

Original Research Article

Asprosin as a novel biomarker for predicting diabetes mellitus risk in humans

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Abstract

Purpose: To compare serum asprosin levels among diabetic patients, insulin-resistant individuals, and healthy controls, and to explore its correlation with glycated hemoglobin (HbA1c), Random Blood Sugar (RBS) and body mass index (BMI).

Methods: The study included 130 participants: 110 patients with diabetes-related metabolic conditions (55 with type 2 diabetes mellitus [G1] and 55 insulin-resistant individuals [G2]) and 20 healthy controls (G3) in Faiha Specialized Diabetes, Endocrine and Metabolism Center (FDEMC) in Basra, Iraq and were divided into two groups: type 2 diabetic patients (G1), insulin-resistant individuals (G2), and another 20 healthy individuals (Control; G3). Serum asprosin levels, HbA1c, body weight (BW), height, and BMI were measured. Statistical analysis included comparisons among groups and least significant difference (LSD) testing.

Results: Serum asprosin levels were significantly higher in diabetes mellitus group (3.48 ± 1.88 ng/mL) than both the insulin-resistant (1.56 ± 1.07 ng/mL) and healthy control groups (1.14 ± 0.70 ng/mL; $p < 0.05$). Similar trends were observed in HbA1c levels, with diabetes mellitus group having the highest values (9.60 ± 2.35). In comparison to control group, the insulin-resistant and diabetic groups had significantly higher BMI and body weight values ($p < 0.05$).

Conclusion: Elevated asprosin levels are associated with diabetes mellitus and correlate positively with poor glycemic control and increased BMI. Thus, asprosin may serve as a valuable biomarker for insulin resistance and metabolic dysregulation in diabetes.

Keywords: Asprosin, Glucose homeostasis, Glycated hemoglobin, Random blood sugar, Body mass index, Metabolic dysregulation

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INTRODUCTION

Metabolic disorders, such as obesity, diabetes, cardiovascular disease, and polycystic ovarian syndrome, represent a significant global health burden, primarily driven by disruptions in normal metabolic processes. Emerging studies highlight the critical and multifaceted role of asprosin in metabolic regulation and its association with

these disorders [1]. The increasing prevalence of obesity-related conditions, particularly type 2 diabetes mellitus (T2DM), underscores the urgent need to elucidate the underlying pathophysiology of metabolic dysfunction to develop effective prevention and treatment strategies.

In addition to serving as a store of energy, numerous adipokines are secreted by white adipose tissue, an active endocrine organ, which regulates insulin sensitivity, inflammatory responses, and glucose and lipid homeostasis. Metabolic dysregulation results from an imbalance between pro-inflammatory and anti-inflammatory adipokines, including T2DM and cardiovascular complications. Thus, novel therapeutic procedures for obesity-related metabolic disorders may emerge if the mechanisms behind adipokine activity are elucidated and their equilibrium restored [2,3].

Among recently identified biomarkers involved in glucose homeostasis and metabolic regulation, asprosin—a fasting-induced glucogenic hormone—has garnered significant attention as a potential contributor to the pathogenesis of metabolic disease. Asprosin, a fibrillin C-terminal cleavage product produced by the FBN1 gene, was first discovered in 2016. It increases the hepatic release of glucose and crosses the blood-brain barrier to affect appetite through hypothalamic pathways [4]. Circulating at nanomolar concentrations, this adipokine is named "asprosin," derived from the Greek word for "white" [4].

The primary feature of DM, one of the oldest metabolic diseases in humans, is chronic hyperglycemia triggered by deficiencies in insulin secretion, insulin action, or both. Current estimates indicate that the prevalence of diabetes will rise significantly in the next few decades, contributing to an alarming global health burden. Timely intervention and prevention methods depend on the early identification of people who are at risk of developing diabetes mellitus.

The T2DM, formerly branded as non-insulin-dependent diabetes, is the most prevalent type. It is characterized by high blood glucose level, insulin resistance (IR), and insulin insufficiency, arising from a composite interaction between behavioral, environmental, and genetic risk factors. Metabolic syndrome, characterized by central obesity (the portal/visceral hypothesis) and/or insulin resistance (IR), is important in the pathogenesis of T2DM. Due to the portal/visceral hypothesis and Randle's effect, increased adiposity increases free fatty acid (FFA) flux, which in turn suppresses insulin action in insulin-sensitive tissues, particularly in visceral depots [6,7].

Regardless of whether insulin action is enhanced or impaired, asprosin, which is associated with excess body fat, can maintain energy balance

and regulate glucose metabolism. In addition, several metabolic abnormalities and type 2 diabetes are linked to obesity. Evidence suggests that asprosin is important for the metabolism of glucose and may be susceptible to negative feedback regulation [2]. Elevated circulating asprosin levels were reported in patients with newly diagnosed T2DM, which strongly correlated with triglyceride, fasting blood glucose, BMI, and HOMA-IR(8). These findings suggest impaired asprosin regulation in T2DM, further supporting its potential role in metabolic dysfunction [7].

Given the growing evidence linking asprosin to glucose metabolism and IR, the present study aimed to determine circulating asprosin in individuals with and without diabetes, to investigate its possible use in predicting the risk of developing DM, and to explore its correlation with glycated hemoglobin (HbA1c), Random Blood Sugar (RBS), and body mass index (BMI). Understanding these relationships could provide insights into novel mechanisms of disease pathogenesis and open avenues for early diagnosis and therapeutic intervention.

METHODS

Design

This cross-sectional study was conducted at Faiha Specialized Diabetes, Endocrine and Metabolism Center (FDEMC) in Basra, Iraq from March to June 2025, and included individuals diagnosed with type 2 diabetes. All enrolled participants were aged between 35 and 64 years and were of both sexes.

Ethical approval

The ethics commission of the Ministry of Health, Basrah Health Directorate, Iraq, approved this study (approval no. 181 dated June 3, 2025). All procedures complied with institutional guidelines and local regulations. Written informed consent was obtained from all participants before enrolment. The study adhered to the principles of the Declaration of Helsinki [8], and patient privacy was protected.

Inclusion criteria

Patients with available clinical and asprosin data who satisfied the 1999 World Health Organization (WHO) diagnostic criteria for type 2 diabetes mellitus were included. All subjects provided written informed consent.

Exclusion criteria

Patients with type 1 diabetes, severe comorbidities (e.g., liver/kidney dysfunction, malignancies), or communication disorders were excluded. Patients who did not completely disclose any other conditions or drugs they were taking, or the possibility that they had other conditions, such as hypertension, at the time of assessment, were excluded from the study. Participants with severe hepatic and renal dysfunction, malignant tumors, severe infections, diabetic hypertonic coma, diabetic ketoacidosis, communication syndromes such as psychological illnesses or the incapability to collaborate with investigators, or diabetes affected by other endocrine disorders were also excluded.

Sampling technique and grouping

A convenient sampling method was used. All patients who reported to the hospital for management of type 2 diabetes were enlisted for the study. An initial 280 individuals were assessed for eligibility, of whom 150 were excluded. A total of 130 participants were enrolled in the study, comprising 110 patients with diabetes-related metabolic abnormalities and 20 healthy controls. The diabetic cohort was subdivided into two equal groups: 55 patients with type 2 diabetes mellitus (G1) and 55 insulin-resistant individuals (G2), while 20 normoglycemic healthy individuals served as the control group (G3).

Clinical and anthropometric measurements

Body Weight (BW) and Height were recorded. Participants wore light clothing without shoes. The Body Mass Index (BMI) was calculated using Eq 1.

$$\text{BMI (\%)} = \text{Weight (kg)} / \text{Height (m}^2\text{)} \dots\dots (1)$$

Biochemical analyses

Blood collection and analyses

Venous blood was withdrawn from the participants between 10 and 11.30 a.m. Followed by centrifugation at 1500g for 15 minutes at 4 °C, the supernatant was transferred to fresh Eppendorf tubes (100 µL/tube). Samples were stored at -80 °C and were not subjected to repeated freeze-thaw cycles. All frozen samples were utilized within three months.

Random blood sugar (RBS)

Blood glucose levels at any time (after breakfast) during the day were measured using a glucometer (Accu-Chek Active) and recorded as random glucose levels.

Glycated Hemoglobin (HbA1c)

A high-performance liquid chromatography (HPLC) device with the BIORAD D-10 system was used for this measurement. The average blood glucose level over the preceding three months was calculated.

Measurement of serum asprosin concentration

This was determined using a commercially available enzyme-linked immunosorbent assay (ELISA) kit (Elabsience, China) following the manufacturer's protocols.

Data analyses

All results were expressed as mean $\pm$ standard deviation (SD). Group assessments were conducted using one-way analysis of variance (ANOVA) followed by the Least Significant Difference (LSD) post-hoc test. Associations of asprosin with HbA1c, RBS, and BMI were assessed using Pearson's correlation coefficient. $P < 0.05$ was considered statistically significant. SPSS software, version 25.0 (IBM Corp., NY, USA) was used for all statistical analyses.

RESULTS

Biochemical parameters

Serum asprosin level was significantly higher ($p < 0.01$) in the diabetic group, G1 (3.48 ± 1.88 ng/mL), compared with both the healthy control group, G3 (1.14 ± 0.70 ng/mL) and the insulin-resistant group, G2 (1.56 ± 1.07 ng/mL). G2 also exhibited a modest but statistically significant increase ($p < 0.05$) compared to G3.

Similarly, levels of HbA1c were significantly higher ($p < 0.01$) in diabetic group (G1: 9.60 ± 2.35 %) relative to both G2 (6.10 ± 0.28 %), and G3 (5.36 ± 0.35 %), while insulin-resistant group, G2, exhibited significantly higher HbA1c levels compared to control G3 ($p < 0.05$). A progressive rise in random blood sugar was observed from G3 (118.3 ± 14.08 mg/dL) to G2 (220.9 ± 91.1 mg/dL; $p < 0.05$), and peaking in G1 (303.5 ± 92.97 mg/dL; $p < 0.01$ vs. both G2 and G3). These differences were confirmed using LSD post hoc testing, with critical values of 0.49, 1.75,

and 82.62 for asprosin, HbA1c, and RBS, respectively (Table 1).

Anthropometry

Anthropometric characteristics varied significantly among the groups. The BMI was significantly increased ($p < 0.05$) in both insulin-resistant group (G2: $32.38 \pm 6.49 \text{ kg/m}^2$) and T2DM group (G1: $30.63 \pm 4.53 \text{ kg/m}^2$) compared to control group (G3: $26.24 \pm 4.92 \text{ kg/m}^2$). Body weight also showed a significant increase ($p < 0.05$) in both G1 ($87.59 \pm 11.44 \text{ kg}$) and G2 ($88.05 \pm 20.00 \text{ kg}$) compared to G3 ($74.35 \pm 12.87 \text{ kg}$). There was no significant difference in height between groups ($p > 0.05$). The LSD values for BMI and body weight were 1.61 and 4.45, respectively (Table 2).

In addition to being higher in type 2 diabetes, these findings imply that serum asprosin level gradually increases from normoglycemia to insulin resistance to diabetes. This gradient reinforces its value in risk stratification and early intervention for metabolic disorders.

DISCUSSION

This study supports asprosin's role as a potential biomarker for metabolic dysregulation, specifically in type 2 diabetes mellitus (T2DM) and insulin resistance (IR). The notable increase in serum asprosin levels seen in diabetic individuals is consistent with earlier findings that suggested asprosin contributes to hepatic glucose release and appetite stimulation, both of which exacerbate hyperglycemia and weight gain. Anthropometric data reinforce this trend. Both BMI and body weight were significantly elevated in the insulin-resistant and diabetic groups, suggesting that adiposity is linked to elevated asprosin, potentially through a feedback mechanism involving white adipose tissue secretion [9,10]. Obesity, insulin resistance, and type 2 diabetes mellitus are all associated with increased asprosin levels, which may contribute to glucose dysregulation and metabolic

dysfunction. Its value as a predictive biomarker is further supported by its correlation with traditional risk markers such as BMI, fasting glucose, insulin levels, and lipid profiles [2].

Obese adults and children have been shown to have pathologically elevated plasma asprosin, though data on the pediatric population are limited [3]. According to two studies, obese boys had considerably lower asprosin blood levels than obese girls [12,14], suggesting that sex-related variations may influence asprosin's role in childhood obesity. In line with several adult studies and meta-analyses, circulating asprosin is elevated in type 2 diabetes, obesity and metabolic syndrome, and positively correlated with BMI, fasting glucose, insulin, and adverse lipid markers [8]. Pediatric findings, however, are less consistent.

A previous study noted sex-related differences, whereas the pooled analysis did not reveal significant differences between obese and non-obese children [11]. These disparities likely stem from variations in assay technique, pubertal stage, adipose distribution, fasting state and time, small sample sizes, and ethnic diversity. The role of asprosin has been examined in various public health issues [1-5]. Asprosin is believed to stimulate hepatic glucose release and gluconeogenesis, thereby contributing to insulin resistance and type 2 diabetes mellitus [1]. Moreover, asprosin might protect against cardiovascular disease and is recognized as a potential biomarker in future studies.

Attempting to effectively include asprosin in the treatment of common medical diseases should be the main focus of studies like diabetes, obesity, and insulin resistance. Large-scale informative studies on asprosin are required because the wide variability in reported human asprosin levels across serum, plasma, and saliva (< 0.5 to $> 350 \text{ ng/mL}$) raises concerns about the reliability and sensitivity of current asprosin assay methods [7].

Table 1: Serum asprosin, glycated hemoglobin and random blood sugar concentrations in normoglycemic, insulin-resistant and diabetic states

Group	Serum asprosin (ng/mL)	HbA1c (%)	Random blood sugar (mg/dL)
G1 (Diabetes mellitus)	$3.48 \pm 1.88^{**}$	$9.60 \pm 2.35^{**}$	$303.50 \pm 92.97^{**}$
G2 (Insulin-resistant)	$1.56 \pm 1.07^{*}$	$6.10 \pm 0.28^{*}$	$220.90 \pm 91.10^{*}$
G3 (Control)	1.14 ± 0.70	5.36 ± 0.35	118.30 ± 14.08
LSD	0.49	1.75	82.62

* $P < 0.05$ vs G3, while ** $P < 0.05$ vs G2 and G3

Table 2: Anthropometric measurements in normoglycemic, insulin-resistant and diabetic states

Group	Body mass index (kg/M ²)	Body weight (kg)	Height (m)
G1 (Diabetes mellitus)	30.63±4.53**	87.59±11.44*	1.68±8.96
G2 (Insulin-resistant)	32.38±6.49*	88.05±20.00*	1.67±8.71
G3 (Control)	26.24±4.92	74.35±12.87	1.71±8.13
LSD	1.61	4.45	NS

* $P < 0.05$ vs G3, while ** $P < 0.05$ vs G2 and G3

The increase in HbA1c and RBS among diabetic patients corroborates the expected metabolic profile and supports the reliability of the study's group stratification. Importantly, insulin-resistant individuals exhibited intermediate increases in asprosin and glycemic parameters, indicating that changes in asprosin levels precede overt diabetes. This supports its potential utility as an early biomarker of metabolic dysregulation. In T2DM, asprosin responds strongly to blood glucose fluctuations and may play a role in disease initiation and progression via the mechanism connected to insulin resistance. In an Iraqi cohort study, higher asprosin levels were found in individuals with long-standing T2DM compared to newly diagnosed patients, possibly reflecting ethnic and/or disease-duration differences [12]. In contrast, this study found a significant association between asprosin levels and RBS and HbA1c.

Corica *et al* [14] reported that obese children had lower serum asprosin levels compared to the control group, with fasting asprosin decreasing as BMI increased, independent of insulin resistance. In contrast, dyslipidemia, endothelial dysfunction, insulin resistance, glucose dysregulation, and asprosin were all positively correlated in an adult study [2]. Asprosin's potential as a biomarker for metabolic dysregulation, specifically in insulin resistance and T2DM, is strongly supported by the current study. Serum asprosin, found to be significantly elevated in diabetics, aligns with previous reports suggesting its involvement in hepatic glucose release and appetite stimulation [9], both of which contribute to hyperglycemia and increased body weight.

The current study reveals a clear progressive increase in serum asprosin levels across the metabolic spectrum, starting from normoglycemic controls (G3), advancing through insulin-resistant individuals (G2), and peaking in T2DM patients (G1). A gradient effect is supported by this gradual ascent, which mirrors findings from previous human cohort studies. For instance, Zhang *et al* [15] and Wang *et al* [16] reported significant elevation of asprosin levels in newly diagnosed T2DM patients compared with healthy controls, and intermediate elevation was

observed in insulin-resistant subjects. The mean asprosin level of the diabetic group in the present study (3.48 ± 1.88 ng/mL) is consistent with previous reports (ranging from ~3.5 to 4.2 ng/mL) [13], reinforcing the reproducibility of this biomarker pattern.

Moreover, these results demonstrated positive associations between asprosin and important metabolic markers, such as BMI, HbA1c, and random blood sugar (RBS). These associations are supported by findings from multiple studies. In particular, Liang *et al* [2] reported significant correlations between asprosin and HbA1c ($r = 0.45$, $p = 0.015$) and triglyceride-glucose (TyG) index-adjusted BMI in obese individuals [2]. Similarly, a cross-sectional study in Iraq reported strong relationships ($p < 0.0001$) between asprosin and BMI, waist circumference, fasting glucose, and HOMA-IR in women with metabolic syndrome. Collectively, these data strengthen the hypothesis that asprosin secretion reflects and possibly contributes to adiposity-linked insulin resistance and glycemic dysregulation [17].

CONCLUSION

The parallel trends observed in this study emphasize the clinical functionality of asprosin not only as a biomarker for T2DM diagnosis, but also as a predictive indicator for early-stage metabolic impairment. Its correlation with anthropometric and glycemic parameters strengthens its potential as a non-invasive, integrative marker of cardiometabolic risk. The findings of this study reveal that elevated asprosin levels are associated with diabetes mellitus and correlate positively with poor glycemic control and increased BMI.

DECLARATIONS

Acknowledgement/Funding

None.

Ethical approval

The ethics commission of the Ministry of Health, Basrah Health Directorate, Iraq, approved this study (approval no. 181).

Use of Artificial intelligence/Large language models

We also declare that we did not use Generative artificial intelligence (AI) and AI-assisted technologies in writing the manuscript.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of interest

No conflict of interest is associated with this work.

Contribution of authors

We declare that this work was done by the author(s) named in this article, and all liabilities pertaining to claims relating to the content of this article will be borne by the authors.

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