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A STUDY ON CLINICAL & CARDIOVASCULAR PROFILE OF RHEUMATOID ARTHRITIS PATIENTS & IT'S CORRELATION WITH DISEASE ACTIVITY

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ABSTRACT :

Background:
Rheumatoid arthritis (RA) is a chronic inflammatory disorder, characterised by both articular and extra - articular manifestations. The chronic subclinical inflammation in rheumatoid arthritis contributes to accelerated atherosclerosis and various cardiovascular events. In a study, if the clinical disease activity index score falls by 10, the risk of developing cardiovascular disease decreases by 26% has been formulated. So it is necessary to do screening for cardiovascular disease in all Rheumatoid arthritis patients.
Methods: This prospective cross sectional study is carried out in known Rheumatoid Arthritis patients attending General Medicine & Rheumatology outpatient clinic or ward They have been selected after detailed investigations and found to be fulfilling ACR criteria for Rheumatoid Arthritis 2010 and also the inclusion , exclusion criteria of our case study.
Results: Left Ventricular Systolic Function, Left Ventricular Diastolic Dysfunction, and valvular abnormalities such as Mitral Regurgitation and Aortic sclerosis correlates positively with duration of rheumatoid arthritis.Coronary Calcification was found in 4 % patients in our study, was an indirect marker of subclinical atherosclerosis and serves as a marker of cardiovascular events. In our case series, Coronary calcification has no significant association with disease severity and duration of disease
Conclusion: Early identification & effective control of disease activity by DMARDS/Biological agents at correct time can prevent or halt the progression of cardiovascular manifestations in Rheumatoid arthritis patients thereby reducing the mortality and morbidity caused by them.
Keywords: Rheumatoid arthritis, Left Ventricular Systolic Function

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INTRODUCTION:

Rheumatoid arthritis (RA) is a chronic inflammatory disorder, characterised by both articular and extra - articular manifestations. The chronic subclinical inflammation in rheumatoid arthritis contributes to accelerated atherosclerosis and various cardiovascular events. A recent study showed that 50% mortality in rheumatoid arthritis is due to cardiovascular disease related deaths. RA is associated with disability, shortened life expectancy, and increased mortality as compared to the general population. Cardiovascular events seems to occur approximately a decade earlier in Rheumatoid arthritis patients like that in diabetes mellitus.

Moreover, like Diabetes mellitus and Dyslipidemia, there is an independent association of RA with preclinical and overt cardiovascular disease and most of the time it is silent with unfavourable outcome leading to premature death.

In a study, if the clinical disease activity index score falls by 10, the risk of developing cardiovascular disease decreases by 26% has been formulated. So it is necessary to do screening for cardiovascular disease in all Rheumatoid arthritis patients. Also, the influence of disease activity on development of cardiovascular disease should also be studied.

AIM AND OBJECTIVES OF THE STUDY:

- To study and document the occurrence of various cardiovascular manifestations in Rheumatoid arthritis patients
- To assess the disease severity in Rheumatoid arthritis patients
- correlate and compare the association between disease severity and various clinical and cardiovascular manifestations in rheumatoid arthritis patients

MATERIALS AND METHODS:

This prospective cross sectional study is carried out in known Rheumatoid Arthritis patients attending General Medicine & Rheumatology outpatient clinic or ward They have been selected after detailed investigations and found to be fulfilling ACR criteria for Rheumatoid Arthritis 2010 and also the inclusion , exclusion criteria of our case study. Written informed consent was obtained from the patients selected for the study. They have been subjected to detail clinical and laboratory investigations. Routine investigations such as complete blood count, Hemoglobin, Total leukocyte count, Differential count, Platelet count, Renal Function test, Liver Function Test, Serum Electrolytes, Fasting Lipid Profile
, Urine Routine Investigations and Blood sugar.

In addition, investigations such as ESR, CRP, RA factor, Anti- CCP antibody, Electrocardiogram, Chest X-Ray PA view, Echocardiogram and Carotid Doppler to detect Carotid Intima Media Thickness were done for all patients.

Carotid Intima Media Thickness was assessed by Ultrasonagraphy B – Mode with a probe of frequency 5 Hz and was confirmed with colour Doppler sonography. Intima Media Thickness was measured at three sites - along common carotid artery in the distal 1 cm before its bifurcation, at the

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carotid bulb, and at the internal carotid artery. Measurements are taken at diastole, at both sides and the average of six measurements were taken which denotes the mean Carotid Intima Media Thickness of the patient.

Statistical analysis was done using the statistical package for social sciences (SPSS).Different statistical methods were used as appropriate. Mean ± SD was determined for quantitative data and frequency for categorical variables. The independent t- test was performed on all continuous variables. The normal distribution data was checked before any t-test. The Chi-Square test was used to analyze group difference for categorical variables. In logistic regression models, age was adjusted for estimation of each or all the independent effects of hypertension, ischemic heart disease and diabetes mellitus . A p- value < 0.05 was considered significant.

RESULTS:

CDAI SCORE DISTRIBUTION

The disease severity was high among our study group with 60 % of cases occupying High CDAI score with no patients under remission.

	CDAI SCORE	NO OF PATIENTS
Remission	<2.8	Nil
Low	2.8 – 10	3
Moderate	10-22	17
High	> 22	30

TABLE : DESCRIPTIVE STATISTICS

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Mean age, Duration of disease, CDAI score, ESR, CRP, mean CIMT, mean EF in our study population were listed.

	N	Minimum	Maximum	Mean	Std. Deviation
Age	50	21.00	74.00	47.76	11.09
CDAI_Score	50	5.00	44.00	25.16	10.40
Duration	50	.20	20.00	8.63	5.85
CIMT	50	0.00	.99	0.72	0.26
EF	50	38.00	75.00	59.46	9.25
ESR	50	15.00	120.00	49.50	27.97
CRP	50	1.00	2.00	1.46	0.50

TABLE : LV SYSTOLIC DYSFUNCTION DISTRIBUTION

		Frequency	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	No	42	84.0	84.0	84.0
	Yes	8	16.0	16.0	100.0
	Total	50	100.0	100.0	

TABLE: LV DIASTOLIC DYSFUNCTION DISTRIBUTION

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		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	28	56.0	56.0	56.0
	Yes	22	44.0	44.0	100.0
	Total	50	100.0	100.0	

TABLE: PULMONARY HYPERTENSION DISTRIBUTION

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	46	92.0	92.0	92.0
	Yes	4	8.0	8.0	100.0
	Total	50	100.0	100.0	

TABLE LEFT VENTRICULAR SYSTOLIC DYSFUNCTION vs CDAI SCORE

LVSD		N	Mean	Std. Deviation	P value
CDAI_Score	No	42	22.93	9.56	<0.0001
	Yes	8	36.88	5.87	

There is strong correlation between Left Ventricular Systolic Dysfunction and Clinical Disease Severity Index score (p value < 0.0001)

CORRELATION OF ECHOCARDIOGRAPHIC FINDINGS WITH DURATION OF RHEUMATOID ARTHRITIS

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		Correlation Coefficient	P value
EF	Duration of disease	-0.516	<0.0001

There is strong significant relationship between variation in ejection fraction and duration of rheumatoid arthritis (p value < 0.0001).

PERICARDIAL EFFUSION vs DURATION OF RHEUMATOID ARTHRITIS

PERICARDIAL EFFUSION		N	Mean	Std. Deviation	P value
Duration of Disease	No	37	6.29	4.65	0.707
	Yes	12	6.83	3.24	

There is no significant relationship between occurrence of pericardial effusion and duration of rheumatoid arthritis (p value 0.707).

DISCUSSION:

We found that patients among our study group fell in age group of 21- 74 yrs with mean age of 47.76 years. Males among study group occupy 28% & females 72 % respectively. The Mean duration of rheumatoid arthritis among study population is 8.63 ± 5.85 yrs.
The disease severity among patients was assessed with clinical disease severity score and Mean CDAI score among them are 25.16 ± 10.4. The disease severity was high among our study group with 60 % of cases occupying High CDAI score with no patients under remission.
Metacarpophalangeal, proximal interphalangeal joint and wrist joints are the most commonly involved joints among study population.

Anaemia seems to be occur more commonly in rheumatoid arthritis patients, being in 72 % of our study population. Lymphocytosis were found in 20% of our study group. Thrombocytopenia and thrombocytosis occurs in minority group of patients (14 %, 4% respectively).
Dyslipidemia in form of Hypercholesterolemia and hypertriglyceridemia was found in 10% and 4% of our study population respectively.

Markers of inflammation such as ESR and CRP are raised more commonly among rheumatoid arthritis patients, ESR being more commonly raised in 96 % of patients, and CRP raised in 46 % of

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patients in study group.
Most Common ECG abnormality found in study group was Left axis deviation (30%) followed by nonspecific ST-T changes (24%). ST –T changes suggestive of coronary artery disease in asymptomatic patients of our study group was found in 18 % of individuals, which was comparable to Masooleh SI et al(21) in which 15% cases had ST-T changes .
In chest X-ray screening, cardiomegaly was found in 40 % of patients and other abnormalities such as fibrotic changes in lungs, prosthetic heart valve shadows, bronchiectactic changes in lungs were present in minority of patients.
Mean Carotid Intima media thickness (CIMT) (cut off among normal individuals is 0.57 mm) is increased in Rheumatoid Arthritis patients when matched with age related controls which signifies presence of premature atherosclerosis. In our case series, Mean CIMT was found to be increased in 68 % of patients. Asymptomatic Carotid Plaque was present in 8% of patients. Presence of carotid plaque suggests that the patients are in stage of preclinical atherosclerosis and emphasis the need for more aggressive risk reduction strategies in these patients.

In our study group, Echo abnormalities were found in 68 % of patients.In our case series, Most common Echocardiographic abnormality is LV diastolic dysfunction which contributes 44% of study group, comparable to 14.54%in study conducted by Raof RM et al(24)followed by Pericardial effusion contributing to 26 %, which was comparable to the study conducted by Selcuket al(28) in which it was 15%. .High prevalence of this complication (47%) was found in study done by Masooleh SI et al(21). Other abnormalities such as Mitral Regurgitation , LV systolic dysfunction were present in 20 % and 16 % of study population respectively, whereas it was as high as 31%(LVSD) in the study by Dawson et al. Coronary calcifications were found in 2 patients.
ESR correlates positively with Clinical disease activity Index score, duration of Rheumatoid arthritis & Mean Carotid Intima Media Thickness. This proves that increased CIMT was associated with inflammatory burden due to more severe disease, and also the chronic inflammation which reflects the duration of the disease.

Dyslipidemia & CRP shows no significant correlation with CIMT or other CVS abnormalities, as compared to the results by Chung et al. [9] andMahajan et al. [10] who did not find significantly correlated dyslipidaemia with accelerated atherosclerosis in RA patients.
According to Homa et al, CIMT increases linearly from 0.48 mm at 40 years of age to 1.02 mm at 100 years of age.Mean age group in our study was 47.76 yrs & mean CIMT was 0.72 mm

So, In our study group CIMT was higher than age related controls and correlates positively with severity of disease as evidenced by high CDAI score(p value 0.043) & duration of disease(p value 0.015), similar observation made by Gonzalez et al and Alkabbi et al in their respective studies. In an Indian study, Mahajan et al. also showed similar observations which showed higher CIMT values in RA patients when compared to control group matched age and related parameters. [10].
Among echocardiographic findings, LV systolic dysfunction (LVSD), variation in Ejection Fraction and Pericardial Effusion positively correlates with clinical disease severity index (CDAI) score in our study group.

Left Ventricular Systolic Function, Left Ventricular Diastolic Dysfunction, and valvular abnormalities such as Mitral Regurgitation and Aortic sclerosis correlates positively with duration

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of rheumatoid arthritis.

Coronary Calcification was found in 4 % patients in our study, was an indirect marker of subclinical atherosclerosis and serves as a marker of cardiovascular events. In our case series, Coronary calcification has no significant association with disease severity and duration of disease, in contrast to the study by Giles et al., which shows increasing disease severity in RA is associated with increased prevalence and extent of coronary calcification, irrespective of gender and age.

CONCLUSION:

Cardiovascular abnormalities such as nonatherosclerotic features like LV diastolic & systolic dysfunction , valvular abnormalities, pericardial effusion and mainly premature atherosclerosis occurs commonly in Rheumatoid arthritis patients & their occurrence positively correlates with Clinical disease activity Index (CDAI)score, disease duration and treatment duration.
All Rheumatoid arthritis patients should be screened for CVS abnormalities through modalities like Electrocardiography, Echocardiography & CIMT periodically. CIMT, a non-invasive marker of accelerated atherosclerosis is also a marker of coronary atherosclerosis serves as an important tool in developing countries like India , due to its low cost, non-invasive patient convenient procedure and so has been recommended by American Heart Association (AHA) as a screening test for cardiovascular diseases in apparently healthy individuals.
DMARDs & Biological agents have been shown to have cardio protective effects in many studies. In a study cohort, Methotrexate have shown to reduce cardiovascular morbidity and mortality, ranging from 15% to 85%.Biological Agents such as TNF alpha inhibitor therapy improves endothelial function and arterial stiffness in patients with RA as shown in a study by Hürlimann et al. A recent study demonstrated that use of
Tocilizumab (IL -6 inhibitor) and Rituximab improves both endothelial function and arterial stiffness, also reduces carotid atherosclerosis respectively.
Therefore, Early identification & effective control of disease activity by DMARDS/Biological agents at correct time can prevent or halt the progression of cardiovascular manifestations in Rheumatoid arthritis patients thereby reducing the mortality and morbidity caused by them.

LIMITATIONS OF THE STUDY

- The Study population is too small
- History of usage of drugs such as DMARDs or Biological agents were not obtained
- Effects of patients medication for rheumatoid arthritis on patients disease severity and its influence and correlation on cardiovascular manifestations were not studied.
- RA Factor and Anti-CCP antibody titre levels were not correlated with patients cardiovascular manifestations.

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