurgitation 3.3%, aortic regurgitation 3.3%; mitral regurgitation + aortic regurgitation in 3.3%.

Most of the patients had no clinical manifestations of cardiac involvement, suggesting that cardiac involve ment in rheumatoid arthritis is a sub-clinical disease.

Keywords: Rheumatoid Arthritis, Cardiac Valve, Diastolic Dysfunction, Pericarditis, swollen joint.

Introduction

Rheumatoid arthritis is a chronic systemic disease of unknown etiology. It is characterized by peripheral symmetrical polyarthritis. It has a progressive course with exacerbations and remissions being part of its natural history. Its onset could be at any age, although it usually starts in the fourth decade of life. Overall, there is a 3:1 female preponderance, but this excess is greater in young people and the age-related incidence is approximately equal in elderly people.[1]

Though being principally a disease of joints, several extra-articular manifestations are also noted. The systemic manifestations include involvement of cardiac, pulmonary, hematological, ocular, and neurological systems. The most common cause of death in these patients is cardiovascular disease.

The prevalence of rheumatoid arthritis is between 0.7% to 1.5 %. Malviaya et al found the prevalence in Indian rural population to be 0.75%.[2]

Cardiac manifestations were initially described by Jean Martin Charcot in 1881 who commented that “cardiac lesions occurred pretty frequently in nodular rheumatism” since he could identify postmortem carditis in 4 out of a group of 9 patients, who were clinically suspected to be suffering from RA.[3]

Many cardiac lesions have been described since then including pericardial effusion, constrictive pericarditis, mitral regurgitation, mitral stenosis, aortic root dilatation and aortic regurgitation, left ventricular systolic and diastolic dysfunction, pulmonary arterial hypertension in many Western and European studies.

The first echocardiographic study of patients with rheumatoid arthritis was done by Prakash et al (1973)

who found pericardial involvement in 7 out of 16 RA patients.[4]

Wislowska and Kowalik in their study found that overall cardiac involvement was more common in nodular rheumatoid arthritis as compared to non-nodular RA.[5]

Jaunatey et al found that left ventricular diastolic dysfunction and pulmonary hypertension was more common in patients with RA.[6]

Maione et al studied 39 patients of RA and compared with 40 control subjects. They found left ventricular dysfunction in 26% of patients with RA.[7]

Pericardial disease is a common autopsy finding in patients with rheumatoid arthritis, but is frequently asymptomatic during life. Corrao et al found pericardial effusion as the most common cardiac manifestation in their study of 35 patients of rheumatoid arthritis.[9]

The Rheumatologists in this country feel that Indian patients appear to have a milder disease with lesser systemic manifestations as compared to western patients with RA.

This was supported by Kaushal et al (1988).[8] Malaviya et al (1993) reported only 8.5 % had subcutaneous nodules in north Indian patients in contrast to accepted figures from the white race reported in the range of 20-30 % of RA patients[2].

Materials and methods

Methodology

- The study was performed on rheumatoid arthritis patients attending OPD in PMCH, Patna Bihar. A total of 30 rheumatoid arthritis patients were enrolled and were compared with 15 age and sex matched control subjects.

Type of study

- This is a cross-sectional observational study.

Study place

- The study was done in department of medicine at pmch, Patna.

Study period

- This study was conducted from April 2021 to November 2022.

Inclusion criteria

After clinical evaluation and laboratory investigation those patients satisfying the modified ACR/EULAR criteria (2010) [11] was included in the study. Age and sex matched controls were selected from medical OPD who came for routine health check up or had nonspecific complaints, after taking care to exclude those suffering from hypertension, cardiac disease, and diabetes mellitus.

Exclusion criteria

- Those suffering from congenital heart disease, ischemic heart disease, valvular heart disease with rheumatic history, and diabetes mellitus, were excluded from the study

Result and discussion

The study was done in PMCH, Patna between April 2021 to November 2022, 30 of rheumatoid arthritis diagnosed by modified ACR/EULAR criteria (2010)[11] along with 15 age and sex matched controls were included in the study after they had fulfilled the inclusion and exclusion criteria.

Age and Sex distribution

The study group included 23 females and 7 males. The age and sex distribution of patients with RA is shown in Table 1 below (figure 1), and the control subjects in table 2 (figure 2).

In the study group the maximum incidence was between 26-50 years (93%) age group. The oldest patient was 62 years and the youngest was 26 years. The

mean age group was 40.1 with standard deviation of 9.22 years. The disease was found to be more common in females with the male: female ratio being 1:3.28 (7:23). Cardiac abnormalities were seen maximum in 41-50 years age group.

In the control group the mean age was found to be 39.1 years. A comparisonof baseline characteristics between RA patients and control subjects is detailed intable 4.

Duration of illness

The duration of the disease ranged from 1 year to 15 years and the mean duration being 4.3 years with a standard deviation of 2.45. In general, cardiac ab normalities were more common in patients with longer duration of illness (table 3) and (figure 3). The mean duration in patients presenting with cardiac ab normalities was found to be 6.93±3.94 years.

Clinical features and investigations

History related to rheumatoid arthritis including joint pains, morning stiffness, and swelling of joints was present in almost all the patients in the study group.

Complete evaluation by clinical examination, plain radio graphy, blood tests, electro cardio gram and echo cardio graphy was done.

On physical examination jugular venous pulsation was elevated in one patient and pulmonary component of second heart sound was loud in 1 patient. Three patient had right-sided pleural effusion of which 2 had moderate pleural effusion and 1had mild pleural effusion and rheu matoid subcutaneous nodules were present in 7 patients.

Simplified 28 joint count as described by Fuchs et al21 was used to evaluate for the number of tender and swollen joints. The mean tender joint count was 16.4 with the range being 6-26, and the mean swollen joint count was 10.2 with range of 0 to 20 (Table 4).

Functional status as recorded on the Stein brocker's scale was as follows 8 patients were class I, 18 patients were class II and 4 belonged to class III (Table 4).

On investigations the hemoglobin levels ranged from 8.5 to 15.0 gm% with a mean of 11.75 gms% and in control subjects hemoglobin level ranged from 9.8 to 14 gms% with mean of 11.36 gms%. The mean ESR in the study group was 35.33 mm/hour and ranged from 12 mm/hr to 80 mm/hour and in the control subjects the levels ranged from 12 to 40 mm/hour, with a mean of 25.2 mm/hour. The anti-CCP level in study group ranged from12 units to 70 units with mean of 31.5 units.

Twenty-one patients (70.00%) were found to be rheumatoid factor (RF) positive. In the study group titres ranged from 1:16 to 1:128, with majority of those positive having atitre of 1:64.

The chest roentgenograms revealed pleural effusion in three patients. None of the patients were found to have cardiomegaly, pericardial involvement in the form of effusion or pericardial calcification on chest X ray.

Radiological assessment of the hand X-rays was done and staged based on stein brocker's classification. Number of patients with class I-2, Class II-20, Class III-7 and Class IV-1. Among patients with cardiac valve abnormalities the number of patients in Class I-NIL, Class II-5 Class III-2 and Class IV-NIL. There was significant relationship of patients with cardiac abnormalities having erosive arthritis, as suggested by the stein brocker's staging.

12 lead electrocardiogram was done on all study subjects and revealed minor abnormalities in 4 patients which were comparable with those found in the control group. In the study group one patient had Left ventricular hypertrophy (LVH), one left anterior hemi block (LAHB) and two patients had nonspecific ST-T changes.

In the control group one subject had LVH, one subject had grade I heart block and one non-specific ST-T changes, one subject has sinus tachycardia.

Echocardiography

Structural findings on echocardiography of RA patients (table 6 and 7) revealed mitral regurgitation in 4 patients, Aortic regurgitation in 1 patient, Aortic + Mitral regurgitation, pericardial effusion in 2 patients, peri cardial thickening in one patient, tricuspid regurgitation and pulmonary hypertension in one, and left ventricular diastolic dysfunction in 5 patients (Figure 4) In the control group echocardiographic normal in all patients.

A comparison (table 5) was done between patients and controls for echocardiographic parameters and patients with RA had a increase in left ventricular diastolic and systolic internal diameters compared to controls and significant decrease in the E/A ratio and increase in the S/D ratio suggesting increased left ventricular diastolic dysfunction in RA patients as compared to controls.

Further patients with cardiac valve abnormalities and patients without cardiac valve abnormalities were compared (table 8) and patients with overall cardiac abnormalities and patients without any cardiac valve abnormalities were compared (table 9).

With cardiac valve there was positive correlation of patients with increase in age and mean duration of disease. However there was no significant correlation between cardiac valve abnormalities and swollen joint counts, tender joint count, subcutaneous nodules, ESR, seropositivity and functional class.

There was positive correlation in patients with cardiac abnormalities and increase in age, tender joint counts, and mean duration of disease. However there was no significant correlation between cardiac abnormalities and swollen joint counts, subcutaneous nodules, ESR, seropositivity and functional class.

Patients with cardiac valve abnormalities were found to have lower ESR values and were more likely to be seropositive but both these parameters did not show any statistically significant correlation.

Table 1: Age and Sex distribution in Rheumatoid Arthritis patients

Age groups	No. of cases (%)	Females (%)	Males (%)	Echo valvular Abnormalities (%)	ECG
20-30	6 (20)	5 (83.33)	1 (16.6)	0	-
31-40	12 (40)	10 (83.33)	2 (16.6)	2 (15.4)	AHB-1
41-50	10 (33.3)	8 (80.0)	2 (20.0)	4 (40.0)	Nonspecific ST-T changes-2
51-60	1 (3.33)	0 (0.0)	1 (100.0)	0	
61-70	1 (3.3)	0 (0.0)	1 (100.0)	1 (100.0)	LVH-1

Table 2: Control subjects

Sn.	Age group	No. of cases	Females	Males	Echo cardio-graphic Abnormalities	ECG
1	20-30	3 (20%)	3	-	-	-
2	31-40	5 (33.33%)	4	1		Sinus tachy-1 Grade 1 heart block-1
3	41-50	5 (33.33%)	3	2	-	LVH-1

4	51-60	1(33.33)	1	-	-	
5	61-70	1(6.66%)	-	1	-	LVH-1

Table 3: Duration of disease

Duration of disease	Number of RA patients	Number with cardiac echo-abnormalities		Specifics
		Valve abnormalities	Others cardiac disease	
1-2 years	3	-	1	Pericardial effusion-1
> 2-3 years	6	-	2	Pericardial thickening -1 Diastolic dysfunction-1
> 3-4 years	12	2	3	Mitral regurgitation-1 Tricuspid regurgitation-1 Pericardial effusion-1 LV diastolic dysfunction-2
> 4-5 years	3	1	2	Mitral regurgitation-1 LV diastolic dysfunction-2
>5-10years	3	3	-	Mitral regurgitation + aortic regurgitation-1 Aortic regurgitation-1 Mitral regurgitation-1
>10 years	1	1	-	Mitral regurgitation-1

Table 4: Baseline characteristics of RA patients and control subjects

Characteristic	**Patients**	**Controls**
Sex ratio (M: F)	1:3.28	1:2.75
Age (mean)	40.13±9.23	39.13±10.12
Duration of disease (mean)	4.32±2.45	-
ESR	35.33±16.88	25.2±8.97
TJC	16.40±6.25	-
SJC	10.20±6.24	-
RF Stein Brockers Functional Class I II III IV	21/30 (70%) 8 18 4 -	 - - - -

CDAI Score		
≤2.8	1	-
2.8≤10	11	-
>10≤22	16	-
>22	2	-

Table 5: Echocardiographic variables in patients and controls

Echocardiography	**Control subjects**	**Patients with RA**	**Statistical Significance (p-value)**
Left atrial diameter	3.19±0.34	3.41±0.71	0.133
Aortic root diameter	2.95±0.15	3.14±0.60	0.114
LV diastolic internal diameter	4.36±0.39	4.54±0.63	p<0.05
LV systolic internal diameter	3.13±0.54	3.32±0.48	0.118
Thickness of septum	0.77±0.14	0.89±0.14	p<0.05
Thickness of posterior wall	0.75±0.16	0.81±0.21	0.140
EF%	66.13±8.19	60.80±9.12	p<0.05
E	63.13±5.48	74.86±27.50	
A	50.47±8.74	73.23±18.07	p<0.05
E/A	1.26±0.21	1.06±0.28	p<0.05
S	45.80±2.08	47.83±3.17	p<0.05
D	42.40±3.60	40.50±6.16	0.138745
S/D	1.09±0.08	1.21±0.16	p<0.05
Other cardiac abnormalities			
Pericardial effusion	-	2(6.67%)	
Pericardial thickening	-	1 (3.33%)	
Diastolic dysfunction		5(16.67%)	

Table 6: Profile of patients with cardiac valve abnormalities

Age	**Duration of disease**	**Sex**	**Tjc**	**Sjc**	**Accp**	**Functional stage**	**Treatment**	**Esr**	**Rf**	**Extra-articular**	**Ecg**	**Echo-cardiography**
62	15	M	22	12	64	III	HCQS	40	1:64	-	LVH	MR
50	5	M	18	16	40	II	MTX	54	1:64	-	-	MR
48	6	F	12	0	14	I	MTX	18	1:64	-		MR
39	4	F	20	14	32	II	HCQ	50	1:64	-	-	MR
48	4	F	20	8	44	II	HCQS	50	1:128	RN	-	TR
39	5.5	F	16	10	32	II	-	24	1:64	-	LAHB	MR+AR
50	9	F	18	12	24	II	HCQ	56	1:32	-	-	AR

Table 7: Profile of patients with other cardiac abnormalities

AGE	Duration of disease	Sex	TJC	SJC	ACCP	Functional stage	Treatment	ESR	RF	Extra-articular	ECG	Echo-cardiography
47	4	F	26	12	25	II	HCQ	50	1:64	-	-	Diastolic dysfunction
47	5	M	28	14	70	III	-	54	1:64	RN	-	Diastolic dysfunction
50	5	F	20	8	14	II	-	24	1:32	-	-	Diastolic dysfunction
40	4	F	26	18	30	II	HCQ	46	1:32	-	-	Diastolic dysfunction
39	3	F	12	10	28	I	MTX	22	1:64	-	-	Diastolic dysfunction
30	3	F	12	4	38	II	-	18	1:64	RN	-	Pericardial thickening
28	2	M	16	10	40	II	MTX	54	1:128	RN	-	Pericardial effusion
40	4	M	20	10	24	II	-	56	1:128	RN	-	Pericardial effusion

Table 8: Comparison of variables between patients without cardiac valve abnormalities and with patients with cardiac valve abnormalities

Parameters	***Patients without cardiac valve abnormalities**	**Patients with Cardiac valve abnormalities**	**Significance**
Age	37.74±8.36	48.00 ±8.36	t=2.882, p=0.003*
Sex	M=21.7% F=78.2%	M=28.6% F=71.4%	OR=1.31(Males) Males are 1.3 times more likely to develop disease
Duration of Disease	3.52±0.92	6.93±3.94	t=3.947, p=0.0002*
TJC	15.91±6.89	18.00 ±3.26	t=0.769, p=0.224
SJC	10.17±6.63	10.28± 5.22	t=0.041, p=0.484
ESR	36.17± 17.86	32.57± 14.03	t=0.488, p=0.315
Subcutaneous Nodules	26.09%	14.23%	t=0.63, p=0.27
RA Factor	65.22%	85.71%	t=1.028, p=0.16
Functional class	I -30.43% II -56.52% III-13.04%	I -14.28% II -71.42% III-14.28%	-

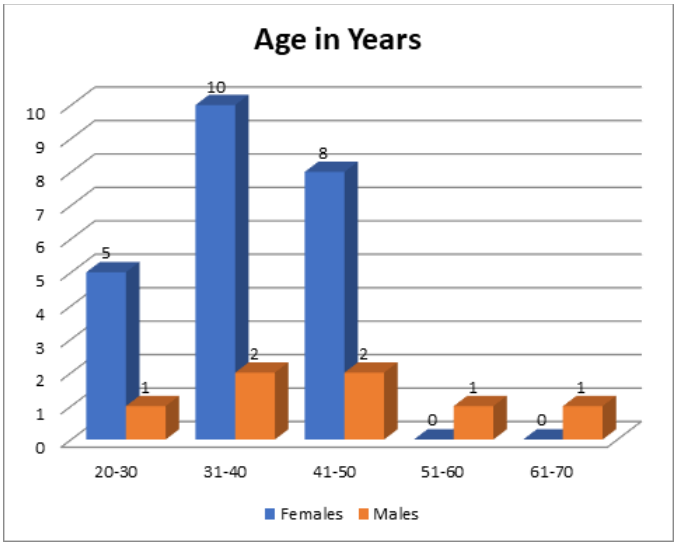
(*Patients without cardiac VALVE abnormalities includes RA patients without any cardiac abnormalities and patients with diastolic dysfunction and patient with pericardial disease.)

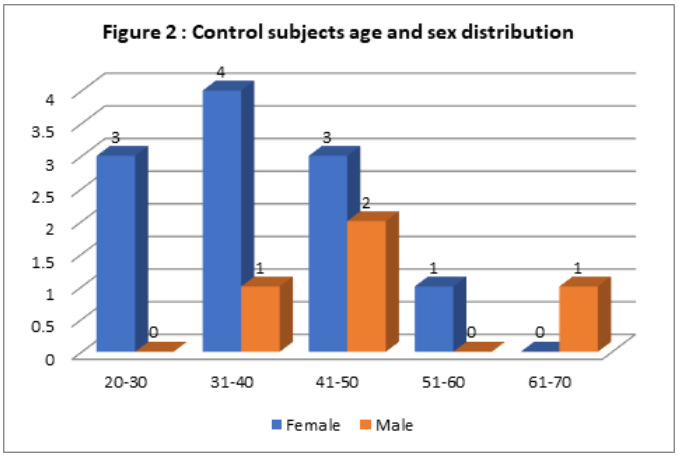
Table 9: Comparison of variables between patients without cardiac abnormalities and with patients having overall cardiac abnormalities

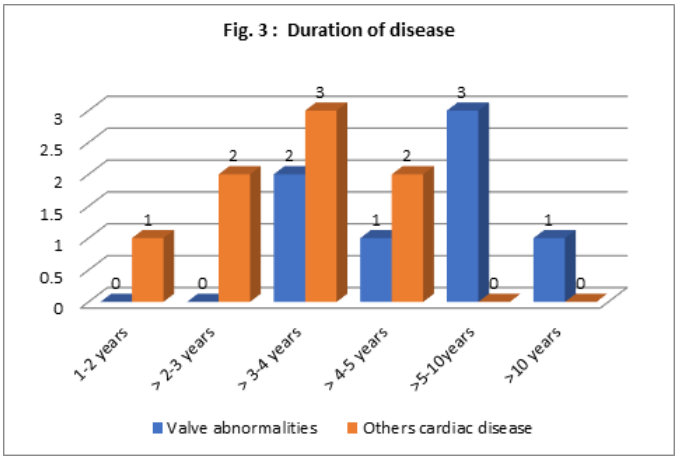
Parameters	**Patients without any cardiac abnormalities**	****Patients with overall Cardiac abnormalities**	**Significance**
Age	36.47±8.56	43.80 ±8.62	t=2.338 p=0.013*
Sex	M=13.33% F=86.67%	M=33.33% F=66.67%	OR=2.5 (Males) Males are 2.5 times more likely to develop disease
Duration of Disease	3.40±0.87	5.23±3.14	t=2.176, p=0.019*
TJC	13.73±6.32	19.07 ±5.06	t=2.551, p=0.008*
SJC	9.87±7.76	10.53± 4.50	t=0.288, p=0.388
ESR	33.87± 18.78	36.80± 15.27	t=0.469, p=0.321
Subcutaneous Nodules	13.33%	33.33%	t=1.28, p=0.104
RA Factor	60%	80%	t=1.18, p=0.12
Functional class	I -40% II -46.67% III-13.33%	I -13.33% II -73.33% III-13.33%	-

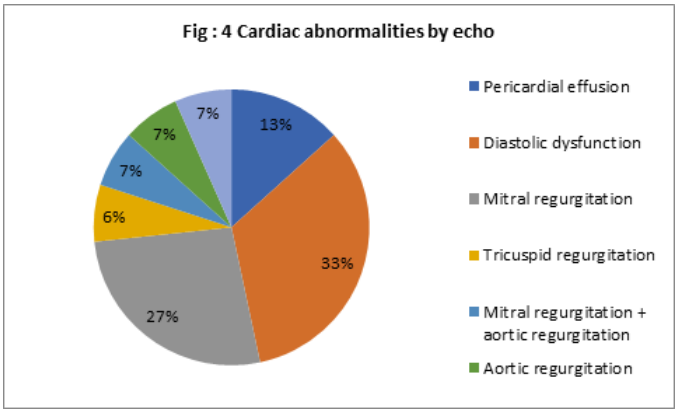
(**Overall cardiac abnormalities includes patient with diastolic and valvular and pericardial diseases).

Figure 1: Age distribution with sex of Rheumatoid Arthritis patients









Conclusion And Summary

Cardiac manifestations were seen in 15 patients (50%), 7 patients with cardiac valve abnormality, 5 patients with diastolic dysfunction, 3 patients with pericardial involvement, out of 30 cases studied the maximum incidence of the disease was seen in the 30-50 years age group and the male to female ratio was 1:3.8.

The mean duration of the disease was found to be 4.32 years in the entire study group and 6.93 years in patients presenting with cardiac valve abnormalities.

There was positive correlation in patients with overall cardiac abnormalities and increase in age(p=0.013); tender joint counts(p=0.008); and mean duration of disease (p=0.019).

However there was no significant correlation between cardiac abnormalities and swollen joint counts, sub cutaneous nodules, ESR, seropositivity and functional class.

With cardiac valve there was positive correlation of patients with increase in age (p=0.003) and mean duration of disease(p=0.0002). However, there was no significant correlation between cardiac valve abnormalities and swollen joint counts, tender joint count, sub cutaneous nodules, ESR, seropositivity and functional class.

Most patients with cardiac abnormalities had normal chest X-ray.

The electrocardiogram revealed minor conduction abnormalities in patients which were comparable to the findings in control subjects.

The most common cardiac abnormality seen in this study was left ventricular diastolic dysfunction in 16.67% followed by mitral regurgitation 13.33%, pericardial disease in 10 % and pulmonary hypertension with tricuspid regurgitation 3.3%, aortic regurgitation 3.3%, mitral regurgitation + aortic regurgitation in 3.3%.

Most of the patients had no clinical manifestations of cardiac involvement, suggesting that cardiac involve ment in rheumatoid arthritis is a sub-clinical disease.

Summary

- Cardiac abnormalities are an important extra-articular manifestation of rheumatoid arthritis.
- These abnormalities are largely sub-clinical.
- The early detection of cardiac abnormalities can be very important in the correct assessment and management of the RA patients, especially in light of the fact that, the 30-50% of the mortality RA patients mortality is due to cardiovascular disorder. [39]
- Therefore, every patient should be submitted to a cardio logical assessment (in particular echocardiography) in order that cardiac involvement can be detected early and treated, and the incidence of morbidity and mortality reduced.

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