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The Effect of Obesity on Fasting/Post-Prandial Glucagon-Like Peptide-1 Levels in People with Type-2 Diabetes

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Abstract

Objectives: To evaluate the impact of obesity on fasting and postprandial glucagon-like peptide-1 (GLP-1) levels in type 2 diabetic cases.

Background: Obesity is a pathological disease described by the excessive accumulation of fat in the body, which can have detrimental effects on one's health.

Methods: This study has been performed on 120 subjects, separated into four groups: **Group A:** normal subjects (30), **Group B:** obese persons without diabetes (30), **Group C:** obese persons with diabetes (30) and **Group D:** non-obese persons with diabetes (30) at the endocrinology outpatient clinic and inpatient of the Internal Medicine Department of Menoufia University Hospital.

Results: There statistically significant variation has been observed among the examined groups according to fasting GLP-1, 1-hour post-prandial GLP1, and 2 hours post-prandial GLP1 (p value less than 0.05). There was a significant negative association among fasting glucagon-like peptide-1 and weight, BMI, HBA1C, & creatinine (r = -0.36, -0.33, -0,23, and -0.23), respectively, with a significant p value <0.05. Also, there was a significant negative association among 1-hour post-prandial glucagon-like peptide-1 and weight, BMI, HBA1C, & creatinine (r = -0.58, -0.56, -0,37, and -0.33), correspondingly, with a significant p value less than 0.05. The same results nearly with 2 h post-prandial GLP-1

Conclusion: The study discovered a significant negative association among fasting glucagon-like peptide-1 and weight, BMI, HBA1C, and creatinine, with a negative correlation observed between 1-hour post-prandial GLP-1 and weight, BMI, HBA1C, and creatinine.

Key words: Glucagon like peptide-1, Obesity, Type 2 diabetes

Introduction

Diabetes mellitus, according to the WHO, is a collection of metabolic illnesses that are described by high concentrations of glucose in the blood due to problems with the production or function of insulin. Diabetes causes persistently high blood sugar levels, which can lead to lasting harm, impairment, and malfunction of several organs, specifically in kidneys, eyes, heart, nerves, and blood vessels [1].

Obesity is a pathological disease characterized by the excessive accumulation of body fat, which can have a negative impact on one's health. Obesity is associated with a range of diseases and ailments, especially cardiovascular disorders, obstructive sleep apnea, type-2 diabetes, some forms of cancer and osteoarthritis [2].

Obese people exhibit elevated levels of non-esterified fatty acids, hormones, glycerol, cytokines, and pro-inflammatory indicators. The pathophysiology of diabetes is rooted in the impairment of the β-islet cells of the pancreas, which leads to a loss of blood glucose regulation. If the failure of β-islet cells in the pancreas is coupled with insulin resistance, the risk of progressing diabetes increases. The association among weight gain, body mass, and the development of diabetes is significant and increasingly prevalent [3].

Incretins are a group of metabolic hormones that promote a reduction in concentrations of glucose in the blood. They are discharged upon consumption & enhance the production of insulin produced by pancreatic beta cells of the islets of Langerhans through a mechanism that depends on the concentration of glucose in the blood. Certain incretins also suppress the secretion of glucagon from the alpha cells located in the islets of Langerhans. Furthermore, they decrease the speed at which nutrients are absorbed into the bloodstream by decreasing stomach emptying, which may directly decrease food consumption [4].

The two primary potential molecules that meet the criteria for an incretin are the intestinal peptides glp-1& gastric inhibitory peptide (GIP). Glucagon-like peptide-1 and gastric inhibitory peptide belong to the glucagon peptide superfamily. Glucagon-like peptide-1 has been formulated as the fundamental management for people with type 2 DM. According to the findings, Caucasian cases with type 2 DM have decrease levels of glucagon-like peptide-1 compared to normal subjects. The overall glucagon-like peptide-1 concentration in non-diabetic Japanese & Caucasians has been found to be similar; however, the concentrations of intact glucagon-like peptide-1 were much lower in Japanese individuals compared to Caucasians. Currently, there is no published data on glucagon-like peptide-1 levels in both normal individuals and cases with T-2DM in Egypt [5].

The purpose of this work was to evaluate the impact of obesity on fasting and postprandial glucagon-like peptide-1 levels in type 2 diabetic cases.

Methods

This investigation has been performed on 120 subjects, separated into four groups: **Group A:** Normal subjects (30) with body mass index (18.5-24.9 kilogram per meters square), **Group B:** Obese persons without diabetes (30) with BMI ≥30kg /m², fasting blood sugar less than one hundred milligrams per deciliter, HbA1C less than 5.7 percent, 2 hours' postprandial blood sugar was < 140 mg/dl, **Group C:** Obese persons with diabetes (30) with BMI ≥ 30 kg/ m², fasting blood sugar ≥ 126 mg/dl, and HbA1c ≥6.5%, and 2 hours' postprandial blood sugar equal two hundred milligrams per deciliter or more, and under treatment of T2DM and **Group D:** non-obese persons with diabetes (30) with body mass index (18.5-24.9 kilogram per meters square), fasting blood sugar equal 126 milligrams per deciliter or more, and HbA1c ≥6.5 percent, and 2

hours postprandial blood sugar equal two hundred milligrams per deciliter or more, and under treatment of T2DM. The investigation has been conducted at the endocrinology outpatient clinic & inpatient department of Menoufia University Hospital's Internal Medicine Department.

Exclusion criteria: cases who are younger than eighteen or older than seventy years of age; cases with type 1 DM; cases with impaired hepatic function; cases with impaired renal function; cases with cancer; and cases with neurological and psychological illnesses.

Method:

All cases have been exposed to complete history-taking, physical examinations, and investigational studies.

Fasting GLP-1 level (pg/L), 1 hour post-prandial GLP-1 level (pg/L), and 2 hours post-prandial GLP-1 level (pg/L) using Human GLP1 (7-36) ELISA Kit.

Materials and Reagents:

ELISA kit (specific for human GLP-1 (7–36)), standard solutions of known GLP-1 concentrations, sample diluent, wash buffer, enzyme-linked antibody (conjugate), substrate solution, stop solution, and microplate reader

Procedure:

Standard Curve Preparation

A standard curve was created using the provided standards with known GLP-1 concentrations. Typically, the standards come in various concentrations. A series of standard solutions were prepared in the microplate wells.

Sample Collection and Preparation: Fasting and post-prandial blood samples have been gathered from study participants. The samples have been centrifuged to obtain clear serum or plasma. Prepare a set of wells for the samples, including the fasting and post-prandial samples.

Incubation: The sample diluent was added to the wells designated for standards, controls, and samples, adding a standard or sample to the respective wells, adding the enzyme-linked antibody (conjugate) to each well and incubating the plate for a specified period to allow binding of GLP-1 to the antibodies.

Washing: Washing the microplate wells to remove unbound substances.

Enzyme Reaction: Adding the substrate solution to each well. Incubating the plate again for a specific period. This incubation allowed the substrate to react with the bound GLP-1.

Stop Reaction: Adding the stop solution to halt the enzymatic reaction in each well.

Measurement: measuring the absorbance of each well in the microplate utilizing a microplate reader set to the appropriate wavelength (usually 450 nanometers).

Data Analysis: Using the standard curve to determine the GLP-1 concentration in each sample well.

Calculations: Calculating the fasting and post-prandial glucagon-like peptide-1 concentrations (in picograms per liter) for each sample based on the standard curve and the measured absorbance values.

Data Interpretation*:* Comparing the glucagon-like peptide-1 levels between fasting and post-prandial samples to analyze the impact of a meal on GLP-1 concentrations, the normal value was 5–10 pmol/L.

Hemoglobin A1C level: HbA1c was a long-term marker of blood glucose control, reflecting average glucose levels over a few months. It was important for diabetes management.

The most common technique for measuring HbA1c was:

High-Performance Liquid Chromatography (HPLC): This method has separated and quantified different forms of hemoglobin, including HbA1c. Blood samples were passed through a chromatography column, and the different hemoglobin components were detected and quantified. The hemoglobin A1C level for people with no diabetes typically falls within the range of four percent to 5.6 percent.

Statistical analysis: Data analysis was carried out using IBM SPSS statistics (V. 27.0, IBM Corp., 2020), values are presented as mean ± standard deviation [43]. Comparison between groups was done using one-way analysis of variance (ANOVA) followed by Bonferroni's post-hoc multiple comparison test. The significance was set at $P \leq 0.05$.

Ethical Consideration

Approval was obtained from Menoufia University Institutional Review Board (IRB# 1342-29/03/2022).The information that was collected from participants is considered confidential. The investigation's participants weren't recognized by name in any report or publication that was related to this investigation. The objective and scope of the investigation, as well as the risk-benefit evaluation, were explained to the participants prior to their admission to this investigation. Consent has been obtained with full knowledge.

Results

A statistically significant distinction has been observed among the examined groups regarding age, sex, weight, height, and BMI (p value fewer than 0.05) **(Table 1).**

There statistically significant distinction has been observed examined groups according to fasting glucagon-like peptide-1, 1-hour post-prandial GLP1, and 2 hours post-prandial GLP1 (p value less than0.05) **(Table 2).**

There statistically significant distinction has been observed examined groups according to postprandial C peptide and fasting C peptide (p value <0.05), as fasting C peptide was higher in control than diabetic-obese, but the range was normal in all of them **(Table 3).**

There statistically significant distinction has been observed examined groups according to fasting blood glucose, postprandial blood glucose, and HBA1C (p value <0.05), as the level was higher in the diabetic-obese group than in other groups **(Table 4).**

A significant negative association has been observed among fasting GLP-1 and weight, BMI, HBA1C, and creatinine (r = -0.36, -0.33, -0,23, and -0.23), respectively, with a significant p value less than 0.05. Also, there a significant negative correlation has been observed between 1 h post-prandial GLP-1 and weight, BMI, HBA1C, & creatinine (r = -0.58, -0.56, -0.37, and -0.33), respectively, with a significant p value less than 0.05. The same results nearly with 2 h post-prandial GLP-1 **(Table 5)**

Table (1): general characteristics between the examined groups

	(Group A) Diabetic obese (number=thirty)	**(Group B) Diabetic non obese (number=thirty)**	**(Group C) Nondiabetic, obese (number=thirty)**	**(Group D) Control (number=thirty)**	**P-value**
Age (years) Mean ± standard	55.2 ±9.2	55.6 ± 11.5		37 ±4.8	**<0.001*** P1-value=0.99
	36:68	28:70		24:56	

deviation (Range)			42.8 ± 9.5 21:58		P2-value <0.001* P3-value <0.001* P4-value <0.001* P5-value <0.001* P6-value =0.13
gander Male Female	4(13.3%) 26(86.7%)	16(53.3%) 14(46.7%)	5(16.7%) 25(83.3%)	7(23.3%) 23(76.7%)	**0001***
Weight Mean ± SD (Range)	95.5 ±11.5 78:120	70.9 ±6.4 61:83	90.1 ±8.3 76:103	63.5 ±6.4 50:74	**<0.001*** P1-value <0.001* P2-value =0.07 P3-value =0.006* P4-value <0.001* P5-value <0.001* P6-value <0.001*
Height Mean ± SD (Range)	158.9 ±7.3 149:175	171.2 ±5.9 161:182	165±4.9 154:173	167.8±4.9 160:178	**<0.001*** P1-value <0.001* P2-value <0.001* P3-value =0.001* P4-value <0.001* P5-value =0.11 P6-value =0.24
BMI Mean ±	37.9±4.7 30.4:47.5	24.1±0.8 22.5:25		22.5±1.6 18.6:24.9	**<0.001***

standard deviation (Range)			33±2.4 30.1:37.8		P1-value <0.001* P2-value <0.001* P3-value <0.001* P4-value <0.001* P5=0.13 P6-value <0.001*

* p value considered significant at level <0.05, P1 =p value amid diabetic obese and diabetic non obese, P2= p value between diabetic obese and non-diabetic, obese, P3= p value between diabetic obese and control, P4= p value between diabetic non-obese and non-diabetic obese, P5= p value between diabetic non-obese and control, P6= p value between non-diabetic obese and control.

Table (2): comparison among the examined groups according to GLP1 fasting and post-prandial

	Diabetic obese **(number=thirty)**	**Diabetic non obese** **(number=thirty)**	**Nondiabetic, obese** **(number=thirty)**	**Control** **(number= thirty)**	**P value**
Fasting GLP-1 Mean ± SD (Range)	58.82 ±13.5 34:79.5	69.3 ± 12.5 44:89	67 ± 10.4 37:79	82±27 57:171	**<0.001*** P1-value =0.11 P2-value =0.54 P3-value <0.001* P4-value =0.79 P5-value =0.03* P6-value <0.002*
1h post prandial GLP1		89.3±12.4		112±27	**<0.001*** P1-value <0.001*

Mean ± SD (Range)	65.8± 13 41:89	64:110	78±14.4 50:105	90:200	P2-value =0.04* P3-value <0.001* P4-value =0.07 P5-value <0.001* P6-value <0.001*
2h post prandial GLP1 Mean ± SD (Range)	62.8±12 38:80	83.8±12 58:100	72±14 64:100	105±24 77:190	**<0.001*** P1-value <0.001* P2-value =0.16 P3-value <0.001* P4-value =0.04* P5-value <0.001* P6-value =0.001*

Table (3): comparison among the examined groups regarding C peptide fasting and post-prandial

	Diabetic obese (number= thirty)	**Diabetic non obese (number=thirty)**	**Nondiabetic, obese (number=thirty)**	**Control (number=thirty)**	**P value**
Fasting c peptide Mean ± SD (Range)	2±0.6 1.1:3.2	2.5 ± 0.38 1.9:3.2	2.5 ±0.56 1.7:3.5	2.9±0.75 1.7:4.1	**<0.001*** P1-value =0.004* P2-value =0.03* P3-value <0.001* P4-value =**0.89**

					P5-value =**0.06** P6-value =0.009*
post prandial c peptide Mean ± SD (Range)	3.8± 0.64 2.9:5.1	4.3±0.66 3.2:5.2	4.2±0.96 2.9:5.7	5.3±1.1 3.9:8.5	**<0.001*** P1-value =0.04* P2-value =**0.17** P3-value <0.001* P4-value =**0.92** P5-value <0.001* P6-value <0.001*

Table (4): comparison among the examined groups according to fasting and post-prandial blood glucose

	Diabetic obese (number=thirty)	**Diabetic non obese (number=thirty)**	**Nondiabetic, obese (number=thirty)**	**Control (number=thirty)**	**P value**
Fasting glucose level Mean ± SD (Range)	141.7 ±27 99:200	126 ± 25.4 87:187	94.1 ± 12.1 84:153	82.4±5.2 74:92	**<0.001*** P1-value =0.01* P2-value <0.001* P3-value <0.001* P4-value **<0.001*** P5-value **<0.001*** P6-value =0.16
post prandial blood glucose	216± 42	184±33 117:265	130.5±17.5	112±8.4 102:128	**<0.001*** P1-value =<0.001* P2-value **<0.001***

Mean ± SD (Range)	160:315		112:213		P3-value <0.001* P4-value **<0.001*** P5-value <0.001* P6-value =0.07
HBA1C Mean ± SD (Range)	7.8±1 6.6:11	7.1±0.6 5.8:8.3	5.5±0.5 5.2:8.3	5±0.18 4.8:5.4	**<0.001*** P1-value =0.002* P2-value **<0.001*** P3-value <0.001* P4-value **<0.001*** P5-value <0.001* P6-value =0.06

Table (5): correlation among GLP1 at different times with other variables

Correlation		**Fasting GLP1**	**1h post prandial GLP1**	**2h post-prandial GLP-1**
fasting GLP1	Pearson Correlation	1	.947**	.874**
	P value	------	<0.001*	<0.001*
1h post prandial GLP1	Pearson Correlation	.947**	1	.924**
	P value	<0.001*	------	<0.001*
2h post prandial GLP1	Pearson Correlation	.874**	.924**	1
	P value	<0.001*	<0.001*	-----
Weight	Pearson Correlation	-.365**	-.581**	-.560**
	P value	<0.001*	<0.001*	<0.001*
BMI	Pearson Correlation	-.331**	-.569**	-.534**
	P value	<0.001*	<0.001*	<0.001*
HBA1C	Pearson Correlation	-.230*	-.379**	-.348**
	P value	0.01*	<0.001*	<0.001*

Hb	Pearson Correlation	0.005	0.042	-0.035
	P value	0.953	0.649	0.706
WBCs	Pearson Correlation	0.026	-0.018	-0.091
	P value	0.777	0.848	0.325
Platelet	Pearson Correlation	-0.032	0.05	0.02
	P value	0.725	0.589	0.808
Urea	Pearson Correlation	-0.173	-.238**	-.214*
	P value	0.059	0.009*	0.01*
Creatinine	Pearson Correlation	-.231*	-.334**	-.348**
	P value	0.01*	<0.001*	<0.001*
AST	Pearson Correlation	-.213*	-.233*	-.242**
	P value	0.02*	0.01*	0.008*
ALT	Pearson Correlation	-0.174	-.210*	-.258**
	P value	0.058	0.01*	0.004*
S.Albumin	Pearson Correlation	-0.038	0.049	0.092
	P value	0.68	0.602	0.321

** Correlation is significant at the 0.01 level (2-tailed), * Correlation is significant at the 0.05 level (2-tailed).

Discussion

A statistically significant distinction has been observed among the examined groups regarding age, sex, weight, height, and BMI (p value<0.05).

The findings of **Ten Kulve et al. [6]** align with our results, as they investigated whether endogenous GLP-1 is responsible for the decrease in activation in satiety areas & central reward after a meal in cases with type 2 diabetes. They observed that obese cases with type 2 diabetes had significantly greater weight, age, and BMI compared to healthy individuals.

A statistically significant distinction has been observed among the examined fasting glucagon-like peptide-1, 1 h postprandial GLP1, and 2 h postprandial GLP1 (p value lower than 0.05).

There was significant higher in control group than nondiabetic obese group. Our results agreed with **Muñoz et al. [7],** who stated that fasting glucagon-like peptide-1 was significantly greater in the non-diabetic obese group than the control group.

In the same study, **Lastya et al. [8]** found that cases of type 2 DM who weren't obese had significantly lesser concentrations of GLP-1 both while fasting and following eating, compared A statistically significant distinction has been observed among the examined groups regarding postprandial C peptide and fasting C peptide (p value <0.05), as fasting C peptide was higher in control than diabetic-obese, but the range was normal in all of them.

Our results are supported by **Byun et al. [9],** who reported that there a statistically significant distinction has been observed among non-diabetic obese and control groups regarding fasting C-peptide, **p**<0.01. Fasting C-peptide was significantly greater in the control group than in the in the nondiabetic obese group.

In the same vein, **Anoop et al. [10]** reported that fasting and postprandial c peptide were significantly greater in diabetic non-obese people than the control.

In addition, **Khan et al. [11]** found insignificant variation in C-peptide levels among diabetic non-obese cases (951.17 ± 100.69 millimoles per litre) and controls (861.18 ± 63.66 millimoles per litre), which contradicts our results.

A statistically significant distinction has been observed among examined groups according to postprandial blood glucose, fasting blood glucose, & HBA1C (p value <0.05), as the level was greater in diabetic obese groups compared to other groups.

There was a significant negative correlation among fasting glucagon-like peptide-1 & weight, BMI, HBA1C, and creatinine (r = -0.36, -0.33, -0,23, and -0.23), respectively, with a significant p value less than 0.05. Also, there was a significant negative association among 1 h post-prandial GLP-1 and weight, BMI, HBA1C, and creatinine (r = -0.58, -0.56, -0,37, & -0.33), respectively, with a significant p value less than 0.05. The same results nearly with 2 h post-prandial GLP-1

Our results are supported by **Hussein et al. [12],** who reported that GLP-1 levels are negatively associated with body mass index (BMI).

Also, our results agreed with those of **Otten et al. [13],** who reported that postprandial glucagon-like peptide-1 levels were inversely associated with body mass index at baseline (r_S = 0.42, P = 0.005).

On the other hand, our results disagree with **Reinehr et al. [14],** who reported that GLP-1 wasn't significantly related to body mass index.

Conclusion

We concluded that there was a significant negative association among fasting glucagon-like peptide-1 & weight, BMI, HBA1C, and creatinine. Also, there was a significant negative association among 1 h post-prandial GLP-1 and weight, BMI, HBA1C, & creatinine, and a significant negative correlation between 2 h post-prandial GLP-1 and weight, BMI, HBA1C, and creatinine.

Funds:

Not applicable

Conflict of Interests:

No conflict of interests

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