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The role of serum nesfatin-1 in predicting metabolic syndrome among patients with overweight

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Nesfatin-1 biomarker could have a promoting key role in the diagnosis and management of many metabolic disorders. However; till now, the exact role of nesfatin-1 in humans still needs further studies. The study presented here was conducted on 40 individuals who were divided into two groups, 20 patients with metabolic syndrome (cases) and 20 healthy people (controls). In addition to sociodemographic and anthropometric measurements, circulating levels of serum lipid profile, fasting blood sugar, insulin resistant (HOMA), serum nesfatin-1 level were measured. All of the study participants also had their blood pressure measured. No significant difference was found between the two groups regarding nesfatin-1 level, but nesfatin-1 was significantly in negative correlation with serum triglyceride, and lastly nesfatin-1 showed accepted prediction outcome of metabolic syndrome.

Keywords: appetite suppression; nesfatin-1; obesity; metabolic syndrome.

Introduction

Metabolic syndrome is a group of disorders that increase the risk of type II diabetes and various cardiovascular diseases. These disorders include obesity, insulin resistance, dyslipidemia, and hypertension (Bovolini et al., 2021; Masenga et al., 2023; Mohamed et al., 2023). Metabolic syndrome is a global multifactorial condition, with high prevalence in recent decades, coinciding with the obesity and sedentary lifestyle epidemics (Anton-Păduraru et al., 2025). Therefore, it is crucial to find predictive indices and reliable biomarkers that clarify the complex pathophysiological process behind metabolic syndrome and the cardio-metabolic issues that are linked to it (Jha et al., 2023).

Lifestyle changes have long been recognized as effective preventive measures against metabolic syndrome. It is recommended to increase consumption of unprocessed cereals, legumes, and fruit, as well as meals high in fiber, dairy products, fish and nuts. Monounsaturated and polyunsaturated fatty acids can be used to substitute saturated fatty acids, and consumption of free sugar should be limited (Fahed et al., 2022; Angelico et al., 2023; Ambroselli et al., 2023). Furthermore, there is accumulating evidence that there is a link between dietary habits and nesfatin-1 levels in metabolic syndrome, which has drawn interest due to its pleiotropic effects on energy balance, cardiovascular function and insulin sensitivity (Karvane et al., 2024). Studies suggest that a high fat diet reduces nesfatin-1 levels; in turn, nesfatin-1 decrease leads to suppression of food intake and thus, improves glucose metabolism and body weight gain (Abed et al., 2024; Nasri et al., 2024).

In addition to its function in energy balancing, nesfatin-1 is essential for the pathophysiology of cardiovascular complications associated with metabolic syndrome as it may protect against atherosclerosis, oxidative stress, and endothelial dysfunction (Luo et al., 2021).

Nesfatin-1 is a neuropeptide that was first discovered in 2006. It originates from nucleobindin 2, a more substantial intermediate molecule. Nesfatin-1 is mostly expressed in the brain, specifically in the hypothalamus, brainstem, and pituitary gland, as well as in adipose tissue, the stomach, and the pancreas (Gan et al., 2024). Researchers have successfully suppressed appetite in animal models with synthetic nesfatin-1 administered subcutaneously, intraperitoneally, and intracerebroventricularly. However, more researches are needed for clinical application in humans (Toh, 2021). The current study aims to determine the impact of nesfatin-1 levels in predicting metabolic syndrome among individuals with weight-related abnormalities.

Material and methods

This study was cross-sectional and enrolled forty participants, who were split into two groups. The case group included twenty subjects who fit the criteria of the National Cholesterol Education Program-Adult Treatment Panel III (Palmeira et al., 2025) and who had been diagnosed with metabolic syndrome by their internist. The control group consisted of 20 volunteers who were around the same age as the case group. The study's participants were between the ages of 25 and 69.

The case group excluded individuals with cancer, type 1 diabetes mellitus, systemic disorders (liver, kidney, and lung disease), gestational diabetes mellitus, major depressive disorder, pregnancy, hormone replacement therapy, and severe acute or chronic infectious infections. In contrast, the control group excluded individuals who had a history of smoking, those who regularly took vitamin-mineral supplements, or those who had a specified medical condition.

German weight scale (Beurer) was used to assess the participants' body weights while they wore thin clothing, wore no shoes, and had an empty stomach. To measure the participants' heights, they had to stand in a vertical position with their heads horizontal, their legs together, and their heels, buttocks, and back contacting the wall. The body mass index was determined by dividing weight (in kilograms) to the height (in meters squared) (Mohajan et al., 2023). To measure the waist circumference, a tape measure was inserted halfway between the lowest rib and the iliac crest.

Blood samples were drawn after at least 8 hours of fasting and analyzed for glucose, HbA1c, total cholesterol, LDL, HDL, and triglyceride levels. In addition, a 5 mL blood sample was collected for serum nesfatin-1 level testing. Blood samples were delivered to the laboratory by cold chain and centrifuged at 2500 rpm for 10 minutes at +4 °C. The separated serum was stored at –40 °C in Eppendorf tubes until analysis. Using ELISA Microplate Reader (BioTek, USA), Labscience Human Nesfatin-1 ELISA Kit (China) was chosen to determine nesfatin-1 level. The results were presented in nanograms per milliliter.

The data was analyzed using SPSS software (version 30). Data are presented as mean ± standard deviation (mean ± SD). Categorical data was analyzed using the χ^2 significance test. To compare two independent groups, Student's t-test was utilized. Pearson correlation was used to estimate the degree of correlation between two quantitative variables. A P-value of <0.05 was considered statistically significant for all statistical tests.

Results

The mean age of the study participants was 45.3 ± 11.44 years. Of the 40 individuals included in study; 15 were males versus 25 were females with male: female ratio of 1:1.66. It's evident that there was a statistically significant difference between patients with metabolic syndrome and those without it regarding: gender (P = 0.012), body weight (P < 0.001), body mass index (P < 0.001), waist circumference (P < 0.001, Table 1).

Table 1
Comparison between the study groups regarding sociodemographic and anthropometric variables

Variable	Cases, n = 20	Controls, n = 20	P-value
Gender: n (%)			
Male	9 (45%)	6 (30%)	0.012
Female	11 (55%)	14 (70%)	
Age, mean ± SD	46.4 ± 11.9	44.2 ± 10.8	0.378
Body weight, kg, mean ± SD	84.9 ± 6.2	66.8 ± 7.7	<0.001
Height, cm, mean ± SD	165.4 ± 5.5	165.2 ± 6.8	0.940
BMI, mean ± SD	31.0 ± 1.6	24.2 ± 1.1	<0.001
WC, cm, mean ± SD	94.6 ± 5.7	79.7 ± 8.2	<0.001

Table 2 shows comparison between the study groups regarding biochemical investigations. Cases with metabolic syndrome were found to have a statistically significantly higher fasting blood glucose (P < 0.001), triglyceride level (P < 0.001), total cholesterol level (P < 0.001) and insulin resistance (P < 0.001). On the other hand; controls found to have a statistically significant ly higher high-density lipoprotein level (P = 0.0012).

Table 2
Comparison between the study groups regarding biochemical variables

Variable, mean ± SD	Cases, n = 20	Controls, n = 20	P-value
FBG, mg/dL	121.0 ± 20.8	90.1 ± 5.2	<0.001
TG, mg/dL	259 ± 104	96 ± 18	<0.001
TC, mg/dL	233 ± 42	162 ± 27	<0.001
HDL, mg/dL	41.3 ± 6.1	52.0 ± 9.1	0.0012
HOMA-IR	4.43 ± 0.93	2.16 ± 0.28	<0.001
Nesfatin-1, ng/mL	515 ± 54	552 ± 103	0.176

Table 3 shows the frequencies of metabolic syndrome component among the case group. All of the case group patients reported hypertension followed by high triglyceride level, while 15 (75%) patients had high density lipoprotein and wide waist circumference.

Table 3
Frequency of metabolic syndrome components among the case group

Variable, n = 20	n (%)
FBG, ≥100 mg/dL	18 (90)
TG, ≥150 mg/dL	19 (95)
HDL *	15 (75)
Waist circumference **	15 (75)
Blood pressure ***	20 (100)

Notes: * – high density lipoprotein was considered low if it is less than 40 mg/dL in men and less than 50 mg/dL in women; ** – waist circumference was considered abnormal if it was more 102 cm in men and more 88 cm in women; *** – blood pressure was considered high if it was more than 130/85 mmHg.

Table 4 illustrates a significant moderately negative correlation between nesfatin-1 and triglyceride levels, while no significant correlation was found with other variables.

Table 4
Correlation analysis between nesfatin-1 and other parameter in the case group

Variable	Correlation coefficient	P-value
Age, years	–0.360	0.118
WC	–0.007	0.976
BMI	0.212	0.369
FBG	–0.041	0.863
TG	–0.449	0.047
HDL	0.099	0.677

The receiver operation characteristic curve (ROC) for nesfatin-1 prediction of metabolic syndrome was shown in Figure 1. And it showed accepted outcome (area under the curve = 0.705) at cut off point of 588.7 ng/dL with sensitivity of 67.9%, specificity of 91.7%, positive predictive value of 95.0%, negative predictive value of 55.0% and the accuracy of the test of 75.0%.

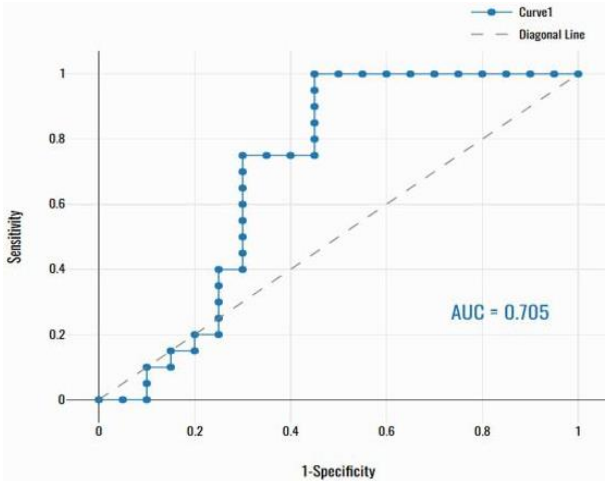

Fig. 1. Nesfatin-1 prediction of metabolic syndrome (ROC)

Discussion

Noncommunicable diseases have become the leading cause of morbidity and mortality in almost all countries (Madan et al., 2023). Metabolic syndrome is defined as a collection of interconnected cardiometabolic risk factors, including glucose intolerance, hypertension, abdominal obesity, atherogenic dyslipidemia, and proinflammatory and prothrombotic states. Furthermore, people with metabolic syndrome are more likely to develop type II diabetes, coronary artery disease, and die within five to 10 years (Luna-Luna et al., 2015).

The current study found that metabolic syndrome tended to affect females more than males, which fits in with a study conducted in Wasit, Iraq (Zamil & Amin, 2021) and another study conducted in Sulaimaniyah, Iraq. Moreover, in the present study the means of weight, BMI and waist circumference were significantly higher in patients with metabolic syndrome than controls, which is similar to many studies (Nouri et al., 2023; Chen et al., 2024). Additionally; fasting blood sugar, serum triglyceride, cholesterol, and insulin resistance were found to be significantly higher in the case group whereas high density lipoprotein was lower when compared to controls. Numerous studies have shown comparable results (Yang et al., 2015; Srivastav et al., 2022; Abdel Wahab et al., 2024). On the other hand, the mean of nesfatin-1 levels between cases and controls was not different in this study, which is supported by one study (Tekin et al., 2020), in contrast to another study (Alotibi et al., 2019). These differences might be due to different sample size and nesfatin-1 ELISA kit used in each study.

Regarding the case group, the study found that 75.0% of the patients had at least 3 of 5 components of metabolic syndrome, which is comparable to 76.6% found by another study (Tekin et al., 2020).

In this study, nesfatin-1 was found to have significant negative correlation with serum triglyceride, which means that as nesfatin-1 decreases serum triglyceride increases and vice versa. In other words, nesfatin-1 could have a potential role in triglyceride regulation and it may play a significant role in the pathogenesis of metabolic syndrome (Alotibi et al., 2019). Moreover, the present study found positive but not significant correlations between nesfatin-1 and body mass index, which means that despite the presence of a relationship, this relationship is not reliable enough to be considered a definitive correlation (Saldanha et al., 2012). In same way, the study found positive and not significant correlation between nesfatin-1 and high-density lipoprotein, which is consistent with a new study conducted among Vietnamese patients (Duc et al., 2023). While negative and not significant correlations were found in this study between; nesfatin-1 and patients'ages, as nesfatin-1 decreases

with age (Baydaa et al 2024), nesfatin-1 and waist circumference (Tekin et al., 2020), and nesfatin-1 and fasting blood sugar (Israa et al., 2023).

This study found the accuracy of nesfatin-1 for prediction of metabolic syndrome was 75%, with accepted outcomes at area under the curve of 0.705, whichconcurs with a study comparing metabolic syndrome associated with fatty liver and normal individuals (Mohamed et al., 2024). In any case, serum nesfatin-1 levels can provide a high degree of accuracy in predicting people at risk for metabolic syndrome when combined with other diagnostic criteria (Tekin et al., 2020).

Conclusion

Nesfatin-1 is an accepted biomarker for the diagnosis of metabolic syndrome, as it showed a moderate accuracy in predicting metabolic syndrome. Nefatin-1 has a significant negative correlation with serum triglyceride, and triglyceride regulation could play the key role in the diagnosis and treatment of metabolic syndrome consequences.

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