RISK OF CARDIOVASCULAR DISEASE IN PATIENTS OF RHEUMATOID ARTHRITIS (RA) PRESENTING IN A TERTIARY CARE HOSPITAL OF PAKISTAN

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ABSTRACT

Objective: To assess the cardio vascular disease (CVD) risk using framingham risk score and frequency of other co-morbidities associated with rheumatoid arthritis (RA).

Study Design: Cross sectional descriptive study.

Place and Duration of Study: Rheumatology department of Fauji foundation hospital (FFH), Rawalpindi. The duration of the study was six months, from Nov 2017 to Apr 2018.

Material and Methods: RA Patients between 40 to 80 years of age were selected from rheumatology outpatient department (OPD) at Fauji Foundation Hospital (FFH) Rawalpindi. After 12 hours of fasting, venous blood was taken for total serum cholesterol (TC), triglycerides (TG), low density lipoproteins (LDL), high density lipoproteins (HDL) and ESR (mm/1st hour). Framingham risk score was calculated using online calculator and it was multiplied by a factor 1.5 as per European League against Rheumatism (EULAR) recommendations to find the correct cardiovascular risk. This gave us 10 year cardiovascular risk in each RA patient.

Results: The study included 205 RA patients with a mean age (in years) of 53.12 ± 10.60. Mean duration of disease (years) was 9.71 ± 7.1. The commonest comorbidity in RA patients was hypertension found in 82 (40%) patients. 100 (48.78%) patients were overweight with mean body mass index (BMI) of 25.35 ± 4.96. Diabetes was found in 38 (18.5%) patients. 51 (24.87%) patients had high low density lipoprotein (LDL) with mean LDL of 116.75 ± 29.50 (mg/dL) whereas 88 (42.92%) patients had either borderline high or high total cholesterol with mean of 194.64 ± 30.62 (mg/dL). 104 (50.73%) patients had borderline high triglyceride levels with a mean of 166.48 ± 63.03 (mg/dL). 25 (12.2%) patients were smokers. 24(11.7%) patients had dexa scan proven osteoporosis (T score <-2.5). Amongst all, 54 (26.3%) patients had low cardiovascular risk, 93 (45.4%) had moderate risk and 58 (28.3%) had high risk according to Framingham risk score.

Conclusion: RA patients have high cardiovascular risk. Other co-morbidities like hypertension, high BMI, diabetes, dyslipidemia, smoking and osteoporosis add to the morbidity and mortality of these patients.

Keywords: Cardiovascular disease risk, Framingham risk score, Rheumatoid Arthritis.

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INTRODUCTION

Rheumatoid arthritis (RA) is a lifetime, chronic debilitating disease with a high morbidity and mortality rate. It affects 0.5% to 1% of the world population[1]. According to local studies the prevalence of RA in Pakistan has been reported to be around 0.5%[2]. It is a disease with continuous inflammation in the patient with formation of auto-antibodies leading to the production of cytokines. The RA patients have increased risk of advance atherosclerosis at a younger age. The risk of cardiovascular death is also associated with the disease activity level, the presence of Rheumatoid factor (RF) and anti-cyclic citrullinated peptide (ACCP) antibodies, disease duration of more than 10 years and presence of extra articular manifestations like rheumatoid nodules, interstitial lung disease, scleritis, and episcleritis[3]. Patients with RA as a result of chronic inflammation are more susceptible to cardiovascular events like myocardial infarction (MI) and stroke[4]. Acute MI is the most common cause of death in RA patients[5]. Patients with RA have a two to five times increased risk of developing premature cardiovascular disease (CVD) that shortens life expectancy by 5-10 years[6]. Along with coronary events, risk of ischemic stroke is also increased in RA patients[7]. Methotrexate and other disease

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modifying antirheumatic drugs decrease the risk of cardiovascular events by controlling the overall inflammatory process[8]. A number of medicines like non-steroidal anti-inflammatory drugs and steroids that are used in the treatment of RA are also responsible for this increase risk[9]. Hence, early detection of all the risk factors in this group of people is essential along with the management of chronic inflammation. A number of cardiac risk assessment scores are used to find the CVD risk in general population like Framingham risk score, systemic coronary risk evaluation (SCORE), American college of cardiology/American Heart Association risk score ASCVD risk score and Reynolds risk score[10]. Validation of these risk scores is questionable in population with RA[11]. Nonetheless, these can be applied in RA population to find the CVD risk and categorize them into low, moderate and high risk[11]. The benefit of this categorization is to screen all patients of RA to detect the risk earlier and intervene about these risk factors. According to european league against rheumatism (EULAR); cardiovascular risk assessment in patients with RA should be performed according to national guidelines and the SCORE risk prediction model should be used if no national guidelines are available. The calculated risk score should be multiplied with a factor of 1.5 as the risk is higher[2]. Hence, risk stratification should be done and patients having high risk or moderate risk should be counseled regarding lifestyle modification and aggressively modifying the risk factors[12]. According to study done by Boo *et al*[13], most of the RA patients underestimate the CVS risk. Managing them according to guidelines and providing awareness to patients to change their daily habits and life styles is of paramount importance to lower the morbidity and mortality. The purpose of the study is to calculate CVD risk using Framingham risk tool and apply EULAR recommendations to find the correct cardiovascular risk[2]. Local data about the utilization of such tools remains scarce. Hence, awareness and emphasis on these risks should be done by the treating physician at the time of diagnosis and every 5 years in low risk patientsand more frequent in patients in moderate to high risk groups[3].

PATIENTS AND METHODS

This is a cross sectional descriptive study conducted in the Rheumatology department of Fauji Foundation Hospital (FFH), Rawalpindi. Approval was taken from the institutional ethical review board. Patients were selected by non-probability consecutive sampling and informed written consent was taken from the patients. The duration of the study was six months (from 1st Nov 2017 to 30th Apr 2018). Two hundred and twenty patients were selected and the sample size was calculatedusing WHO sample size calculator (24% anticipated population, 6% absolute precision, 95% confidence interval). Patients diagnosed as case of RA based upon ACR 2010 criteria[14], between 40 to 80 years were selected. Patients, who donot fulfill the above criteria orhad aprevious history of ischemic heart disease or stroke or using any lipid lowering drug were excluded from the study. Patients were assessed at baseline and after one week. Demographic details of the patients including age, gender, duration of the disease, medications used, were entered in the study proforma. Previous history of hypertension, diabetes, ischemic heart disease, stroke and smoking was asked from the patients. Blood pressure was measured using sphy gmomanometer after resting the patient for 5 minutes both at first visit and after one week and the mean of the two readings was taken. At first visit disease activity was assessed clinically by noting number of tender joints (TJ), swollen joints (SJ) and visual analogue score (VAS) for pain (0-10). Blood sample was drawn forfasting lipid profile and erythrocyte sedimentation rate (ESR). DAS28 of the patient was calculated using online calculator. Body mass index was measured using the BMI formula i.e. weight in kilograms /(height in meter). Framingham risk score was calculated by using patient's age, blood pressure, total cholesterol (TC), high density lipoproteins (HDL), history of smoking, diabetes and hypertension using the online calculatorand it was multiplied

by a factor 1.5 as per european league against rheumatism (EULAR) recommendations to find the correct cardiovascular risk. This gave a 10 year cardiovascular risk in each RA patient (low risk:less than 10%, moderate risk: 10% to 20% or high risk more than 20%. Data was analyzed using SPSS version 23.0. Mean and Standard deviation (SD) were calculated for numeric variables like age, systolic blood pressure (SBP), diastolic blood pressure DBP and Framingham risk score (FRS). Percentage sand frequencies was calculated for risk factors like number of patients with high BMI, hypertension, diabetes, smokers, high LDL andlow, moderate and high FRS.

Table-I: Baseline Characteristics of the study population.

Characteristics	Number (%) or Mean ± SD
Total number of patients	n=205
Gender	Female 202 (98.54%) Male 3 (1.46%)
Age (years)	53.33 ± 10.31
Duration of disease (years)	9.89 ± 7.00
Age of RA diagnosis (years)	43.73 ± 9.13
Low density lipoprotein (mg/dL)	116.75 ± 29.50
High density lipoprotein (mg/dL)	41.42 ± 7.17
Total Cholesterol (mg/dL)	194.64 ± 30.62
Triglycerides (mg/dL)	166.48 ± 63.03
Systolic blood pressure (SBP) mmHg	128 ± 17.64
Diastolic blood pressure (DBP) mmHg	78.63 ± 8.80
Body mass index	25.35 ± 4.96
Framingham risk score	15.60 ± 6.84
Seropositive (Either RA or Anti CCP positive)	138 (67.31%)
Seronegative (Both RA factor and Anti CCP negative)	67 (32.68%)

RESULTS

Out of 220 patients 15 patients lost to follow up. The baseline demographics characteristics of the study population are as shown in table-I. According to the calculated FRS; 54 (26.3%) patients had low cardiovascular risk, 93 (45.4%) had moderate risk and 58(28.3%) had high risk. The comorbidities found in the study population are as shown in table-II.

DISCUSSION

Rheumatoid arthritis is a chronic disease with high morbidity not only because of the disease itself but due to associated comorbidities as well. RA was previously thought to be a disease of joints with no impact on overall body of the patients. But the use of NSAIDs, steroids and systemic inflammation in RA leads to increased cardiovascular risk and early death as compared to general population[15]. Boo *et al* in a South Korean study conducted on 200 patients showed that 60% and 12% patients have moderate and high FRS risk respectively. It also showed that 43% had high BMI, 39% had hypertension, 7% had diabetes and 5% were smokers[13]. As compared to our study about 45.4% and 28.3% have moderate to high scores respectively. And 40% patients have hypertension, 48.8% patients have either borderline BMI or obese, 18.5% had diabetes, 12.2% had history of smoking. In a study conducted locally[16].

Wagan *et al*, observed a high BMI of 48.4%, high LDL 43.5%, hypertension 37.4%, Diabetes 22.8% and smoking 15.9%, moderate to high FRS of 40.2% with males having higher FRS score than femalesin a sample of 246 RA patients[16]. The FRS risk scores are higher in our sample as compared to this study which could be due to multiplication with factor 1.5 as per EULAR guidelines. Along with traditional risk factors that include hypertension, diabetes mellitus, smoking, dyslipidemia, obesity, older age and male gender; other contributing factors may be seropositive status for antibodies, high disease activity and disease duration. In our study, hypertension is present in 40% of the sample size,

the reason to this increase prevalence of hypertension may be due to RA itself or the drugs that are used for the treatment of RA especially steroids and NSAIDs. Diabetes is also prevalent in 18.5% of population. Smoking adds to morbidity of most of the patients are huqqa smokers in the sample. Another risk factor which is important is high BMI; about 48.8% of the patients lie in range more than 25, this is mostly due to physical inactivity as most of the patients with RA are not very active or there may be contribution from drugs which are used to suppress the immune process in the body. The study conducted in accordance with the EULAR guidelines and calculating the CVS risk with multiplication with factor 1.5 as per guidelines. There are very few of these studies with consideration of all these factors and comorbidities done. The purpose of study is to calculate the actual risk of the patients of RA so that it will be communicated and counseled to patients and rheumatologist who is mainly managing the joint symptoms of the patients, should also guide and manage these risk factors so that mortality and morbidity of this moderate and high risk group should be reduced. It is the responsibility of the treating rheumatologist to ensure that CVS risks are being treated and managed in a proper way[2]. The high risk group is very important in this regard that these patients have risk of myocardial infarction about 70% higher than in the general population[4]. A study demonstrated 42% excess risk of death among subjects with RA as compared with the general population[5]. Screening of all patients at baseline and every 5 years for CVS risk factors should be done and if they have intermediate and high risk CVS evaluation should be done more often[12]. Proper guidance regarding physical activity to reduce weight and maintaining ideal weight, control of hypertension either by using antihypertensive or lifestyle modification, keeping diabetes in limits

Table-II: Comorbidities in the study population.

Variables	Number and percentages
Hypertension	82 (40%)
Diabetes mellitus	38 (18.5%)
Smoking	25 (12.2%)
High BMI	
Over weight=25 to 30	69 (33.7%)
Obese= above 30	31 (15.1%)
Low Density Lipoprotein(LDL)	
Borderline high=130-159	37 (18.04%)
High=more than 160	10 (4.87%)
Very high=more than 190	4 (1.95%)
Total cholesterol	
Borderline high=200-239	78 (38.04%)
High=more than 240	10 (4.87%)
Triglycerides	
Borderline high=150-199	58 (28.29%)
High=200-499	45 (21.95%)
Very high=more than 500	1 (0.48%)
High density lipoprotein	9 (4.39%)
Low=less than 40	
Optimal = 40 to 60	74 (36.09%)
High=more than 60	122 (59.51%)
Osteoporosis	24 (11.7%)
Framingham risk score	
Low	54 (26.3%)
Moderate	93 (45.4%)
High	58 (28.3%)

with medicines or diet, managing osteoporosis with anti-resorptive therapy, guidance about quitting smoking, and vaccination of these patients against common pathogen and lastly keeping lipid levels in normal range by dietary modification and statins is a must. Methotrexate and other DMARDS also decrease systemic inflammation[17]. It should be the plan in all patients of RA especially the moderate and high risk group, along with joint symptoms management these risk factors should be identified and treated aggressively and proper counseling of these patients should be done as under treatment of CVS risk factors is a cause of increase mortality[19]. Lifestyle modification physical activity, maintaining ideal body weight, low salt diet, quitting smoking should be emphasized in every patient in every visit along with drug compliance. The study could have been done on different settings with different study groups which could have generated a comparison.

LIMITATION OF STUDY

Our study had certain limitations which include limited time duration, non-probability sampling technique, very few numbers of male RA patients, one center study and no comparison group. Disease activity co relation was not seen with CVD risk as it is not the primary goal of the study so correlation is not seen.

CONCLUSION

RA patients have a high cardiovascular risk score and there is increased prevalence of other comorbidities like hypertension, diabetes, smoking, dyslipidemias, and obesity in this group of patients.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any of the authors.

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