

**β- Cell function in a sample of Iraqi Patients with type 2 diabetes mellitus****Isam Noori Salman***National Diabetes Center/ AL-Mustansiriyah University**esam.kirwi@yahoo.com*DOI: <https://doi.org/10.32947/ajps.18.01.0363>**Abstract:****Back ground:** Type 2 diabetes is mostly due to impaired β-cell mass and dysfunction which expressed by Insulin secretion, sensitivity and resistance.**Aim of study:** to evaluate β- cell function in newly diagnosed and ongoing diabetics.**Method:** Eighty-eight subjects enrolled in this study with age range (30-59) years, (20) healthy individuals as controls group with mean age (42.95±9.80) years. (68) Diabetic Patients was divided into two groups, (26) newly diagnosed diabetic, mean age (45.81±8.16) years and (42) ongoing diabetics, mean age (49.33±6.64) year. "Fasting glucose", "lipid profile", "glycosylated hemoglobin", "C-peptide levels" were evaluated. Insulin secretion, sensitivity and resistance "HOMA B %", "HOMA S %"and "HOMA IR" respectively were estimated by "Homeostasis Model Assessment" "HOMA2 calculator program".**Results:** "Insulin secretion" and "sensitivity" were found to be lower (P 0.001) in both groups of diabetes than that controls, while a high level of insulin resistance in both diabetic groups than controls (P>0.0001)."C-peptide" level is higher in "newly diagnosed" diabetics than" ongoing diabetics" and controls (p<0.0001).**Conclusion:** Patients with low c- peptide level has poor insulin reserve and may need insulin while patients with high level of c- peptide have good insulin reserve and not need insulin to control his blood glucose.**Key words:** Diabetes, "Insulin resistance", "Insulin sensitivity", "HOMA", "c-peptide".

وظيفة خلايا بيتا في نموذج من المرضى العراقيين المصابين بداء السكري من النوع الثاني

عصام نوري سلمان

المركز الوطني لعلاج وبحوث السكري

**الخلاصة:****خلفية البحث:** أن تطور داء السكري من النوع 2 يرجع في الغالب إلى انخفاض كتلة الخلية وينتج عن ذلك خلل قلة افراز الانسولين وقلة حساسيته بالنسبة للخلايا ومقاومة الانسولين .

الهدف من البحث: لتقييم وظيفة خلايا بيتا لدى مرضى السكري حديثي التشخيص والمصابين بالسكري لفترة طويلة.. المرضى وطريقة العمل: تم أخذ ثمانين قوثمانون مواطنا من الفئة العمرية (30-59) سنة، (20) من الأفراد الأصحاء كمجموعة ضابطة مع متوسط العمر (42.95 ± 9.80) سنة. (68) مريض مصاب بداء السكري من النوع الثاني وتم تقسيمهم إلى مجموعتين، (26) مريض مصاب حديثا بالسكري ومتوسط العمر (45.81 ± 8.16) سنة و (42) مريضا مصاب بالسكري لفترة طويلة، متوسط العمر (49.33 ± 6.64) سنة. تم تقييم الجلوكوز في البلازما في حالة الصيام ،

وتم حساب مستويات البيبتيد-س، والنسبة المئوية لخضاب الدم المعسل ومقاومة الانسولين

(هو ما أ) وحساسية الانسولين (هو ما-أس) وتوازن افراز الانسولين (هو ما-ب)

**النتائج :** ان مستوى البيبتيد -س وجد مرتفعا بشكل ملحوظ لدى مرضى السكري حديثي التشخيص مقارنة بالمرضى المشخصين سابقا والمجموعة الضابطة وتبين ان افراز الانسولين وحساسيته كان وطا جدا عند كلتا المجموعتين من مرضى السكري من المجموعة الضابطة بينما ظهرت زيادة معنوية في مقاومة الانسولين في كلتا المجموعتين مقارنة بالمجموعة الضابطة**الاستنتاج :** المرضى الذين يعانون من انخفاض مستوى البيبتيد لديهم احتياطي الأنسولين قليل وربما تحتاج إلى الأنسولين في حين أن المرضى الذين لديهم مستوى عال من البيبتيد احتياطي الأنسولين جيد وليس في حاجة الأنسولين للسيطرة على السكري في الدم.

مفاتيح الكلمات: داء السكري من النوع 2، حساسية الأنسولين، مقاومة الأنسولين، هوما، البيبتيد ج

## Introduction:

Insulin resistance is a core defect which is responsible for development of "type 2 diabetes". "Insulin resistance" means a reduction in the tissue sensitivity to insulin which increases progressively till development of diabetes. Individuals may have insulin resistance for many years and yet with normo glycemia and continue increasing insulin secretion until reach a state of decomposition which resulting into hyperglycemia. [1]

In "Beta cell dysfunction", the "insulin secretion" is reduced while in "insulin resistance", insulin secretion may be not affected but the presence of insulin insensitivity is the problem. Both "Beta cell dysfunction" and "insulin resistance" leads to hyperglycemia and development of "type 2 diabetes". [2]

Many factors can trigger insulin resistance, of which central obesity is an important one. To develop diabetes,  $\beta$ -cell should loss its mass  $>65\%$  and reduced its insulin secretary capacity and this needs 10-12 years before clinical diagnosis of diabetes, so subjects will develop fasting hyperglycemia late and impairment of glucose tolerance appears early when there is reduction in " $\beta$ -cell function". [3]

HbA1C increased with time as the " $\beta$ -cell function" decline. Insulin sensitivity and B-cell function are considered as a measurement of " $\beta$ -cell power" and they are proportionally and inversely related to compensate for "insulin resistance". [4]

Not all individuals with insulin resistance develop diabetes because subjects who can increase insulin secretion sufficiently to overcome hyperglycemia may not develop diabetes, while those whom their B cells cannot maintain adequate amount of insulin secretion can develop the disease and this because of presence of a trigger high risk factor such as central obesity, smoking and decline of physical fitness. [5]

Evaluation of "insulin secretion" is difficult depending on the venous blood sample because of the clearance of most of insulin secreted when it pass through hepatic cells and frequent samples may be needed for monitoring of insulin function because of its short half-life (6 minutes only). [6]

Also, people takes external insulin has antibodies in their blood which interfere with the insulin assessment, so c-peptide which released from the pro-insulin and not cleaned by hepatic cells and have a half life time of 30 minutes is more accurate to evaluate insulin secretion. [7] Evaluation of insulin sensitivity can be done indirectly by using HOMA model using fasting blood glucose and c-peptide.

## Aims of the study

To estimate the "Beta cell function" in newly diagnosed, ongoing diabetic patients expressed by "insulin secretion", sensitivity" and "resistance" using homeostasis model assessment (HOMA 2 calculator program).

### Patients and methods:

A cross sectional, prospective study was conducted at the National Diabetic Center / Al-Mustansiriyah University, period from December 2016 to May 2017. The study included (88) subjects (42 females and 46 males) with age (30-59) years, (20) apparently healthy as "control group" and (68) patients with "type 2 diabetes". The patients were grouped into (26) "newly diagnosed" diabetics and (42) ongoing "diabetic". Patients taking external insulin were excluded. "Fasting glucose "and "C-peptide" was measured.

Insulin secretion, sensitivity and resistance were estimated from "fasting glucose" and "C-peptide" values by HOMA using HOMA-CIGMA software (HOMA2 calculator program) [8] [The homeostasis model assessment" (HOMA) estimate

"beta cell function" (B %) and "insulin sensitivity" (S %), as percentages of referral normal population.

#### Statistical Analysis:

Data were Analyzed of data was done using the "statistical packages for social sciences" (SPSS –version 11.5).

"ANOVA" and "student t-test" to test the "significance of difference" in mean between more than and two groups

**Table 1: Fasting glucose, duration and HbA1C in newly diagnosed diabetics, ongoing diabetic patients and controls.**

	Newly diagnosed diabetics	Ongoing diabetic patients	Healthy controls	P value
<b>Fasting plasma glucose (mg/ml)</b>	185.31±65.64	203.02±358.49	93.85±7.31	0.0001*
<b>Duration (months)</b>	5.81±2.08	68.29±48.47		0.0001*
<b>HbA1C%</b>	6.70±0.32	9.38±2.10	5.77±0.64	0.0001*

The mean serum "C-peptide" for "newly diagnosed" diabetics (4.41±1.78 ng/ml) and for "ongoing diabetic" patients (2.28±1.03 ng/ml) which was "significantly" higher ( P >0.001) than

respectively. P value ≤ 0.05 was considered significance.

#### Results:

There was significant increase in fasting plasma glucose (FPG) in both, "newly diagnosed" and "ongoing diabetics" comparing to controls (P <0.001), "table 1".

controls mean (2.09±0.90 ng/ml), while no "significant differences" in serum "C-peptide" levels between males and females ( P> 0.05) as shown in "table 2".

**Table 2: Serum C-peptide levels in newly diagnosed diabetics, ongoing diabetic patients and controls.**

	Newly diagnosed diabetics	Ongoing diabetic patients	Healthy controls	P value
<b>C-peptide (ng/ml)</b>	4.41±1.78	2.28±1.03	2.09±0.90	0.0001*
<b>Males</b>	3.88±1.89	2.13±0.95	2.44±1.04	> 0.05
<b>Females</b>	4.93±1.56	2.48±1.12	1.80±0.68	> 0.05
<b>P value</b>	0.137	0.280	0.116	

P< 0.05 level of significance using ANOVA test for difference of more than two means.

The mean Insulin Secretion for the newly diagnosed diabetic patients was (73.49±33.98) % and in "ongoing diabetic" patients was (37.09±19.67) % which was

"significantly" lower (P>0.001) than controls mean (115.00±37.70) % as shown in "table 3".

**Table 3: The level of Insulin Secretion (B %), Insulin Sensitivity (S %) and Insulin resistance (IR) in newly diagnosed diabetics, ongoing diabetic patients and controls.**

	Newly diagnosed diabetics	Ongoing diabetic patients	Healthy controls	P value
<b>Insulin secretion (B%)</b>	73.49±33.98	37.09±19.67	115.00±37.70	0.0001*
<b>Insulin Sensitivity (S%)</b>	29.29±17.84	58.60±38.36	80.81±42.10	0.0001*

<b>Insulin Resistance (IR)</b>	4.35±1.94	2.25±0.98	1.52±0.65	0.0001*
--------------------------------	-----------	-----------	-----------	---------

P< 0.05 level of significance using ANOVA test for difference of more than two means.

The mean Insulin Sensitivity for the newly diagnosed diabetic patients was (29.29±17.84) % and for Ongoing diabetic patients was (58.60±38.36) % which was "significantly" lower (P>0.001) than controls mean (80.81±42.10) % as shown in "table 3".

A significant increase in insulin resistance level of newly diagnosed diabetics (4.35±1.94) and ongoing diabetic patients (2.25±0.98) when compared with healthy controls (1.52±0.65) as shown in table (3).

### Discussion

serum "C-peptide" level was more in "newly diagnosed" diabetics than "ongoing diabetic" patients and controls, This finding has been in consistent with the study done by "La-or Chailurkit et al" study [9] where the "C-peptide" level was more in "newly diagnosed" diabetes and this may be explained the role of "insulin resistance" and a compensatory augmentation in "beta cell mass" and "insulin secretion" to overcome the hyperglycemia and those patients seems with adequate insulin reserve and may only require diet and exercise modalities of treatment to improve insulin sensitivity ,in addition to anti-diabetic drugs.[10] The load of "insulin resistance "cannot be overcome when the "beta cell mass" and function lost its compensatory power,[11], resulting in "type 2 diabetes ".While, in ongoing diabetic patients group the level of "C-peptide" was significantly lower, which coincide with "Bo. Set al" study results, and this can be explained as those patients with low "c-peptide" levels means have poor insulin reserve and such people may require insulin therapy. [12], the study declared that low c-peptide level patients usually with long duration of diabetes and high HbA1c% and these findings explained the supposition that patients with long duration of diabetes has more reduction of "insulin secretion" due to B cells exhaustion. Insulin secretion power

depends on mass and function of cells. Continuous hyperglycemia renders the-cells" into a reservoir of insulin in those volunteers in" insulin resistance" state. [13]

Fasting "C-peptide" level may reflect "insulin sensitivity" and "pancreatic secretion" more clear than "fasting insulin" because it is co secreted from the "beta cell" together with insulin, but is not metabolized by the liver like insulin, so it is less to be affected.[14].Also insulin estimation cannot distinguish endogenous from exogenous one.[15],this can be achieved by using fasting C-peptide level to estimate the "Insulin secretion", sensitivity and IR (HOMA B %, S % and IR) respectively by (HOMA2 calculator program).[8].

"Asakawa et al" have also announced that poorly controlled diabetics with long duration of diabetes have impaired insulin secretion because of "glucose toxicity", so "HOMA B%" is lower in "ongoing diabetics". It is stated that as glucose increase, it will result in a vicious cycle that develop frank "insulin resistance" and poorer "β-cell function". [16], a reduction of "β-cell mass" and "insulin secretion" is complicated by "insulin resistance" at the onset of "type 2 DM". [17]

Also, Tzeng TF, et al found that fasting hyper insulinemia and higher "insulin resistance" as well as, "insulin sensitivity and secretion" were lower in newly diagnosed diabetics than normal subjects. [18]

### References

- 1- American Diabetes Association. Standards of medical care-2013. Diabetes Care. 2013; 36 (Supple 1): S11–66.
- 2- Tura A, Pacini G, Kautzky-Willer A, et al. Estimation of prehepatic insulin secretion: comparison between standardized C-peptide and insulin kinetic models. Metab Clin Exp. 2012; 61:434–43.

- 3- Page KA, Reisman T. Interventions to preserve beta-cell function in the management and prevention of type 2 diabetes. *Current diabetes reports*. 2013 Apr; 13(2):252–60.
- 4- Kanat M, Winnier D, Norton L, et al. The relationship between  $\beta$ -cell function and glycated hemoglobin: results from the Veterans Administration Genetic Epidemiology Study. *Diabetes Care*. 2011; 34:1006–10.
- 5- Malandrucchio I, Pasqualetti P, Giordani I, et al. Very-low-calorie diet: a quick therapeutic tool to improve  $\beta$  cell function in morbidly obese patients with type 2 diabetes. *Am J Clin Nutr*. 2012; 95:609–13.
- 6- Nowak C, Sundström J, Gustafsson S, Giedraitis V, Lind L, Ingelsson E, et al. Protein Biomarkers for Insulin Resistance and Type 2 Diabetes Risk in Two Large Community Cohorts. *Diabetes*. 2016; 65(1):276–84.
- 7- Klein D, Misawa R, Bravo-Egana V, Vargas N, Rosero S, Piroso J, et al. MicroRNA Expression in Alpha and Beta Cells of Human Pancreatic Islets. *PLoS ONE*. 2013; 8(1).
- 8- Levy, J. C.; Mathews, S. R. and Hemans, M. P. “Correct Homeostasis Model Assessment (HOMA) Evaluation Uses the Computer Program”. *Diabetes Care*, 1998; 21:2191-2.
- 9- La-orChailurkit, Wallaya Jongjaroenprasert, Suwannee Chanprasertyothin, Boonsong Ongphiphadhanakul. “Insulin and C-peptide levels, pancreatic beta cell function, and insulin resistance across glucose tolerance status in Thais”. *Journal of Clinical Laboratory Analysis*. 2007; 21:85-90.
- 10- An de Bunt M, Gaulton KJ, Parts L, Moran I, Johnson PR, Lindgren CM, et al. The miRNA Profile of Human Pancreatic Islets and Beta-Cells and Relationship to Type 2 Diabetes Pathogenesis. *PLoS ONE*. 2013; 8(1):92-
- 11- Curran AM, Ryan MF, Drummond E, Gibney ER, Gibney MJ, Roche HM, et al. Uncovering Factors Related to Pancreatic Beta-Cell Function. *PLoS ONE*. 2016; 11(8): e0161350.
- 12- Bo, S.; Cavallo-Perin; P. and Gentile, L. et. al. “Relationship of residual beta-cell function, metabolic control and chronic complications in type 2 diabetes mellitus”. *Acta Diabetol*. 2000; 37:125-129.
- 13- Kareem, I.; Jaweed, S.A. And Bardapurkar, V.p .et. al. “Study of magnesium, Glycosylated hemoglobin and lipid profile in diabetic retinopathy”. *Clinical biochemistry*, (2004):19(2): 124- 127.
- 14- Anne Clark; Lucy, C.; and Jones et. al. “Decreased Insulin Secretion in Type 2 Diabetes: A Problem of Cellular Mass or Function?”. *Diabetes*, 2001; Vol. 50, Suppl 1.
- 15- Jenny Tong, Wilfred Y. Fujimoto and Steven E. Kahn et. al “Insulin, C-Peptide, and Leptin Concentrations Predict Increased Visceral Adiposity at 5- and 10-Year Follow-Ups in Nondiabetic Japanese Americans”. *Diabetes*, 2005; Vol.(54).
- 16- Asakawa, H.; Tokunaga, K. and Kawakami F. “Relationship of leptin level with metabolic disorders and hypertension in Japanese Type 2 diabetes mellitus patients”. *J Diab Comp*, 2001; 15: 57-62.
- 17- Maharani, U. and Karam, J.H. *Diabetes mellitus and hypoglycemia*. Tierney LM. Jr, McPhee SJ, Papadakis MA. *Current Medical Diagnosis and Treatment*, New York, Lange Medical Books / McGraw-Hill, 2002; (4th ed): p.1203-50.
- 18- Tzeng, T. F.; Chen, J. H. and Hsiao, P. J. et al. “Insulin action and insulin secretion in newly diagnosed type 2 diabetic patients”. *Kaohsiung J Med Sci*. Sep 2001; 17(9):468-74.