ORIGINAL RESEARCH PAPER
Volume - 10 | Issue - 07 | July - 2021 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

ASSOCIATION BETWEEN GLUCOSE PROFILE AND INSULIN RESISTANCE WITH DISEASE ACTIVITY IN PATIENTS WITH EARLY UNTREATED RHEUMATOID ARTHRITIS: A CROSS SECTIONAL STUDY.

Medicine

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

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

ABSTRACT

Introduction – Rheumatoid arthritis (RA) is a chronic multisystem disease of unknown cause, with a wide variety of systemic manifestations but a persistent inflammatory synovitis as the characteristic feature

Method: This cross-sectional study was conducted at SRN hospital MLN medical college; a tertiary care centre, Prayagraj (U.P) India to find out Correlation between Glucose profile and Insulin Resistance with Disease Activity Score in patients with Early Untreated Rheumatoid Arthritis.

Results: A total of 60 RA patients (diagnosed as per the ACR-EULAR criteria) either sex and age >18 years were selected. Subjects underwent OGTT and glucose profile (FPG, 2HrPPG, A1c) values were observed. RA disease activity and IR was assessed using the Disease Activity Score 28 (DAS 28) and HOMA-IR respectively. RA patients included in the present study were divided into two subgroups according to their DAS28; the first subgroup (n=40, 66.7%) exhibited low/moderate disease activity defined by DAS28≤5.1 and the second (n=20, 33.3%) showed high disease activity (DAS28>5.1). Out of 60 subjects, one-third subjects 20 (33.3%) had high DAS while 36 (60.0%) had moderate DAS. On OGTT, prevalence of IFG/IGT was 36.7% while 6 (10.0%) patient of RA were found diabetic.37 patients (61.7%) in patients with RA were defined as having IR (HOMA-IR≥2.50).

Conclusions: It has observed that patient subgroup with high DAS revealed significantly higher FPG, 2Hr PG,A1C and IR in comparison to the low/moderate DAS.

KEYWORDS

Glucose Profile, Rheumatoid arthritis, Insulin resistance, Disease Activity Score

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory disorder of unknown etiology, characterized by systemic symptoms that particularly involve the joints and may lead to deformities during the course of the disease.[1] Its most apparent feature is the chronic inflammatory synovitis symmetrically covering the peripheral joints.[2] .However, RA may also have extra-articular manifestations such as involvements of the cardiovascular system, haematological system, liver, respiratory system, eyes, muscles, kidneys and the neurological system.[3,4]

Insulin resistance (IR) is a key feature of obesity, metabolic syndrome, and type 2 diabetes mellitus (T2DM). IR is not a disease unto itself, but rather a physiological abnormality that greatly increases the chances of developing diabetes and metabolic syndrome.[5] Although RA patients have a high prevalence of metabolic syndrome and factors related to obesity, dyslipidemia, and metabolism disorders, only few studies have been specifically designed to investigate IR in this population.

Several studies have discussed the association between chronic inflammatory disease states and disorders in intermediary metabolism,[6,7] particularly peripheral IR. In addition, numerous independent studies have implicated the association of multiple immune regulatory components (including tumor necrosis factor-α [TNF-α] and interleukin-6 [IL-6]) in RA, IR, and T2DM.[8,9,10]Disease-associated reduction in lean muscle mass and sedentary lifestyle likely further contribute to IR in patients with RA.[11].

MATERIALS AND METHODS

The study was carried out at the Department of general Medicine/orthopaedics of SRN Hospital, MLN Medical College, Prayagraj, Uttar-Pradesh, India. After taking approval from the Scientific Research and Ethics Committee, patients who fulfilled the inclusion criteria were taken up for the study. First, the purpose of the study was explained to the study subjects who were diagnosed as rheumatoid arthritis as per the ACR-EULAR criteria and presented to OPD/IPD of general Medicine/ orthopedics in the local language with the help of the information sheet. After Obtaining Informed Consent, each patient was assessed clinically with detailed History and thorough Physical Examination and lab investigations.

It was a cross sectional observational study. The study was carried out over a period of months from 2019 to 2020.

A total of 60 RA patients (diagnosed as per the ACR-EULAR criteria) of either sex and age >18 years were selected. Subjects underwent OGTT and glucose profile (FPG,2HrPPG, A1c) values were observed. RA disease activity and IR was assessed using the Disease Activity Score 28 (DAS 28) and HOMA-IR respectively. Patients with diagnosed diabetes mellitus, chronic kidney disease, acute inflammatory conditions other than RA, hypertension and congestive cardiac failure were excluded from this study.

After overnight fasting, blood samples were obtained for laboratory evaluation and a standard OGTT was performed in all patients according to the recommendations of World Health Organization. According to OGTT results patients were classified in subgroups of glucose tolerance; according to ADA patients were classified as norm tolerant if FPG< 100 mg/dL and 2-h postload glucose < 140; IFG if FPG 100–125 mg/dL and 2-h postload glucose < 140 mg/dL; IGT if FPG < 100 and 2-h postload glucose 140–199 mg/dL and diabetic if 2-h postload glucose ≥200 mg/dL.

DATA ENTRY AND STATISTICAL ANALYSIS

The collected data were transformed into variables, coded and entered in Microsoft Excel. Data were analyzed and statistically evaluated using SPSS-PC-20 version.

Quantitative data was expressed in mean, standard deviation and difference between two comparable groups were tested by student's t-test (unpaired) or Mann Whitney 'U' test. Three or more group's mean was analyzed using one-way ANOVA, while qualitative data were expressed in percentage. Statistical differences between the proportions were tested by chi square test or Fisher's exact test. Pearson correlation coefficient was used to see the correlation between two quantitative variables. 'P' value less than 0.05 was considered statistically significant.

RESULTS

It was a hospital based observational prospective study conducted in Department of general Medicine/orthopaedics of SRN Hospital, MLN Medical College, Prayagraj, Uttar-Pradesh, India enrolling a total of 60 rheumatoid Arthritis patients (diagnosed as per the ACR-EULAR criteria) of either sex and age >18 years. Subjects were divided into two subgroups according to their DAS28; the first subgroup (n=40, 66.7%) exhibited low/moderate disease activity defined by DAS28≤5.1 and the second (n=20, 33.3%) showed high disease activity (DAS28>5.1).

Out of 60 subjects most of the subjects with RA were between the age group of 31-45 years (45.0%) followed by 46-60 years (36.7%).

RA was more commonly seen in female subjects (76.7%) compare to male (23.3%) subjects

Most of the females were in the age group of 31-45 years (41.3%) or 46-60 years (41.3%) while male were maximum in the age group of 31-45 years (57.1%).

One-third subjects 20 (33.3%) had high disease activity score while 36 (60.0%) had moderate disease activity score. Mean Disease activity score was 4.92±0.61.

Out of 60 subjects plasma glucose level was≥126 mg/dL in 7 (11.7%) subjects while in 21 (35.0%) subjects it was in prediabetic range (100-125 mg/dL).

2 hr postprandial glucose was in diabetic range (≥200 mg/dL) in 5 (8.3%) subjects while 33 (55.0%) subjects were in prediabetic range (140-199 mg/dL).

On OGTT, prevalence of impaired fasting glucose/impaired glucose tolerance was 36.7% while 6 (10.0%) patient of RA were found diabetic**.**

Out of 60 subjects with RA, HbA1C was in diabetic range (≥6.5%) in 4 (6.7%) subjects while in 30 (50.0%) subjects HbA1C was in prediabetic range (5.7-6.5%).

Thirty seven patients (61.7%) in patients with RA were defined as having IR (HOMA-IR≥2.50).

Table 1 shows clinical and laboratory characteristics of RA subgroups according to DAS 28 Scoring which shows significant difference in low/moderate DAS 28 with high DAS 28.

In Fig 2 and Fig 3 Pearson's correlation revealed a statistically significant positive correlation between HOMA-IR values and DAS-28 (r=0.73, p <0.001) and HOMA-IR values and DAS-28 (r=0.426, p <0.001) respectively.

Table 1 Clinical and laboratorial characteristics of RA subgroups according to DAS 28 scoring

Variable	Low/moderate DAS-28 (n=40)	High DAS-28 (n=20)	P value
Age	41.88±10.75	41.15±11.08	0.81
Duration of symptoms	9.85±5.10	9.93±5.04	0.95
HOMA-IR	2.59±0.86	3.84±0.84	<0.001
Fasting plasma insulin	10.95±2.84	13.40±2.01	<0.001
Fasting plasma glucose	94.38±9.07	118.25±20.41	<0.001

Rheumatoid arthritis patients included in the present study were divided into two subgroups according to their DAS28; the first subgroup (n=40, 66.7%) exhibited low/moderate disease activity defined by DAS28≤5.1 and the second (n=20, 33.3%) showed high disease activity (DAS28>5.1). The patient subgroup with high disease activity revealed significantly higher fasting glucose, VAS disease activity score and fasting insulin levels in comparison to the low/moderate disease activity score. Similarly, the subgroup of RA with high disease activity score showed significant higher HOMA-IR compared with low/moderate disease activity group of patients.

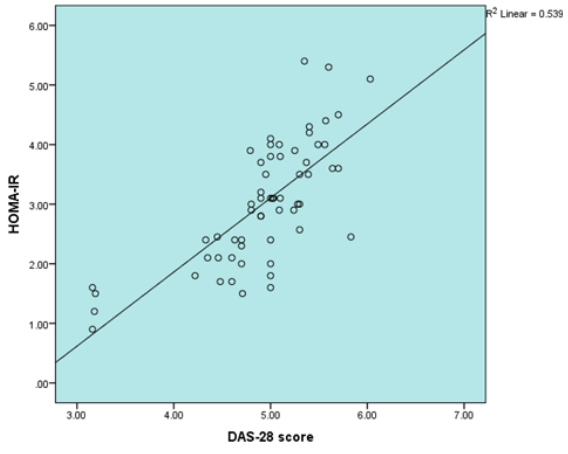

Fig 2 : Scatter plot showing correlation of Disease activity score-28 with HOMA-IR

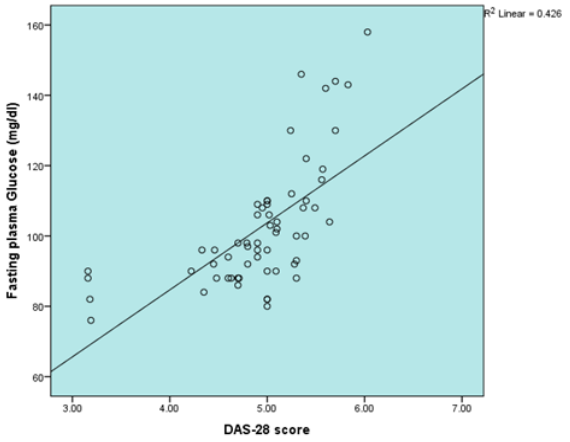

Figure 3 :Scatter plot showing correlation of Disease activity score-28 with fasting plasma glucose

DISCUSSION

The present study was a hospital based cross sectional observational study conducted in 60 rheumatoid Arthritis patients. Rheumatoid arthritis patients included in the present study were divided into two subgroups according to their DAS28; the first subgroup (n=40, 66.7%) exhibited low/moderate disease activity defined by DAS28≤5.1 and the second (n=20, 33.3%) showed high disease activity (DAS28>5.1). The patient subgroup with high disease activity revealed significantly higher fasting glucose, A1C, HOMA-IR and fasting insulin levels in comparison to the low/moderate disease activity score. Similarly, the subgroup of RA with high disease activity score showed significant higher HOMA-IR compared with low/moderate disease activity group of patients. Disease activity score-28 was significantly correlated with Fasting plasma Glucose (r value = 0.65; p value<0.001), Fasting plasma Insulin (r value=0.66; p value<0.001), HOMA-IR (r value=0.73; p value<0.001) and HbA1C (r value = 0.72; p value <0.001).

CONCLUSION

Most of the subjects were having symptoms since last 7-12 months (41.7%) while more than one fourth subjects (26.7%) subjects were presented to us within 1-6 months of symptoms. Mean duration of symptoms in study subjects was 9.90±5.02 months. Out of 60 subjects with RA, 32 (53.3%) were found overweight as per Asian BMI classification while 4 (6.7%) were obese. Mean BMI of study subjects was 23.99±2.95 kg/m2. Out of 60 subjects with RA, HbA1C was in diabetic range (≥6.5%) in 4 (6.7%) subjects while in 30 (50.0%) subjects HbA1C was in prediabetic range (5.7-6.5%).

Our study there was a 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), DAS-28 (r=0.73, p <0.001).

LIMITATIONS

It was a cross-sectional design, and finding of our study need to be confirmed in a longitudinal investigation. Sample size was only 60 in our study. An analysis of a larger data set may reveal a greater number of significant associations between the independent variables assessed in the current study and insulin resistance.

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