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To Evaluate the Frequency of Newly Diagnosed Ischemic Heart Diseases in RA Patients

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Abstract **Original Research Article**

Background: Patients with RA have higher rates of morbidities and mortalities than in general population, which is highly attributed to an increased risk of CVD among RA patients and often untreated, leading to a decrease in life expectancy. Owing to its high prevalence and prognostic importance, professional societies and experts groups have increasingly emphasized the importance of CVD prevention and prompt recognitions in patients hospitalized with RA. ***Objective:*** To evaluate the frequency of newly diagnosed ischemic heart diseases in RA patients. ***Methods:*** It was a hospital based cross- sectional study. Study was conducted at Medicine Department of Chittagong Medical College Hospital (CMCH) for six months period from July'2018 to December'2018. A total 58 diagnosed RA case were selected purposively from both outdoor and indoor of Medicine Department of CMCH. Those having different comorbid condition like stroke, heart failure, chronic kidney disease, diabetes, pregnancy, encephalopathy, bleeding disorder, hypothyroidism, hyperthyroidism or unwilling to be included in the study were excluded. Patients' demographics, serology results including rheumatoid factor (RF), anti-cyclic citrullinated peptide antibody (anti-CCP) and antinuclear antibody (ANA), as well as, disease activity score in 28 joints (DAS28) were recorded in a case record form. ***Results:*** Percentage of the patients newly diagnosed as hypertensive and diabetic were 8.6% and 5.2% respectively. RA patients with IHD were 14%, had prolonged disease duration 3.56 ± 2.16 and high disease activity 27.6%. Percentages of patients had hypercholesterolemia, low high density lipoprotein (HDL), High Low density lipoprotein (LDL) were 81%, 98.3% and 100% respectively. ***Conclusion:*** Proportions of the patients were newly diagnosed as hypertensive and diabetic were 8.6% and 5.2% respectively. RA patients with IHD were more aged, had prolonged disease duration and high disease activity.

Keywords: Rheumatoid arthritis, cardiovascular diseases, ischemic heart disease.

INTRODUCTION

Rheumatic inflammation of cardiac structures can manifest itself as pericarditis, myocarditis, or endocarditis. The heart valves and the intracardiac conduction system can be affected as well, leading to AV block [1]. Functional sequelae, e.g., congestive heart failure, can arise as a consequence of any inflammatory rheumatic disease. The long-term mortality of rheumatic diseases is elevated predominantly because of the increased risk for cardio vascular comorbidities [2]. The cardiovascular risk profile should therefore be re-evaluated regularly (e.g., at 5-year intervals) in cooperation with the patient's primary care physician. In patients with inflammatory rheumatic diseases, the elevated cardiovascular risk should be kept in mind and preventive measures should be initiated early. This subject should be further studied in controlled trials so that the treatment options for patients with cardiac involvement can be evaluated [3].

To evaluate the prevalence of comorbidities and compare their management in RA patients from different countries worldwide an international, cross-sectional study was conducted by Dougados *et al.,* 2014 [4] Demographics, disease characteristics (activity, severity, treatment), comorbidities (cardiovascular, infections, cancer, gastrointestinal, pulmonary, osteoporosis and psychiatric disorders) data were collected for consecutive RA patients [5]. Of 4586 patients recruited in 17 participating countries, 3920 were analysed (age, 56±13 years; disease duration,

10±9 years (mean±SD); female gender, 82%; DAS28 (Disease Activity Score using 28 joints)–erythrocyte sedimentation rate, 3.7±1.6 (mean±SD); Health Assessment Questionnaire, 1.0±0.7 (mean±SD); past or current methotrexate use, 89%; past or current use of biological agents, 39%. The most frequently associated diseases (past or current) were: depression, 15%; asthma, 6.6%; cardiovascular events (myocardial infarction, stroke), 6%; solid malignancies (excluding basal cell carcinoma), 4.5%; chronic obstructive pulmonary disease, 3.5%. High intercountry variability was observed for both the prevalence of comorbidities and the proportion of subjects complying with recommendations for preventing and managing comorbidities. The systematic evaluation of comorbidities in this study detected abnormalities in vital signs, such as elevated blood pressure in 11.2%, and identified conditions that manifest as laboratory test abnormalities, such as hyperglycaemia in 3.3% and hyperlipidaemia in 8.3% [6]. The study revealed that, among RA patients, there is a high prevalence of comorbidities and their risk factors. In this multinational sample, variability among countries was wide, not only in prevalence but also in compliance with recommendations for preventing and managing these comorbidities. Systematic measurement of vital signs and laboratory testing detects otherwise unrecognized comorbid conditions [7].

There is now a large body of epidemiological evidence linking RA with the premature development of cardiovascular disease [8]. This relates, at least in part, to the systemic inflammatory burden in RA, which has been shown to predispose to the development of premature atherosclerosis in individuals with this condition. Several traditional risk factors such as obesity, dyslipidemia, type 2 diabetes mellitus (T2DM), metabolic syndrome (MetS), hypertension, physical inactivity, advanced age, male gender, family history of CVD, hyperhomocysteinemia, and tobacco have been associated with CVD in RA patients [9-14]. In fact, seropositive RA may, like diabetes, act as an independent risk factor for CVD [15]. A proinflammatory state, insulin resistance [16], hyperhomocysteinemia [17], and oxidative stress [18] are common characteristics of both RA and atherogenesis. The finding and understanding of these predisposing factors will allow us to better describe cardiovascular sub-phenotypes including hypertension, stroke, coronary artery disease (CAD), angina, myocardial infarction (MI), arrhythmias, ventricular diastolic dysfunction, congestive heart failure (CHF), thrombosis, and peripheral arterial disease [19-21].

OBJECTIVES

To evaluate the frequency of newly diagnosed ischemic heart diseases in RA patients.

METHODOLOGY

Type of study	Hospital based cross-sectional study
Place of study	Indoor and outdoor of Department of Medicine Chittagong Medical College Hospital, Chattogram, Bangladesh
Study period	Six months from 01/07/2018 to 31/12/2018.
Study population	Patients who are the Diagnosed Case of Rheumatoid Arthritis admitted in Indoor Department and Visited OPD in Medicine Department CMCH
Sampling technique	Consequence sampling
Sample size	Considering the resources (time & fund) limitation 58 conveniently collected cases were included in the study

Inclusion Criteria

1. Diagnosed patients of RA by ACR/EULAR Criteria, visited in indoor or OPD of CMCH.
2. Age above 18 years.
3. Both sex.

Exclusion Criteria

1. Patients who had other rheumatic disease like SLE, osteoathitis etc.
2. Patients who had previously diagnosed comorbid condition like DM, HTN, IHD, acute confusional state (stroke/encephalopathy).
3. Subjects who did not provide written consent to participate in the study.

Procedure of the Study

After getting approval from the Research and Training Monitoring Department of Bangladesh College of Physicians and Surgeons, diagnosed RA patients was included in this study. Informed written consents were taken after explaining purpose and procedure of the study from the patient. After getting consent, clinical history and physical examination was done. Next blood sample was collected and sent for biochemical analysis and other relevant investigations were done.

Data Processing and Analysis

After collection data were compiled in a Microsoft Office Excel Worksheet. Then thet were fed into SPSS (Statistical Package for Social Science) for Windows version 23 software to process and analyze the data. Continuous variables were reported as the

means ± SD and categorical variables were reported as frequency (percentages). Mean of the different continuous variables were compared between ischemic and non-ischemic group by independent student' test. Statistical significance was defined as $P < 0.05$ and confidence interval set at 95% level.

RESULT

Most of the patients were rheumatoid factor (55%) and anticyclic citrulinated peptide antibody (58 %) positive. All of them were taking MTX and 48% were on steroid during data collection. Mean ± SD disease duration was 3.56±2.16 years (Table I).

Table I: The disease characteristics of the patients

Variables		
Disease duration, in years	Mean ± SD	3.56±2.16
	Range	0.6-11
Rheumatoid factor	Positive	55 (94.9%)
	Negative	3 (5.2%)
ACPA	Positive	58 (100%)
	Negative	0 (0%)
Current medication	Methotrexate	58 (100%)
	Hydroxychloroquine	5 (8.6%)
	Steroid	10 (%)
	Salazine	3 (5.2%)

Data are expressed as frequency (and percentage) if not otherwise mentioned.
ACPA: Anticyclic citrullinated peptide antibodies

On blood pressure measurement only 5 (8.6%) RA patients were found to be hypertensive (Table II).

Table II: Distribution of Blood pressure among the patients

Variables		
Systolic blood pressure, mmHg	Mean±SD	131.12±11.5
	Mnimum-maximum	110-180
Diastolic blood pressure, mmHg	Mean±SD	88.3±4.83
	Mnimum-maximum	70-105
Hypertension	Yes	5 (8.6%)
	No	53 (91.4%)

Data are presented as frequency (percentage) if not otherwise mentioned.
SD: Standard deviation.

Figure 1 shows that out of 58 patients 40 (69%) had normal ECG. Eight (13.8%) patients had ECG findings compatible with myocardial ischaemia.

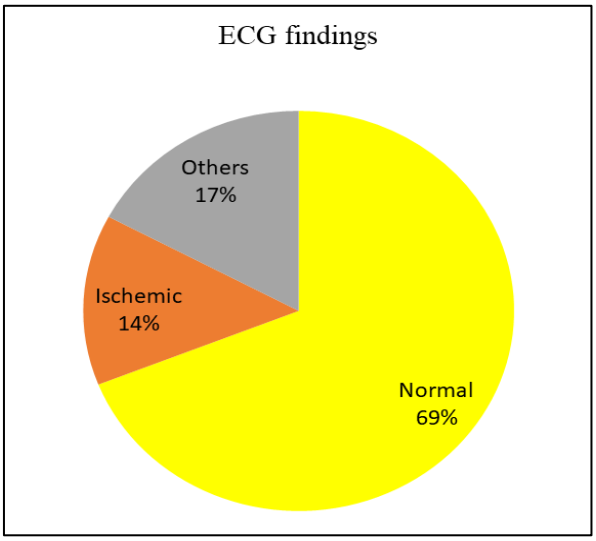

Figure 1: Distribution of the study subjects by their ECG findings (n=58)

Among the 8 ECG proven ischaemic patients 4 (50.0%) patients has inferior ischaemia, 2 (25.0%) has anterior ischaemia and 2 (25.00%) has lateral ischaemia. Only 4 (6.9%) patients had decreased or absent wall motion of heart (compatible with ischaemia) on echocardiography (Table III).

Table III: Distribution of the patients with asymptomatic ischaemia by type of ischaemia (n=8)

	Frequency	Percentage (%)
Types of ischemia		
Anterior ischaemia	4	50.0
Inferior ischaemia	2	25.0
Lateral ischaemia	2	25.0
Wall motion abnormality on Echocardiography		
Present	4	50.0
Absent	4	50.0

According to fasting lipid profile most of the patients had dyslipidemia (Table VI).

Table IV: Distribution of the study subjects by lipid profile status

Risk factors	Frequency (n)	Percentage (%)
Total Cholesterol mg/dl		
Normal	11	19.0
Hypercholesterolaemia	47	81.0
Triglyceride(TG), mg/dl		
Normal	1	1.7
Hyper TG	57	98.3
High density lipoprotein level (HDL), mg/dl		
Normal HDL	6	10.3
Low HDL	52	89.7
Low density lipoprotein level(LDL), mg/dl		
Normal	0	0.0
High LDL	1	100.0

Prevalence of DM in 58 patients after based on fasting and 2 hours after blood sugar is presented in Figure 2. It shows that, out of 58 RA patients 55 (94.8%) have normal glycemic status and 3 (5.2%) are diabetic.

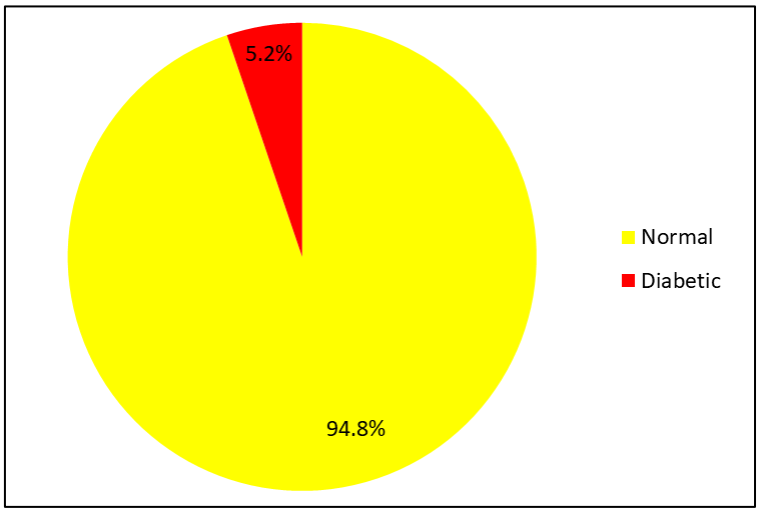

Figure 2: Glycemic status of the patients (n=58) with rheumatoid arthritis

There are significant association between increase in Age, RA duration, DAS 28 and occurrence of newly detected ischemic heart disease in RA patients as shown in Table V.

Table V: Comparison between ischemic and non-ischemic group regarding history, clinical and laboratory characteristics in RA patients

Variables	Ischaemic (n=8)	Non ischaemic (n=50)	P value
Age in years	57.8±4.56	50.51±10.13	0.032*
Disease duration in years,	8.56±2.2	3.56±2.16	0.014*
BMI, kg/m^2	26.01±2.6	25.14±3.66	0.665
Waist hip ratio	0.98±0.13	0.97±0.25	0.896
SBP, mmHg	135.32±10.4	131.12±11.5	0.875
DBP, mmHg	87.23±4.34	88.3±4.83	0.546
DAS-28	6.18±0.20	3.76±0.61	0.001*
FBS	5.99±1.9	5.92±1.36	0.345
2 HABS	8.1±1.23	7.9±1.08	0.465
Cholesterol, mg/dl	230±34	221±25	0.671
Triglyceride. mg/dl	222±50	223±54	0.899
LDL, mg/dl	140±19	137±20	0.874
HDL, mg/dl	38±1.5	39.6±1.6	0.886
Serum creatinine, mg/dl	0.89±0.3	0.88±0.29	0.896

Data are expressed as mean±SD;*Statistically significant.
P value are derived from independent sample t test.
BMI: Body mass index. SBP: Systolic blood pressure. DBP: Diastolic blood pressure.
DAS28: Disease activity score 28.FBS: Fasting blood sugar.2HABS: Two hours after breakfast sugar. LDL: Low density lipoprotein. HDL: High density lipoprotein.

DISCUSSION

In our study, age was found not to have significant association with IHD in patients with RA. This is inconsistent with the results of Dala *et al.*, [22] and Kadrekar *et al.*, [23]. We also found that the occurrence of newly detected IHD is significantly increased in patients with RA in association with the high disease activity.

According to the inclusion criteria we have only included the RA patients who had no previous history of HTN, DM and any other CVDs. On blood pressure measurement 5 (8.6%) patients were found to be hypertensive and by blood sugar measurement 3 (5.2%) patients were newly detected as diabetic. Association between traditional risk factors, like history of hypertension, DM or dyslipidemia was pointed out by other international studies among RA patients [24, 25]. However, we did not find any association between blood pressure, blood sugar and lipid profile level between patients with or without IHD. Beside small sample size we have excluded the RA patients who were already diagnosed as HTN or DM. Other studies [26] have confirmed that the risk factor obesity was not associated with ischemic cardiac morbidity a finding in line with the results of our study.

Out of the 58 RA patients there was female predominance with a male to female ratio of 1:5.4. Mean age was 51.74± 8.41years with a range of 37-72 years. About half of the patients were illiterate. These demographic and socioeconomic distributions of RA patients are similar with regional studies.

CONCLUSIONS

Primary cardiovascular diabetic prevention counseling should be a part of the treatment of RA patients. New population-based studies with more specific and sensitive technique are needed in order to increase the consistency of information on cardiovascular disease in RA patients and also to investigate associated factors in other regions of Bangladesh.

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