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A Biochemical Analysis for Glucose homeostasis regulated by certain hormones

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ABSTRACT

The aim of this study was performed to compare ghrelin and GLP-1 levels in individuals with normal blood sugar levels. This study was performed to compare ghrelin and Glucagon like peptide -1 (GLP-1) levels in individuals with normal blood sugar levels. Participants and methods: The study included a total of 200 individuals, with 58% of being male. The mean age of the participants was 37.2 ±4.2 years. BMI mean was 31.9 ±4.4 kg/m². The subjects were tested in a condition of fasting, as well as 30 and 60 minutes after ingesting a standard liquid meal. Throughout this testing, we evaluated the concentrations of ghrelin and GLP-1. Results: Patients exhibited the most unfavorable metabolic profile, defined by higher levels of glucose. It was noted that the levels GLP-1 and insulin exhibited a similar increase in all groups after consuming a standard meal, regardless of whether the participants were fasting or had eaten 30- or 60-minutes prior. Glucose levels exhibited a rise in all groups following the consumption of food. However, the rise was significantly more pronounced in the DOB group as compared to the NOB as well as CON groups at the 30 and 60-minute marks after the meal ($p < 0.00$). Conclusion: It has been concluded that GLP-1 and ghrelin levels in individuals with different levels of glucose tolerance had similar responses after consuming a typical liquid meal.

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1- INTRODUCTION

The gut-brain axis has a crucial role in regulating energy balance and is involved in the progression and control of metabolic diseases. Insulin, glucagon, Ghrelin, and glucagon-like peptide-1 (GLP-1) are synthesized by enteroendocrine cells located in the gastrointestinal tract (GI) and pancreas [1]. Many experiments had been performed to evaluate the fluctuating patterns of glucose and insulin regulation, as well as the existence of autoantibodies associated with diabetes, in a sample of persons who do not have diabetes [2]. GLP-1, an incretin hormone, is secreted by enteroendocrine L cells situated in the distal jejunum and ileum, as well as by neurons in the brainstem and hypothalamus, following a meal. GLP-1 stimulates the release of insulin from pancreatic islets in reaction to glucose levels [3]. β-cells experience suppression, glucagon secretion is hindered, and stomach emptying is postponed, leading to a decrease in the rate of nutritional absorption. These actions aid in reducing the levels of glucose in the blood after a meal and increasing the feeling of fullness [4]. Ghrelin, a peptide that enhances hunger, is mostly secreted by the

stomach and duodenum. Individuals with a normal body weight who are not consuming food experience an elevation in levels of ghrelin, which is a hormone [5]. The rise in ghrelin levels increases appetite and aids in the prevention of hypoglycemia by enhancing the synthesis of glucagon and decreasing the release of insulin in response to glucose [6].There is a proposition that individuals who are obese and have insulin resistance or type 2 diabetes mellitus (T2DM) nevertheless exhibit a response to the impacts of gut hormones. Individuals suffering from obesity commonly have decreased levels of ghrelin and GLP-1, both prior to and following meals [7]. However, our understanding of the time course of ghrelin and GLP-1 levels after a meal, as well as their relationship with body fatness and glucose regulation, is currently restricted [8]. There is a concept proposing that excessive body fat and specific metabolic and inflammatory disorders are independently associated with reduced levels of ghrelin following meals [2]. Therefore, this study was performed to compare ghrelin and GLP-1 levels in individuals with normal blood sugar levels

2- METHOD

Study population and Subject recruitment

Approximately 200 people with various diagnoses related to glucose intolerance problems. This is because conducting an oral glucose tolerance test would be inappropriate for individuals with known diabetes, and the results would be difficult to interpret due to the use of antidiabetes medication. Eligible participants were discovered by searching the hospital database. These participants were not diagnosed with diabetes during their last visit to our program. Subsequently, the study was deliberated during patient appointments, and their inclination to participate was evaluated. Prior to recruitment, subjects were given informed consent, as well as assent. The protocol obtained approval from the Institutional Review Board under the reference number 197-152-3.

Study procedures

Body weight was assessed. The Body Mass Index (BMI) was computed and all categories were assessed as referenced by Center of Disease Control and Prevention (CDC, 2020).

Laboratory testing

Blood samples were obtained via venipuncture and collected in serum EDTA, and fluoride tubes. To inhibit the breakdown of the active forms of ghrelin, GLP-1, and insulin. Next, plasma EDTA tubes were subjected to centrifugation at a speed of 1,000 revolutions per minute at a temperature of 4 ºC for a duration of 10 minutes. Similarly, tubes containing plasma fluoride and serum were centrifuged at a speed of 4,000 revolutions per minute at a temperature of 18 ºC for a duration of 10 minutes. The samples were placed into cryotubes and stored at a temperature of -80 ºC until they were analyzed.Plasma levels of active ghrelin, insulin, and active GLP-1 were measured at three different time points: baseline (fasting), 30 minutes after a meal, and 60 minutes after a meal. The measurements were done using the Milliplex® and GLP-1 Active Chemiluminescent Kit (Merck-Millipore, USA). In addition, plasma glucose levels were assessed in plasma samples using the glucose oxidase colorimetric technique. All these studies were conducted using commercially available kits specifically designed for the Automatic Analyzer A25. The coefficients of variance for both within-assay and between-assay analyses were all below 15%..Following a period of fasting lasting 10 hours, all individuals were subjected to an oral glucose tolerance test (OGTT). During the initial venipuncture, samples were obtained for measuring fasting insulin and glucose levels [9].

Statistical considerations

The statistical power was computed using the G*Power version 4.1.4 software, this calculation yielded a total sample size of 200 participants. The relationships between insulin sensitivity, insulin resistance, insulin secretion, glucose status, and patient treatment variables. The study evaluated changes in average GLP-1, and Ghrelin levels over a period of time using generalized estimating equations.

3- RESULTS

From a total 200 patients with majority (n=116) are males (Figure 1), those with diabetes exhibited the most unfavorable metabolic profile, defined by higher levels of glucose, insulin, and HbA1c. The mean age of the participants was 37.2 ±4.2 years. The mean BMI of the subjects was 31.9 ±4.4 kg/m² (Table 1). Moreover, there was a considerably higher rise in glucose levels in those with diabetes compared to those without diabetes following a meal ($p < 0.00$). There were no notable differences observed in ghrelin and GLP-1 levels between the groups during fasting ($p > 0.07$). After 60 minutes, all groups exhibited a reduction in ghrelin levels relative to the fasting state following the standard meal ($p < 0.03$). Furthermore, we noted that the levels of both GLP-1 and insulin exhibited a similar increase in all groups after consuming a standard meal, regardless of whether the participants were fasting or

had eaten 30- or 60-minutes prior. Glucose levels exhibited a rise in all groups following the consumption of food. However, the rise was significantly more pronounced in the DOB group as compared to the NOB as well as CON groups at the 30 and 60-minute marks after the meal ($p < 0.00$), all ghrelin and GLP-1 values are presented in Table (2).

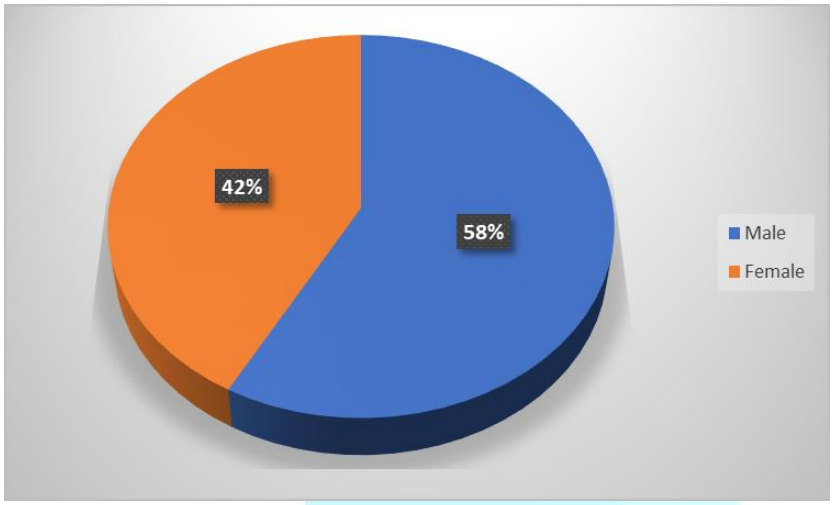

Figure 1. The gender distribution among patients (n=200)

Table 1 The demographic data for patients in this study (n=200)

All patients		**(n=200)**
Age median (range)		**37.2 ±4.2 years**
Gender,	**No.**	**(%)**
Female	**84**	**42**
Male	**116**	**58**
Weight status category	**No.**	**(%)**
Underweight	**18**	**9**
Normal/healthy weight	**71**	**35.5**
Overweight	**11**	**5.5**
Obese	**100**	**50**

Table 2 Glucose haemostasis controlling hormones level in this study

Variable	**Normal glucose tolerance (n=101) (Control)**	**Impaired glucose tolerance (n=99)**	**P value**
Fasting insulin level (µU/mL)	**4.7**	**8.1**	**0.00**
Thirty-minute insulin level (µU/mL)	**49.9**	**82.1**	**0.00**
Two-hour insulin level (µU/mL)	**21.9**	**61.1**	**0.00**
Ghrelin (pg/ml)			
CON (certificate of need a document issued by a health systems)	**81.1**	**88.12**	**0.03**
NOB(new obstetric visit)	**71.2**	**79.3**	
DOB(date of birth)	**44.5**	**47.1**	
Glucagon like peptide (GLP-1) (pM)			
CON	**0.69**	**0.71**	**0.00**

NOB	**0.55**	**0.49**
DOB	**0.72**	**0.81**

4- DISCUSSION

The primary conclusions of our investigation are as follows: a) The levels of active ghrelin consistently decreased in all groups from the fasting period to 60 minutes after the meal. b) The concentrations of active GLP-1, insulin, and plasma glucose exhibited an increase in all groups over the period from fasting to 30 minutes and 60 minutes after the meal. c) Individuals with dysglycemia and obesity had significantly greater increases in plasma glucose levels compared to both control individuals and individuals with obesity who had normal glycemic levels, at both the 30-minute and 60-minute time points after the meal [10]. Ghrelin exerts a deleterious influence on energy equilibrium and/or calorie limitation, hence averting hypoglycemia. Furthermore, it functions as a therapeutic intervention for individuals with clinical problems marked by inadequate body weight, as it enhances appetite and augments caloric consumption. However, inhibiting ghrelin could potentially offer benefits in regulating body fat levels through its key influence on food intake [11].

Unlike GLP-1, levels of ghrelin rise during the fasting period before eating and then decline after a meal is ingested. The results of our investigation corroborate this observation. Swiftly consuming a meal leads to a reduction in ghrelin levels, a hormone that triggers hunger, while simultaneously increasing glucose intake, a form of sugar [12]. GLP-1 promotes the release of insulin throughout meals, which causes a decrease in ghrelin levels due to the gradual increase in insulin and glucose levels. Moreover, it is important to examine the inhibitory impacts of additional gastrointestinal hormones, such as CCK, GIP, and PYY, on ghrelin levels after a meal, as their collective interactions hold promise for future investigation [13,14].

5- CONCLUSION

Our findings showed that GLP-1 and ghrelin levels in individuals with different levels of glucose tolerance had similar responses after consuming a typical liquid meal. Further research is required to examine the time sequence of gastrointestinal hormones following a meal and their influence on the clinical and metabolic of individuals with metabolic disorders.

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التحليل الكيميائي الحيوي لإستتباب الجلوكوز الذي تنظمه بعض الهرمونات

الخلاصة

تم إجراء هذه الدراسة لمقارنة مستويات الجريلين وGLP-1 لدى الأفراد ذوي مستويات السكر في الدم الطبيعية. تم إجراء هذه الدراسة لمقارنة مستويات الجريلين والجلوكاجون مثل الببتيد -1 (GLP-1) لدى الأفراد ذوي مستويات السكر في الدم الطبيعية. المشاركون والطرق الخاصة بالبحث: شملت الدراسة 200 فرد، 58% منهم ذكور. وكان متوسط عمر المشاركين 37.2 ±4.2 سنة. كان متوسط مؤشر كتلة الجسم 31.9 ±4.4 كجم/م^2. تم اختبار الأشخاص في حالة الصيام، وكذلك بعد 30 و60 دقيقة من تناول وجبة سائلة قياسية. خلال هذا الاختبار، قمنا بتقييم تركيزات الجريلين وGLP-1. النتائج: أظهر المرضى المظهر الأيضي غير المواتي، والذي تم تحديده بمستويات أعلى من الجلوكوز. وقد لوحظ أن مستويات GLP-1 والأنسولين أظهرت زيادة مماثلة في جميع المجموعات بعد تناول وجبة عادية، بغض النظر عما إذا كان المشاركون صائمين أو تناولوا الطعام قبل 30 أو 60 دقيقة. أظهرت مستويات الجلوكوز ارتفاعًا في جميع المجموعات بعد تناول الطعام. ومع ذلك، كان الارتفاع أكثر وضوحًا بشكل ملحوظ في مجموعة DOB مقارنةً بمجموعات NOB وكذلك مجموعات CON عند علامتي 30 و60 دقيقة بعد الوجبة (P <0.00). الاستنتاج: لقد تم التوصل إلى أن مستويات GLP-1 والجريلين لدى الأفراد الذين لديهم مستويات مختلفة من تحمل الجلوكوز كان لديهم استجابات مماثلة بعد تناول وجبة سائلة نموذجية.