Ghrelin and Leptin and Their Relations with Insulin Resistance in Diabetes Mellitus Type 2 Patients

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Abstract:

Ghrelin and leptin are hunger hormones related to type 2 diabetes mellitus (T2DM), and the pathogenesis of T2DM is the abnormality in insulin secretion and insulin resistance (IR). The aim of this study is to evaluate ghrelin and leptin concentrations in blood and to specify the relationship of these hormones as dependent variables with some biochemical and clinical measurements in T2DM patients. In this study, forty one T2DM and forty three non-diabetes mellitus (non-DM) subjects, aged between 40-60 years and with normal weight, were enrolled. Fasting serum ghrelin and leptin were estimated by enzyme-linked immunosorbent assay (ELISA). In our results ghrelin was significantly increased, and leptin was significantly decreased, in T2DM patients compared with non-DM subjects. Ghrelin was positively correlated with the fasting blood glucose (FBG) and IR, but inversely related to the insulin sensitivity (IS). Leptin was negatively correlated with mean arterial pressure (MAP), FBG, glycated hemoglobin (HbA1c), IR, low-density lipoprotein cholesterol, nitric oxide (NO), and alanine aminotransferase (ALT), as well as showed a linear correlation with IS and a strong dependence on sex. The area under the curve (AUC) value shows ghrelin and leptin as biomarkers for T2DM. In conclusion ghrelin and leptin hormones have predictive ability to predict T2DM, as they are significantly associated with IR, IS, free radicals, and lipid profile.

Keywords: Diabetes, HOMA-IR, Hunger hormones (ghrelin and leptin), Oxidative stress, QUICKI.

Introduction:

Type 2 diabetes mellitus is a chronic disease due to deficiency in insulin secretion and insulin actions [1]. Many studies are presented to explain the association of hunger hormones (ghrelin and leptin) with IR [2-5].

Ghrelin is an orexigenic hormone, first isolated from the stomach of humans and rats in 1999 [6]. Studies have focused on the relationship between ghrelin and diabetes complications, especially hypertension, atherosclerosis, and obesity [7]. Patients with T2DM has a lower ghrelin level than healthy subjects [4]. Ghrelin has a role in glucose metabolism, and involved in insulin secretion and IS [8, 9].

Leptin is an anorexigenic hormone synthesized in adipose tissue, and affects the hypothalamus to alter food intake behavior and energy expenditure [10]. The role of hyperleptinemia in the pathogenesis of IR and T2DM has been postulated, and a higher level of leptin was found in patients with T2DM than in healthy subjects [11, 12]. Additionally, strong associations of leptin with body mass index (BMI), IR, and insulin production in T2DM patients have been found [3]. Leptin may affect cardiovascular functions and increasing blood pressure [13]. Leptin may be a marker of hepatic fibrosis [14], and thus it may be associated with alanine aminotransferase (ALT), which is a liver injury marker. Becerril revealed the physiological relationship between leptin and nitric oxide (NO, a nitrogen-based free radical

secreted by endothelial cells) [15]. Leptin concentrations depend on sex, as female subjects have higher serum leptin concentrations than males [16, 17].

However, no sufficient studies clearly show the association of both orexigenic and anorexigenic hormones with almost all biochemical parameters related to T2DM. The purpose of our study is to evaluate ghrelin and leptin concentrations in blood and to specify the relationship of these hormones as dependent variables with some biochemical and clinical measurements in T2DM patients.

Material and Methods:
Subjects

This study included eighty four subjects from Sulaimani Governorate, Kurdistan Region of Iraq. Forty-one participants (16 men and 25 women) with T2DM attended the Diabetic and Endocrine Clinical Center of Sulaimani Governorate. The rest of the subjects (14 men and 29 women) were healthy and selected randomly as the control group. The age of the participants ranged between 40-60 years, they had BMI ≤ 25 kg/m^2. The present study excluded those with chronic diseases (hypertension, cancer, cardiovascular, gastrointestinal, liver, kidney, autoimmune, and thyroid diseases), pregnant, smokers, or alcoholic. The blood samples were collected from April to October 2018.

This study was approved by the ethics committee of the College of Medicine at University of Sulaimani-Kurdistan Region of Iraq.

Clinical Parameters

The clinical history of each subject was recorded by questioning them orally on the day of sample collection and the participants provided informed verbal consent. A mechanical scale was used to measure the height and weight of the participants, and the BMI was calculated, by applying BMI formula [18]. Blood pressure was measured with mercury sphygmomanometer from the right hand while the subject was kept at rest, after resting for five minutes. By applying the mean arterial pressure (MAP) equation, MAP was calculated according to Yu, et al [19].

IR was calculated by applying the homeostasis model assessment-insulin resistance (HOMA-IR) formula described by Matthews, et al [20]. The quantitative insulin-sensitivity check index (QUICKI) was used for assessing IS [21].

Laboratory Measurements

About 10 mL of fasting blood was withdrawn from the antecubital vein of all participants, while they were seated. We collected 1 mL of blood in a vacuumed ethylenediaminetetraacetic acid (EDTA) tube for assessing the HbA1c test immediately, while the rest of the blood was collected in a vacuumed gel tube to obtain serum. Sera were separated from the blood and stored in small Eppendorf tubes for later analysis.

Diagnosticum Zrt (TOKYO BOEKI MEDISYS) Biolis kits were used for estimation of all biochemical parameters including fasting blood glucose (FBG), HbA1c, total cholesterol, triglyceride, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), aspartate transaminase (AST), and ALT by using BiOLiS 24i Premium analyzer (Tokyo Boeki Medisys Inc., Tokyo, Japan). For the quantitative determination of insulin, MAGLUMI 1000 fully-auto chemiluminescence immunoassay were used by utilizing MAGLUMI Insulin (CLIN) Snib kit. Ref. number 130205002M (Shenzhen New Industries, Shenzhen, China). Very low-density lipoprotein-cholesterol (VLDL-C) was calculated by Friedewald's equation [22].

NO was estimated by the colorimetric method based on the Griess reaction [23]. Malondialdehyde (MDA) was determined by a simple and sensitive spectrophotometric method and Thiobarbituric acid (TBA) reagent from (Merck KGaA, Darmstadt, Germany) used [24].

Fasting serum ghrelin and leptin hormones were estimated by enzyme-linked immunosorbent assay (ELISA). Human ELISA kits, Product number CEA991Hu (Cloud-Clone Corp., Houston, TX, USA), and BioVendor research and diagnostic products, Cat number RD191001100 (Brno, Czech Republic), were used for ghrelin and leptin estimation, respectively.

Statistical Analysis

The data of ghrelin and leptin hormones were expressed as a median (interquartile range, IQR). A p-value <0.05 was considered

statistically significant. By using GraphPad Prism 7 (San Diego, CA, USA), a Mann-Whitney non-parametric t-test was applied to compare all the studied variables between non-DM controls and T2DM patients. The receiver operating characteristic (ROC) curve was created to compare the sensitivity and specificity of variables in both control and patient groups.

All the data were log-transformed. Pearson (r) and non-parametric Spearman (r_s) correlations were used to analyze the correlation coefficient of ghrelin and leptin, respectively. To predict the relationship of ghrelin and leptin with all other variables, stepwise multiple regression was performed. All the analyses were performed with Statistical

Package for Social Sciences (SPSS) version 24.0 (IBM, Armonk, NY, USA).

Results

As shown in Table 1, there were significant differences between T2DM and non-DM subjects in serum ghrelin and leptin concentrations. Depending on Mann-Whitney test, ghrelin was significantly higher in T2DM patients compared with non-DM subjects, while leptin was highly significantly lower in T2DM patients compared with non-DM subjects (Table 1). Serum ghrelin was higher in both men and women with T2DM, but the difference was significant only in men. On the other hand, by applying unpaired t-test, both men and women showed significantly lower serum leptin concentrations in T2DM patients compared with non-DM subjects, respectively (Table 1).

Table 1. Serum ghrelin and leptin concentration (ng/mL) in males, females and all subjects of non-diabetes mellitus (non-DM) and type 2 diabetes mellitus (T2DM) patients.

Parameters			Median	IQR	p-value	n
Ghrelin(ng/ml)	**All Subjects**	Non-DM	20.19	19.57-20.46	**0.0157**	32
		T2DM	20.4	20.19-20.57		33
	Males	Non-DM	19.95	11.86-20.17	**0.0016**	9
		T2DM	20.33	20.17-20.54		15
	Females	Non-DM	20.33	19.7-20.54	0.123	23
		T2DM	20.5	20.23-20.61		18
Leptin(ng/ml)	**All Subjects**	Non-DM	9.716	4.695-16.41	**<0.0001**	39
		T2DM	3.448	1.752-5.788		38
	Males	Non-DM	3.087	2.189-4.788	**0.0218**	12
		T2DM	2.037	1.037-2.758		16
	Females	Non-DM	12.04	9.59-19.25	**<0.0001**	27
		T2DM	5.419	3.524-10.05		22

IQR: interquartile range; N.S. Not significant; n: number of sample

Table 2 demonstrates the ROC curve analysis and presents ghrelin and leptin as biomarkers for T2DM according to the area under the curve (AUC) values. Ghrelin presented as a biomarker for male but not for female T2DM patients. On the other hand,

leptin appears as a marker for both men and women T2DM patients. Thus, leptin was regarded as a useful marker for both sexes, while ghrelin is considered a biomarker for male T2DM patients only.

Table 2. ROC curve for ghrelin and leptin in males, femals and all subject.

Parameters	Ghrelin (ng/ml)			Leptin (ng/ml)		
	All Subjects	Male	Female	All Subjects	Male	Female
AUC	0.673	0.874	0.642	0.759	0.755	0.825
SE	0.067	0.070	0.086	0.054	0.092	0.061
p-value	**0.016**	**0.002**	0.1212	**<0.0001**	**0.022**	**0.0001**
n	65	24	41	77	28	49

AUC: Area under the curve; SE: Standard error

Serum ghrelin showed a significant positive correlation with FBG and HOMA-IR, and a negative correlation with weight and QUICKI. It was not correlated with the rest of the studied parameters according to Spearman correlation coefficient (r_s) analysis. Leptin showed a strong inverse correlation with most of the studied parameters, including height, systolic blood pressure (SBP), MAP, FBG, HbA1c, HOMA-IR, LDL-C, ALT and NO. It showed a positive correlation with sex and QUICKI. The remaining parameters showed no significant relation with serum leptin levels on Pearson correlation (r) analysis (Table 3).

Stepwise multiple regression was performed to test the relation between ghrelin and leptin with all the studied parameters, and the results are shown in Tables 4 and 5.

As shown in Table 4 the independent predictors for ghrelin in the total studied population group are ALT, FBG, and age as first, second, and third predictors, respectively.

The independent predictors for leptin in the total studied group are illustrated in Table 5. Sex was the major predictor for serum leptin. FBG, weight, and NO were the second, third and fourth entrant predictors for leptin.

Table 3. Correlation coefficient of ghrelin and leptin hormones with anthropometrics and metabolic parameters of the study parameters.

Parameters	Ghrelin (n=82)		Leptin (n=82)	
	r_s	p-value	r	p-value
Age	-0.183	0.095	-0.076	0.246
Sex	0.100	0.365	0.645	**0.0000**
Weight	-0.236	**0.030**	-0.089	0.212
Height	-0.200	0.068	-0.226	**0.019**
BMI	-0.117	0.290	0.162	0.070
SBP	-0.004	0.973	-0.338	**0.001**
DBP	-0.051	0.646	-0.061	0.290
MAP	-0.039	0.728	-0.222	**0.021**
FBG	0.238	**0.030**	-0.394	**0.0001**
Insulin	0.089	0.423	0.081	0.232
HOMA-IR	0.238	**0.029**	-0.240	**0.014**
QUICKI	-0.239	**0.029**	0.239	**0.014**
HbA1c	0.192	0.081	-0.249	**0.011**
Cholesterol	0.017	0.880	0.080	0.235
Triglyceride	0.162	0.141	-0.113	0.153
HDL-C	0.214	0.051	0.014	0.449
LDL-C	0.168	0.127	-0.204	**0.031**
VLDL-C	0.163	0.138	-0.109	0.162
AST	-0.174	0.113	-0.001	0.497
ALT	-0.024	0.828	-0.300	**0.003**
NO	-0.077	0.484	-0.285	**0.004**
MDA	0.151	0.169	-0.103	0.175
Ghrelin			-0.083	0.226
Leptin	-0.007	0.951		

Spearman (r_s) correlation coefficient was used for ghrelin data while, for leptin data Pearson correlation (r) was used. (B: the unstandardized coefficient regression, Beta: the standardized coefficient regression, R^2: the coefficient of determination (squared correlation), F: F-test)

Table 4. Stepwise multiple regression analysis reveals alanine aminotransferase (ALT), fasting blood glucose (FBG), and age as independent predictors for ghrelin in total population subjects.

Model	B	Beta	Partial correlation	R^2	Adjusted R^2	F	P-value
1			0.218	0.048	0.036	4.107	**0.046**
Constant	4.311						**0.000**
ALT	-0.724	-0.218					**0.046**
2			0.368	0.136	0.114	6.358	**0.003**
Constant	2.392						**0.003**
ALT	-1.108	-0.334					**0.003**
FBG	1.111	- 0318					**0.005**
3			0.433	0.187	0.157	6.146	**0.001**
Constant	8.936						**0.004**
ALT	-1.046	-0.315					**0.005**
FBG	1.367	0.392					**0.001**
Age	-4.231	-0.242					**0.027**

The excluded variables are sex, weight, height, BMI, systolic and diastolic blood pressure, MAP, cholesterol, triglyceride, LDL-C, HDL-C, VLDL-C, insulin, HOMA-IR, QUICKI, leptin, HbA1c, NO, and MDA. (B: the unstandardized coefficient regression, Beta: the standardized coefficient regression, R^2: the coefficient of determination (squared correlation), F: F-test)

Table 5. Stepwise multiple regression analysis reveals sex, fasting blood glucose (FBG), weight, and nitric oxide (NO) as predictors for leptin hormone in the total population subjects.

Model	B	Beta	Partial correlation	R^2	Adjusted R^2	F	P-value
1			0.645	0.416	0.408	58.316	**0.000**
Constant	-0.124						0.280
Sex	0.511	0.645					**0.000**
2			0.746	0.557	0.546	50.879	**0.000**
Constant	1.058						**0.000**
Sex	0.502	0.634					**0.000**
FBG	-0.548	-0.376					**0.000**
3			0.780	0.608	0.593	41.321	**0.000**
Constant	-2.479						**0.030**
Sex	0.617	0.778					**0.000**
FBG	-0.482	-0.330					**0.000**
Weight	1.791	0.271					**0.002**
4			0.808	0.652	0.635	37.029	**0.000**
Constant	-2.654						**0.015**
Sex	0.625	0.789					**0.000**
FBG	-0.399	-0.274					**0.000**
Weight	1.963	0.297					**0.000**
NO	-0.312	-0.218					**0.002**

The excluded variables are age, height, body mass index, systolic and diastolic blood pressure, MAP, cholesterol, triglyceride, LDL-C, HDL-C, VLDL-C, insulin, HOMA-IR, QUICKI, ghrelin, HbA1c, and: MDA. (B: the unstandardized coefficient regression, Beta: the standardized coefficient regression, R^2: the coefficient of determination (squared correlation), F: F-test)

Discussion:

This study showed the prevalence of both ghrelin and leptin in T2DM patients and non-DM subjects in Iraqi Kurdistan Region.

We found that ghrelin significantly increased in T2DM patients, in contrast to previous studies [4, 7, 25]. The increment of ghrelin may be related to hyperglycemia and IR in our population with T2DM, as ghrelin induces insulin resistance [26] or may be related to BMI as our subject were within normal BMI, a previous study reported the peripheral ghrelin is inversely correlated with BMI and they had lower ghrelin level in

T2DM patients with higher BMI [4]. It may also be due to the compensatory effect of diabetes on energy expenditure, as patients with DM have a lower level of energy in their bodies. Thus, they have a higher appetite than non-DM subjects. This explanation was supported by Dong, et al and Gelling, who indicated the physiological role of ghrelin in the regulation of energy homeostasis in mice with Streptozotocin-induced diabetes [27, 28]. Another possible reason for significantly higher ghrelin concentration is the antidiabetes medication, metformin, which causes an elevation in plasma ghrelin level and this explanation approved by Nabel M, as they found serum ghrelin level in control diabetic patients was lower than that of control healthy group while it was higher in diabetic patients' using metformin daily [29].

On the other hand, serum leptin showed a highly significant lower concentration in T2DM compared with non-DM subjects. Previous studies observed a variation in the level of serum leptin, so our result may be partly explained by ethnic differences. For instance, Abdelgadir, et al observed that the Sudanian T2DM patients had lower leptin levels than non-DM subjects with BMI $\leq$25 [30], whereas in a Polish study, a reverse outcome was obtained [12]. Saudi Arabians with DM had a moderately higher leptin level than non-diabetic subjects [31]. And Iraqi diabetic normal weight men had lower serum leptin than normal weight healthy subjects [32]. As with our ghrelin results, metformin may also explain the lower leptin levels [11]. The other possible reason of decreasing in leptin level of T2DM patients in our study may be related to the BMI, Zamil, et al result confirmed our result as they concluded that obesity had a significant effect on leptin concentration [32].

In our population, women showed a higher concentration of serum ghrelin in both T2DM patients and non-DM subjects than men. This result is frequently recorded and several studies have explained the interactions between ghrelin and estrogen, as they reported stimulatory effect of plasma estrogen on ghrelin receptors expression [33]. Testosterone also has an inverse relation with ghrelin, overexpression of ghrelin may inhibit production of testosterone in human testes which may be due to the activities of ghrelin receptor [34]. And

another possible reason of the sexual dimorphism of ghrelin is the difference in fat mass contents and distribution in female than in male [35] however, body fat content was not estimated in our study. On the other hand, subjects with T2DM showed significantly lower serum leptin levels in our population, both men and women. Women had higher leptin concentrations than men, which accords with previous studies [16, 17]. Higher leptin levels in women may be attributed to a higher ratio of adipose tissue and higher leptin production rate per unit mass of adipose tissue [36] and estrogen levels in women, which stimulate leptin mRNA expression [37].

Our results, established by ROC curve analysis, show that ghrelin is a useful T2DM disease marker for male subjects and this is possibly because of the regulatory effect of steroid hormone on ghrelin level as the ghrelin and ghrelin receptor expression occurs in the Leydig and Sertoli cells of human testes and ghrelin affect testosterone secretion via stimulation of cyclic guanosine monophosphate (cGMP) and cyclic adenosine monophosphate (cAMP) [34], or due to the stimulatory effect of estrogen hormone on ghrelin, while leptin is a useful biological marker for T2DM regardless of sex which may be explained by many possible reasons. Including the body fat mass distribution, and the stimulatory effect of estrogen and progesterone on serum leptin in women. In men, testosterone inhibits leptin production in adipose tissue. Leptin may have a direct role on spermatogenesis and the function of testes due to the distribution of leptin receptors in the seminiferous tubules and seminal plasma on the testes cells [38].

According to the nonparametric Spearman's coefficient (r_s) of correlation, ghrelin exhibits a positive correlation with FBG and HOMA-IR. This result is in line with Vestergaard et al, who found that ghrelin administration induced IR [39]. The main reason for that association is the stimulatory effects of ghrelin on glucose synthesis and decreasing the peripheral glucose uptake [40] and in turn, it causes insulin resistance due to defect in insulin action and leads to reduced insulin sensitivity.

By applying stepwise multiple regression analysis, ALT was found to be a significant predictor for ghrelin, along with

FBG and age. ALT is the first predictor for ghrelin and this is due to the effect of ghrelin on liver inflammation [41], and the inhibitory effect of ghrelin O-acyltransferase administration on serum ALT activity [42]. FBG was another independent predictor of ghrelin hormone. This is due to the enhancement effect of ghrelin on glucagon secretion via its effect on the liver and brain, and stimulate hepatic glucose production through its effect on the brain [43].

Pearson correlation (r) was used to determine the relationship of leptin with other studied biochemical parameters. Serum leptin inversely correlated with FBG, HbA1c, HOMA-IR, LDL-C, MAP and NO concentrations. Leptin deficiency causes a severe IR, which is associated with hyperglycemia [44, 45]. The inverse correlation between leptin and HbA1c mechanism may be due the prolonged hyperglycemia which lowers serum leptin level. As previous study found a negative correlation between serum leptin level and HbA1c in T2DM [46]. The negative correlation between leptin and IR may be related to the normal body weight of our population as obesity has an important linear effect on increasing serum leptin and IR [3]. Consistent with our results, Mohiti-Ardekani, et al found that leptin and HOMA-IR had a negative correlation in non-obese T2DM patients [47]. Leptin has a linear relation with QUICKI, which accords with the findings of previous studies as they found a strong significant correlation of leptin with QUICKI [48, 49]. This indicates the improvement effects of leptin on hepatic IS, which is due to the effect of leptin on liver through autonomic nervous system [50].

Our stepwise regression found that the major predictor for leptin in the total studied subjects is sex, which accounts for 41% of the leptin variation. The sex differences in leptin may be due to factors such as subcutaneous fat in women [46], estrogens, which stimulate leptin mRNA expression [51], and glucocorticoids, which may play an important role on leptin synthesis. Fat mass is a significant determinant of plasma leptin concentrations, as mentioned by Fujita, et al [52] and Zamile et al, also found a higher serum leptin in overweight diabetic than normal weight T2DM patients [32]. These support

our result about the effect of weight on leptin level. A hypoglycemic effect is another physiological function of leptin, and leptin is a key regulator of glucose homeostasis in rodents and humans [53]. Finally, NO is a predictor of leptin, which contributes to NO metabolism in humans [15]. Interestingly, the current results showed ghrelin a linear correlation with higher FBG and IR. Also, it is evident from our results that leptin is associated with lower FBG, LDL-C levels, IR, hypertension, reactive oxygen species, and oxidative stress in DM patients.

Conclusion:

Ghrelin induced IR and hyperglycemia in our subjects, because of the stimulatory effects of orexigenic hormones on glucose and insulin secretion. While, lower level of leptin is associated with higher FBG and IR in T2DM patients. Ghrelin is a biomarker of T2DM in male subjects, but leptin is a useful marker for the disease regardless of sex. Ghrelin and leptin have predictive ability to predict T2DM disease, as they were significantly associated with IR, IS, free radicals, and lipid profile.

Authors' declaration:

- Conflicts of Interest: None.
- We hereby confirm that all the Figures and Tables in the manuscript are ours. Besides, the Figures and images, which are not ours, have been given the permission for re-publication attached with the manuscript.
- The author has signed an animal welfare statement.
- Ethical Clearance: The project was approved by the local ethical committee in University of Sulaimani.

Authors' contributions statement:

- Author contribution: As the authors we certify that we have participated in different roles as follows:
- 1*:Sample collection, analysis and interpretation of data. Drafting, writing, and proofreading the MS.
- 1: Revision and proofreading the manuscript.
- 2: Conception and designing the project, revision and proofreading of the manuscript..
- Both 1 and 2 supervised the project.
- All the authors discussed the results and contributed to the final version of the manuscript.

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الغريلين واللبتين وعلاقتهما مع مقاومة الأنسولين في مرضى داء ألسكري من النوع ألثاني

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الخلاصة:

إن مرض السكري من النوع الثاني هو ناتج عن خلل في إفراز هرمون الأنسولين، ومقاومة الأنسولين. الهدف من الدراسة هو قياس تركيزالجريلين واللبتين في الدم وتحديد طبيعة العلاقة الموجودة بين هذه الهرمونات كمتغيرات تابعة مع بعض القياسات البيوكيميائية والسريرية في مرضى السكري من النوع الثاني. شملت الدراسة واحد و أربعين مريضاً بداء السكري من النوع الثاني و ثلاثة و أربعين شخصاً أصحاء كمجموعة ضابطة ، تتراوح أعمارهم بين 40-60 سنة و ضمن الوزن الطبيعي. وتم قياس نسبة هرمون الغريلين و اللبتين باستخدام تقنية الفحص المناعي المرتبط بالإنزيم (الإليزا). أظهرت النتائج إن نسبة الغريلين اعلى واللبتين أقل معنوياً في مصل مرضى السكري من النوع الثاني مقارنة بالجموعة الضابطة. وتبين ان غريلين ترتبط إيجابيا مع، نسبة السكر في الدم و مقاومة الأنسولين ومن ناحية اخرى ترتبط عكسياً بحساسية الأنسولين. أماعلاقة اللبتين مع سكر الدم، الهيموجلوبين الجلوكوزيلاتي، مقاومة الأنسولين والبروتين الدهني المنخفض الكثافة، أكسيد النيتريك وأنزيم الكبد (ألانين أماينوترانسفيريز) هي علاقة عكسية. و ترتبط اللبتين خطياً بمعدل ضغط الدم، حساسية الأنسولين و نوع الجنس. وفقًا لاختبارات التشخيص بأستعمال منحنى الخاصية العملياتية للمستقبلية أعتبرت هرمون الغريلين واللبتين علامات حيوية لداء السكري من النوع الثاني. استنتجت هذه الدراسة أن الغريلين واللبتين يمكن إستخدامهم كأدوات تنبؤية للأصابة بمرض السكري من النوع الثاني، نظراً لعلاقتهما المعنوية بمقاومة وحساسية الأنسولين، الشوارد الحرة و مستوى الدهون.

الكلمات المفتاحية: هورمونات الجوع، مؤشر مقاومة الأنسولين، مؤشر حساسية الأنسولين، الإجهاد التأكسدي، داءالسكري