Are different Metabolic Syndromes, associated with Rheumatoid Arthritis?

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ABSTRACT

This study cross-sectional analytic study was conducted at Department of Medical Unit-1, Services Hospital, Lahore, from 3rd June 2019 to 3rd December 2019 with an objective to measure the frequency of metabolic syndrome in patients with newly diagnosed (treatment naïve) Rheumatoid Arthritis. A total 74 Rheumatoid Arthritis (RA) patients diagnosed according to 2010 American College of Rheumatology-European League against Rheumatism classification criteria were included and were treatment naïve. Age and sex matched apparently healthy controls were also included. Metabolic syndrome (MetS) was diagnosed based on the National Cholesterol Education Program (Adult Treatment Panel III 2004 revised criteria). It was found that 50% of the patients with Rheumatoid Arthritis had Metabolic syndrome and in control group this frequency was 32.43%. The diagnostic criteria used to diagnose MetS was 'National Cholesterol Education Program (Adult Treatment Panel III 2004 revised criteria)' ($p<0.05$). Rheumatoid Arthritis (RA) group was seen to be more prone to have lower high density lipoproteins (62.16%), higher triglycerides (50%), higher blood pressure levels (40.54%), higher FBG (20.27%) and increased waist circumferences (35.13%). In conclusion, it was observed that metabolic syndrome (MetS) is more prevalent in Rheumatoid Arthritis (RA) group when compared to control group.

Keywords: Rheumatoid arthritis, Metabolic syndrome, Prevalence, Frequency, Treatment naïve

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INTRODUCTION

WHO, in 1998, defined the first criteria of MetS. It was the three years after the original criteria, the new National Cholesterol Education Program criteria of MetS were proposed. Metabolic syndrome (Syndrome X) by definition is a cluster of conditions that are cardiovascular disease risks, such as diabetes, high blood pressures, dyslipidemia and obesity. The pathophysiology of metabolic syndrome is thought to be due to insulin resistance along with abnormal adipose distribution and function. Dysfunctional adipose tissue also play an important role in pathogenesis of insulin resistance[1]. All of these conditions accelerate atherogenic state increasing the risk for cardiovascular diseases like coronary heart disease and stroke; fatty liver and several cancers.

Rheumatoid arthritis is a persistent symmetrical polyarthritis that can affect any joint that is lined by a synovial membrane and is one of the major reasons for higher disability burden and mortality[2]. Rheumatoid arthritis is thought to be an independent risk factor for increased atherogenesis causing an increased mortality due to cardiovascular diseases[3,4]. In addition to this, treatment of rheumatoid arthritis and the sedentary lifestyle secondary to disability, in turn add on to the risk for cardiovascular disease[5]. The rheumatoid arthritis may associated with higher chances of a cardiovascular disease and this may be a consequence of metabolic syndrome associated with RA patients[6].

There are several criteria to define metabolic syndrome like National Cholesterol Education Program- Adult Treatment Panel III (NCEP-ATP III) 2004 revised criteria or the WHO criteria. However, NCEP-ATP III 2004 revised criteria is widely used.

There isn't much data in Pakistani community about the frequency of MetS in RA patients. The goal of this study is to assess the prevalence of MetS in treatment naive RA patients with a rationale to assess every new RA case for MetS with the objective to avoid complications associated with metabolic syndrome. So this study was conducted with an objective to assess the frequency of metabolic syndrome in newly diagnosed (treatment naïve) Rheumatoid Arthritis.

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METHODOLOGY

This cross-sectional analytical study has included 74 patients with RA that came to Medicine Department, Services Hospital, Lahore for evaluation between 3rd June 2019 and 3rd December 2019, and fulfilled the criteria laid down by 2010 American College of Rheumatology and European League Against Rheumatism.

The criteria for inclusion of subjects in this study was newly diagnosed RA patients or those patients with RA that had been diagnosed earlier but did not take any DMARD ever either due to any reason. The exclusion criteria comprises of dyslipidemia causing conditions like Hypothyroidis, Nephrotic syndrome or Familial Dyslipidemia. Any patient receiving Lipid lowering drugs as well as any Urate lowering drugs or non-compliant with the treatment with DMARDs was also excluded. Those diagnosed with chronic inflammatory conditions like chronic kidney disease, neoplastic disorders, chronic liver disease were also excluded. Those having infections like human immunodeficiency virus were also excluded as well as any patient with the age below 16 years. Female patients that were pregnant or any patient on oral contraceptive pills was not included in this study. A total sample size of 148 individuals where the control group included 74 subjects, with age and sex matched candidates from the general population of Lahore. All the candidates had given informed consent and approval certificate was obtained from the Institutional Review Board, Services Institute of Medical Sciences, Lahore.

MetS was diagnosed with the National Cholesterol Education Program (Adult Treatment Panel III 2004 revised criteria) taking at least three out of five features to diagnose MetS. Weight and Height were measured in both RA and Control group to calculate Body Mass Index (BMI) and categorized as underweight (<18.5kg/m^2), normal (18.5-22.9), overweight (23-27.49) and obese (>27.5 kg/m^2). Circumference of the waist was measured using a measuring tape at mid-way between lower costal margin and anterior superior iliac spine at with the breathing held at end-expiration. Mercury sphygmomanometers were used to measure blood pressures with the patient sitting for five minutes. Serum HDL and Serum Triglycerides were measured by taking venous blood samples post 10 hours overnight fast as well as fasting blood glucose and all of these were analyzed by auto analyzer.

Data Analysis: This data that was gathered was then compiled. This was followed by tabulation and analysis of this data as descriptive statistics using the IBM SPSS version 22.0. Mean ± Standard Deviation is used to represent continuous data whereas the categorical data is represented in terms of percentages. Groups of categorical data were compared using Chi Square test. A $p<0.05$ was taken statistically significant.

RESULTS

A total of 148 patients were studied. The mean age of patients was 40.94 +/_ 5.26 in both groups and mean BMI was slightly more in RA group when it was compared to control group (25.49 ± 2.25 vs. 25.43 ± 2.3). The mean waist circumference was again more in RA group when it was compared to control (86.54 ± 11.31 vs. 86.54 ± 11.31) so was mean systolic BP (134.89 ± 14.52 vs. 113.35 ± 15.13). Over all 16 (21.62%) patients were greater than 45 years in age (Table-I).

Table-I: Demographic and anthropometric Features of RA group and Control Group (N=148)

	Control Group		RA Group		Value of Test used	p-Value
	%	Mean ± SD	%	Mean ± SD		
Age in years		40.94 ± 5.26		40.94 ± 5.26		
Female	78.37		78.37			
Weight (Kg)		62.82 ± 8.75		63.14 ± 8.56		
Height (m^2)		2.48 ± 0.36		2.48 ± 0.36		
Body Mass Index (Kg/m^2)		25.43 ± 2.3		25.49 ± 2.25	1.21	0.9763879
Waist Circumference (cm)		84.44 ± 11.55		86.54 ± 11.31		
Systolic BP (mmHg)		113.35 ± 15.13		134.89 ± 14.52		
SD: Standard Deviation, BP: Blood Pressure						

The median triglycerides levels were found to be higher in RA group compared to the control group whereas the median HDL levels were pound to be lower in RA group compared to the control group (Table -II).

Table-II: Biochemical parameters for RA group and Control Group (N=148)

	Control group	RA group	Value of Test used	p-Value
	Median	Median		
Triglycerides (mg/dL)	142	150	0.207	0.90167602
HDL (mg/dL)	42	41		
FBG (mg/dL)	112	110		
HDL: High Density lipoproteins, FBG: Fasting Blood Glucose				

Table-III: Frequency of MetS criterion in RA group and Control (N=148)

	Control group N=74		RA group N=74		Value of Test used	p-Value
	Frequency	%	Frequency	%		
Increased waist circumference	21	28.37	26	35.13		
Elevated Triglycerides	32	43.24	37	50	0.225	0.99412705
Reduced HDL	41	55.4	46	62.16		
Elevated FBG	11	14.86	15	20.27		
Elevated Systolic BP	25	33.78	30	40.54		
BP: Blood Pressure, HDL: High Density lipoproteins, FBG: Fasting Blood Glucose						

Frequency of MetS in RA group was 50% (N=37) and in control group was 32.43% (N=24) based on NCEP-ATP III 2004 revised

criteria and both groups were compared using Chi Squared test keeping p<0.05 as statistically significant. The Chi square statistic was 4.713 and the p value was .0299 making it statistically significant (Table-III).

RA group was seen to be more likely to have lower high density lipoproteins (62.16%), higher triglycerides (50%), higher blood pressure levels (40.54%), higher FBG (20.27%) and increased waist circumferences (35.13%).

DISCUSSION

Our study was carried out at the Medicine department of Services Hospital in Lahore, Pakistan, with the goal to assess whether or not there is a higher frequency of MetS in treatment naïve RA patients and is this prevalence statistically significant. Our study found out that MetS is in higher frequency in patients diagnosed with RA in compared to control group (50% vs. 32.43%). Only a few studies have been done in Pakistan to study the frequency of MetS in RA and in most of these studies patients were already on DMARD treatment and only a few were treatment naïve[7].

RA in itself is an independent risk for atherosclerosis[8]. The pro inflammatory chemicals like Tumor necrosis factor alpha, interleukin 6 and cytokines all contribute to atherosclerosis and insulin resistance[9,10]. Insulin resistance in turn, results in abnormal levels of blood glucose, HDL and triglycerides, increasing the risk of atherosclerosis and hence, the risks for cardiovascular events like myocardial infarction or stroke[11]. Therefore, RA in itself increases the risk of developing MetS and insulin Resistance.

Dyslipidemia tends to be more frequent in patients with RA. Trends of dyslipidemia similar to our study have also been seen by Castro and colleagues in their study that is frequency of dyslipidemia was higher in RA patients[12]. Dar et al in their study found a higher prevalence of waist circumference, BMI and weight in RA patients[13].

Similarly frequency of hypertension tends to be higher in RA patients. Dao HH, Do QT, Sakamoto J. reported higher proportions of hypertension in RA patients[14]. RA in itself is an independent risk for cardiovascular diseases, which is a consequence of cascade of inflammation. Therefore, any therapy with anti-inflammatory effects, especially the novel biologic drugs may be of value in managing any cardiovascular risk in patients with a newly diagnosed RA and may also be a promising approach among the general population[15]. Therefore, managing RA should be a multi-disciplinary team (MTD) effort to combat not just the RA but also its complications and all the complications associated with metabolic syndrome. It is, therefore, equally important to actively look for all the aspects of metabolic syndrome (diabetes, hypertension, dyslipidemia and central obesity) and treat the patient on all fronts. It should be made a practice to evaluate every new case of RA for diabetes, hypertension, dyslipidemia and central obesity with an early intervention, so that atherosclerosis can be avoided and with that complications like stroke and myocardial infarction can be evaded.

Considering the results of our study and the results of the other studies discussed above, it is important to check for the frequency of MetS in treatment naive RA patients with a rationale to assess every new RA case for MetS with the objective to avoid complications associated with MetS.

CONCLUSION

In conclusion, MetS is more prevalent in RA group in comparison to the control group.

AUTHOR'S CONTRIBUTION

Hussian R: Conceived idea, Designed research methodology, Literature search, Literature review
Fahad M: Data collection, Data analysis, Statistical analysis
Nawaz A: Data collection, Data analysis, Manuscript final reading
Zahid A: Data collection, Data analysis, Manuscript writing

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