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Original Research Paper

Rheumatology

AN ASSOCIATION OF METABOLIC PARAMETERS WITH DISEASE ACTIVITY SCORE IN EARLY UNTREATED RHEUMATOID ARTHRITIS: A CROSS SECTIONAL STUDY.

Anubha Srivastava Associate Professor Medicine MLN Medical College Prayagraj, UP, India, 211002.

Mohit Tripathi Junior Resident Medicine MLN Medical College Prayagraj, UP, India, 211002.

Saransh Baranwal* Junior Resident Medicine MLN Medical College Prayagraj, UP, India, 211002. *Corresponding Author

ABSTRACT

Background: Evaluating the correlation between various metabolic parameters with the disease activity and insulin resistance in early untreated patients of rheumatoid arthritis.

Methods: A cross-sectional study was done. 60 patients of RA(diagnosed by the ACR-EULAR criteria) were studied. Metabolic parameters included FPG, 2Hr PG, A1C, IR, BMI, TG/HDL ratio, and TC/HDL ratio. 20(33.3%) had high DAS while 36(60.0%) had moderate DAS. **Results:** On OGTT, 22(36.7%) patients had IFG/IGT and 6(10%) were diabetic. A1C was in diabetic range(≥6.5%) in 4(6.7%) subjects and in pre-diabetic range in 30(50.0%). 37(61.7%) patients were having IR(HOMA-IR≥2.50). TG/HDL ratio was increased in 36(60.0%) subjects while TC/HDL ratio was increased in 17(28.3%) subjects of RA.

Discussion: There occurs a significant correlation of DAS 28 SCORE with IR, TG/HDL,TC/HDL ratio in early untreated patients of rheumatoid arthritis

KEYWORDS : Metabolic parameters, Rheumatoid arthritis, Disease Activity Score

INTRODUCTION

Rheumatoid arthritis (RA) is a multisystem disorder characterized by a symmetric polyarthritis having several extra-articular manifestations.[1]. There has been advocation of association of Insulin Resistance (IR) between metabolic syndromes and factors related to obesity such as dyslipidemia. [2,3] Insulin resistance (IR) is a key feature of obesity, metabolic syndrome, and type 2 diabetes mellitus (T2DM). Although RA patients have a high prevalence of metabolic syndrome and factors related to obesity, dyslipidaemia, and metabolic disorders, very few studies have been done in this population.[4] Disease-associated reduction in lean muscle mass and sedentary lifestyle likely further contribute to IR in patients with RA.[5]

MATERIALS AND METHODS

A hospital based cross-sectional study was carried out in Department of General medicine/Orthopaedics in SRN Hospital, MLN medical college, Prayagraj, Uttar Pradesh, India over a period of one year in 2019-2020. Patients who were diagnosed as a case of RA based on ACR-EULAR criteria were selected from OPD, after following standard protocol of Ethical and Scientific clearance. After obtaining informed consent, patients were assessed thoroughly via detailed history, physical examination, and laboratory investigations. A total of 60 patients of RA (diagnosed on the basis of ACR-EULAR criteria) underwent oral glucose tolerance test (OGTT) and glucose profile [Fasting plasma glucose (FPG), 2Hr PPG (Postprandial glucose), Glycosylated Haemoglobin (A1C)} was studied. Other metabolic parameters including Insulin Resistance (IR), Basal Metabolic Index (BMI) and Triglycerides (TG) /High Density Lipoprotein (HDL) and TC/HDL (Total Cholesterol) ratio were also studied. Patients with diagnosed hypertension, chronic kidney disease, diabetes mellitus, congestive cardiac failure, and other acute inflammatory conditions (besides RA) were excluded from the study.

Blood samples were withdrawn in morning after overnight fasting and laboratory evaluation was done. Patients were subjected to OGTT according to World Health Organisation (WHO) recommendations. Data was collected and entered in MS Excel sheet and was analysed and statistically evaluated using SPSS-PC-20 version. Pearson correlation coefficient was used to see the correlation between two quantitative variables. 'P' value less than 0.05 was considered statistically significant.

RESULTS

60 RA patients of >18 years age and sex were taken and divided into two subgroups based on their DAS28 score; first subgroup (n=40, 66.7%) had low/moderate disease activity as defined by DAS28≤5.1 and the second (n=20, 33.3%) had high disease activity (DAS28>5.1).

Out of 60 patients, 20(33.3%) patients had high disease activity while 36(60.0%) had moderate disease activity. 7 (11.7%) had FPG of ≥126 while 21 (35.0%) had FPG in pre-diabetic range (100-125).

2Hr PPG was in diabetic range (≥200) in 5 (8.3%) patients while 33 (55.0%) were in pre-diabetic range (140-199). On OGTT impaired fasting glucose/impaired glucose tolerance prevalence was 36.7% while 6 (10.0%) were found to be diabetic.

HbA1C was in pre-diabetic range (5.7-6.4%) in 30 (50.0%) while in 4 (6.7%) patients, it was in diabetic range (≥6.5).

The mean BMI in patients with low/moderate disease activity was 23.56±2.48 and in patients with high disease activity, it was 24.87±3.63. The correlation of increased BMI with increased disease activity (DAS28 score) had p value of 0.11.

TG/HDL ratio in patients with low/moderate disease activity was 1.79±0.38 and in patients with high disease activity, it was 2.65±0.53. The correlation increased TG/HDL ratio with increased disease activity (DAS28 score) had p value of <0.001. TC /HDL ratio in patients with low/moderate disease activity was 2.36±1.05 and in patients with high disease activity, it was 3.15±1.16. The correlation increased TC/HDL ratio with increased disease activity (DAS28 score) had p value of 0.01.

Table 1

Variable	Low/moderate DAS-28 (n=40)	High DAS-28 (n=40)	P value
Age	41.88±10.75	41.88±10.75	0.81
Fasting plasma glucose	94.38±9.07	118.25±20.41	<0.001
BMI	23.56±2.48	24.87±3.63	0.11
TG/HDL	1.79±0.38	2.65±0.53	<0.001
TC/HDL	2.36±1.05	3.15±1.16	0.01

Table 1 shows 40 RA patients (66.7%) had low/moderate disease activity (defined by DAS28≤5.1) and 20(33.3%) had high disease activity (defined by DAS28>5.1). The subgroup with high disease activity had significantly higher fasting glucose, 2-hour post prandial glucose, TG/HDL ratio and TC/HDL ratio as compared to subgroup with low/moderate disease activity. Correlation between BMI and high disease activity was not found to be significant.

Figure 1 and 2 shows significant correlation of DAS score with FPG, HOMA IR and Fig 3 shows significant correlation of HOMA IR and TG/HDL.

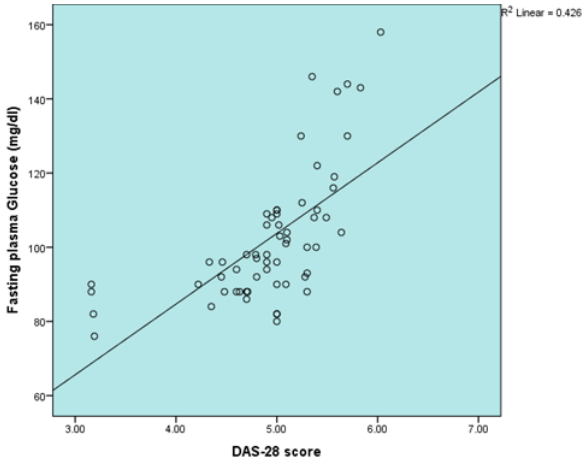

Fig 1 Scatter plot showing correlation of Disease activity score-28 with fasting plasma glucose

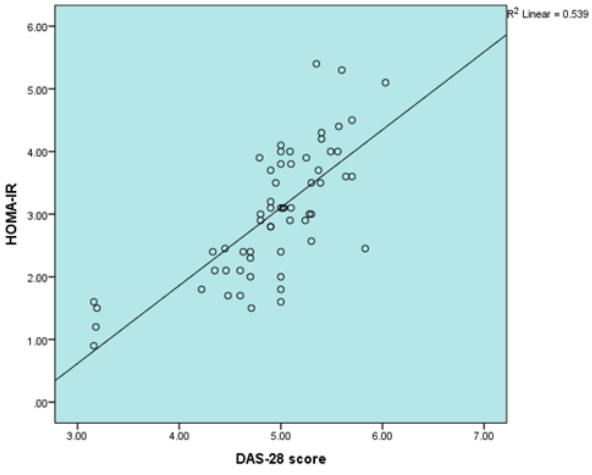

Fig 2 Scatter plot showing correlation of Disease activity score-28 with HOMA-IR

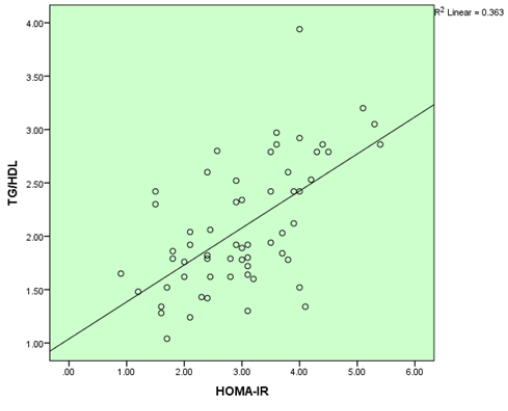

Figure 3: Scatterplot showing correlation of HOMA-IR with TG/HDL in RA subjects

DISCUSSION

In this observational prospective study patients with high disease activity was found to have significantly higher FPG(r value=0.65, p valve<0.001), 2 hour PPBG (r value=0.67, p value<0.001), HbA1C (r value=0.72, p value<0.001), TG/HDL ratio(r value=0.25, p value=0.05) and TC/HDL ratio(r value=0.53, p value<0.001). Association between increased BMI with high disease activity in RA patients was found to be insignificant (p value=0.11).

37(61.7%) patients among all the patients of RA were defined as having IR (HOMA-IR≥2.50).

There was a statistically significant positive correlation between HOMA-IR values and each of the fasting serum insulin (r=0.92, p<0.001), TG/HDL ratio (r =0.60, p<0.001) and DAS-28 (r=0.73, p <0.001).

Steiner G et al (2009) tried to describe the impact of rheumatoid arthritis (RA), and its treatment, on lipoprotein levels with potential implications for atherosclerosis. Patients with RA face an increased risk of developing premature cardiovascular disease and limited ability to modify risk factors, eg, through exercise. RA is associated with an abnormal lipoprotein pattern, principally low levels of high density lipoprotein (HDL) cholesterol. Most treatments for RA tend to improve the atherogenic index (total/HDL cholesterol ratio), with more evidence for biologics in this regard. The improvement in the lipoprotein profile in RA appears to be associated with suppression of inflammation. It was concluded that lipid levels should be monitored and managed in patients with RA to minimise the long-term risk of cardiovascular disease. More research is needed to quantify the relationship between systemic inflammation.[6]

Chen DY et al (2015) investigated the associations of RA-related inflammation or rheumatoid factor (RF)/anti-cyclic citrullinated peptide (anti-CCP) positivity with lipid profiles and IR. There was an inverse correlation between disease activity (disease activity score for 28 joints, or DAS28) and low-density lipoprotein cholesterol (LDL-C) levels (r = −0.226, P <0.05) and a positive correlation between DAS28 and IR (r = 0.361, P <0.005). There was also a positive correlation between IR and levels of IL-6 or TNF-α. HDL-C levels significantly increased in patients receiving 6-month anti-TNF-α therapy, and levels of total cholesterol, LDL-C, and triglyceride increased in tocilizumab-treated patients. IR significantly decreased in patients under biologic therapy but was unchanged in biologic-naïve patients. Age, IR, and DAS28 were significant predictors of severe subclinical atherosclerosis (odds ratios of 1.08, 2.77, and 2.52, respectively).[8]

These finding are similar to our study. Ostojic P et al (2016) tried to estimate the impact of disease activity, obesity, functional disability, and depression on lipid status, glycoregulation, and risk for coronary heart disease (CHD) in patients with rheumatoid arthritis (RA). 36 patients with RA were included in this study. Out of 36 patients, 11 (30.6 %) fulfilled the criteria for metabolic syndrome (MS). Ten of 11 patients (90.1 %) with MS had a 10-year risk for CHD greater than 10 % compared to only 3 of 25 patients (12 %) without MS (p = 0.0001). Patients with high disease activity had lower HDL values than patients with mild or moderate disease activity (1.4 vs. 1.7 mmol/l, p = 0.04). Significant correlations were observed between CRP level and insulinemia (ρ = 0.57, p = 0.003), as well as CRP level and the HOMA index (ρ = 0.59, p = 0.002). The body mass index (BMI) correlated significantly with total cholesterol (r = 0.46, p = 0.02), LDL (ρ = 0.41, p = 0.04), and TG (ρ = 0.65, p < 0.001) in blood. The HAQ-DI did not correlate either with parameters of glycoregulation or lipid status. It was concluded that active RA is independently

associated with decreased HDL cholesterol and increased insulin resistance. Obesity was found to be an independent risk factor for increased total cholesterol, LDL cholesterol, and TG. Depressed patients with RA tend to be overweight or obese and, therefore, have an unfavorable lipid profile.[9]

Erum U et al (2017) conducted a study to determine the frequency of dyslipidemia in patients with RA. Out of 200 patients, 23 (11.5%) were male and 177 (88.5%) were female. A total of 107 (53.5%) patients had dyslipidemia. The most common abnormality seen was a low HDL, seen in 83 (41.5 %) patients. This may be considered as a secondary impact of chronic inflammatory state, seen in RA. It was concluded that lipid abnormalities should be sought at regular intervals, and corrective actions taken to mitigate increased cardiovascular disease risk.[10]

These finding are similar to our study.

CONCLUSION

In our study there was a significant positive correlation between DAS28 score and fasting plasma glucose ® value=0.65, p valve<0.001), 2 hour post prandial glucose ® value =0.67, p value<0.001), HbA1C(r value=0.72, p value <0.001), TG/HDL ratio(r value=0.25, p value=0.05) and TC/HDL ratio(r value=0.53, p value<0.001). Insulin resistance defined as HOMA-IR≥2.50 was associated with increased values of fasting serum insulin (r=0.92, p<0.001), TG/HDL ratio (r =0.60, p<0.001) and DAS-28 (r=0.73, p <0.001). Though the association between increased BMI with high disease activity in RA patients was insignificant (p value=0.11). Further, patients of Rheumatoid arthritis should be subjected to A1C and lipid profile evaluation at early stages. Detection of derangement in metabolic parameters at early stages can lead to improved disease outcomes.

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