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The Biochemical Importance of Arginase in Type 2 Diabetes Pathophysiology: Relationships with Cystatin C, GIP, and GLP-1

Salam Noman Hattawi Ghadeer
College of science / University of Kirkuk / Iraq

Asst. Pof. Dr. Nawal Abdullah Murtadha
Ph.D. in Clinical biochemistry, College of science / University of Kirkuk / Iraq

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Annotation: This is also referred to as adult-onset diabetes mellitus. In this form of diabetes, levels of insulin may be usual, thereby raised, or depressed. This meant the majority of people have insulin resistance and insulin resistance, although insulinopaenia can occur as the illness progresses; or we as a species may define T2DM encompasses primarily resistant to insulin coupled with a relative deficiency of insulin to overwhelmingly a hormonal the secretary deficiencies alongside glucose resistance.

There were 180 participants in two distinct categories of individuals with T2DM were included in this investigation. and controls (140 patients, aged 35 to 65, including 40 apparently healthy controls, 70 uncontrollable DM patients (G1), and 70 managed DM patients (G2). All patients received care at the Kirkuk Teaching the Hospital, El-emel Diyaliz Merkezi, and Azadi Education Hospital in Kirkuk, Iraq, as well as private medical clinics between June 2024 and December 2024. After an overnight fast, venous blood samples were aseptically extracted from the participants via venipuncture. Two sections of the six milliliters were collected. Four milliliters that were kept in a plain tube containing any anticoagulation for 30 minutes at ambient temperatures.

Arginase level and GLP_1 (glocagon-like peptide) and GIP (gastric inhibitory polypeptide) levels have been shown to be negatively correlated in the present investigation and Cystine C Level in patients Diabetic Mellitus compared with Control groups.

Keywords: Arginase, Diabetes mellitus DM, biochemical markers, Cystatin C, GIP, and GLP-1.

Introduction

People with T2DM make up Ninety to ninety-ive percent of people with diabetes do not need insulin to survive.

Most likely, a number of variables combine to develop this kind of diabetes.

Most people with this kind of metabolic disorder are obese, and there is no aggressive suppressio n of ß-cells., which produces some insulin resistance (1). Patients who are not considered obese by conventional weight criteria might have a large amount of fat concentrated in their abdominal cavity. Ketoacidosis does not occur spontaneously in diabetics with type 2. It usually rises in reaction to the strain brought on by another illness, like an infection (2).

Being overweight or obese and not engaging in intense physical activity raise the risk of developing diabetes of the type 2 variety. This type of diabetes is consistently linked to an exceptional genetic susceptibility than T1DM, which is autoimmune in nature. However, the biological factors underlying this type of diabetes are complex and poorly understood (3).

Because diabetes is so closely linked to renal disease, it is critical to identify diabetes patients have developed kidney failure in order that they can receive timely care. The investigation was based on the idea that diabetic are more likely to have renal impairment than non-diabetics. As a result, the study sought to explore the renal function of diabetes mellitus patients in comparison to age-matched non-diabetics (4). The particular goals were to use a questionnaire to determine the signs and signs of kidney disease experienced by diabetic patients, to determines the frequency of overweight or obesity, to determine plasma values for uric acid, urea, and creatinine, and to determine the relationship between the BMI, FBS, plasma therapy uric acidic solution, urea, and creatinine and the duration of the illness. In the last reaction of the urea cycle (UC), this metalloenzyme, which contains binuclear manganese, initiates the conversion of L-arginine to Lornithine and urea (5). Information that is accessible show that abnormal arginase expression plays a pathophysiological role in hypertension, obesity, aging, diabetes, and other conditions. The scientific community is currently considering arginase as a possible predictor of the severity and course of a medical condition. Patients with type 2 diabetes had a 50% increase in plasma arginase enzyme activity when when compared to the members of the control group (6). In the past few decades, more participants have been investigated using more sophisticated techniques. A modest reduction in GLP-1 responsiveness was seen in contrast to nondiabetic patients, particularly during the subsequent hour after the food stimulus (7). Individuals with type 2 diabetes showed a reduced response to peripheral doses of intact, biologically active GLP-1. In patients with type 2 diabetes and healthy control subjects, the proportion of intact GLP-1 to total GLP-1 seemed to be similar (8). Together, our findings suggest that reduced insulinotropic activity throughout GIP is a major abnormality in the entero-insular axis in people with type 2 diabetes. Because GIP functions as a physiological incretin hormone, its diminished responsiveness may help to explain type 2 diabetes's reduced incretin impact and the abnormalities in insulin secretion linked to the disease (9). It has been suggested that decreased

regulation of the responsible B-cell GIP receptors is an early, possibly both genetically passed on incrementally in the clinical progression of type 2 diabetes, based on the finding that more than half (50%) of nondiabetic neighbors in the initial wave individuals with diabetes of type 2 exhibit diminished GIP effect (10). A variety of research investigations have looked into the production of Cys C in patients with T2DM. Some studies found that T2DM patients had higher levels of Cys C than normal individuals; however, others found a more mixed picture120. Although there have been numerous studies on the relationship between blood Cys-C and diabetes, major studies have yielded conflicting results. To investigate further independent proof of Cys-C serum's diagnostic value for Diabetes (11).

Aim of the Study: to evaluate the levels in the blood of GIP, GLP-1, Cystatin C, and blood arginase translocation in individuals with diabetes who have type 2.

Equipment and Procedures

There were 180 participants in the study (140 cases) as well as 40 seemingly healthy control) aged thirty-five to sixty-five years old, divided divided into two distinct categories: standards and patients with T2DM. These groups were categorized based on the patients' HbA1c levels, which refer to their hyperglycemia control. The first group (G1) consisted of 70 patients (31 males and 39 females) with a HbA1c value of over eight percent (Diabetic nephropathy) The individuals were using Metformin or Glucophage. The subsequent group (G2) consisted of 70 patients (30 male, 40 female) using HbA1c values below 7% (fully controlled with metformin and this medicine). 40 individuals (20 men and 20 women) made up the third group, the Controls (G3), which appeared to be healthier. All patients received care at the Kirkuk Academic the Hospital, El-emel Diyaliz Merkezi, until Azadi Learning Hospital in Kirkuk, Iraq, as well as private healthcare facilities between June 2024 and December 2024. Under the supervision of medical professionals, they received diagnostics and confirmed. Using the ELISA approach, important components in the current study were identified. An ELISA is the instrument in question. The individual's GIP an antibody was coated beforehand on the produced medium. Arginase, Cystine C, GLP_1 (glocagon-like polypeptide), and GIP (gastric inhibiting polypeptide) assay kits.

Statistical analysis:

The ANOVA test was performed on all data using Minitab software. Nevertheless, the average is compromised by the ducun multiple ranges test if the P-value is less than 0.05.

Results:

Arginase levels in people with diabetes (G1+G2) and seemingly healthy controls (G3) were measured.

As shown in Table (1), the current investigation found that the amount of activity of Arginase was considerably ($P < 0.001$) higher in diabetes patients (G1 + G2) than in seemingly healthy controls (G3).

Table (1): DM sufferers' (G1+G2) and seemingly healthy controls' (G3) arginase levels.

(mean ± SD)				
Variables	**DM patients uncontrolled (R.F+D.M) (G1) N= 70**	**DM patients (controlled HbA1c)(G2) N= 70**	**healthy controls (G3) N= 40**	**P value**
Arginase ng\ml	10.59± 1.3	8.26±0.3	7.152± 0.07	<0.001
Maximum	13.46	7.61	7.27	
Minimum	8.54	9.36	7.01	
P ≤ 0.05 Significant P > 0.05 Non significant				

measurement of gastric inhibitory polypeptide (GIP) and glocagon-like peptide (GLP_1), as well as seemingly normal controls (G3).

According to the current investigation, diabetes patients (G1 + G2) had non-significantly higher levels of GLP_1 (glocagon like peptide) activity (P^ 0.0001) than apparently regular controls (G3) (mean ± S.D.). GIP (gastric inhibiting polypeptide) concentrations rose sharply (P < 0.01) (mean ± deviation from normal) in diabetes patients.compared to controls (G3) that appear to be in good condition, as indicated in Table (2).

Table (2): Glocagon-like peptide (GLP_1) and the gastric inhibitory polypeptide (GIP) levels, along with those of seemingly normal controls (G3)

(mean ± SD)				
Variables	**DM patients uncontrolled (R.F+D.M) (G1) N= 70**	**DM patients (controlled HbA1c)(G2) N= 70**	**healthy controls (G3) N= 40**	**P value**
GLP_1 (glocagon like peptide)	21.10±4.8	20.98±15.2	10.27±1.2	<0.0001
Maximum	36.18	20.98	12.94	
Minimum	13.06	11.17	8.10	
GIP (gastric inhibitory polypeptide)	11.74±10.6	8.12±7.20	4.33±0.11	<0. 01
Maximum	34.4	29.1	4.52	
Minimum	4.1	4.12	4.11	
P ≤ 0.05 Significant P > 0.05 Non significant				

Cystine C levels in people with diabetes (G1+G2) and seemingly healthy controls (G3) were measured.

As shown in Table (3), the current investigation discovered that the activity level of Cystine C was considerably (P < 0.009) higher in patients with diabetes (G1 + G2) as opposed to seemingly healthy controls (G3).

Table (3): Cystine C levels among G1+G2 DM patients as well as G3 seemingly healthy individuals

(mean ± SD)				
Variables	**DM patients uncontrolled (R.F+D.M) (G1) N= 70**	**DM patients (controlled HbA1c)(G2) N= 70**	**healthy controls (G3) N= 40**	**P value**
Cystine C	3.662±3.2	2.965±2.7	1.355±0.02	<0.009
Maximum	5.984	4.70	1.385	
Minimum	1.319	1.343	1.312	
P ≤ 0.05 Significant P > 0.05 Non significant				

Research parameter correlation

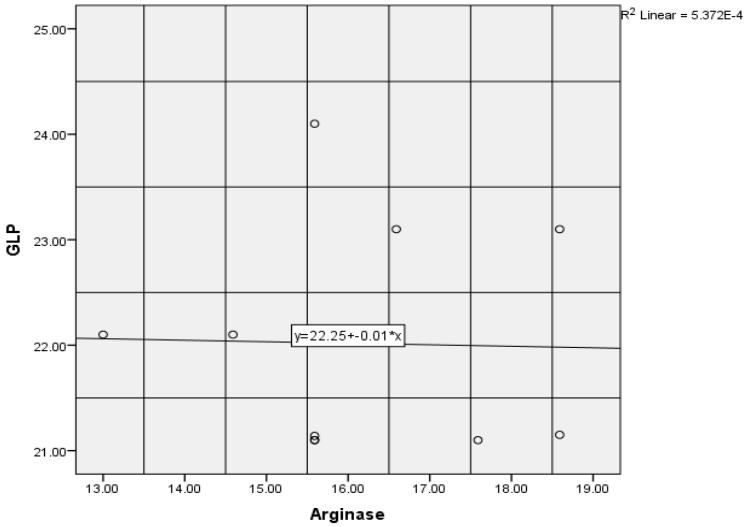

Figure (1): Correlation between Arginase Level and GLP_1 (glocagon like peptide) Level in patients Diabetic Mellitus compared with Control groups

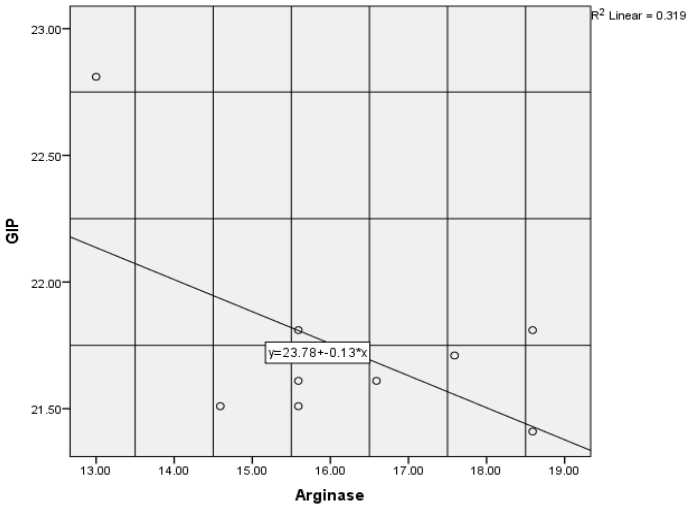

Figure (2): Correlation between Arginase Level and GIP (gastric inhibitory polypeptide) Level in patients Diabetic Mellitus compared with Control groups

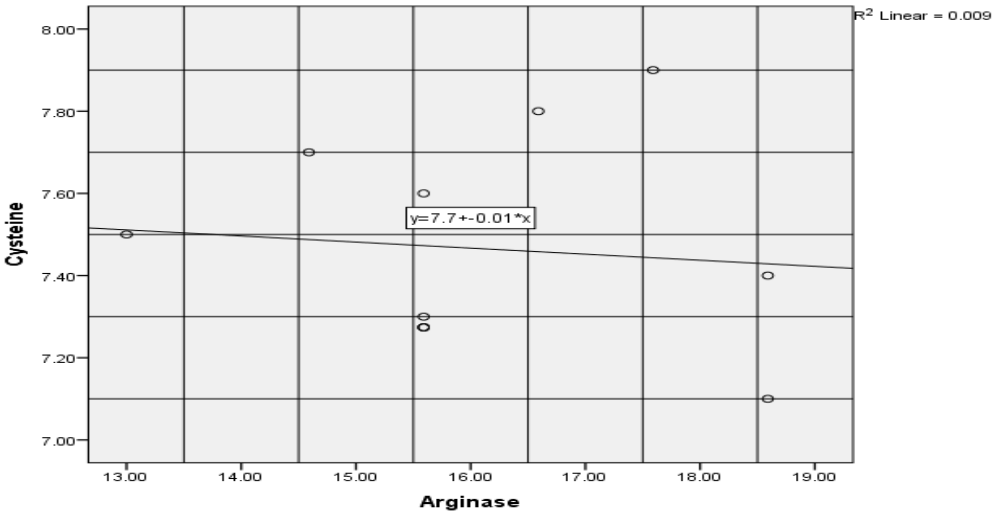

Figure (3): Correlation between Arginase Level and Cystine C Level in patients Diabetic Mellitus compared with Control groups

Discussion

The result suggests that arginase protein contributes significantly to the occurrence of type 2 diabetes, as previous studies have shown. People experiencing type 2 diabetes have been reported to have higher blood levels of the arginase I activity, and blocking arginase I is being shown to be protective in DM (12).

This enzyme activity and level of expression were much higher in diabetics compared to controls, and they were found to correlate favorably with the control's circulating glucose levels. These findings suggest that arginase could be employed as a prospective or predictive marker for DM patients. Thus, arginase inhibitor may be regarded a promising tool for diagnosing diabetes in medical settings (13). After eating, consuming sugar, or overloading on fatty tissue, plasma GLP-1 levels increase. Peak concentrations of 15–40 pmol/l happen an hour after nutrient administration, with typical baseline (fasting) levels ranging from 5 pmol/l.

In those with type 2 diabetes, inconsistent data has been presented about GLP-1 release in responses to oral hyperglycemia. Both enhanced postchallenge reactions were earlier observed in previous research (14). In the past few decades, more participants have been conducted investigated using more sophisticated techniques. Compared to patients without diabetes, there was a slight decrease in GLP-1 reactivity, particularly in the initial period following the food stimulation. Liu and Yupeng discovered that those with diabetes who have type 2 react less well to complete, physiologically active GLP-1 in their plasma concentrations (15,16). This provides more evidence that the minor changes in GIP (gastric inhibitory polypeptide) secretion found in type 2 diabetic individuals are not pathophysiologically significant. In patients with impaired glucose tolerance, gastric inhibitory polypeptide, or GIP, is totally effective. Researchers looked into how GIP (gastric inhibitory polypeptide) affected relatives in the first degree of those with diabetes of the type 2 variety (17,18). According to research, cysteine C measurement can be beneficial in determining kidney function in diabetic patients (G1+G2) while comparing it to healthy individuals (G3). A low-molecular-weight polypeptide called cysteine C is believed to provide a more accurate measure of the rate of glomerular filtration than creatinine. Serum cysteine C values were higher in type 2 diabetics than in healthy individuals, according to research. Additionally, measuring cysteine C can help identify diabetic kidney damage early. Compared to creatine and creatinine-based assays, an early increase in blood blood cystatin C levels and cystatin D-derived GFR may be a more reliable indicator of diabetes (19,20,21).

Conclusion

The present research discovered a negative link between Arginase Level, Diabetic Mellitus Patients' GLP_1 (glocagon-like peptide), GIP (gastric inhibitory polypeptide), and Cystine C Levels in Comparison to Control Groups. In Nepalese T2DM patients, researchers recommend assessing GFR to monitor the development of retinopathy. In patients with type 2 diabetes, this could help forecast their risk for heart mortality and morbidity.

Conclusion

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