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Study of plasma level of Glucagon-like peptide 1 (GLP1) as a new marker for diabetes in Egyptians with prediabetes

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Abstract

Background: Prediabetes is a subset of hyperglycemia wherein blood glucose levels are higher than usual but not yet high enough to be diagnosed as diabetes mellitus. Screening for prediabetic state is crucial for the prevention of type 2 diabetes mellitus (DM). This research aimed to examine the association between GLP-1 levels and poor glucose tolerance in Egyptian prediabetics.

Methods: One hundred and twenty patients of both sexes were included in this research at Beni-Suef University Hospital. Patients were classified into one of three categories according to their OGTT results: 40 people with normal weight and glucose tolerance (NGT) made up Group 1 serving as a baseline. In the second group, 40 patients with impaired fasting glucose (IFG) were included. In the third group, 40 patients with combined IFG/IGT were enrolled. A comprehensive history, physical examination, and laboratory tests were performed on all patients. Overnight fasting insulin hormone levels (between 8 and 12), blood glucose levels, concentrations of (a) total plasma GLP-1 (b) total plasma triglyceride (c) low-density lipoprotein cholesterol (d) high-density lipoprotein, ALT, and AST levels, together with serum creatinine, were used to calculate insulin hormone resistance.

Results: We found that GLP-1 and HOMA-IR had an important impact in predicting IFG and IFG with IGT. For predicting IFG and IFG/IGT subgroups, the corresponding (GLP1) cut-offs were ≤ 23.6 and ≤ 19.1 , respectively. The cut-off for using HOMA-IR in predicting IFG and IFG & IGT groups was 3.6. (GLP1) was greatest (39.6 ± 18.3) in individuals with NGT, followed by IFG (17.6 ± 4.1) and IGT (13.6 ± 3.1). Moreover, compared to individuals with IFG (11.7 ± 10.6) and IGT (16.5 ± 10.2), those with NGT had the lowest HOMA IR (1.5 ± 0.9).

Conclusion: GLP-1 had good sensitivity and specificity as an associated new biomarker in prediabetic individuals with impaired fasting glucose or glucose tolerance that may progress to type 2 DM.

Keywords: GLP-1 – HOMA-IR – Prediabetes – IFG – IGT.

Background:

One of the world's leading public health problems, diabetes mellitus, has far-reaching consequences for people's health and the economy. In 2019, 9.3 percent of people (463 million) had diabetes across the globe, as reported by the International Diabetes Federation (IDF). with no effective prevention in place, the rate is expected to increase to 10.2 percent (578 million) by 2030 and 10.9 percent (700 million) by 2045. Likewise, it's estimated that this year prediabetes will affect 374 million individuals (7.5% of the global population), 454 million people (8%) by 2030, and 548 million (8.6%) by 2045 [1].

Glycated hemoglobin (HbA1C) levels ranging from 5.7% to 6.4%, fasting glucose levels between 100 and 125 mg/dL, or glucose levels of 140 to 199 mg/dL measured 2 hours after a 75-g oral glucose challenge indicate prediabetes. Approximately 10% of Americans diagnosed with prediabetes progress to full-blown diabetes annually [2].

Early detection of prediabetes may lead to successful early therapies, preventing the development of type 2 diabetes (T2D) and its associated problems, such as cardiovascular disease, blindness, and renal failure, which can have devastating effects if left untreated. Global data suggests that T2D may be avoided by properly controlling glucose and insulin dysregulation [3].

When exposed to macronutrients, the small intestine secretes glucagon-like peptide-1 (GLP-1). GLP-1 may be responsible for the incretin effect. Post-meal insulin secretion is significantly affected by the incretin impact. Insulinotropic and glucagonostatic features of GLP-1 are generally preserved in T2D, prompting the development and broad implementation of GLP-1-based treatment [4].

This study aimed to evaluate the correlation between the level of GLP 1 and impaired glucose tolerance in Egyptian prediabetics and whether GLP1 could possibly be used as a marker for progression to type 2 high blood glucose.

Methods:

This case-control study was performed on 100 patients of both sexes recruited from the outpatient endocrinology clinic at Beni-Suef University Hospitals between November 2019 and November 2021. All participants in the study provided their informed consent before enrollment.

Each participant underwent a 75 gm glucose oral glucose tolerance test (OGTT). Prediabetes is characterized by impaired fasting glycemia (IFG), impaired glucose tolerance (IGT), or a combination of both. IFG is confirmed by a fasting glucose level between 100-125 mg/dL, while IGT is diagnosed by a 2-hour plasma glucose (2hPG) level of 140-199 mg/dL following the 75gm oral glucose challenge. Conversely, normal glucose tolerance (NGT) is indicated by a fasting blood glucose (FBG) level of <100 mg/dL and a 2hPG level of <140 mg/dL. Diabetes mellitus (DM) is diagnosed when FBG exceeds 126 mg/dL and/or 2hPG surpasses 200 mg/dL.

Following the oral glucose tolerance test (OGTT), cases were divided into three categories; the control group, including 20 people with normal weight, and the glucose tolerance group comprised **Group 1 (NGT)**. The second group, composed of 40 people diagnosed with **IFG**, is called **Group 2**. Group 3 had 40 patients with both **IFG and IGT**.

Patients with a history of DM, advanced liver disease, on treatment with drugs affecting GIT motility, thyrotoxicosis, GIT malignancies, or surgical procedures to GIT were all excluded from the study.

Full history was obtained from all patients, including age, residence, occupation, and any special habits of clinical importance. Past history of medical illness was obtained, including DM, HTN, CVS diseases, Dyslipidemia, bleeding tendencies, DVT, history of previous operation, blood transfusion, and any allergy to drugs. Clinical examination was performed on all patients with a special focus on weight and height, and then BMI was calculated according to the equation $[BMI = \frac{\text{weight in kg}}{\text{height in meters}^2}]$. Waist circumference was estimated at the highest point of the iliac crest with minimal respiration; the result was then rounded to the nearest 0.1 cm.

The following parameters were evaluated in the laboratory: fasting blood glucose, 2HPP, fasting insulin after overnight fasting (from 8-12), glucose-stimulated GLP-1 (30 min after 75 g glucose), the total GLP-1 level in plasma, total cholesterol (TC), triglyceride (TG), and high-density lipoprotein cholesterol (HDL-C), serum creatinine, ALT, and AST.

HOMA-IR Calculation:

Analyzing the performance of islet cells, the homeostasis model assessment of cell function (HOMA-IR) was employed to measure basal insulin secretion since this investigation only utilized blood samples taken after the OGTT. In the meantime, we decided to use the HOMA evaluation of IR (HOMA-IR) to provide a rough estimate of IR when fasting. The formulas are as follows:

$$\text{HOMA-IR} = \frac{\text{FPG} - \text{FINS}}{22.5}$$
 where FPG (Fasting plasma glucose) and FINS (Fasting serum Insulin Concentration).

Data Analysis and Statistics:

Numbers and percentages of patients were given for categorical variables, which were then compared across groups using Pearson's Chi-square test. Group differences in continuous variables were determined by calculating their means $\pm$ standard deviations, and medians (interquartile range) according to their normal distribution; then, using the one-way ANOVA or Kruskal Wallis, we

compared the groups according to the distribution of the continuous variables. Pairwise comparison (Tukey HSD) between every 2 groups was used. The ROC curve was used to detect the best cut-off, sensitivity, specificity, positive predictive, and negative predictive values for the studied markers in the prediction of IFG and IFG with IGT. Pearson's and Spearman's correlations were employed in the correlation of continuous variables according to the normality distribution. We used IBM's SPSS version 20 statistical software for our analysis, and our alpha was set at 5 Percent. Thus, a P value of 0.05 was considered statistically significant.

Ethical considerations:

This study protocol was revised and approved by the research ethics committee of the Faculty of Medicine of Beni-Suef University. The study followed the Helsinki Declaration for research ethics standards.

Results:

Group I (NGT). Group II (IFG). Group III (IFG and IGT).

Demographic and baseline characters of patients (table 1):

The demographic and baseline characteristics of the patients are shown below in Table (1), including age, sex, BMI, and waist circumference. There was no statistically significant difference between the studied groups regarding age and sex distribution (P-value>0.05). Nevertheless, there was a statistically significant difference between the studied groups regarding their BMI and WC.

Table (1): Baseline characteristics of the studied groups.

Items	Group I (no=20)	Group II (no=40)	Group III (no=40)	P-value
Age	46.8±9.1	47.5±9.2	46.2±7.8	0.901
Sex				
Males	10(50.0%)	16(40.0%)	21(52.5%)	0.510
Females	10(50.0%)	24(60.0%)	19(47.5%)	
BMI	25±1.8	30.7±2.4	31±3.1	<0.001*

Post hoc				
P1<0.001*		P2<0.001*		P3=0.805
WC	89.4±7.1	95.8±12.4	99±16.2	0.036*
Post hoc				
P1=0.195		P2=0.027*		P3=0.529

*P-value is significant P1 (group I vs group II), P2 (group I vs group III), P3 (group II vs group III)

The laboratory results of patients within the study revealed a statistically significant difference between the studied groups regarding their GLP1 (P-value<0.05). Group 1 (controls) had the highest level of GLP1 (39.6±18.3) compared to groups 2 (17.6±4.1) and 3 (13.6±3.1). Regarding the HOMA-IR, there was a statistically significant difference between the studied groups regarding their HOMA IR (P-value<0.05). Group 1 (controls) had the lowest HOMA IR (1.5±0.9) compared to groups 2 (11.7±10.6) and 3 (16.5±10.2). Also, there were statistically significant differences between the three groups regarding FBG, 2hPP, fasting insulin level, total cholesterol, triglycerides, HDL, ALT, AST, and serum creatinine levels. Detailed laboratory results for different groups are presented in Table (2)

Table (2): Comparison of the studied groups' laboratory results.

Items	Group I (no=20)	Group II (no=40)	Group III (no=40)	P-value
FBG	93.8±11.1	108.8±7.7	120±19.4	<0.001*
P1=0.001* P2=0.001* P3=0.001*				
2 hr. PPG	119.5±19.3	132.6±7.9	176.9±20	<0.001*
P1=0.010* P2=0.001* P3=0.001*				
Fasting insulin	6.7±3.9	42.9±38.3	55.6±34.2	<0.001* (KW)
P1=0.010* P2=0.001* P3=0.194				
T. cholesterol	163.6±31.5	193.3±35.1	194.9±34.2	0.002*
P1=0.010* P2=0.001* P3=0.194				
TG	123.3±29.9	168.4±61.7	156.1±65.7	0.022*

P1=0.017* P2=0.107 P3=0.620				
HDL	66.9±10	55.9±11	54.9±11.1	<0.001*
P1=0.001* P2=0.001* P3=0.927				
ALT	17.1±5.2	18.4±4.8	21.1±6.3	0.018*
P1=661 P2=0.026* P3=0.082				
AST	18.6±3.6	16.8±5.1	21.1±7	0.006*
P1=0.471 P2=0.284 P3=0.004*				
Creatinine	0.6±0.1	0.8±0.1	0.8±0.2	0.001*
P1=0.001* P2=0.004* P3=0.834				
GLP1	39.6±18.3	17.6±4.1	13.6±3.1	<0.001*(KW)
Median (IQR)	30(26.1,55.6)	18.2(15.2,21.3)	13.9(11.5,15.7)	
P1<0.001* P2<0.001* P3=0.107				
HOMA IR	1.5±0.9	11.7±10.6	16.5±10.2	<0.001*(KW)
Median (IQR)	1.4(0.8,2.1)	5.8(4.4,13.3)	14.9(6.3,22.1)	
P1<0.001* P2<0.001* P3=0.063				

*P-value is significant KW: Kruskal Wallis test

Pairwise comparison (Tukey HSD) between every 2 groups was used. P1 (group I vs group II), P3 (group I vs group III), P3 (group II vs group III)

Role of GLP-1 and HOMA-IR in the prediction of prediabetes (Figures 1 & 2):

Table (3) showed that there was a significant role of GLP1 and HOMA IR in the prediction of IFG with IGT. The GLP1 and HOMAIR cut-off was ≤ 19.1 , 3.6 in the prediction of IFG&IGT with sensitivity, specificity, PPV, and NPV equals 100%.

Table (3): Sensitivity, specificity, Positive predictive value, and Negative predictive value of HOMAIR and GLP1 in prediction of IFG with IGT (referenced by free healthy controls).

Items	GLP1 in prediction of IFG & IGT	HOMAIR in the prediction of IFG & IGT
AUC	1.000	1.000
P-value	<0.001*	<0.001*

Cut off	≤ 19.1	> 3.6
Sensitivity (95%CI)	100(91.2 – 100)	100(91.2 – 100)
Specificity (95%CI)	100(83.2 – 100)	100(83.2 – 100)
PPV (95%CI)	100(83.2 – 100)	100(83.2 – 100)
NPV (95%CI)	100(85- 100)	100(85- 100)

*P-value is significant

Table (4) showed that there was a significant role of GLP1 and HOMA IR in the prediction of IFG. The GLP1 and HOMAIR cut-off was ≤ 23.6 , 3.6 in prediction of IFG & IGT with high sensitivity, specificity, PPV, and NPV.

Table (4): Sensitivity, specificity, Positive predictive value, and Negative predictive value of HOMAIR and GLP1 in prediction of IFG (referenced by free healthy controls).

Items	GLP-1 in prediction of IFG	HOMA-IR in the prediction of IFG
AUC	0.997	1.000
P-value	$< 0.001^*$	$< 0.001^*$
Cut off	≤ 23.6	> 3.6
Sensitivity (95%CI)	100(91.2 – 100)	100(91.2 – 100)
Specificity (95%CI)	95(75.1 - 99.9)	100(83.2 – 100)
PPV (95%CI)	97.6(85.6 - 99.6)	100(83.2 – 100)
NPV (95%CI)	100(91.2 – 100)	100(85- 100)

*P-value is significant

Relation between GLP-1 and HOMA-IR and different parameters of patients:

Correlation between HOMA IR, GLP1, and different parameters in the healthy control group revealed a strong positive linear correlation between the HOMA-IR and fasting insulin (p-value < 0.001 and correlation Coefficient ($r=0.979$) in the control group.

Correlation between HOMA-IR, GLP1, and different parameters in a group with IFG revealed that there was a strong positive linear correlation between the HOMA-IR and fasting insulin (p-value <0.001 and correlation coefficient ($r= 0.977$) and moderate negative linear correlation with the triglycerides (p-value 0.038 and correlation coefficient ($r= -0.330$) in the second group. Regarding the GLP1, it was moderately correlated negatively with waist circumference (p-value 0.048 and correlation coefficient ($r= -0.315$), fasting insulin (p-value= 0.025) and correlation coefficient ($r= -0.354$), total cholesterol (p-value 0.019 and correlation coefficient ($r= -0.371$) and positively correlated with 2 hours postprandial glucose (p-value 0.032 and correlation coefficient ($r= 0.339$).

Correlation between HOMA-IR, GLP1, and different parameters in the group with IFG and IGT combined revealed that there was a strong positive linear correlation between the HOMA-IR and fasting insulin (p-value <0.001 and correlation coefficient ($r= 0.972$), and moderate positive correlation with BMI (p-value 0.004 and correlation coefficient ($r= 0.446$) and 2 hours postprandial (p-value= 0.041) and correlation coefficient ($r= 0.325$) in the third group, the GLP1 did not correlate with any of the studied parameters.

Discussion:

The majority of people are diagnosed with prediabetes before they acquire type 2 diabetes. Prediabetes is an asymptomatic illness that is not connected with any functional impairment. According to the most recent estimations, the majority of prediabetics will ultimately acquire diabetes. However, the progression from impaired glucose tolerance (IGT) and impaired fasting glucose (IFG) to diabetes may take several years [5].

This study was conducted at Beni-Suef University Hospital to evaluate the correlation between GLP-1 levels and impaired glucose tolerance in Egyptian pre-diabetic patients.

Our study showed a significant role of GLP1 and HOMA-IR in the prediction of IFG and IFG combined with IGT. The GLP1 cut-off was ≤ 23.6 , and ≤ 19.1 in the prediction of IGF and IFG & IGT groups, respectively. The HOMA-IR cut-off was 3.6 in IGF and IFG & IGT group prediction. There was a statistically significant difference between the groups' HOMA IR and GLP-1. Patients with NGT had the highest level of GLP1 (39.6 ± 18.3) compared to patients with IFG and IGT (17.6 ± 4.1 and 13.6 ± 3.1), respectively. Also, patients with NGT had the lowest level

of HOMA IR (1.5 ± 0.9) compared to patients with IFG and IGT (11.7 ± 10.6 and 16.5 ± 10.2), respectively. Patients in IFG and IGT groups did not differ significantly from each other regarding the HOMA IR and GLP-1.

Consistent with our findings, **Hussein et al. (2014)** demonstrated that GLP-1 levels could predict impaired glucose tolerance accurately in obese Egyptian individuals using ROC curves. They observed a notable decrease in GLP-1 levels in patients with IFG and IGT compared to those with NGT. This was attained by an increased HOMA-IR in patients with IFG and IGT [5]. Similarly, **Marathe et al. (2020)** identified a significant association between blood glucose levels and plasma GLP-1 concentrations. They found an increase in plasma GLP-1 levels following glucose ingestion in both NGT and IGT groups, with higher GLP-1 levels observed in the NGT group compared to the IGT group [4]. Additionally, **Zhang et al. (2012)** reported a deficiency in the secretion of total GLP-1 concentration and its response to glucose challenge in prediabetic patients, particularly in those with IFG and IGT. The HOMA-IR was markedly elevated in patients with IFG and IGT compared to those in the NGT group [6].

Contrary to our results, the study of **Chong et al., (2020)** demonstrated significantly lower GLP-1 levels in individuals with normal glucose tolerance (NGT) compared to those with prediabetes and type 2 diabetes mellitus (T2DM). NGT mean GLP-1 levels were 16.24 ± 7.79 , while for prediabetes and T2DM, they were 21.99 ± 10.16 and 27.18 ± 11.56 respectively. Additionally, HOMA-IR was notably higher in prediabetic (4.23 ± 2.24) and diabetic (6.2 ± 4.68) individuals compared to those with NGT (2.4 ± 1.35) [7]. **Lee et al., (2010)**, in their study about glucagon-like peptide-1 levels in Japanese patients with type 2 diabetes, demonstrated that compared with the NGT group, the IGT and T2DM groups had significantly higher levels of HOMA-IR and lower levels of GLP-1. However, they found that GLP-1 couldn't predict the change in blood glucose levels [8].

Possible causes of this discrepancy include differences in sample size, duration of diabetes mellitus (DM), and inclusion of all prediabetes (PD) persons with isolated IFG, isolated IGT or IFG combined with IGT. Different hyperglycemic circumstances and PD/DM lengths may cause cell function and insulin sensitivity (IS) to vary, which in turn may cause varying amounts of GLP-1.

GLP-1's ability to bring down blood glucose levels makes it useful for predicting DM in people with IFG and IGT. Intestinal epithelial endocrine L-cells produce GLP-1 in response to food consumption. Reduced blood glucose levels result from GLP-1's ability to increase insulin secretion from pancreatic beta cells and inhibit glucagon release from alpha cells [9]. Additionally, it reduces the rate at which food is emptied from the stomach, increases insulin sensitivity, and promotes the regeneration of beta cells as well as inhibits their death. Significant decreases in HbA1C levels (positive effects on weight) and a low risk of hypoglycemia are all hallmarks of GLP-1 RAs. It is not only the pancreas that has GLP-1 receptors; but also the heart, blood arteries, stomach, intestines, visceral fat, kidney, and brain have them, too [10].

Our results revealed that BMI was higher in the IFG and IGT groups than the NGT group, while the waist circumference was significantly higher in the IGT group than the NGT group. Groups with NGT, IFG, and IFG combined with IGT didn't differ significantly from each other.

Consistent with our study was Zhang et al., (2012) who revealed that patients with IFG and IGT had a significantly higher BMI and WC than those with NGT. The mean BMI for cases with NGT was 23.93 ± 2.89 , with WC 84.0 ± 8.4 . On the other hand, patients with IFG and IGT had a BMI of 24.92 ± 2.95 and 24.75 ± 3.15 respectively, while their WC was 84.6 ± 8.4 and 86.0 ± 9.3 [6]. In addition, the study by Wang et al., (2016) reported that patients with IGT and T2DM had a higher BMI and WC than those with NGT but without statistically significant differences [11].

We found that the mean fasting blood glucose and the 2hPP blood glucose levels were significantly higher among patients in group III (IFG and IGT) than in group II (IFG) and group I (NGT). The fasting insulin was higher in patients with IGT 55.6 ± 34.2 than the normal control group 6.7 ± 3.9 . The mean value for patients with IFG was 42.9 ± 38.3 . Similarly, Marathe et al., (2020) [4], in their study about the relationship between plasma GIP and GLP-1 levels in individuals with normal and impaired glucose tolerance, demonstrated that blood glucose concentrations were greater in IGT with significant differences compared to NGT cases. Moreover, serum insulin concentration was greater in the IGT group. Also, the study of Hussein et al., (2014) reported that patients with impaired glucose tolerance had significantly higher FBG, 2HPP, and fasting insulin levels when compared to NGT cases. The mean FBG level was (86.10 ± 6.36) Vs. (111.50 ± 6.75) for patients with IGT. The mean 2HPP blood glucose level was

(123.30±8.68) for NGT cases and (129.95±8.07) for IGT cases. The mean fasting insulin level was (11.85±4.30) for NGT cases and (14.75±3.61) for IGT cases [5].

Another notable finding in our study was the mean total cholesterol level which was significantly higher among patients with IGT and IFG (194.9±34.2 Vs. 193.3±35.1) respectively compared to those with NGT (163.6±31.5). Also, the triglyceride level was significantly higher among patients with IFG and IGT (168.4±61.7 Vs. 156.1±65.7), respectively, compared to those with NGT (123.3±29.9). On the other hand, the mean serum HDL was significantly lower among patients with IGT and IFG (54.9±11.1 Vs. 55.85±11.007) compared to the NGT group (66.95±10.045).

Lee et al. (2010) reported findings consistent with our study, indicating a significant elevation in serum triglycerides and cholesterol levels in the IGT group and patients with T2DM compared to the NGT group. They also found a significant decrease in HDL levels in the IGT and T2DM groups relative to the NGT group [8]. Similarly, Wang et al. (2016) observed significantly higher levels of total cholesterol and triglycerides in the IGT and T2DM groups compared to the NGT group. Their data revealed mean total cholesterol levels of 3.94±0.88 mmol/L for the NGT group and 4.44±0.95 mmol/L vs. 5.36±2.09 mmol/L for the IGT and T2DM groups, respectively. The mean triglyceride levels were 1.94±1.06 mmol/L for the NGT group and 2.10±0.87 mmol/L vs. 2.70±1.24 mmol/L for the IGT and T2DM groups, respectively. Consistent with our findings, they also observed a significant reduction in HDL levels in the IGT (1.40±0.63 mmol/L) and T2DM (1.10±0.28 mmol/L) groups compared to the NGT group (1.60±0.59 mmol/L)[11]. Furthermore, Yabe et al. (2015) demonstrated that total cholesterol levels (mg/dL) were significantly higher in patients with T2DM (203 ± 33.1) and IGT (195.3 ± 25.8) compared to those with NGT (186.4 ± 36.4). Additionally, triglyceride levels (mg/dL) were notably elevated in the T2DM group (121.5 ± 55.6) and IGT group (112.2 ± 70) relative to the NGT group (80.5 ± 64.4). Conversely, HDL cholesterol levels (mg/dL) were significantly reduced in the T2DM group (55.6 ± 13.8) and IGT group (62.9 ± 15.1) compared to the NGT group (64.4 ± 15.8).

When present, hypertriglyceridemia and low HDL-C in PD are clinically concerning because they might promote glucose dysregulation by causing insulin resistance and beta cell dysfunction. Hyperglycemia may both result from and contribute to the dyslipidemia condition characterized by elevated plasma triglyceride and free fatty acid levels and decreased HDL-C [12].

In diabetes, dyslipidemia is typically an early sign of insulin resistance before the onset of full-blown diabetes. Hypertriglyceridemia is a common precursor to atherogenic dyslipidemia that characterizes insulin resistance. In addition, the reduced activity of tissue lipases, many of which are controlled by insulin, seems to be the primary cause of poor clearance of VLDL cholesterol in insulin resistance situations. Insulin resistance also causes reduced FFA absorption and enhanced lipolysis by adipocytes both of which cause increased circulating FFA levels. Overproduction of triglyceride-rich lipoproteins from the liver and the intestine was caused by insulin resistance and the enhanced transport of FFA to peripheral organs, including the liver and intestine. In addition, elevated FFA levels are associated with insulin resistance. Potentially, this might set off a domino effect of insulin resistance and FFAs [13].

Liver functions and serum creatinine were normal in all groups. However, there was a statistically significant difference between the studied groups regarding liver function and creatinine level. Like our study, **Ribeiro et al., (2019)** showed in their study about managing hyperglycemia and reversal of prediabetes condition that patients had a normal liver function. The mean Aspartate transaminase (U/L) in their study was 22.1 ± 7.5 and the mean Alanine transaminase (U/L) was 25.6 ± 15.1 [14]. Also, **Açar et al., (2019)** found that the mean creatinine level was within normal for prediabetic cases (0.90 ± 0.23) [15].

Conclusion:

In conclusion, GLP-1 and HOMA-IR have good sensitivity and specificity as associated biomarkers in prediabetic individuals with impaired fasting glucose or glucose intolerance that may progress to type 2 DM.

Declarations

Conflicts of Interest:

The authors have no potential conflicts of interest to declare.

Funding:

None.

Data Availability Statement:

Data is released upon reasonable request from the corresponding author.

Ethics approval

This study protocol was revised and approved by the research ethics committee of the Faculty of Medicine of Beni-Suef University. The study followed the Helsinki declaration for research ethics standards.

Consent to participate

Each person who participated in the study provided informed consent before enrolling.

Written Consent for publication

All authors read and approved the final manuscript

Code	availability	NA
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Authors' contributions

-A.M.N: Author, participated in data interpretation, writing and reviewing the manuscript, Conceptual design and data collection, and data analysis. K.E.E: Author, participated in, writing and reviewing the manuscript. Study design. Y.B.I: Author, participated in design, analysis, data interpretation, writing, and reviewing the manuscript. A.S.A.M: Author, participated in the design, analysis, data interpretation, writing, and reviewing the manuscript. S.A.E: Corresponding Author, participated in data interpretation, write and review the manuscript. T.M.A: Author, participated in the design, analysis, data interpretation, writing, and reviewing the manuscript.

Abbreviations:

IFG Impaired fasting glucose.
 IGT Impaired glucose tolerance
 OGTT Oral glucose tolerance test.
 T2DM Type 2 Diabetes Mellitus.
 OGTT: oral glucose tolerance test
 NGT: normal glucose tolerance
 FFA: Free Fatty Acid

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