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Serum nesfatin-1 is a biomarker of pre-diabetes and interplays with cardiovascular risk factors

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Abstract

Background and objectives: Nesfatin-1 as a potent anorexigenic peptide is secreted by pancreatic β cells. Conflicting data are available about its level among diabetic patients. Our study aimed to assess nesfatin-1 levels in newly diagnosed drug-naïve diabetic and pre-diabetic patients and its association with cardio-metabolic risk and insulin resistance (IR). This case-control study included drug-naive patients with DMT2 (group 1, $n = 30$) and pre-diabetes (group 2, $n = 30$) in addition to healthy subjects (group 3, $n = 28$). Anthropometric and routine biochemical assessments were performed. Serum nesfatin-1and plasma insulin levels were assessed by ELISA methods. Homeostatic model for assessment of IR (HOMA-IR) was calculated.

Results: Serum nesfatin-1 was significantly lower in diabetic and pre-diabetic compared to healthy subjects (3.89 ± 1.1 ng/dl and 7.47 ± 1.22 ng/dl versus 15.39 ± 3.53 respectively, $p < 0.001$). Also diabetic patients had statistically significant lower nesfatin-1 levels than pre-diabetic patients ($p < 0.001$) Roc curve analysis identified cut-off values of ≤ 9 ng/dl and ≤ 5.5 ng/dl with an AUC of 0.94 and 0.97, sensitivity of 96.7 and 100%, and specificity of 93.3% and 96.7% for diagnosis of pre-diabetes and diabetes respectively. Using bivariate analysis, nesfatin-1 was negatively correlated with glycemic parameters (fasting and 2 h postprandial blood sugar, HBA1c), IR parameters (fasting insulin and HOMA-IR) and atherogenic lipid profile (triglyceride, cholesterol, and LDL-c); and positively correlated to HDL-c in both diabetic and pre-diabetic but not in healthy.

Conclusion: Nesfatin-1 is an excellent predictor for pre-diabetes and DMT2. It is associated with favorable glucose and lipid metabolism probably via insulin signaling pathway.

Keywords: Nesfatin-1, Pre-diabetes, HOMA-IR, Atherogenic lipid profile

Introduction

Pre-diabetes is classified as either impaired fasting glucose (IFG) or impaired glucose tolerance (IGT). Pre-diabetes is initiated primarily by insufficient insulin secretion via pancreatic beta cells and insulin-resistance (IR). It is frequently accompanying with the metabolic syndrome and it is risk factor for diabetes mellitus type2 (DMT2) [1].

Nesfatin-1, a new satiety peptide, is expressed in the brain mainly in the hypothalamus. Accordingly, this peptide became first known for its anorexigenic effect. However, subsequent studies demonstrated the fact that it is synthesized in peripheral tissues such as pancreatic islets, gastric endocrine cells and adipocytes. Moreover, its expression level was 20 times higher in endocrine cells of the oxyntic gastric mucosa than in the brain [2, 3]. Molecular and animal studies suggested its beneficial effects on glucose and lipid metabolism as it augments

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insulin sensitivity [4, 5]. It regulates energy homeostasis via its central anorexigenic effect and decreased body weight effect [6]. Interestingly, some evidences revealed the regulatory effect of nesfatin-1 on adipogenesis [7]. Peripheral nesfatin-1 administration may possess an anti-hyperglycemic effect which is time dose and insulin-dependent effect [8]. Nesfatin-1 is involved in enhancement of insulin sensitivity either peripheral or hepatic through promoting peripheral glucose uptake and decreasing gluconeogenesis via different mechanistic pathways [4, 5].

However, there were conflict data about nesfatin-1 levels in diabetic subjects [9–11]. Recently, little unmatched data in pre-diabetic patients were reported [12, 13]. Currently, the reasons for such discrepancy are unclear. Racial factor or medication intake in many of these studies may be a contributor. We investigated serum nesfatin-1 levels in newly diagnosed, drug -naive patients with pre-diabetes and DMT2 and explored its relationships with anthropometric, metabolic, and IR in these patients particularly in pre-diabetic, an aspect sparsely mentioned before among Egyptian population.

Subjects and methods

This prospective cross-section study was conducted on 88 subjects who included 60 newly diagnosed, drug-naive patients with DMT2 ($n = 30$) and pre-diabetes ($n = 30$) in addition to age and sex matched- twenty eight healthy persons who served as control group. Subjects had any of the following criteria was excluded from our study: overt hepatic, renal, cardiovascular neuropsychiatric malignancy, and chronic inflammatory disease, or taking any anti-hyperglycemic medications, insulin sensitizers, steroid, statin. The patients were selected from attendant of diabetic out-patient clinic. Our study was conducted in Diabetic and Endocrinology Unit, Internal Medicine Department and Clinical Pathology department, along the period from March 2016 to July 2017.

Ethical aspect

The study protocol was approved by the local Institutional Ethics Committee and conducted in accordance with the ethical guidelines of the Declaration of Helsinki. All patients gave informed consents to participate in this study.

Criteria of diagnosis of pre-diabetes and DMT2 were according to The American Diabetes Association's (ADA's) Standards of Medical Care 2014). Pre-diabetes" is the term used for individuals with IFG as fasting plasma glucose (FPG): 100–125 mg/dL; IGT as 2-h PG in the 75-g oral glucose tolerance test (OGTT) 140–199 mg/dL or glycosylated hemoglobin (HbA1C):5.7–6.4%. DM was diagnosed either FPG $\geq$ 126 mg/dL, 2 h PG $\geq$ 200 mg/dL during an OGTT, HbA1C $\geq$ 6.5%; or in a patient with classic symptoms of hyperglycemia and a random plasma glucose $\geq$ 200 mg/dL [14].

All subjects answered a standardized questionnaire including age, conventional cardiovascular disease risk factors, and current medication. Arterial blood pressure (BP) was measured and anthropometric measurements were taken in a standardized manner. Laboratory investigation into two categories (a) routine investigation: renal, liver function tests and lipid profile (b) special one: oral glucose tolerance test (OGTT), fasting serum insulin, HbA1c, HOMA-IR, and serum Nesfatin-1.

Sampling protocol

Seven ml of venous blood samples were withdrawn after overnight fasting. Sample was divided into (1) One milliliter in EDTA tube for analysis of HbA1c via Immunoturbidimetric method (Genius Diagnostics) (2) 6 ml in two serum separator gel tube, 3 ml in each tube, samples were allowed to clot for 30 min at 37 °C before centrifugation for 15 min at 3500 rpm. The expressed serum was used for measurement of routine investigation. And the Remaining serum and plasma were stored at − 20 °C for further assessment of special investigation. Routine investigation done via automated chemistry autoanalyzer system Selectra proM, ELITech group, Finland. As well, plasma levels of fasting Insulin level (assayed by Insulin Human EIA Kit, abcam, ab100578). Oral glucose tolerance test (OGTT) was done for each subject in our study, the test had special precaution subject must (1) 3 days prior to test, subject receives a diet containing 150 g of carbohydrate/day, (2) all medication that impair glucose tolerance should be avoided, (3) 10- to 16-h fast, and (4) no exercise before or during the test. 1.75 (g/kg) of body weight glucose, up to 75 g glucose prepared, then dissolved in 290–300 ml water (allowed to drink within 10 min). Blood samples for blood glucose were measured at fasting and every half an hour for 2 h (we obtained five samples). Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) was calculated according to the following equation: HOMA-IR = fasting insulin uIU/mL X fasting glucose (mg/dl)\405 [15].

Concerning serum Nesfatin-1 was measured by EIA kit (kit was supplied via EIAab Science Co. Ltd. E-PP-1585).

Statistical analysis

All statistical analyses were performed with the SPSS version 20. Quantitative data are expressed as mean ± SD and compared by ANOVA test for comparison between the three groups followed by the post Hoc Tukey correction between each two groups for normally distributed data. Non-parametric quantitative data are expressed as median and interquartile and compared with the

Kruskal-Wallis test for the three groups and the Mann-Whitney test for each two groups. Qualitative data are expressed as frequencies and the differences between groups were assessed by the chi-square test. Correlation analysis was performed using the Pearson correlation method. Receiver operating characteristic (ROC) curve analysis was done to assess cut-off point of nesfatin-1 for diagnosis of pre-diabetes and DM. $P < 0.05$ was considered statistically significant.

Results

Baseline characteristics of diabetic, pre-diabetic, and healthy subjects are summarized in Table 1. This study involved three groups: pre-diabetic and diabetic and healthy control groups. Ranges of age were from 34 to 66 years with mean ± SD of 48.7 ± 8.8 in diabetic group (male/female {m/f}: 17/13), from 36 to 65 years with mean ± SD of 48.1 ± 6.4 in pre-diabetic group (m/f: 18/12); and from 34 to 65 years-old with mean ± SD of 48.16 ± 10.6 among healthy control group (m/f: 15/13). Serum nesfatin-1 levels were significantly decreased in diabetic and pre-diabetic subjects compared with healthy control (3.89 ± 1.1ng/dl and 7.47 ± 1.22 ng/dl versus 15.39 ± 3.53 respectively with $p < 0.001$ for both). Also, diabetic patients had statistically significant lower nesfatin-1 levels than pre-diabetic patients ($p < 0.001$) Fig. 1.

ROC curve analyses identified nesfatin-1 levels ≤ 5.5 ng/dl as cut off value for diagnosis of DMT2 with area under the curve (AUC), sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV), and accuracy were 0.97, 100%, 96.7%, 100%, and 98.3% respectively (Fig. 2); and identified nesfatin-1 cut-off value ≤ 9 ng/dl for diagnosis of pre-diabetes with AUC of 0.94 and 96.7% for sensitivity, 93.3% for specificity, 93.5% for PPV, 96.6% for NPV, and accuracy of 95% (Fig. 3).

Biivariate correlations were performed among diabetic patients, serum nesfatin-1 levels were negatively correlated with systolic BP ($p = 0.006$), parameters of insulin and glucose metabolism (fasting glucose, 2hpp blood glucose, Hb A1c, fasting insulin, and HOMA-IR with $p < 0.001$, $p = 0.03$, $p = 0.013$, $p = 0.004$, $p = 0.026$, respectively) and atherogenic lipid profile (total cholesterol, TG, and LDL-cholesterol ($p = 0.002$, $p = 0.005$, $p = 0.02$,

Table 1 Baseline characteristics of studied groups

Variables	Group I (diabetic) ($N = 30$)	Group II (pre-diabetic) $N = 30$	Group III (control) $N = 28$	A	B	C	D
Nesfatin-1 (ng/dl)	3.89 ± 1.1	7.47 ± 1.22	15.39 ± 3.53	< 0.001*	< 0.001*	< 0.001*	< 0.001*
Age (years)	48.76 ± 8.81	48.1 ± 6.43	48.06 ± 10.61	0.94	0.95	0.95	1
Male/female *n* (%) $	17/13 (57/ 43)	18/12 (60/40)	15/13 (54/46)	0.87	0–79	0.79	0.61
Waist cir (cm)	104 ± 10.6	93.03 ± 9.5	83.56 ± 9.64	< 0.001*	< 0.001*	< 0.001*	0.001*
Waist/hip ratio	0.92 ± 0.04	0.96 ± 0.04	0.82 ± 0.05	< 0.001*	0.03*	< 0.001*	0.001*
BMI (kg/m^2	30.07 ± 5.14	34.33 ± 5.09	23.8 ± 1.65	< 0.001*	0.001*	< 0.001*	< 0.001*
SBP (mmHg)	138.5 ± 11.75	130.13 ± 11.94	111.16 ± 5.36	< 0.001*	0.009*	< 0.001*	< 0.001*
DBP (mmHg)	88 ± 5.95	83.83 ± 7.03	74 ± 4.96	< 0.001*	0.08	< 0.001*	< 0.001*
F glucose (mg/dl)	152.33 ± 32.62	117.06 ± 4.73	81.3 ± 7.37	< 0.001*	< 0.001*	< 0.001*	< 0.001*
2hPP glucose (mg/dl)	276.76 ± 52.38	171.5 ± 14.6	110.9 ± 6.33	< 0.001*	< 0.001*	< 0.001*	< 0.001*
Hemoglobin A1c(%)	10.41 ± 2.01	6.26 ± 0.35	4.65 ± 0.46	< 0.001*	< 0.001*	< 0.001*	< 0.001*
F insulin (μU/mL)#	19 [16–28]	22 [16–28.3]	8 [5–11.5]	< 0.001*	0.83	< 0.001*	< 0.001*
HOMA- IR #	8.[6–12]	6.5 [4–8]	2 [1–2.1]	< 0.001*	0.007*	< 0.001*	< 0.001*
cholesterol (mg/dl)	220.83 ± 15.57	201.2 ± 10.33	168.9 ± 10.63	< 0.001*	< 0.001*	< 0.001*	< 0.001*
Triglycerides (mg/dl)	165.96 ± 15.29	141.8 ± 13.85	96 ± 5.55	< 0.001*	< 0.001*	< 0.001*	< 0.001*
HDL-c(mg/dl)	50.3 ± 2.36	50.3 ± 2.36	66 ± 3.92	< 0.001*	1	< 0.001*	< 0.001*
LDL-c (mg/dl)	137.33 ± 16.44	122.4 ± 11.02	88.6 ± 11.97	< 0.001*	< 0.001*	< 0.001*	< 0.001*
Creatnine (mg/dl)	0.87 ± 0.23	0.81 ± 0.18	0.81 ± 0.21	0.41	0.69	0.81	1

Waist cir waist circumference, *BMI* body mass index, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *F* fasting plasma, *HOMA-IR* homeostasis model assessment of insulin resistance, *HDL-c* high-density lipoprotein cholesterol, *LDL-c* low-density lipoprotein cholesterol. Quantitative data are expressed as mean ± SD and compared by ANOVA test for comparison between the three groups followed by post hoc Tukey correction between each two groups for normally distributed data

#Non-parametric quantitative data are compared with Kruskal-Wallis test for the three groups and Mann Whitney test for each two groups. $=qualitative variables are expressed as frequency and compared by $\chi 2$ test

*Significant difference at *p* value < 0.05. *A p* value between the three groups. *B p* value when group I compared with group II. *C p* value when group I compared with group III. *D p* value when group II compared with group III

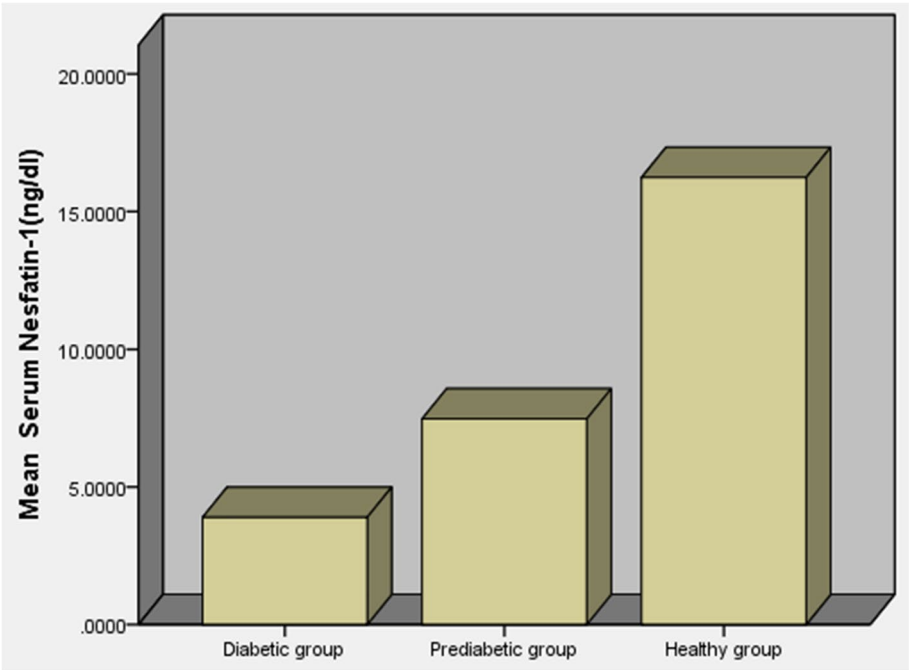

Fig. 1 serum nesfatin-1 levels in diabetic, pre-diabetic, and healthy subjects

respectively). However, its levels were positively associated with HDL-cholesterol ($p = 0.021$). By contrast, no association of nesfatin-1 with age, diastolic BP, and parameters of obesity (BMI, waist circumference, and WHR) was demonstrated (Table 2).

Bivariate correlations were performed in pre-diabetic patients: serum nesfatin-1 had similar correlations as that in diabetic group, serum nesfatin-1 levels were negatively correlated with systolic BP ($p = 0.003$), parameters of insulin and glucose metabolism (fasting glucose, 2hpp blood glucose, Hb A1c, fasting insulin, and HOMA-IR with $p = 0.012$, $p = 0.003$, $p < 0.001$, $p = 0.001$, $p = 0.018$), total cholesterol, TG, and LDL-cholesterol ($p = 0.015$, $p = 0.003$, $p = 0.002$, respectively) and were positively associated with HDL-cholesterol ($p = 0.001$) (Table 2).

Bivariate correlations were performed in healthy subjects in whom no correlation was observed between these mentioned parameters and nesfatin-1 levels (Table 2).

Discussion

In the current study, we found significantly decreased serum nesfatin-1 levels among newly diagnosed drug-naive patients with either pre-diabetes or DMT2 than healthy control. Moreover, serum nesfatin-1 level progressively decreased from pre-diabetic to overt DMT2 with novel identification of cut-off value ≤ 9 and ≤ 5.5 ng/dl for their diagnosis, respectively. An issue was rarely explored before. We were pioneering to identify association of serum nesfatin-1 levels with many cardio-metabolic risk factors, IR indices among pre-diabetic and diabetic patients.

There is sparse data in the literature that studied association of pre-diabetes and nesfatin-1**.** Algul et al., 2016 found insignificant lower level among pre-diabetic compared to healthy control in Turkey [12]. In their study, these patients were not newly diagnosed and some of them had already on anti-hyperglycemic therapy. In addition, their HOMA-IR values were much lower compared to our study. Contrarily, another study in newly diagnosed treatment-naive diabetic and pre-diabetic patients (one group) in Jordan reported elevated nesfatin-1 level compared to euglycemic subjects as a control group. However, selection of control group was biased as they were obese and had atherogenic lipid profile (were not healthy control) [13]. Similar to our results, previous decreased nesfatin-1 level among Chinese patients with DMT2 and among women gestational diabetes compared to healthy control was reported [9, 11]. Particularly, variable participation of extra pancreatic sources of nesfatin-1 in its circulating level, racial factor, and differences in study design including control selection and previous treatment may contribute to these discrepancies.

Our result of decreased serum nesfatin-1 level among pre-diabetic and diabetic may be a cause or consequent of IR and hyperinsulinemia. Nesfatin-1 may improve both hepatic and

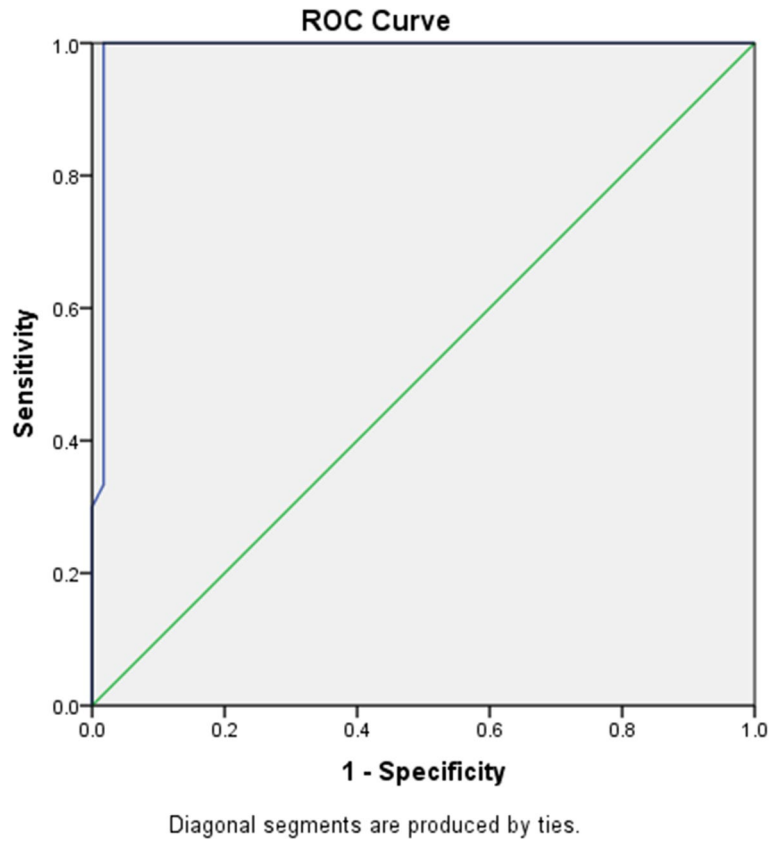

Fig. 2 ROC curve analyses identified nesfatin-1 levels of ≤ 5.5 ng/dl as cut-off value for diagnosis of DMT2 with 0.97 for area under curve (AUC), 100% sensitivity, 96.7% specificity, 96.8% positive predictive value (PPV), 100% negative predictive value (NPV), and 98.3% accuracy

peripheral insulin sensitivity as it enhances glucose uptake by peripheral tissues and inhibits gluconeogenesis via different pathways [4, 5]. Higher nesfatin-1 levels augments glucose-provoked insulin secretion by stimulating Ca^{+2} influx through L type channel l [16]. Moreover, nesfatin-1 mRNA is colocalized almost completely with insulin in β pancreatic islets cells. Also, its processing physiologically occurs in pancreatic islet cell [17]. Nesfatin 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 [18]. On the other hand, nesfatin-1 synthesis and release from islet cells can be triggered by glycolipotoxic conditions in euglycemic but not in in diabetic mice (DMT1, DMT2) [19, 20].

In our study, serum nesfatin-1 level had significant negative correlation with blood glucose level in diabetic and pre-diabetic but not in healthy control. These findings were supported by animal studies that showed the anti-hyperglycemic effect of nesfatin-1. This effect was dosage, duration, and insulin dependent in hyperglycemic db/db mice (mimic DMT2) but not in streptozocin-mediated diabetes model (mimic DMT1) nor in euglycemic [9]. Also, anti-hyperglycemic effect of nesfatin was associated with significant reduction of obesity markers, IR parameters and improved lipid profile with decreased LDL and TG, and increased HDL-c levels with nesfatin-1 intake for 4 weeks in diabetic rats [21]. In contrast to our results, raised nesfatin-1 levels were significantly associated with impaired glycemic and obesity parameters and higher insulin resistance [10].

In the present study, we reported significant negative associations of serum nesfatin-1 and systolic BP among diabetic and pre-diabetic but not in healthy control. In contrast, nesfatin-1 administration (peripherally) increase mean blood pressure via impairment the endothelial nitric oxide synthase enzyme activity in prolonged restraint stress animals [22, 23]. Recently, endogenous central NUCB2/nesfatin-1 in the paraventricular nucleus of hypothalamus controls plasma level of both vasopressin and oxytocin [24]. In line with our results, positive association with systolic BP was demonstrated among euglycemic-obese hypertensive subjects but not in dysglycmic-obese hypertensive subjects. Dysglycemia may be linked to lower nesfatin-1 levels or diminished its hypertensive action in obese

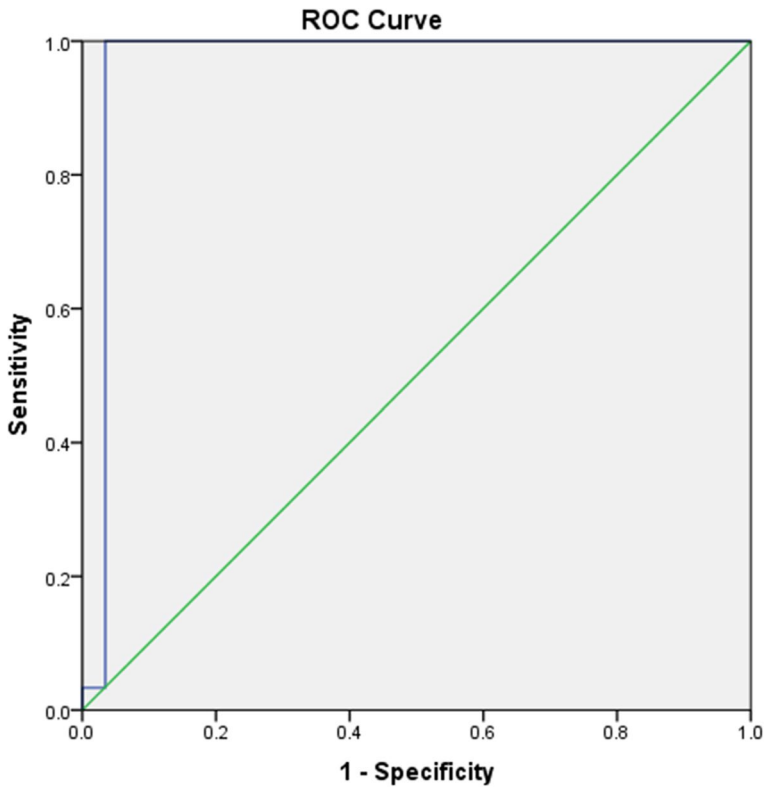

Fig. 3 ROC curve analyses identified nesfatin-1 levels of ≤ 9 ng/dl as cut-off value for diagnosis of pre-diabetes with 0.94 for area under curve (AUC), 96.7% sensitivity, 93.3% specificity, 93.5% positive predictive value (PPV), 96.6% negative predictive value (NPV), and 95% accuracy

Table 2 Correlations of serum nesfatin-1 with clinical and biochemical parameters among studied patients groups and healthy control

	Diabetic group (*n* = 30)		**Pre-diabetic group (*n* = 30)**		**Healthy subjects (*n* = 28)**	
	r	***P***	***r***	***P***	***r***	***P***
Age (years)	0.032	0.868	− 0.240	0.200	0.060	0.755
Waist circumference (cm)	− 0.285	0.126	0.203	0.283	0.054	0.779
Waist/ hip ratio	0.295	0.114	0.094	0.622	− 0.027	0.889
Body mass index (kg/m^2)	0.221	0.241	− 0.178	0.346	− 0.265	0.157
Systolic blood pressure (mmHg)	− 0.490	0.006*	− 0.531	0.003*	− 0.127	0.505
Diastolic blood pressure (mmHg)	− 0.033	0.864	0.339	0.067	0.170	0.369
Fasting plasma glucose (mg/dl)	− 0.619	< 0.001*	− 0.454	0.012*	− 0.095	0.618
2hPP plasma glucose (mg/dl)	− 0.390	0.033*	− 0.523	0.003*	− 0.226	0.229
Hemoglobin A1c(%)	− 0.447	0.013*	− 0.601	< 0.001*	− 0.239	0.203
Fasting insulin (μU/mL	− 0.515	0.004*	− 0.569	0.001*	0.128	0.499
HOMA-IR	− 0.406	0.026*	− 0.428	0.018*	0.162	0.392
Total cholesterol (mg/dl)	− 0.549	0.002*	− 0.440	0.015*	− 0.279	0.136
Triglycerides (mg/dl)	− 0.503	0.005*	− 0.518	0.003*	− 0.242	0.197
High-density lipoprotein (mg/dl)	0.573	0.001*	0.562	0.001*	0.265	0.156
Low-density lipoprotein (mg/dl)	− 0.419	0.021*	− 0.543	0.002*	− 0.298	0.109

HOMA-IR = homeostasis model assessment of insulin resistance; correlation by Pearson coefficient significant difference at *p* value < 0.05, *r* correlation coefficient weak (*r* = 0–0.24), fair (*r* = 0.25–0.49), moderate (*r* = 0.5–0.74), strong (*r* = 0.75-1)

hypertensive patient via improvement of insulin sensitivity [25]. Moreover, decreased serum nesfatin-1 levels are linked with the presence and severity of preeclampsia [26]. Other reported no association of blood pressure and nesfatin-1 in diabetic patients [27].

In the present study, we did not found any correlation of serum nesfatin-1 levels and obesity parameters as previously described in one study [28]. We reported its negative correlation with insulin and HOMA-IR. There was unmatched data in clinical studies. Serum levels of nesfatin-1 were negatively associated with BMI and HOMA-IR in diabetic patients, non-obese male patients, and among women with polycystic ovary syndrome and gestational diabetes [27, 29, 30]. Contrarily, other reported the reverse findings in diabetic patients [10]. Moreover, serum nesfatin-1 level in the obese children was significantly lower and correlated to BMI not to IR [31].

Finally, our study was the first to show a negative correlation between nesfatin-1 and lipids in pre-diabetic and diabetic subjects. So, nestafin may have anti-atherogenic effect on lipid profile. This association was recently reported among coronary artery disease patients [32]. Other researchers have failed to observe any association, even in diabetic patients [10, 27] meanwhile positive correlation of nesfatin with triglyceride in pre-diabetic/diabetic Jordan patients [13]. Animal studies reported that Nesfatin-1 may regulate lipid metabolism. Nesfatin-1 stimulates fatty-acid oxidation by activating AMP-activated protein kinase in diabetic rats [33], chronic subcutaneous infusion of nesfatin-1 reduced plasma cholesterol and triglyceride and elevate HDL-c levels in other animal models [21, 34]. Central nesfatin-1 in the brain may reduce the lipogenic activity and enhance fatty acid oxidation in the rainbow trout liver [35]. Theoretically, anti-atherogenic effect of nesfatin-1 may be mediated via by its anti-oxidant and anti-inflammatory properties and its enhancing effect on insulin sensitivity [4, 5, 36].

Our study was limited by its cross-sectional design and a relatively small sample size; therefore, it cannot prove a causal relationship between altered nesfatin-1 levels and the development of type 2 DM or pre-diabetes. Baseline characteristics of pre-diabetic, diabetic, and control groups were not comparable, which may have had an effect on the conclusion. We recommended further follow-up studies for pre-diabetic subjects to assess role of circulating nesfatin levels for progression from pre-diabetes to diabetes

Conclusion

Serum nesfatin-1 level may be a potential protective factor against hyperglycemia, ,atherogenic lipid profile , hypertension and IR. We demonstrate that nesfatin-1 is an excellent marker for diagnosis of pre-diabetes. It is negatively associated with many cardiovascular risk factors.

Abbreviations

ADAs: American Diabetes Associations; AUC: area under curve; BMI: Body mass index; BP: Blood pressure; DMT2: Diabetes mellitus type2; FPG: Fasting plasma glucose; HDL-c: High-density lipoprotein-cholesterol; HOMA-IR: Homeostatic model for assessment of insulin resistance; IFG: Impaired fasting glucose; IGT: Impaired glucose tolerance; IR: Insulin resistance; LDL-c: Low-density lipoprotein-cholesterol; NPV: Negative predictive value; OGTT: Oral glucose tolerance test; PPV: Positive predictive value.

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Authors' contributions

Prof . El Hini provided the ideas and the design of the study and wrote the protocol. She shared in conducting the literature review and data collection, recruited the participants, Dr matter shared in Data collection, analysis of the result and wrote the draft of the manuscript. Prof. Salama followed all stages of the study. Dr. Moaness did the laboratory work of this study. And the authors approved the final draft. The author(s) read and approved the manuscript.

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Availability of data and materials

The datasets generated and analyzed during the present study are not publicly accessible due to concerns of participates confidentiality but are offered by the corresponding author on realistic request.

Declarations

Ethics approval and consent to participate

Our study was approved by local ethical committee of our institute. All procedures performed in our clinical study including human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the Helsinki Declaration. All individual participants gave informed consent to be included in the study.

Consent for publication

All the authors involved in this study give their consent for this article to be published in The Egyptian Journal of Internal Medicine

Competing interests

All authors declare that they have no competing interests.

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