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Association between Nesfatin-1 Levels and C-Peptide in Sera of Obese/Non-Obese Type 2 Diabetic Women

Israa Khalil Ibrahim Al-Yassiri[1*], Fadhil Jawad Al-Tu'ma[1], Maher Abbood Mukheef[1], Khosay Baqir Jawad[2]
Baraa Abdul-Kareem Mutar[1]

[1]Department of Chemistry and Biochemistry, College of Medicine, University of Kerbala, Kerbala, Iraq.
[2]Al-Hassan Center of Diabetes and Endocrinology Unit, Al-Hussein Medical City, Kerbala Health Directorate, Kerbala, Iraq.
*Correspondence to: Israa Khalil Ibrahim Al-Yasiri (E-mail: aalyasiri1@gmail.com)

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Abstract

Objectives: The aim of the presented word was to assess the diagnostic accuracy of serum Nesfatin-1 in type 2 diabetes mellitus and its relationship with C-peptide level in obese and non-obese type-2 diabetic women of Iraqi population.

Methods: (A case-control study was performed on 50 type 2 diabetic patients admitted in Al-Hussein Teaching Hospital and Al-Hassan center of diabetes and endocrinology unit/Kerbala health directorate – Iraq and another 50 control individuals, during the period from April, 2022 – Jan. 2023). The T2DM groups were divided into two groups 25 obese and 25 non-obese; also the control group was divided into 25 obese and 25 non-obese as apparently healthy groups. The ELISA Kit was used to measure serum Nesfatin-1 and C-peptide, and random serum glucose was measured by enzymatic colorimetric method, and lipid profile test were measured through spectrophotometric technique, instead of HbA1c% was determined using HPLC method.

Results: The results observed indicated that Nesfatin-1 levels shown a non-significant decrease in all of type 2 diabetic groups as compared with apparently healthy control group, while the C-peptide were significantly decreased in type 2 diabetic patients when compared with apparently control group. In addition, the random blood glucose and HbA1c% were shown significant elevation in type 2 diabetic patients as compared with apparently healthy control groups. The observed data indicated that Nesfatin-1 and C-peptide levels when comparing between type 2 diabetic patients and control in obese groups shown a risk factors depending upon the odd ratio observed (OR = 1.064 (1.011–1.119), 1.0200 (0.992–1.08)) respectively, but only Nesfatin-1 was shown to be significant. In BMI the levels of Nesfatin-1 and C-peptide, as shown the Nesfatin-1 was significant in obese groups, while the C-peptide as shown significant in normal weight groups. The optimal diagnostic points for Nesfatin-1 were (sensitivity = 98%, specificity = 90%) at a level (Cut-off points) = 39.13, while C-Peptide levels: (sensitivity = 98%, specificity = 94%) at a level (Cut-off points) = 15.99. Both markers have *P*-values of the AUC were <0.001 and statistically significant.

Conclusion: Accordingly, it was concluded that a significant relationship between circulating Nesfatin-1 levels and type 2 diabetes. Nesfatin-1 appears to be able to contribute to the treatment of obesity and diabetes because of its anorexigenic and antihyperglycemic effects. In addition, C-peptide is a known biomarker of insulin resistance and beta-cell function. High specificity and sensitivity analyzed results were obtained by ROC analysis for both markers in T2DM.

Keywords: Nesfatin-1, C-peptide, obese, diabetes mellitus, type 2, body mass index, hypoglycemic agents

Introduction

Diabetes mellitus (DM) is a metabolic disorder where in human body does not produce or properly uses insulin, a hormone that is required to convert sugar, starches and other food into energy. Absence or reduced insulin in turn leads to persistent abnormally high blood sugar and glucose in tolerance. It is probably an oldest disease known to man.[1] Immunohistochemical studies have shown that the precursor of Nesfatin-1, non-esterified fatty acid/nucleobinding 2 (NUCB2), is localized in many places such as the pituitary gland, hypothalamus, brain stem, the forebrain and midbrain nuclei, central amygdaloid nucleus, ventrolateral medulla, and cerebellum. It is linked with developing of various serious diseases like micro vascular (nephropathy, retinopathy, neuropathy) and macro vascular (peripheral vascular disease and coronary heart diseases).[2] Diabetes and its complications are complex, multifactorial conditions with both major environmental and genetic components. When early studies identified differences in diabetic complication susceptibility in patients who seemed otherwise equal with regard to their diabetes glucose control, clinical features and management.[3]

Obesity and T2DM are two of the most pressing public health concerns worldwide because of their association with life-threatening diseases, including cardiovascular diseases and cancers.[4] Obesity, especially pathologic expansion of visceral white adipose tissue (vWAT), increases the risk of developing T2DM. Depending on the race, more than 75–90% of patients with T2DM are overweight or obese. The strong association of obesity and T2DM is supported by the term "disability."[5]

Nesfatin-1 that discovered in 2006 is secreted from the hypothalamic nuclei, which are responsible for controlling appetite. In the same study, it was reported that nesfatin-1 suppresses food intake, even in obese mice with a knockdown leptin gene.[6] The secretion is distributed in the body; nesfatin-1 is thought to affect many functions. Previous studies have reported that nesfatin-1 has regulatory effects on energy metabolism through suppression of food intake. In addition, it has been reported that nesfatin-1 regulates cardiac functions, decreases blood glucose levels, acts as a neuroendocrine regulator, and causes weight loss along with reduction in energy intake.[7]

The relationship between obesity and nesfatin-1 was investigated because of the effects of nesfatin-1 on food intake and energy consumption. There was a relationship between the polymorphism of the nucleobindin-2 gene and obesity. This may be a risk factor for the development of

obesity.[8] A study compared the fasting plasma nesfatin-1 levels of healthy individuals and type 2 diabetic individuals. Thus, fasting nesfatin-1 levels were found to be lower in individuals with type 2 diabetes than healthy individuals.[9] The effect of nesfatin-1 on insulin secretion is affected by blood glucose concentrations. Nucleobindin-2/Nesfatin-1 released from the pancreas increased in response to glucose.[10] Nesfatin-1 can increase the synthesis of pre-proinsulin mRNA and stimulate glucose-enhanced insulin release.[11] Peripheral nesfatin-1 may have a potential effect on the control of glucose homeostasis.[12]

Nesfatin-1 may be involved in long-term changes of energy expenditure. Because nesfatin-1 reduces food intake and increases energy expenditure, it induces a negative energy balance, which might be relevant in states of over nutrition but also might reflect conditions of stress.[13]

C-peptide is a substance that is created when the hormone insulin is produced and released into the body. C-peptide is a sign that the body is producing insulin. A low level (or no C-peptide) indicates that pancreas is producing little or no insulin. C-peptide is secreted in equimolar amounts with insulin from pancreatic beta cells and is reported to be a more useful laboratory parameter than insulin in evaluating endogenous insulin reserve.[14] C-peptide is a useful and widely used method of assessing pancreatic beta cell function and is measured to tell the difference between insulin the body produces and insulin that is injected into the body.[15] After cleavage of proinsulin, insulin and the 31-amino-acid peptide c-peptide are produced in equal amounts.[16]

The presented word aimed to assess the diagnostic role of serum Nesfatin-1 in obese and non-obese type 2 diabetes mellitus and its association with C-peptide level as compared with apparently healthy control women of Iraqi population.

Materials and Methods

A case-control study was performed on 50 blood samples obtained from types 2 diabetic women divided into two patients groups (25 obese and 25 non-obese) which were admitted in Al-Hussein Teaching Hospital and Al-Hassan center of diabetes and endocrinology unit/Kerbala health directorate – Iraq, during the period from May, 2022 – Jan. 2023), and another 50 blood samples obtained from apparently healthy women and also divided into two control groups (25 obese and 25 non-obese). The ELISA Kit was used to measure serum Nesfatin-1 and C-peptide levels, random blood glucose were measured by enzymatic colorimetric method, and lipid profile test were measured through spectrophotometric technique, while HbA1c% was determined using HPLC method. The mean ± SD data observed of BMI was determined from (Fendler et al., 2021):[17]

BMI (kg/m^2) = Weight (kg)/ Height (meter)^2

These results for both type 2 diabetic women patients and control groups, weight was classified according to their BMI as shown below (Organization, 2016).[18]

a. Underweight < 18.5
b. Normal weight 18.5–24.9
c. Over weight 25.0–29.9
d. Obese ≥ 30.0

The Waist/Hip ratio (W/H ratio) was calculated by dividing waist circumference by hip circumference as indicated below:

W/H ratio = Waist (cm)/Hip (cm)

According to World Health Organization (WHO, 2021) a W/H ratio chart is:

Health risk	Women
Low	0.80 or lower
Moderate	0.81–0.85
High	0.86 or higher

The data were analyzed using the Statistical Package for Social Sciences (SPSS version 22.0). Continuous variables were expressed as means ± standard deviation, SD). Mean comparisons were made using one-way analysis of variance (ANOVA) test. Receiver operator characteristic curves (ROC) were drawn to compare different sensitivity indices of each marker studied.

Results

The clinical demographic characteristics of type 2 diabetic patients group were summarized in Figure 1 which indicates that 50% of women included in this study of type 2 diabetic patients group were within normal weight (non-obese) and 50% were obese.

Therefore, higher percentage of risk was observed (48%) in obese type 2 diabetic women, and lower risk factor was observed low and moderate (1%) W/H ratio, Figure 1B.

Fig. 1 **Baseline characteristics and demographic description of the study population in type 2 diabetic women patients compared to apparently healthy control.**

Table 1 illustrated that effect of type 2 diabetes non-obese women ($N = 25$) on some biochemical parameters studied in patients and apparently health control groups ($N = 25$). The mean ± SD observed in non-obese type 2 diabetic women include Nesfatin-1 levels which was non-significantly decreased in type 2 diabetic patients and reached to (67.42 ± 33.49 ng/dl) as compared with apparently non-obese healthy control (87.54 ± 68.09 ng/dl, $P = 0.19$), while the level of C-peptide was significantly decreased to (107.82 ± 21.23 nmol/l) in non-obese type 2 diabetic patients as compared with apparently non-obese healthy control (176.44 ± 111.53 nmol/l, $P = 0.004$). The level of random blood glucose and and HbA1c% were significantly increased markedly in non-obese type 2 diabetic patients group and they reached to (279.76 ± 59.33 mg/dl) (9.72 ± 2.20%) as compared with apparently healthy control group (98.04 ± 13.74 mg/dl, $P < 0.001$) (4.13 ± 0.62%, $P < 0.001$) respectively.

The mean ± SD of lipid profile levels shown in the same table including total cholesterol (TC), high density lipoprotein-cholesterol (HDL-C), low density lipoprotein-cholesterol (LDL-C) and triglycerides (TG) which were studies in each type 2 diabetic patients group and healthy control. The data observed indicated that each of total cholesterol (184.44 ± 19.66 mg/dl) and triglycerides (185.28 ± 37.99 mg/dl) were significantly increased as compared with apparently non-obese healthy control group (164.36 ± 29.60 mg/dl) and (109.36 ± 20.78 mg/dl) respectively ($P < 0.05$), while the HDL-C and LDL-C were non-significantly changes, $P = 0.73$ and $P = 0.94$ respectively.

Table 2 illustrated that effect of obese type 2 diabetes women ($N = 25$) on the same biochemical parameters studied and compared with control groups ($N = 25$). The mean ± SD results obtained indicated that Nesfatin-1 levels was significantly decreased in obese type 2 diabetic patients and reached to (50.79 ± 12.08 ng/dl) as compared with apparently obese healthy control (75.48 ± 68.53 ng/dl, $P = 0.007$) and the level of C-peptide was non-significantly decreased to (134.69 ± 83.39 nmol/l) in type 2 diabetic patients as compared with apparently obese healthy control (143.11 ± 59.49 nmol/l, $P = 0.68$). While the level of random blood glucose and HbA1c% were significantly increased in obese type 2 diabetic patients group and they reached to (260.80 ± 72.38 mg/dl) (9.30 ± 1.85%) as compared with apparently obese health control groups (100.48 ± 11.64 mg/dl, $P < 0.001$) (4.58 ± 0.75%, $P < 0.001$) respectively.

The mean ± SD of lipid profile levels shown in the same table including also total cholesterol (TC), high density lipoprotein-cholesterol (HDL-C), low density lipoprotein-cholesterol (LDL-C) and triglycerides (TG) which were studies in each type 2 diabetic patients group and healthy control. The data observed indicated that each of total cholesterol was significantly increased and they reached to (205.52 ± 35.74 mg/dl) as compared with apparently obese healthy control group (178.00 ± 34.95 mg/dl, $P = 0.008$), while the mean ± SD of triglyceride was non-significantly decreased to (168.32 ± 22.83 mg/dl) as compared to apparently obese health control (205.28 ± 105.97 mg/dl, $P = 0.10$), while HDL-C and LDL-C were non-significantly decreased and the reached to (45.48 ± 5.47 mg/dl) (154.25 ± 33.76 mg/dl) as compared with obese control group (47.31 ± 6.18 mg/dl, 0.27) (161.40 ± 42.62 mg/dl, $P = 0.51$) respectively.

Binary logistic regression was performed and forward logistic regression was adopted to analyze the results. It was found that Nesfatin-1 in non-obese type 2 diabetic patient has a protective factor (OR: 0.987; 95% CI: (0.960–1.015)) respectively, while in obese type 2diabetic women patients groups were independent risk factors (OR: 1.064; 95% CI: (1.011–1.119).

In addition, C-Peptide was shown to be a risk factor for T2DM in normal and obese cases (OR: 1.058 and 1.02, 95% CI: (1.021–1.097), 0.992–1.08) as shown in Table 3.

The correlation coefficient was used for determining linear relationships between Nesfatin-1 and obese T2DM and non-obese T2DM, with each of BMI, C-Peptide, RBG and HbA1c% in obese T2DM groups as compared with Non-obese T2DM group. The results showed that there was moderated relationship and a significant correlation between Nesfatin-1 and BMI ($P = 0.015$, $r = 0.4$), C-peptide ($P = 0.015$, $r = -0.4$), RBG ($P = 0.007$, $r = -0.4$), and HbA1c% ($P = 0.004$, $r = -0.42$) as shown in Figure 2.

The results of the receiver operating curve (ROC) and AUC analysis for the Nesfitin-1 and C-peptide (73%, 71.6%)

Table 1. **The biochemical parameters studied in non-obese T2DM and control groups**

Variables	(Non-obese) Samples, $N = 50$		
	T2DM Patients, $N = 25$ Mean ± SD	Control $N = 25$ Mean ± SD	*P* value
Nesfatin-1, ng/dl	67.42 ± 33.49	87.54 ± 68.09	0.19[NS]
C- Peptide, nmol/l	107.82 ± 21.23	176.44 ± 111.53	**0.004[S]**
RBG, mg/dl	279.76 ± 59.33	98.04 ± 13.74	**<0.001[S]**
HbA1c%	9.72 ± 2.20	4.13 ± 0.62	**<0.001[S]**
TG, mg/dl	185.28 ± 37.99	109.36 ± 20.78	**<0.001[S]**
TC, mg/dl	184.44 ± 19.66	164.36 ± 29.60	**0.007[S]**
HDL-C, mg/dl	45.02 ± 3.42	44.71 ± 2.93	0.73[NS]
LDL-C, mg/dl	191.54 ± 33.84	176.38 ± 28.76	0.94[NS]

RBG, Random blood glucose; HbA1c, Glycated hemoglobin; TG, Triglyceride; TC, Total cholesterol; HDL-C, High density lipoprotein-cholesterol; LDL-C, Low density lipoprotein-cholesterol.

Table 2. **The biochemical parameters studied in obese T2DM and control groups**

Variables	(Obese) Samples, $N = 50$		
	T2DM Patients, $N = 25$ Mean ± SD	Control $N = 25$ Mean ± SD	*P* value
Nesfatin-1, ng/dl	50.79 ± 12.08	75.48 ± 68.53	**0.007[S]**
C- Peptide, nmol/l	134.69 ± 83.39	143.11 ± 59.49	0.68[NS]
RBG, mg/dl	260.80 ± 72.38	100.48 ± 11.64	**<0.001[S]**
HbA1c%	9.30 ± 1.85	4.58 ± 0.75	**<0.001[S]**
TG, mg/dl	168.32 ± 22.83	205.28 ± 105.97	0.10[NS]
TC, mg/dl	205.52 ± 35.74	178.00 ± 34.95	**0.008[S]**
HDL-C, mg/dl	45.48 ± 5.47	47.31 ± 6.18	0.27[NS]
LDL-C, mg/dl	154.25 ± 33.76	161.40 ± 42.62	0.51[NS]

RBG, Random blood glucose; HbA1c, Glycated hemoglobin; TG, Triglyceride; TC, Total cholesterol; HDL-C, High density lipoprotein-cholesterol; LDL-C, Low density lipoprotein cholesterol.

Table 3. **Estimation the associated of analyzed factors in patients compared to control group**

Variables	Normal weight		Obese	
	T2DM OR (Lower–Upper)	Control *P* value	T2DM OR (Lower–Upper)	Control *P* value
Nesfatin-1, ng/dl	0.987(0.960–1.015)	0.37[NS]	1.064(1.011–1.119)	**0.01[S]**
C- Peptide, nmol/l	1.058(1.021–1.097)	0.002[S]	1.0200(0.992–1.08)	0.94[NS]
TG, mg/dl	0.891(0.819–0.969)	**0.007[S]**	1.005(0.996–1.013)	0.29[NS]
TC, mg/dl	0.969(0.897–1.047)	0.42[NS]	0.974(0.953–0.996)	**0.023[S]**
HDL-C, mg/dl	0.986(0.596–1.630)	0.95[NS]	1.005(0.987–1.023)	0.57[NS]
LDL-C, mg/dl	0.898(0.807–0.998)	**0.04[S]**	1.066(0.956–1.189)	0.24[NS]

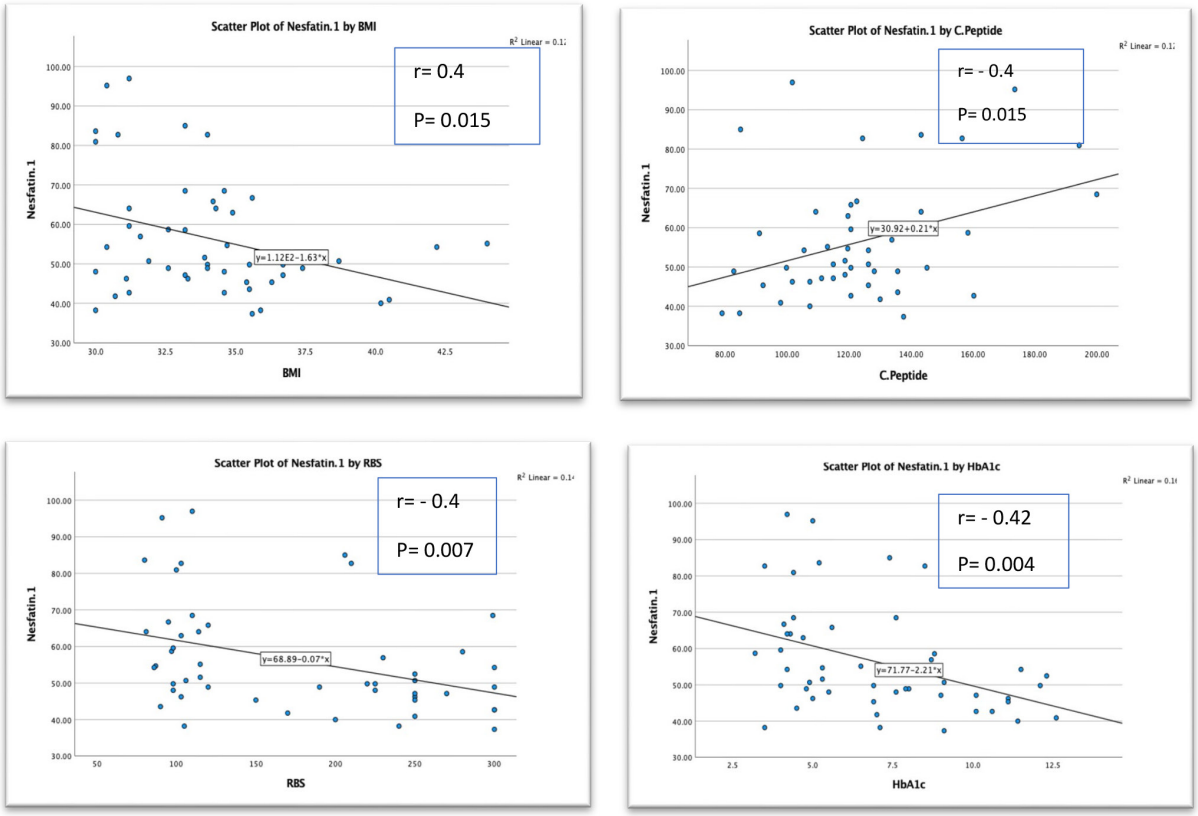

Fig. 2 **Simple linear regression of Nesfatin.1 by (a) BMI, (b) C-peptide, (c) RBS and (d) HbA1c between obese (DM & non DM).**

respectively, as possible diagnostic parameters. Nesfitin-1 was shown a good diagnostic performance for prediction of T2DM patients compared to control group, data are presented in Figure 3 and Table 4. For Nesfitin-1 (sensitivity = 98%, specificity = 90%) at a level = 39.13, while C-peptide levels: (sensitivity = 98%, specificity = 94%) at a level = 0.15.99, both Nesfitin-1 and C-peptide *P* values of the AUC for IMA were <0.001 and statistically significant.

Discussion

Nesfatin-1 is reported to exert an antihyperglycemic effect under impaired glucose metabolism conditions.[19] It may also act in the brain to upregulate insulin sensitivity (Yang et al., 2012),[20] and increase insulin release in beta cells in response to hyperglycemia.[21] Various studied including the roles of different biomarkers associated with the pathogenesis of T2DM in obese and non-obese male and females subjects have been studied in various region including Iraqi individuals.[22] Nesfatin-1 was also found to inhibit food intake in the central nervous system and acts as an anorexigenic agent, but the regulatory mechanism remains not clear,[6] but the regulatory mechanism remains unclear. Since Nesfatin-1 can cross the brain-blood-barrier and hypothalamic Nesfatin-1 can significantly inhibit food intake.[23] Li et al. proposed that diabetic polyphagia is caused by decreased circulating Nesfatin-1 levels and positively correlated with age.[9] Studies have also shown that Nesfatin-1 can stimulate the lipid metabolism and exhibit anti-inflammatory effects.[24] Nesfatin-1 may improve both hepatic and peripheral insulin sensitivity as it enhances glucose uptake by peripheral tissues and inhibits gluconeogenesis via different pathways.[25] Moreover, Nesfatin-1 mRNA is colocalized almost completely with insulin in β pancreatic islets cells. Also, its processing physiologically occurs in pancreatic

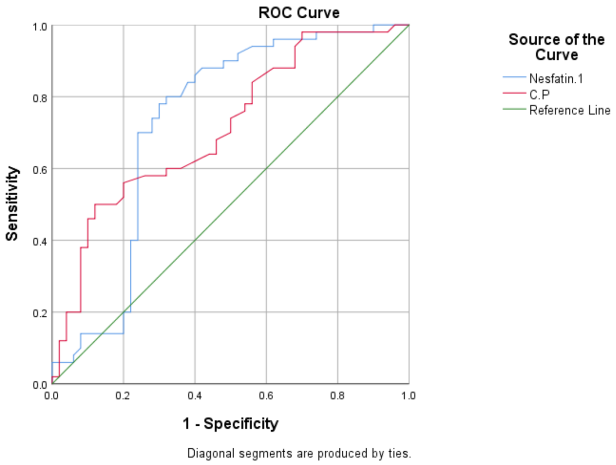

Fig. 3 **ROC curves for Nesfitin-1 and C-peptide in patients to analyses the optimal diagnostic points for predicting of cases compared to control group.**

Table 4. **Receiver operating characteristic curve showing sensitivity and specificity of Nesfitin-1 and C-peptide in patients compared to control group**

Test result variable(s)	Nesfatin-1	C-Peptide
AUC	73%	71.6%
Sensitivity %	98%	98%
Specificity %	90%	94%
Youden index	0.369	0.346
Cut-off points	39.13	15.99
CI (95%)	0.624–0.835	0.616–0.816
PPV	52.13%	51.04
NPV	47.87%	48.96%
P value	<0.001	<0.001

islet cell.[26] Nesfatin-1 mRNA expressed on pancreatic islet cells from type 2 diabetic patients was lower than that from healthy subjects. This was significantly correlated with insulin secretion capability.[27]

On the other hand, the role of C-peptide is not well defined in type 2 diabetes, of which insulin resistance and insulin secretion defect both exist. Some studies found that C-peptide level was a protective effect on microvascular complications. Serum C-peptide had been used in assessing pancreatic function in DM patients for a long time.

This study demonstrates a continuous decline in serum C-peptide levels following diagnosis and an especially significant decline from baseline after 3 years. Several hypotheses are presented to explain the clinical implications of residual C-peptide secretion in T1DM. Some previous studies suggested that C-peptide acts as an endogenous antioxidant, which protects pancreatic beta cells by increasing catalase expression and reducing peroxisomal oxidative stress.[28] Additionally, other reported postulate an association between residual C-peptide levels and reduction in response to glucagon-like peptide-1 (GLP-1).[29] Although the mechanism is not clearly elucidated yet, the clinical benefit from preserved C-peptide secretion in DM patients is widely known. Microvascular complications such as diabetic retinopathy and nephropathy were found to be less likely to develop in patients with residual C-peptide production, but the results were not always consistent among studies.[30] Also, preserved beta cell function is reported to be related to a decreased risk of hypoglycemia and decreased insulin requirement.[31] Moreover, with the wide use of continuous glucose monitoring (CGM) systems, recent studies reported on the importance of glycemic variability and its association with C-peptide levels. Patients with residual C-peptide production had a lower mean blood glucose level and higher time in range (Rickels et al., 2020),[32] and fasting C-peptide levels were negatively correlated with glucose coefficient of variation by CGM.[33]

Diabetes mellitus (DM), a metabolic disorder characterized by hyperglycaemia, associated with deficiency or resistance to insulin indicates endocrinal abnormality of the pancreas. Lipid abnormalities are prevalent in T2DM patients because of IR which affects key enzymes and pathways in lipid metabolism: Apo protein production, regulation of lipoprotein lipase, action of cholesterol ester transfer proteins and hepatic and peripheral actions of insulin.[34,35] Hyperglycemia and the high level of IR associated with T2DM has multiple effects on fat metabolism which results in the production of atherogenic dyslipidemia characterized by lipoprotein abnormalities: elevated very low density lipoprotein cholesterol (VLDL) elevated low density lipoprotein cholesterol (LDL-C), elevated triglyceride (TG) and decreased high density lipoprotein cholesterol (HDL-C).[36] The main cause for lipid abnormalities in T2DM patients is impaired secretion of insulin that affects the liver apolipoprotein production and regulates the enzymatic activity of lipoprotein lipase (LpL) and cholesterol ester transport protein (CETP). Moreover, its deficiency reduces the activity of hepatic lipase; therefore, several steps involved in the production of biologically active LpL might be altered in T2DM compared to controls.[37]

Many studies were confirmed the association of nesfatin-1 levels in obese individuals. It has been reported that the expression of nesfatin-1 was up-regulated in adipose tissue of a high-fat diet. This suggests a potential role for Nesfatin-1 in the lipid accumulation pathway and perhaps diet-induced obesity.[38]

The mean fasting C-peptide level of the obese T2DM was higher than that of the non-obese T2DM. They were moderately positively correlated, although not linear. Hence this study suggests that obese patients are hyperinsulinemic. Other study observed lesser insulin levels in non-obese T2DM as compared to obese which also noted by anothers, in which they measured insulin and C-peptide levels during a three hour oral glucose tolerance test.[39] A positive correlation between BMI and basal serum C-peptide levels was also observed previous reports.[40] According to Banerji et al, Asian Indians have an unexpectedly high percentage of body fat relative to BMI and muscle mass; this is associated with a proportionate increase in visceral fat. They are markedly insulin resistant and hyperinsulinemic.

The condition of obesity is caused by excessive intake of nutrients continuously causing fat deposits to become excessive. Deposits of fatty acids in the form of chemical compounds in the form of triacylglycerol contained in adiposity cells can protect the body from the toxic effects of fatty acids. Freeform fatty acids can circulate in blood vessels throughout the body and cause oxidative stress which we are familiar with lipo-toxicity. The emergence of lipo-toxicity effects caused by

several free fatty acids released by the triacylglycerol to compensate for the destruction of excessive fat deposits affects the adipose and non-adipose tissue and plays a role in the pathophysiology of diseases in various organs such as the liver and pancreas. This release of free fatty acids from excessive triacylglycerol can also inhibit fat synthesis and reduce the clearance of triacylglycerol. This can increase the tendency of hypertriglyceridemia. The release of free fatty acids by endothelial lipoprotein from triglycerides which increases in the increase of lipoprotein β causes lipo-toxicity which also interferes with the function of insulin receptors. The consequence of insulin resistance is hyperglycemia, which is compensated by glucose synthesis from the liver (gluconeogenesis), which contributes to aggravating hyperglycemia. Free fatty acids also contribute to hyperglycemia by reducing glucose use from insulin-stimulated muscles. Lipotoxicity due to excess free fatty acids also decreases insulin secretion from pancreatic β cells, which ultimately β cells will experience fatigue.[41]

Diabetes is associated with the development of insulin resistance. With multiple indices available, examination the validity of the (Nesfitin-1) and C-peptide to determine DM by receiver operating characteristic analysis was performed. Nesfitin-1 was shown a good diagnostic performance for prediction patients compared to control group. For Nesfitin-1 (sensitivity = 98%, specificity = 90%) at a level = 39.13, while C-peptide levels: (sensitivity = 98%, specificity = 94%) at a level = 0.15.99, both Nesfitin-1 and C-peptide *P*-values of the AUC for IMA were <0.001 and statistically significant. Since metabolic syndrome is associated with elevated risk for developing diabetes, many studies were investigating the insulin resistance and many types of adipokines. A key component of metabolic syndrome is the development of insulin resistance (IR). The homeostatic model assessment (HOMA-IR) can determine IR by using insulin or C-peptide concentrations; however, the efficiency of adipokines (Nesfitin-1) and C-peptide to determine metabolic syndrome/ or their complication namely diabetes has not been compared. C-peptide is a strong indicator of metabolic syndrome. Since C-peptide has recently emerged as a biomolecule with significant importance for inflammatory diseases, monitoring C-peptide levels will aid clinicians in preventing Metabolic Syndrome.[42] Also, Serum Nesfatin-1 is possibly associated with weight-related abnormalities in otherwise healthy subjects and type 2 diabetes. Obesity and type 2 diabetes may share a common pathologic point in this regard.[43]

Conclusion

1. Nesfatin-1 levels which was non-significantly decreased in non-obese type 2 diabetic patients, while the level of C-peptide was significantly decreased to in non-obese type 2 diabetic patients.
2. The Nesfatin-1 levels was significantly decreased in obese type 2 diabetic patients, while, the C-peptide was non-significantly decreased in obese type 2 diabetic patients.
3. Nesfatin-1 appears to be able to contribute to the treatment of obesity and diabetes because of its anorexigenic and antihyperglycemic effects. In addition, C-peptide is a known biomarker of insulin resistance and beta-cell function. High specificity and sensitivity analyzed results were obtained by ROC analysis for both markers in T2DM.

Conflict of Interest

None.

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