Original Article

Serum Ghrelin Level in Type 2 Diabetes Mellitus Postmenopausal Women in Relation to Body Mass Index

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Abstract

Background: People living with type 2 diabetes mellitus (DM) are more vulnerable to various forms of both short- and long-term complications, which often lead to their premature death. **Objectives:** The aim of this study was to evaluate the effects of serum level of ghrelin in diabetic postmenopausal, nondiabetic obese menopausal, and control healthy women. **Materials and Methods:** This case–control study included 90 participants (30 diabetic postmenopausal women, 30 nondiabetic obese menopausal women with body mass index (BMI) equal or >30, and 30 control healthy participants). Full history for referred individuals was taken and height and body weight were measured. BMI <18.5 was considered underweight, between 18.5 and 24.9 was a normal, between 25 and 29.9 was overweight, and more than 30 was obese. **Results:** Age ranged between 45 and 80 years old. Serum ghrelin had highly significant difference in obese comparison to both diabetes and control groups, and there is a significant difference between obese and diabetes with higher concentration in obese than diabetic group. Mean fasting blood glucose (FBG) showed a highly significant difference between obese, diabetes, and control groups with higher concentration in both obese and diabetes participants, and specifically, there is a significant difference between diabetes and obese groups with higher concentration in diabetic than obese group. BMI showed a significant difference and higher level in obese in comparison to other two groups. The serum ghrelin had a moderate significant correlation with FBG in obese but insignificant correlation with both diabetes and control groups. FBG shows no significant correlation with BMI in all three groups. **Conclusion:** There is an inverse relationship between fasting glucose and ghrelin level in type 2 diabetic patients and positive correlation in obesity. The study also shows that hyperglycemia due to disturbance in glucose metabolism may result in suppression of ghrelin level in type 2 DM.

Keywords: Body mass index, obesity, serum ghrelin, type 2 diabetes mellitus

Introduction

Type 2 diabetes mellitus (DM) is a metabolic disorder, in which the insulin is used for controlling glucose which is not properly used by the body[1] and accounted for approximately 90% of all cases of diabetes.[2] Type 2 diabetes is commonly manifested by middle-to-late-aged adults (40 years); however, its prevalence is increasing in younger populations. A diabetic patient cannot metabolize carbohydrates, proteins, or fats due to improper production of insulin or resistance to insulin.[3]

Genetically predisposed obesity in people is considered to be one of the main causes of type 2 DM (T2 DM). As in prediabetes, it has no classical symptoms of diabetes and remains undiagnosed for many years because hyperglycemia develops gradually at an early stage.[4] Often symptoms come on slowly,[5] many people, however, have no symptoms during the first few years and are diagnosed on routine testing.[6]

People living with T2 DM are more vulnerable to various forms of both short- and long-term complications, which often lead to their premature death.[7]

As obesity is associated with numbers of physiological changes resulting in diseases such as insulin resistance, cardiac diseases, and hypertension (HT), and numerous studies have reported a strong association of obesity with diabetes.[8]

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Postmenopausal describes women who have not experienced any menstrual flow for a minimum of 12 months, forward that they have uterus and do not seem to be pregnant or lactating[9] and her ovaries become inactive.[10]

Ghrelin is a peptide hormone produced predominantly by P/D1 cells that present in the lining of the stomach and also it is secreted in small amount from epsilon cells of pancreas. In pituitary gland, hypothalamus, kidney, placenta, and brain also have a smaller amount of ghrelin. Ghrelin increases appetite by acting on the hypothalamus which is a part of the brain control appetite and promotes fat storage.[11] Besides regulation appetite, ghrelin plays a major role in regulation energy homeostasis.[12]

The aim of this study was to evaluate the effects of serum level of ghrelin in diabetic postmenopausal, nondiabetic obese menopausal, and control healthy women.

Materials And Methods

Study design and patients

This case–control study was done at the Baghdad Medical City Complex. Collection of sample was conducted during the period from January to April 2019.

The research is designed to study 90 participants including 30 diabetic postmenopausal women, 30 nondiabetic obese menopausal women with body mass index (BMI) equal or >30, and 30 control healthy participants which their relatives free from signs and symptoms of type 2 DM. Full history for referred individuals was as follows: name, age, DM, HT or chronic illness, medication, smoking, and alcohol, and then, height and body weight were measured. BMI was calculated as weight (kg)/square of height (m^2). According to the WHO associate adult who encompasses a BMI <18.5 was considered underweight, between 18.5 and 24.9 was a normal, between 25 and 29.9 was overweight, and more than 30 was obese.

Blood samples (5 ml) were collected from the antecubital vein after fasting for ≥10 h. Two milliliters of blood sample was taken in gel vials for glucose estimation, and 3 ml was taken in gel vials and allowed to clot for serum separation. Finally, clear serum was then carefully transferred to Eppendorf Tubes using micropipettes and stored at − 20°C for further analyses. Glucose was measured by Reflotron® Plus system, and normal range was 74–106 mg/dl (4.1–5.9 mmol/l). Serum ghrelin was measured by ELISA and detection range was 0.16–10 ng/mL.

Statistical analysis

Statistical analysis was carried out using SPSS version 22.0 (SPSS, IBM Company, Chicago, IL 60606, USA). Continuous data were expressed as means ± standard deviation. Comparison of continuous variables was analyzed using ANOVA tests if the data are normally distributed. If the data are not normally distributed, differences between groups were examined by nonparametric test. The correlation between continues variable is measured by Pearson test if the data are normally distributed. $P < 0.05$ was statistically significant.

Ethical consideration

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with patients verbal and analytical approval before sample was taken. The study protocol and the subject information and consent form were reviewed and approved by a local ethics committee.

Results

Total postmenopausal women (90 participants) are arranged into three groups as following: obese (30 participants), diabetes (30 patients), and control (30 participants) with age ranging between 45 and 80 years old. Serum ghrelin had highly significant difference in obese comparison to both diabetes and control groups as shown in Table 1, exclusively, there is a significant difference between obese and diabetes with higher concentration in obese than diabetic group [Table 2]. In general, mean fasting blood glucose (FBG) showed a highly significant difference ($P = 0.000$) between obese, diabetes, and control groups with higher concentration in both obese and diabetes participants, and specifically, there is a significant difference ($P = 0.001$) between diabetes and obese groups with higher concentration in diabetic than obese group [Table 2].

Clinical characteristics of age parameters demonstrated no significant difference ($P = 0.351$) in comparing all three group (obese, diabetes, and control groups) with each others. However, BMI showed a significant difference and higher level in obese in compare to other two groups – *post hoc* test displayed significant difference between control group versus obese, control group versus diabetes, and obese group versus diabetes group as shown in Table 3.

The serum ghrelin had a moderate significant correlation with FBG in obese but insignificant correlation ($P > 0.05$) with both diabetes and control groups [Table 4a and Figure 1].

Table 1: Biochemical level of both fasting blood sugar and plasma ghrelin in three groups (obese, diabetic, and healthy participants) and their significant difference (ANOVA test)

Parameters	Mean±SD			*P*
	Obese	Diabetes	Control	
FBS (mg/dl)	143.4±39.33	243.8±89.32	117.3±11.89	0.000
Ghrelin level (ng/dl)	5.1±0.85	4.3±0.82	4.8±1.01	0.008

SD: Standard deviation, FBS: Fasting blood sugar

Table 2: Biochemical association of both fasting blood sugar and plasma ghrelin in obese and diabetic patients

Parameters	Mean±SD		*P**
	Obese	Diabetes	
FBS (mg/dl)	143.4±39.33	243.8±89.32	0.000
Ghrelin level (ng/dl)	5.1±0.85	4.3±0.82	0.001

*Independent samples *t*-test. SD: Standard deviation, FBS: Fasting blood sugar

There was no significant correlation between FBG and age in all three groups, except there was a significant correlation between FBG with age factor in control group. FBG shows no significant correlation with BMI in all three groups [Table 4b].

Discussion

The present study showed that mean ghrelin levels were significantly different between obese and diabetes groups as in with higher level in obese than diabetic group. These results disagree with a study conducted by Cruz-Domínguez *et al*.[13] in which control has higher level of ghrelin as compared to diabetics and obese whereas the present study shows that obese has higher level of ghrelin (although still within a reference normal detection range) than diabetic group. It could be due to hormonal changes (postmenopause), patient selection, or due to small sample number. Furthermore, it may be as a result of ghrelin changes with age as ghrelin plasma concentration increases with age and this may contribute to the tendency for weight gain as people age.[14]

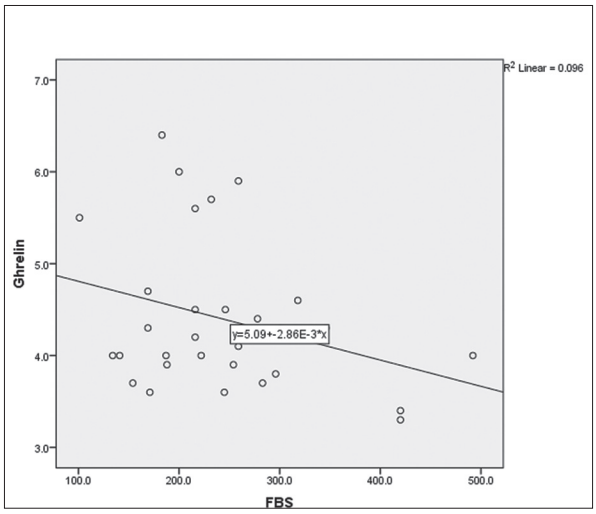

Figure 1: The correlation between plasma level of ghrelin and fasting blood sugar in patients with type 2 diabetes mellitus. There are a negative and insignificant correlation between these parameters ($R = -0.31$, $P = 0.095$)

Table 3: Clinical characteristics in obese, diabetic patients, and healthy people and their significant difference (ANOVA test)

Parameters	Mean±SD			*P*
	Obese	Diabetics	Control	
Age (years)	57±7.49	57.2±6.98	54.6±8.68	0.351
BMI (kg/m^2)	35.5±3.27	31.2±4.86	26.3±1.56	0.000

SD: Standard deviation, BMI: Body mass index

Table 4: The correlation between plasma ghrelin (A) and fasting blood sugar (B) with each other and with other clinical parameters (age and body mass index)

Parameters	Obese		Diabetics		Control	
	r	*P*	*r*	*P*	*r*	*P*
A: Ghrelin						
FBG	0.414	0.023*	−0.310	0.095	0.110	0.562
BMI	0.077	0.685	0.087	0.646	−0.125	0.512
Age	−0.042	0.827	0.027	0.889	0.359	0.520
B: FBS						
Age	0.228	0.225	−0.051	0.789	0.428	0.018*
BMI	−0.029	0.878	−0.056	0.787	−0.172	0.362

*Significant correlation at the *P*=0.05. FBS: Fasting blood sugar, BMI: Body mass index

Ghrelin showed insignificant negative correlation with FBG ($r = -0.310$ and $P = 0.095$). This was consistent with the findings of Jawed *et al*.[15] who found that ghrelin levels and serum glucose level are inversely related to each other and further added that ghrelin levels are lower in patients with type 2 DM, and this insignificant correlation may be related to small sample number. Whereas there was significantly positive correlation of ghrelin ($r = 0.414$, $P < 0.05$) with FBG in obese.

These results disagree with the findings of Jawed *et al*.[15] which show nonsignificant correlation between ghrelin and glucose in obese participants. This may occur as ghrelin which is an appetite inducer when increased lead to enhance appetite which in turn lead to increase blood glucose; and this may be due to patients selection and small number sample. No significant correlation of ghrelin with BMI was found in all three groups. These results were consistent with study conducted by Cruz-Domínguez *et al*.[13] in which diabetics with high BMI had low ghrelin levels. These findings also in accordance to the findings of McLaughlin in which no association of ghrelin was observed with BMI ranges 29–35 kg/m^2.

Conclusion

There is an inverse relationship between fasting glucose and ghrelin level in type 2 diabetic patients and positive correlation in obesity. The study also shows that hyperglycemia due to disturbance in glucose metabolism may result in suppression of ghrelin level in T2 DM. The present study showed that ghrelin levels are different in obesity and DM.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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