Risk Factors and Early Detection of Diabetes Mellitus in Early Rheumatoid Arthritis Women

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Abstract:

Background: Patients with rheumatoid arthritis show predominance of metabolic disorder characterized by overweight, central obesity, dyslipidemia and impaired glucose tolerance, specifically, few studies have explain insulin resistance in this disease.

Objective: The aim of present study is to examine insulin resistance and the risk of developing diabetes mellitus in middle age Iraqi women with early rheumatoid arthritis.

Patients and methods: This work involved seventy female with early rheumatoid arthritis. Who was attending to the National Diabetic Center (NDC) of Al-Mustansiriya University and 35 healthy subjects as a control group. From all subjects blood sample was drawn in fasting state to measure the biochemical parameters which including plasma glucose level and fasting insulin concentrations. Other measurements (RF and anti-CCP) were made by routine methods. Homeostasis model of assessment insulin resistance (HOMA-IR) by using the formula HOMA model Insulin sensitivity was calculated in RA patients and healthy control.

Results: Results revealed a highly significant in the level of rheumatoid factor (RF), anti-CCP and fasting insulin, and HOMA-IR when compared patient group with control group. While a significant increase in level of FBG in RA group than control group. Also there was a positive correlation with high significance among, Anti-CCP, and RF with HOMA-IR in rheumatoid arthritis group.

Conclusions: This study shows that patient with rheumatoid arthritis have abnormal insulin secretion with high value of IR than group of healthy control and these patients may be at risk of diabetic mellitus.

Keywords: Rheumatoid arthritis, RF, anti-CCP, insulin resistance.

Introduction:

Rheumatoid arthritis (RA) is an autoimmune disease cause's inflammation of joint swelling, tenderness, and synovial joints destruction, which lead to severe disability and premature mortality. The immune system attacks healthy tissue mistakenly, and it is unknown causes. Rheumatoid arthritis progress at any age; however, widespread this disease among middle age (1) in particularly women more prone to disease than men. Infection, genes, also hormonal changes properly related with RA. In beginning of the disease the patients always suffer from only minor joint pain, stiffness, and fatigue. One of the most common symptoms is morning stiffness. In addition, May be accompanied by a warm joint, tender, and stiff. The joint pain can be felt to the same degree on both sides of the body. By the time, the joint may become deformed due to lack of motion (2).

Insulin resistance is a common metabolic condition defined as rising concentration of insulin related to inappropriate response to glucose in normal levels of glycemia or high. Therefore, a pathological condition characterized by a loss of the Physiological response of peripheral tissues to insulin activity (endogenous or exogenous), the presence of hyperglycemia is very common with IR in the presence of high insulin doses (3). Importantly, IR has a role in pathogenesis of metabolic defect like obesity or diabetic (4). Other studies have found a higher association between chronic disease and dysfunction metabolism, basically presence of insulin resistance. Patients with Rheumatoid disease have been found to have altered impaired glucose metabolism and insulin resistance (IR) (5-8). Dessein, *et al* (9) notify patients with inflammatory arthritis have higher levels of insulin resistance than healthy control group, and presence a correlation between high levels of c-reactive protein and insulin resistance. Dessein *et.al* (10) concluded that IR was associated with inflammatory markers and disease activity such as CRP and ESR. Similarly, Chung *et al* (11) provided that patients with RA have a higher Homeostasis assessment model (HOMA) index that lupus patients, that it correlates with weight adjusted for age, gender and steroid use. Other studies (12-13) have also shown a positive correlation between C reactive protein levels and HOMA index in patients with RA. The only study provided by Garcia Díaz, (14) who found no differences in HOMA values between RA patients. So that, the objective of this work was focused to examine insulin resistance and increased

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risk of progressive diabetes mellitus in middle age Iraqi women with newly rheumatoid arthritis (RA).

Materials and Methods:

Seventy females with newly rheumatoid arthritis mean age (45± 0.65) years. The classification criteria for RA according to American College of Rheumatology 2010 (15) attending to the National Diabetic Center (NDC) of Al-Mustansiriya University from October to December 2016 and 35 healthy subjects as a control group with mean age (43± 0.57) years. Excluded any of patients have a history of hypertension, smoking, diabetes mellitus, kidney, liver, heart, and endocrine disease.

Blood was drawn from patients in the morning after an overnight fast for at least 12 h to measure glycated hemoglobin HbA1c (16) and plasma glucose level (17), also. Other measurements: Test of rheumatoid factor (RF) and anticyclic citrullinated peptide antibody (anti-CCP) and fasting insulin concentrations was detected by using enzyme-linked immune sorbent assay (ELISA) method (18). Homeostasis model of assessment (HOMA) IR was calculated according to the formula in the HOMA Insulin resistance index was determined by using the formula ([fasting plasma glucose (mmole/L) × fasting insulin (μU/ml)]/22.5) (19).

Statistical test: The parameters analyzed statistically by applying student's T-test to comparison difference between control and patients groups. All results set as mean ± SD and to characterize the relationship among parameters of two groups' correlation coefficient test was used.

Results:

Data in table (1) show a non-significant increase in age between patient (45± 0.65) years and control group (43± 0.57) years. Also, the mean level of rheumatoid factor (RF), anti-CCP, fasting insulin, and HOMA- IR were highly significantly increased when compared patient group with control group. While a significant increase in level of FBG in RA group than healthy group.

Table 1: Characteristics of the patients group and healthy control group.

Variables	Patients RA	Healthy control	P-value
Age (Yrs)	45 ± 0.65	43± 0.57	>0.05*
RF(IU/Ml)	45.67 ± 19.1	5.1 ± 1.52	<0.001
Anti-CCP(U/mL)	101.5 ± 33.1	17.7 ± 5.23	<0.001
FBG (mg/dl)	91.60 ± 6.62	88.6 ± 4.67	<0.01
HbA1c %	6.8 ± 0.82	4.57 ± 1.43	<0.001
Insulin (μIU/mL)	11.14 ± 3.22	3.88 ± 1.1	<0.001
HOMA IR	2.55± 0.87	0.77 ± 0.24	<0.001

P-values <0.05 was considered statistically significant*

Data in table (2) indicate the presence a positive correlation with high significant among, Anti-CCP, and RF in rheumatoid arthritis group.

Table 2: correlation between HOMA-IR and RF, anti- CCP

	r	P-value
HOMA-IR& RF	0.218	<0.001
HOMA-IR& anti- CCP	0.374	<0.001

P-values <0.05 was considered statistically significant

Discussion:

Insulin resistance results from defect of the insulin receptor or abnormality metabolic process that effect of insulin. Resistance usually develops long before diabetes mellitus type 2 appears, identifying and treating insulin-resistance patients has potentially great preventive value (20). IR linked with increased risk to cardiovascular disease also to dyslipidemia and metabolic syndrome (21). So that, importantly estimation of IR and understand their mechanisms in RA patients especially with new diagnosis as a risk for developing diabetic mellitus. In the present study, with respect to acute-phase reactants FBG and insulin concentration and HOMA, there was statistically highly significant in rheumatoid arthritis patients than in controls; also, a positive correlation was founded between HOMA-IR and RF and anti-CCP. This is in agreement with the conclusion of Chung *et al*. (22) who showed that rheumatoid arthritis individual with hyperinsulinemia had highly significant in RF and anti-CCP. On the other hands this results was supported by the Borba's study (23) who concluded that systemic chronic inflammation has been proposed to have a prominent role in the pathogenesis of IR and metabolic syndrome. The explanation for hyperinsulinemia in patients with rheumatoid arthritis may be insulin have an anti-inflammatory effect not just related to metabolism of glucose within reason insulin inhibit many factors of pro inflammatory transcription and regulation their genes (24).This explain confirming the result of this study that hyperinsulinemia was correlated to inflammation markers. This higher HOMA b-cells core leads to compensate for reduced lower levels of insulin sensitivity.

Conclusion:

This study shows that patient with rheumatoid arthritis have abnormal insulin secretion with high value of IR than group of healthy control and these patients may be at risk of diabetic mellitus. This conclusion was obtained on measurement concentration of insulin, HOMA IR. Hence, there is an imperious want into strategies to manage inflammation, dyslipidemia, and most importantly evaluation of IR in patients with RA.

Author's contributions:
Mohammad Hasan Ali: supervisor, writing and literature reviewer
Dr. Abeer J. Hassan: data analysis and writing
Enas Jabbar Hasan**:** samples collection

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