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Assessment of Neudesin Serum Levels in Pre-Diabetes and Newly Diagnosed Type 2 Diabetes Mellitus

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Abstract

Background Type 2 Diabetes Mellitus (T2DM) is a metabolic disorder characterized by chronic hyperglycemia due to insulin resistance and impaired insulin secretion. Prediabetes, an intermediary condition where blood glucose levels are elevated but not yet diagnostic for diabetes, poses a significant risk for progression to T2DM. Neudesin (NENF), a neurotrophic factor with known roles in adipocyte differentiation and myoblast inhibition, has emerged as a potential biomarker for metabolic dysregulation.

Objective To evaluate serum NENF levels in individuals with prediabetes and T2DM, and establish a diagnostic cutoff value with optimal sensitivity and specificity to distinguish diabetic and prediabetic patients from healthy individuals.

Methods A total of 120 Iraqi individuals aged 28–66 years participated in this study, including 30 patients with T2DM, 30 individuals with prediabetes, and 60 healthy controls. Serum levels of NENF were determined using a commercially available enzyme-linked immunosorbent assay kit, body mass index was calculated from participant height and weight, fasting blood glucose and glycated hemoglobin were measured using standard enzymatic colorimetric methods.

Results The findings revealed significantly higher serum NENF levels in T2DM patients compared to prediabetic and control groups (P <0.001). Mean NENF concentrations were 651.61±184.08 ng/ml in healthy controls, 745.56±231.23 ng/ml in prediabetic individuals, and 1034.78±496.45 ng/ml in T2DM patients.

Conclusion Elevated NENF levels are associated with T2DM and prediabetes, suggesting its potential as a sensitive and precise biomarker for early detection, screening, and monitoring of metabolic dysregulation.

Keywords Type 2 diabetes mellitus, neudesin, prediabetes, metabolic dysregulation

List of abbreviations: ADA = American diabetes association, the BMI = Body mass index FBG = Fasting blood glucose, HbA1c = Glycated hemoglobin, T1DM = Type 1 diabetes mellitus, T2DM = Type 2 diabetes mellitus

Introduction

Type 2 diabetes mellitus (T2DM) is a rising health issue in Iraq, influenced by factors such as unhealthy lifestyles, obesity, and limited healthcare resources. Effective management through patient education and lifestyle changes is essential to reduce complications and healthcare burdens. [(1)]. The global prevalence of diabetes has more than doubled over the past three decades, making it the 9th leading cause of death worldwide [(2)]. Currently, approximately 1 in 11 people globally are affected, with T2DM accounting for nearly 90% of cases [(3)].

According to the International Diabetes Federation, about 1.1 million children and adolescents aged 14-19 have type 1 diabetes mellitus (T1DM) [4]. The number of individuals with diabetes is projected to rise from 425 million in 2017 to 629 million by 2045, driven by increasing obesity and sedentary lifestyles associated with socioeconomic and nutritional transitions [5]. Furthermore, T2DM is on the rise among adolescents and young adults, with obesity, family history, and physical inactivity being the major risk factors [6].

Pre-diabetes represents an intermediate state of elevated glucose levels and carries a high risk of progression to T2DM. Each year, approximately 10-15% of individuals with pre-diabetes develop T2DM [7,8]. Insulin resistance—central to T2DM—results from reduced tissue responsiveness to insulin in the liver, muscles, and adipose tissue. This resistance may stem from impaired insulin receptor binding or defects in post-receptor signaling mechanisms [9,10].

Neudesin (NENF), a neurotrophic factor, has recently gained attention for its potential role in metabolic disorders. It is expressed primarily in the brain and adipose tissue, with additional presence in the heart, kidneys, and lungs [11]. NENF belongs to the membrane-associated progesterone receptor (MAPR) family, though its functions are distinct from other members of this subclass [12]. Its biological activity is attributed to its cytochrome b5-like heme/steroid-binding domain [13]. NENF is involved in neuronal differentiation, energy homeostasis, and intracellular signaling pathways such as phosphatidylinositol-3 kinase (PI3K) and mitogen-activated protein kinase (MAPK), which are closely related to glucose metabolism and insulin sensitivity [14].

Emerging evidence suggests that MAPK may contribute to obesity-induced insulin resistance by modulating lipid storage and metabolic signaling in adipose tissue. These findings indicate its potential link to the pathogenesis of T2DM, positioning NENF as a promising biomarker for metabolic dysregulation [15].

Therefore, this study aimed to evaluate serum levels of NENF in individuals with T2DM, prediabetes, and healthy controls as well as its potential diagnostic value using Receiver Operating Characteristic (ROC) curve analysis.

Methods

This case-control study included 120 Iraqi participants aged between 31 and 65 years, grouped as follows: 30 prediabetic individuals, 30 T2DM patients, and 60 healthy controls. The study was conducted at the Department of Chemistry and Biochemistry Laboratories, Al-Imamein Al-Kadhimein Medical City, Baghdad, Iraq.

Participants underwent structured interviews and physician consultations. Height and weight of each one was measured to calculate the body mass index (BMI). Blood samples were collected after a minimum overnight fast of 8 hours to ensure standardized measurements. Diagnoses of prediabetes and T2DM were based on the American Diabetes Association (ADA) 2023 guidelines [16].

Each participant provided 8 ml of venous blood. Of this, 2 ml were collected in Ethylene diamine tetra acetic Acid (EDTA) tubes for glycated hemoglobin (HbA1c) analysis, while 6 ml were drawn into gel tubes for fasting blood glucose (FBG). Samples were allowed to clot at room temperature for 20 min and were then centrifuged for 10 min. The serum obtained was aliquoted for immediate biochemical analysis. Biochemical parameters, including FBG and lipid profiles, were assessed using enzymatic and colorimetric methods.

Remaining serum samples were stored at −20°C for subsequent analysis of NENF concentrations using enzyme-linked immunosorbent assay (ELISA) kits, adhering to the manufacturer's protocol.

Statistical analyses

Statistical analyses were conducted using statistical package for social sciences (SPSS) (Version 26, IBM Corp., Armonk, NY, USA). Results were expressed as mean±standard

deviation (SD). Graphical representations and data visualizations were performed using GraphPad Prism (Version 9.0, GraphPad Software, San Diego, CA, USA). The significance level for all statistical tests was set at P <0.05.

Results

To confirm the diagnosis of diabetes and prediabetes, BMI, FBG and HbA1c was compared among the three studies groups, it was found a significant difference in BMI among the three studied groups (P = 0.048), an insignificant difference in FBG (P = 0.134) among the three studied groups, while a significant difference in HbA1c was present (P = 0.008).

The analysis demonstrated a progressive increase in serum NENF levels across the study groups. The mean NENF concentration for the entire study cohort was 810.65±368.32 pg/ml. Group-specific stratification revealed mean levels of 651.61±184.08 pg/mL in the control group, 745.56±231.23 pg/mL in the prediabetic group, and 1034.78±496.45 pg/mL in the diabetic group

Intergroup comparisons indicated statistically significant differences in serum NENF levels across all groups (P <0.001). While no significant difference was observed between the control and prediabetic groups (P = 0.096), the diabetic group exhibited significantly higher levels compared to both the control (P <0.001) and prediabetic groups (P = 0.005) as shown in (Figure 1 and Table 1).

Table 1. Comparison of Clinical and Biochemical Parameters Between Study Groups

Parameter	Control (n = 60) Mean±SD	Prediabetes (n = 30) Mean±SD	Diabetes (n = 30) Mean±SD	P value
BMI (kg/m²)	26.89±4.23	27.52±4.36	30.58±3.95	0.048
FBG (mg/dl)	89.74±11.74	118.76±12.47	176.68±49.20	0.134
HbA1c (%)	5.24±0.30	6.17±0.27	8.22±1.17	0.008
Neudesin (pg/ml)	651.61±184.08	745.56±231.23	1034.78±496.45	<0.001

BMI = Body mass index, FBG = Fasting blood glucose, HbA1c = Glycated hemoglobin, HDL-C = High-density lipoprotein cholesterol, LDL-C = Low-density lipoprotein cholesterol, VLDL-C = Very low-density lipoprotein cholesterol

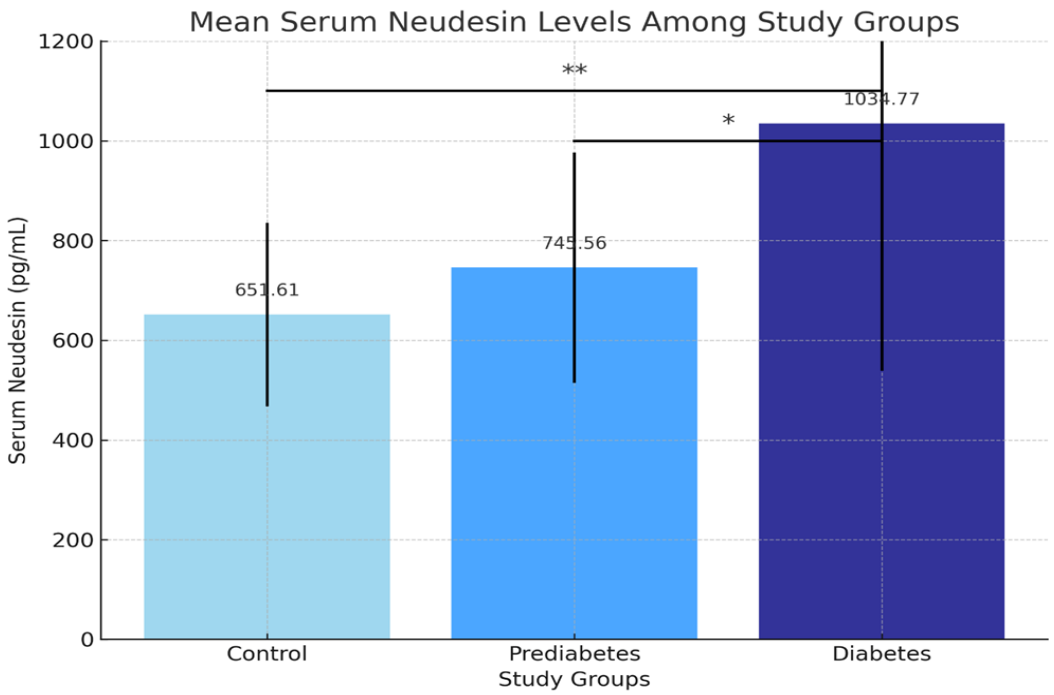

Figure 1. Comparison of serum Neudesin (NENF) levels among the study groups. Data are expressed as mean ± standard deviation (SD). Statistical analysis was performed using one-way ANOVA followed by post hoc test. *p < 0.05, **p < 0.01, and *p < 0.001 indicate statistically significant differences compared with the control group

Receiver Operating Characteristic (ROC) curve analysis was conducted to evaluate the diagnostic performance of serum NENF in identifying dysglycemic states. A threshold value of >633.29 pg/ml yielded an area under the curve (AUC) of 0.81, with a sensitivity of 83.3% and a specificity of 60.0% (Table 2; Figure 2). These findings underscore the potential utility of serum NENF as a biomarker for distinguishing diabetic and prediabetic individuals from healthy controls.

Table 2. Diagnostic performance of serum NENF in distinguishing diabetic and non-diabetic subjects based on ROC curve analysis

Cutoff Value (pg/ml)	AUC (%)	Accuracy (%)	P value	Sensitivity (%)	Specificity (%)
>633.29	81.0	71.7	0.000	83.3	60.0

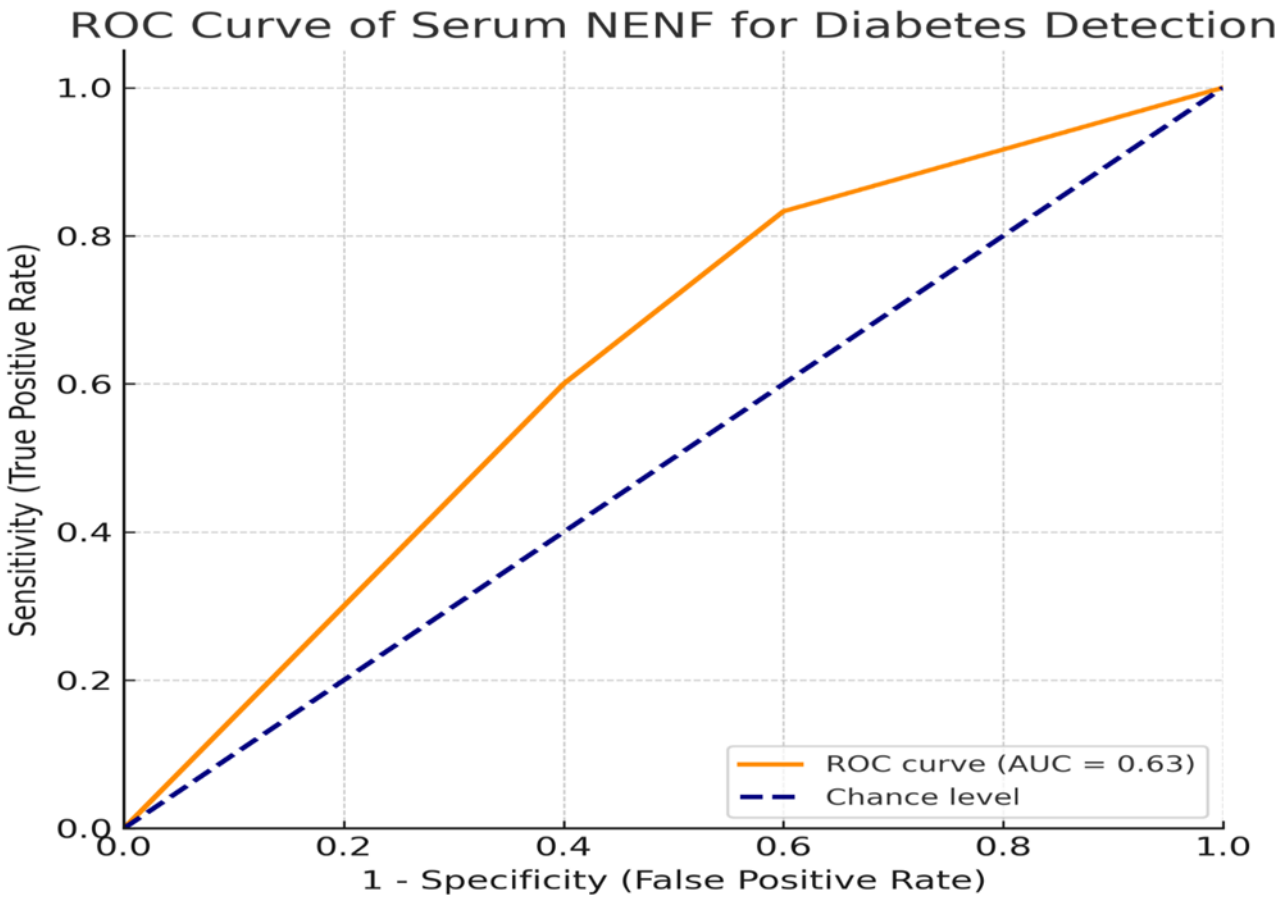

Figure 2. Receiver operating characteristic (ROC) curve of serum Neudesin (NENF) for distinguishing patients with type 2 diabetes mellitus (n = 30) from prediabetic individuals (n = 30)

Discussion

This study highlights that plasma levels of NENF were significantly higher in individuals with diabetes compared to those with prediabetes and the control group. Additionally, the prediabetic group exhibited intermediate NENF levels, suggesting a progressive rise in NENF along the continuum from normoglycemia to diabetes. These findings are consistent with prior research, which reported elevated NENF levels in diabetic individuals relative to healthy controls [17]. This underscores the potential of NENF as a biomarker for early detection and monitoring of diabetes progression.

The ROC curve analysis further emphasizes the diagnostic value of NENF. A threshold value of >633.29 pg/mL yielded an area under the curve (AUC) of 81.0%, reflecting good discriminatory capacity. Sensitivity and specificity values of 83.3% and 60.0%, respectively, support its reliability as a biomarker, albeit with some specificity limitations. These observations align with the growing emphasis on sensitive biomarkers to enable early intervention in diabetes management [18].

The rise in NENF levels may be associated with its role in metabolic regulation and inflammatory pathways, both critical in the pathophysiology of diabetes. A recent study suggests that NENF contributes to lipid metabolism and insulin sensitivity, which may explain its elevation in prediabetic and diabetic conditions [19]. However, the underlying mechanisms remain unclear, necessitating further research.

Despite these encouraging findings, certain limitations must be acknowledged. The relatively small sample size may limit the broader applicability of the results. Moreover, the cross-sectional design prevents establishing causal relationships. Future longitudinal studies with larger cohorts are required to validate these findings and investigate the mechanistic links between NENF and diabetes progression.

In conclusion, this study underscores the potential of NENF as a valuable biomarker for differentiating between diabetes and prediabetes. The significant elevation of plasma NENF levels in diabetic individuals, along with the progressive rise observed in prediabetic subjects, highlights its importance in the early detection and monitoring of diabetes progression.

These findings contribute to the growing body of research linking NENF to the pathophysiology of diabetes, underlining its potential clinical applications. However, further studies with larger sample sizes are essential to validate these results and elucidate the mechanisms driving the observed associations. Expanding our understanding of NENF could open new avenues for innovative diagnostic and therapeutic strategies in diabetes management.

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Author contribution

Abdul Haleem: Data collection, including and laboratory measurements (ELISA and biochemical assays), statistical analysis, data interpretation, and preparation of tables and figures. Dr. Hamzah: Conceptualization and study design, supervision of the project, and manuscript drafting. Dr. Khudhair: Diagnosis of diabetes among participants. Deli: Assisted in laboratory measurements (ELISA and biochemical assays).

Conflict of interest

The authors affirm that there are no conflicts of interest associated with this study.

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