



(RESEARCH ARTICLE)



## The role of betatrophin at onset of the Iraqi type II Diabetes Mellitus patients

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### Abstract

**Background:** Type II diabetes mellitus It is one of the most important metabolic disorders that the body suffers from, which affects glucose metabolism. It begins first with insulin resistance and then develops into type II diabetes mellitus disorder. One of the most famous pathological complications of type II diabetes mellitus disorder is the inhibition of insulin secretion and hyperlipidemia. Betatrophin which is a protein hormone produced at the beginning of infection with type II diabetes mellitus disorder. It works as a protective factor as it activates the growth and development of pancreatic beta cells and also has a role in regulating lipid metabolism at the beginning of infection with the disorder.

**Materials and methods:** The present study included the selection of 28 individuals suffering from type II diabetes mellitus disorder, and 28 healthy individuals as control. The study individuals were of both sexes and their ages ranged between 38-55 years. Many of biochemical markers were measured for all study individuals include Insulin hormone, random blood sugar, glycated hemoglobin, Betatrophin hormone and C-peptide, where special kits from the best international companies were used for this. On the other hand, the t-test method was used for statistical analysis to compare the two groups.

**Results:** After comparing the control group with the patients group with type II diabetes mellitus disorder, it was found that there was elevate in the levels of random blood sugar, glycated hemoglobin, Betatrophin hormone and C-peptide in the group of patients compared to the control group, except insulin hormone which was not affected. The values of mean  $\pm$  standard deviation (SD) and p-value were relied upon to determine the clinically significant values.

**Conclusion:** The current study results conclude that the hormone Betatrophin begins to rise as a protective factor for the body at the onset of insulin resistance, which causes with type II diabetes mellitus disorder This increase in the level of the hormone Betatrophin is an attempt by the body to rebuild parts of the pancreas to enhance insulin secretion and also to regulate the metabolism of fat in the body, which is considered a complication of with type II diabetes mellitus disorder

**Keywords:** Betatrophin; Type II diabetes mellitus disorder; Insulin resistance

### 1. Introduction

Type II diabetes mellitus can be defined as an inherited metabolic disorder that affects the human body and often occurs after age of 38 years. The pathological cause of type II diabetes mellitus is an effect that occurs in the shape of insulin receptor proteins, and this effect causes cells to resist insulin, which is called insulin resistance (1). The occurrence of this pathological condition in the body cause the body's cells unprepared to respond for the effect of insulin, which is responsible for the catabolism of glucose molecules in the body, which causes an elevate in glucose level in the

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bloodstream. The state of insulin resistance can cause the process of inhibiting the secretion of insulin from pancreatic beta cells and thus atrophy of pancreatic secretion. In addition, the other pathological complications caused by insulin resistance are hypertension, hyperlipidemia and others. The most important symptoms and signs that begin to appear at the onset of type II diabetes mellitus are nausea, vision problems, frequent thirst and others (2).

Betatrophin is a protein hormone that is encoded by hepatocytes in most cases, as the number of amino acids that compose it is 198 and is encoded by special gene located on 19p13 chromosome. Where its encoding and secretion are stimulated by several stimuli, the most important of which are the calories consumed, irisin, insulin, and sometimes thyroxin hormone (3). Betatrophin is considered one of the most famous recently discovered hormones because there are studies about it that show its role in metabolic disorders such as hyperlipidemia and diabetes and how it regulates the level of fat in the body as well as its role in enhancing the secretion of insulin. However, until now, there are many studies about the precise and physiological role that betatrophin plays in the body. In this research, we highlight on the role of betatrophin in type II diabetes mellitus patients at the onset of suffering (4).

Our current study addressed the results of evaluating the level of betatrophin and its role with other parameters in Iraqi type II diabetes mellitus disorder patients.

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## **2. Material and methods**

### **2.1. The study design**

This study was designed by dividing the individuals included in it into two groups.

Group 1 included 28 individuals who did not suffer from any disease and was called the control group, which included individuals from both genders and their ages were 38-55 years.

Group 2 included 28 individuals who were newly diagnosed with type II diabetes mellitus disorder and was called the patient group, which included individuals from both genders and their ages were 38-55 years.

Both groups were diagnosed as patients or healthy based on the appearance of symptoms and signs related to type II diabetes mellitus disorder, as there are many characteristics of symptoms and signs used in this diagnosis. In addition, the patient's history and laboratory tests were used as well, and all of these investigations are stated in the American Diabetes Association Releases 2023 to diagnose type II diabetes mellitus that was used in this study (5).

### **2.2. The Study ethics**

This study was conducted at Al-Furat General Hospital in May 2024, where it included collecting all study individuals from both groups. The process of diagnosing the study individuals from patients and healthy people was subject first to diagnosis and then obtaining the individuals' consent to include them in the study orally, in order to achieve the characteristics of correct scientific research. The study was conducted after the 2013 Helsinki Declaration on the Ethics of Scientific Research.

### **2.3. Measurements and collect samples**

The process of collecting blood samples from all study individuals (both groups) began after diagnosing them and dividing them into healthy and patients individuals. After drawing blood samples, they were divided into two parts.

Part 1 of the blood sample was separated by centrifugation to obtain serum after being left in a water bath for 3 minutes. The blood serum was used to measure Insulin hormone, random blood sugar, Betatrophin hormone and C-peptide for all study individuals.

Part 2 of the blood sample was treated with a tube containing Ethylenediaminetetraacetic acid (EDTA) to preserve the blood components from damage via coagulation, because it was used to measure Glycated haemoglobin (HbA1c) percentage for all study individuals.

Materials and kits were used to measure the above parameters from the best manufacturers company of these materials, as all details of the materials are fixed in kit leaflets that mention in table below, see table 1.

**Table 1** The details of kits for the all biochemical markers that used in current study

Biochemical marker	Company name for the kit	Principle test	Lot Number
C-peptide	IBL International GMBH	Solid phase ELISA	RE53011
Random blood sugar	SPINREACT	Spectrophotometer	MDBSIS46-E 03/05/17
Betatrophin hormone	AvisceraBioscience	quantitative sandwich enzyme-linked immunosorbent assay( ELISA)	SK00528-02
HbA1c	Dx gen	Chromatographic assay	C1301a
Insulin hormone	ABCAM	The enzyme-linked immunosorbent assay (ELISA)	ab278123

### 2.4. Statistical analysis

Using statistical analysis methods to determine the extent of the difference in measured values between two or more groups. In the current study, the t - test method was used for comparison between groups 1 and 2. The t-test method uses mean, standard deviation (SD ) and p-value, where the p-value is considered clinically important if it is less than 0.05. At this study was use the 18 of SPSS program ( 2022 ) version (6)

### 3. Results

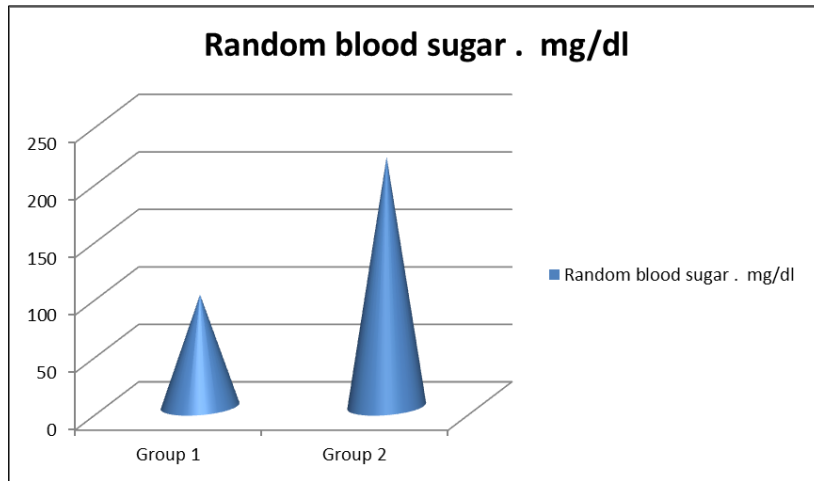
The current study used the statistical method know t-test, that using the values of the mean  $\pm$  standard deviation (SD) and the p-value in comparison between the groups. The results of this study showed after comparing the newly diagnosed type II diabetes mellitus disorder patients group and the control group and based on the values of p-value that there was an increase (significant clinical different ) in all parameters in the newly diagnosed type II diabetes mellitus disorder patients group compared to the control group except for the value of Insulin hormone which was not affected. The table below and the figures show these clinical differences.

See table 2 and figure 1,2,3&4.

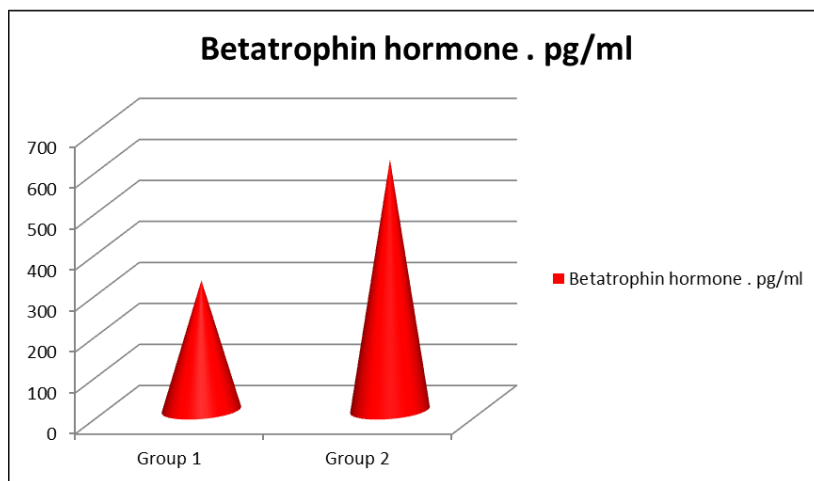
**Table 2** The newly diagnosed type II diabetes mellitus disorder patients group and control group comparison based on the many of Biochemical markers

Biochemical markers	Group 1 (control group) (No.28) Mean $\pm$ SD	Group 2 (newly diagnosed type II diabetes mellitus disorder patients group) (No.28) Mean $\pm$ SD	p-value
Random blood sugar (mg/dl)	97.3 $\pm$ 19.1	217.1 $\pm$ 8.6	0.001*
Insulin hormone ( $\mu$ IU/ml)	56.3 $\pm$ 8.5	63.2 $\pm$ 6.9	0.05
Betatrophin hormone (pg/ml)	316.5 $\pm$ 12.6	611 $\pm$ 25.8	0.001*
C-peptide (ng/ml)	4.2 $\pm$ 1.3	6.1 $\pm$ 3.2	0.001*
HbA1c (%)	5.1 $\pm$ 0.3	9.13 $\pm$ 2.4	0.001*

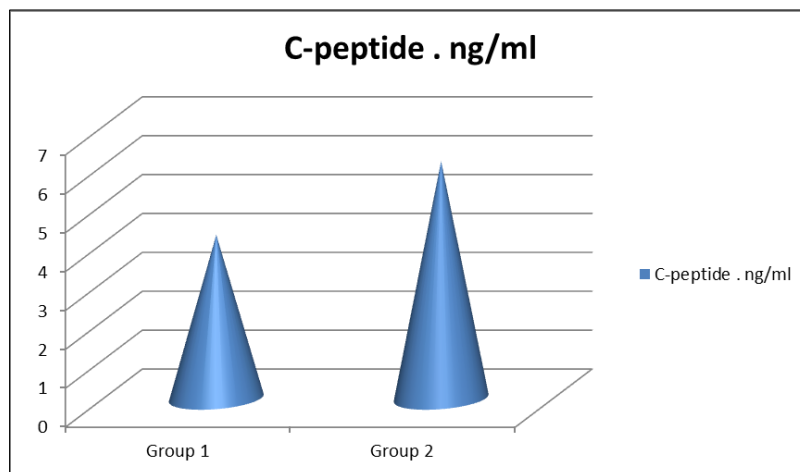
\* P-value less than 0.05 (Significant value)



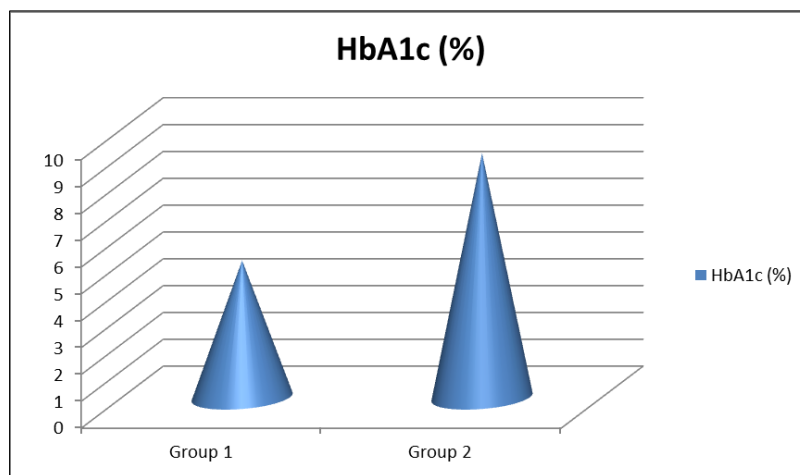
**Figure 1** Comparison between Group 1 (control group) & Group 2 (newly diagnosed type II diabetes mellitus disorder patients group) according to the level of Random blood sugar



**Figure 2** Comparison between Group 1 (control group) & Group 2 (newly diagnosed type II diabetes mellitus disorder patients group) according to the level of Betatrophin hormone



**Figure 3** Comparison between Group 1 (control group) & Group 2 (newly diagnosed type II diabetes mellitus disorder patients group) according to the level of C-peptide



**Figure 4** Comparison between Group 1 (control group) & Group 2 (newly diagnosed type II diabetes mellitus disorder patients group) according to the HbA1c percentage

#### 4. Discussion

The prolonged elevation of blood sugar levels due to insulin resistance is called type II diabetes mellitus disorder, which in turn can reduce the production and secretion of insulin from pancreatic beta cells due to the process of inhibition. The reason for the low insulin level is the inhibition of differentiation of these cells, which leads to a decrease in pancreatic function (7). Previously, there was a scientific theory that supported that the liver cell can release signals capable of multiplying and developing pancreatic beta cells. However, the more scientifically accepted idea is that the liver-specific depletion of the insulin receptor that produces the growth of pancreatic beta cells by the insulin receptor antagonist (S961) from liver cells. We were able to confirm the elevation of Betatrophin hormone by S961 insulin resistance (8). Therefore, the research results indicate the growth and development of pancreatic beta cells stimulated by the elevation of Betatrophin hormone, which means the enlargement of the pancreas gland accompanied by the elevation of the missing insulin level. (9).

The most important stimulant for the activation and production of Betatrophin is the relative increase in insulin at the onset of suffer with type II diabetes mellitus disorder due to the occurrence of insulin resistance at this stage. The reason for the increase in Betatrophin is primarily for the purpose of protection, as from the beginning of infection with insulin resistance the body senses the damage to the pancreas, in addition to the increase in fats accompanying this condition. The increase in Betatrophin at the beginning of type II diabetes mellitus disorder is an attempt by the body to reduce complications by regulating fat metabolism (hyperlipidemia ) and preventing it from accumulating. On the other hand, the increase in Betatrophin is an attempt by the body to restore the inhibition part of the pancreatic tissue. (10).

There are many studies that agree with the idea of our research and also agree with the results of our current research, as it was proven that Onalan, E., Bozkurt, A. and et al (2022) the level of Betatrophin hormone is high in the type II diabetes mellitus disorder patients at the beginning stage of infection. Therefore, Onalan, E., Bozkurt, A. and et al (2022) agrees with the results of our present study that proved the level of Betatrophin hormone is high in patients newly diagnosed with type II diabetes mellitus disorder. (11).

#### 5. Conclusion

The results of the current study conclude that the hormone Betatrophin begins to rise as a protective factor for the body at the onset of insulin resistance, which causes with type II diabetes mellitus disorder This increase in the level of the hormone Betatrophin is an attempt by the body to rebuild parts of the pancreas to enhance insulin secretion and also to regulate the metabolism of fat in the body, which is considered a complication of with type II diabetes mellitus disorder.

## Compliance with ethical standards

### *Disclosure of conflict of interest*

There are no conflicts of interest in this study.

### *Statement of informed consent*

Informed consent was obtained from all individual participants included in the study.

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### *Authors' contributions*

All authors contributed to data analysis, drafting and revising of the paper and agreed to be responsible for the all work aspects.

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