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Relation between Renal Function and Insulin Resistance of Type 2 Diabetic Iraqi Patients

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Abstract

Type 2 diabetes mellitus (T2DM) is a condition where the body's ability to regulate and utilize glucose as fuel is compromised. As a result of this chronic ailment, excess sugar circulates in the bloodstream. Thus, it can be described as a cluster of metabolic disorders that manifest through factors like insulin resistance and give rise to various complications. These conditions impact several physiological organs, leading to reduced efficiency in their functioning. The objective of this study was to assess the level of insulin in patients with Type 2 diabetes mellitus (T2DM) and to interpret the relationship between insulin resistance (HOMA-IR) and renal function. The methods employed in this investigation were designed to achieve these specific aims, seventy patients and twenty controls were involved for this study. The patients of T2DM was divided into three group according to them eGFR, 20 stage I patients (G1), 25 stage II diabetic patients (G2) and 25 stage III diabetic patients (G3). Insulin, fasting plasma glucose (FBG), HbA1c, and renal function were measured in all subject. The study's findings indicated that patients in Group 3 (G3) with elevated glomerular filtration rate (GFR) exhibited significantly higher insulin levels (14.48 µIU/ml) and HOMA-IR values (8.66) compared to other patients. Moreover, diabetic patients had significantly higher serum insulin levels than those in the healthy control group (P<0.001). The diabetic group also demonstrated a marked

degree of insulin resistance compared to the healthy control group. Additionally, a negative correlation was observed between HOMA-IR, eGFR, and Duration in the diabetic patients.
Conclusion: higher insulin levels and insulin resistance appear to contribute to the development of chronic kidney disease (CKD).

Keywords: type 2 Diabetes (T2DM), Insulin Resistance (HOMA-IR), Serum insulin, Serum Creatinine (S.Cr).

Introduction

The occurrence of chronic kidney disease (CKD) and the prevalence of diabetes in CKD patients have been consistently increasing [1, 2]. As kidney function declines, there is a common development of metabolic acidosis and insulin resistance (IR), which adversely affect bone health, nutritional status, and contribute to the elevated mortality risk associated with CKD [3, 4]. Insulin resistance refers to the suboptimal response of the liver, skeletal muscle, and adipose tissue to normal insulin levels. Several factors have been linked to insulin resistance among individuals with CKD, including metabolic acidosis, anemia, inflammation, hyperactivity of the Renin-Angiotensin-Aldosterone System (RAAS), vitamin D deficiency, physical inactivity, excess fat mass, and accumulation of nitrogen catabolites [5].

Insulin resistance has notable clinical implications, including its role in promoting endothelial dysfunction and raising cardiovascular mortality. Although the evidence is not definitive, certain data indicate that insulin resistance might play a part in the onset and advancement of CKD. As a result, viewing insulin resistance as a modifiable risk factor and a potential target for therapeutic interventions to enhance CKD outcomes is a reasonable approach [4, 6].

The association between metabolic acidosis, insulin resistance, and cardiovascular risk has been documented in scientific literature since 1924[7]. Despite the widespread use of nutritional therapy and oral administration of sodium bicarbonate to correct metabolic acidosis in CKD [8, 9, and 10]. It remains unknown whether such correction can reduce insulin resistance or enhance insulin's effectiveness in target cells among diabetic individuals.

Emerging research indicates that the kidney plays a significant role in maintaining glucose balance within the body. Studies utilizing radiolabeled glucose have shown that the kidneys are actively involved in both producing and utilizing glucose as part of human glucose metabolism

[11]. Consequently, it is suggested that impaired kidney function could disrupt the normal appearance of glucose in the bloodstream, the development of insulin resistance has been associated with investigations conducted on individuals with type 2 diabetes. These studies have shown that, akin to hepatic gluconeogenesis, renal gluconeogenesis is not adequately suppressed by insulin, as observed in healthy individuals [12].

Materials and Methods

The study involved seventy individuals with Type 2 diabetes mellitus (T2DM) from Iraq, aged between 37 and 70 years, with an average age of (49.33±6.640) years. Patients with Type 2 diabetes, metabolic syndrome, high waist circumferences, and high serum glucose, pregnant women, individuals with liver disease, renal disease, and hypertension were all excluded from the study.

Additionally, twenty healthy individuals, both male and female, were selected as control volunteers, with ages matching the T2DM patients (37-70 years). The criteria for selecting controls included being non-diabetic, non-hypertensive, free from acute diseases, and having no history of alcohol consumption or smoking.

Blood specimens of about 10 ml were collected from both the patients and control individuals after 12-15 hours of fasting, between 8:00 and 11:00 am. The blood samples were divided into two parts. The first part was mixed with ethylene di-amine tetra acetic acid (EDTA) (1.5 mg/ml) to estimate HbA1c within three hours. The second part was used to collect serum by allowing it to clot at room temperature (22°C) and then centrifuged at 3000r.p.m. The serum was divided into two sections and stored in Eppendorf tubes in the freezer (-20°C) until further use.

Anthropometries Measurements

Anthropometric measurements, such as age, weight, and height, were taken for each participant. The Body Mass Index (BMI) was calculated using a formula that involves dividing the weight by the square of the height.

Assessment of the Homeostasis Model Assessment (HOMA-IR)

Various methods were utilized to measure insulin resistance (IR), with the most common one being the calculation of the homeostasis model assessment (HOMA). This involved using fasting insulin levels (μU/ml) and glucose levels (mg/dl) in the following equation.

Investigating insulin resistance is crucial as it significantly impacts the equilibrium of various metabolic pathways (Matthews et al., 1985) [13].

HOMA-IR= [glucose (mg\dl) × fasting insu(µU/ml)] /405

Statistical analysis

Using SPSS, the statistical analysis was completed (version 25). The data was converted into the mean and standard deviation for numerical variables with normally distributed data, respectively, and into frequency/percentage for categorical variables. While a t-test performed independently and an ANOVA test were employed to see whether there was a significant, the distinction lies in the nature of the numerical variables.

Results and Discussion

Anthropometric and biochemical parameters were assessed in both patient groups and healthy subjects

Anthropometric is a measurement body of the human in term of the dimensions of adipose tissue, muscle and bone. It is essential to measurement subcutaneous adipose tissue because individuals with great values are described to be at high risks for diabetes mellitus, hypertension, gallstones, arthritis and cardiovascular disease and some forms of cancer [14], The mean (±SD) values of age, body mass index (BMI), duration of diabetes, and gender for all the groups under study are presented in Table [1].

Table 1: The characteristics related to demographics and clinical features

Parameter	Control	G1	G2	G3	P (Value)
Age (Year) 40-80 Mean ±SD	60.85 ±1.14 (45-70)	55.25 ±9.25 (41-80)	65.2 ±8.30 (48-80)	65.68 ±10.70 (41-80)	P = 0.230
Age (40-60%)	60 % (45-68)	75% (41-59)	32% (48 – 60)	27% (53-59)	-
Age (60-80%)	40 % (60-70)	25% (60-80)	68% (61-80)	73% (60-80)	-
BMI (Kg/h^2) Mean ±SD	23.91 ±3.10	27.38 ±4.14	30.80 ±9.94	27.27 ±5.58	P = 0.07
Male	55 %	40 %	48 %	49%	-
Female	45 %	60 %	52 %	51%	-
Duration Mean ±SD	-	14.55 ±7.83	15.28 ±5.81	17.04 ±8.84	P = 0.001

Table [1] shows mean ± SD of age among different groups for patient groups that including [G1 (55.25 ±9.25), G2 (65.2 ±8.30) and G3 (65.68 ±10.70)], in addition to control group [60.85 ±1.14]. The distribution of age factor among patients indicates no significant difference at ($p>0.05$) between the different groups. The results show in table [1] that is a non-significant value of BMI ($P>0.05$) of CKD groups. The results demonstrated a notable increase in duration ($p<0.001$) in G1 (14.55 ±7.83) and G2 (15.28 ±5.81) and G3 (17.04 ±8.84) diagnosis of CKD.

Description of Gender Distribution of Anthropometric measurement

The results show in table (2) there is no-significant value between gender in all of [Age, BMI and duration]. The gender distribution of Age shows the mean of male (58.81±7.45) and female (56.66±6.74) in control group (P=0.515). While in patient the gender distribution of age show the mean of male (62.36±10.71) and female (62.71±10.33) and (P=0.890).

The gender distribution according to BMI show the mean of male (24.12±3.00) and female (23.77±3.83) in control group (P=0.822). While in patient the gender distribution according age show the mean of male (27.86±5.29) and female (29.40±9.09) and (P=0.381). The gender distribution of Duration show the mean of male (16.68±7.96) and female (14.53±6.96) in patient group (P=0.237).

Table 2: Gender Distribution of Anthropometric measurement

Variables	Control Healthy			GFR Patient		
	M no=11	F no=9	P	M no.=38	F no.=32	P
Age Mean ±SD	58.81±7.45	56.66±6.74	0.515	62.36±10.71	62.71±10.33	0.890
BMI (Kg/h^2) Mean ±SD	24.12±3.00	23.77±3.83	0.822	27.86±5.29	29.40±9.09	0.381
Duration Mean ±SD	-	-	-	16.68±7.96	14.53±6.96	0.237

Metabolic Factors for the Studied Groups

The results show that the fasting blood sugar (FBS) were shown in Table [3]. In patient groups G1 (169.95±0.72), G2 (174.23±8.06) and G3 (204±14.08) The results revealed a high significant difference ($p<0.001$) through all the studied groups in the present study when it`s compared with normal healthy group .Also Table [2] shows the values of insulin as a metabolic factor for T2DM .The mean ± SD of insulin values of patient groups including each of G1

(10.81±1.52), G2 (11.55±2.17), G3 (14.48±1.58) and control group (9.10±2.53). The results showed high significant change (P<0.001) between patient groups with diabetes mellitus and control healthy group whereas mean ± SD values of HOMA-IR for the mentioned patient and control groups are including, [G1 (5.41±1.52), G2 (5.96±1.39), G3 (8.66±1.92) and control group (1.40±0.96)], as shown in Table [2]. The results showed level of serum insulin a significant increase (p=0.042), (p<0.05) in both of G1 group, G2 group and G3 group, when compared with control group, the results showed high significant change (P< 0.001) between patient with diabetes mellitus and control healthy group. The results shows that the HbA1C were shown in Table [2]. in patient groups G1 (8.809±0.49), G2 (8.933±0.533) and G3 (9.933±0.40) The results revealed a high significant difference (p<0.001) through all the studied groups in the present study when it`s compared with normal healthy group (3.855±0.23)

Table 3: Mean ±SD values of FBS, insulin and HbA1C for all the studied groups

Parameter	Control	G1	G2	G3	P (Value)
FBS mg/dL	88.5±2.47	169.95±0.72	174.23±8.06	204±14.08	P=0.001
HbA1C mmol/mol	3.855±0.23	8.809±0.49	8.933±0.533	9.933±0.40	P=0.001
Insulin	9.10±2.53	10.81±1.52	11.55±2.17	14.48±1.58	P=0.001
HOMA-IR	1.40±0.96	5.41±1.52a	5.96±1.39	8.66±1.92a	P=0.001
(a) referred to significant of G1 to control group (b) referred to significant of G1 to G3					

Renal Function

The kidney plays a crucial role in regulating the composition and volume of extracellular fluid in the body, thereby maintaining homeostasis. This is achieved through various renal functions such as filtration, reabsorption, and secretion of substances from the plasma, which help preserve the internal environment of the body [15]. To determine any disorders in the kidney's biological function, several parameters need to be estimated as a part of kidney function examination. These parameters include serum creatinine, urea, and glomerular filtration rate (eGFR), which were measured for all the studied groups using the estimates based on the Modification of Diet in Renal Disease (MDRD) formula are documented in Table [4].

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Table 4: Mean ± SD of renal function parameter for all the studied groups

Parameter	Control	G1	G2	G3	P (Value)
Creatinine mg/dL	0.390±0.18	0.690±0.17 a	0.69±0.144 b	1.573±0.437 c	P=0.001
Blood Urea mg/dL	11.45±3.619	29.25±2.13.83	43.040±12.07	73.68±23.22 c	P=0.001
GFR *mL/min*	299±47.98	117.9±27.62 a	87.84±10.08 b	44.040±9.409 c	P=0.001
(a) referred to significant of G1 to control group (b) referred to significant of G2 to G1 (c) referred to significant of G3 to G2					

Table [4] shows the values of serum creatinine, urea and GFR. The mean ± SD values of serum creatinine (S.Cr) for each patient group of G1, G2, G3 and healthy group are (0.690±0.17) (0.69±0.144), (1.573±0.437) and (0.390±0.18), respectively.

Whereas the mean ± SD values of urea for both the patient and control groups are as follows (29.25±2.13.83), (43.040±12.07), (73.68±23.22) and (11.45±3.619) respectively. The results showed a high significant increase ($p < 0.001$) in level of both creatinine and urea in the diabetes eGFR (G1, G2 and G3) comparison with healthy non-diabetes group included in the study. As shown in Figures (1) and Figure (2). At the same time, there is high significant difference (urea and creatinine) between diabetic groups (G1, G2 and G3) when it compared between each other's and when compared with control group, ($p > 0.001$). Estimated GFR, Early detection and hyperglycemia control in the case of diabetic patients with T2DM and its complications such as diabetic nephropathy may be reducing the progression of disease. Both the National Kidney Foundation (NKF) and the American Diabetes Association (ADA) recommend annual screening of eGFR and assessment of excretion in all individuals with type 2 diabetes. [16].

The mean ± SD values of eGFR for the mentioned patient and control groups include (117.9±27.62), (87.84±10.08), (44.040±9.409) and (299±47.98) respectively, the results showed a high significant increase ($p<0.001$) in level in diabetes eGFR.

Correlation between HOMA-IR and various variables

Table [5] showed the correlation coefficient of HOMA-IR level with each of [age, BMI, duration of diabetic, FBS, insulin, HOMO-IR, HbA1C, creatinine, urea and GFR] in diabetic patients with CKD. The study shows the correlation coefficient showed the presence of positive correlation between HOMA-IR and BMI ($r = 0.184$, $P = 0.083$) and Age ($r = 0.150$, $P =$

0.159). Also the results of correlation coefficient showed a presence negative correlation between HOMA-IR and Duration (r = -0.125, P = 0.286).

The results indicate a strong positive correlation between HOMA-IR and FBS (r = 0.307, P = 0.001), Insulin (r = 0.581, P = 0.001), and HbA1C (r = 0.527, P = 0.001).

Furthermore, the results demonstrate a strong positive correlation between HOMA-IR and S.Cr. (r = 0.759, P = 0.001) and Blood Urea (r = -0.736, P = 0.001) as appear in Figure (1) and (2). and the results show the correlation coefficient showed a presence strong negative correlation (P < 0.01) between HOMA-IR and eGFR (r = -0.562, P = 0.001) , as appear in Figure (3) .

Table 5: Correlation between HOMA-IR and various variables

Variable	HOMA-IR	
	r	P value
Age year	0.150	0.159
BMI kg/h^2	0.184	0.083
Duration year	-0.125	0.286
GFR ml/min	-0.562*	0.001
S.Cr mg/dL	0.759*	0.001
Urea mg/dL	0.736*	0.001
FBS mg/dL	0.307*	0.001
HbA1C mmol/mol	0.527*	0.001
Insulin µU/mL	0.581*	0.001
*. Correlation is significant at the 0.01 level (2-tailed).		

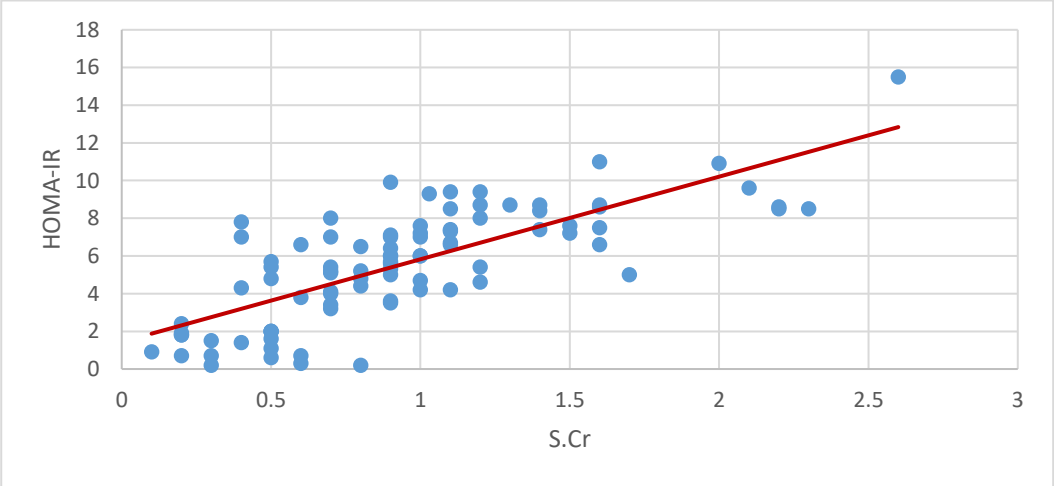

Figure 1 : Relation between HOMA-IR and S.Cr

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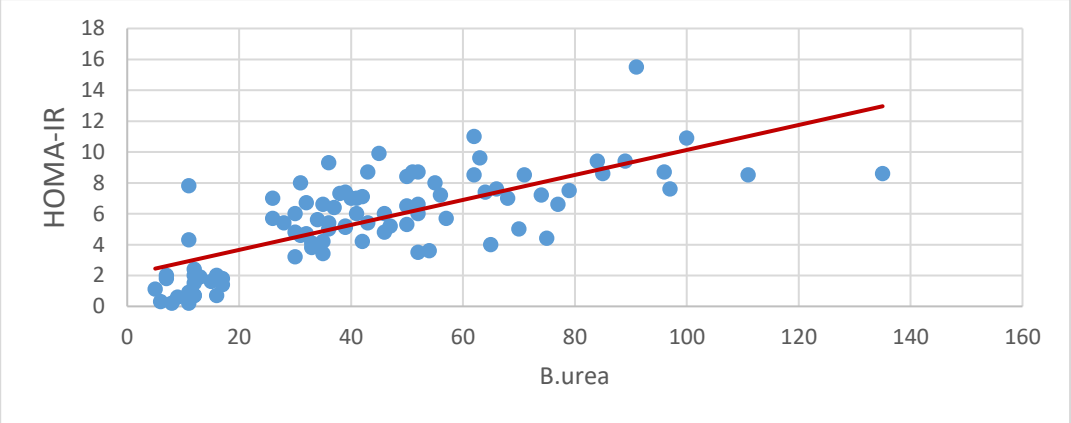

Figure 2: Relation between HOMA-IR and B.Urea

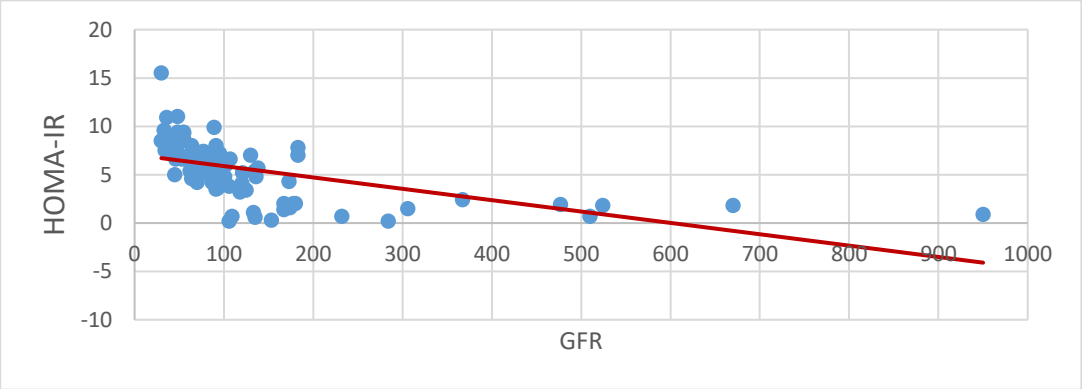

Figure 3: Relation between HOMA-IR and GFR

Conclusion

This paper has discussed the relation between insulin resistance (HOMA-IR) and renal function in type two diabetic patients according to the eGFR. There is a significant higher levels of insulin in G3 patients and HOMA-IR in G3 patients, and also in the patients with elevated GFR levels. The serum insulin levels were significantly elevated in diabetic patients compared to the healthy control group. Furthermore. A significant level of insulin resistance was noted in the diabetic group compared to the healthy control group. Additionally in diabetic patients, a negative correlation was observed between HOMA-IR and eGFR as well as duration.

Additionally, a positive correlation was found between HOMA-IR, blood urea and serum creatinine.

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