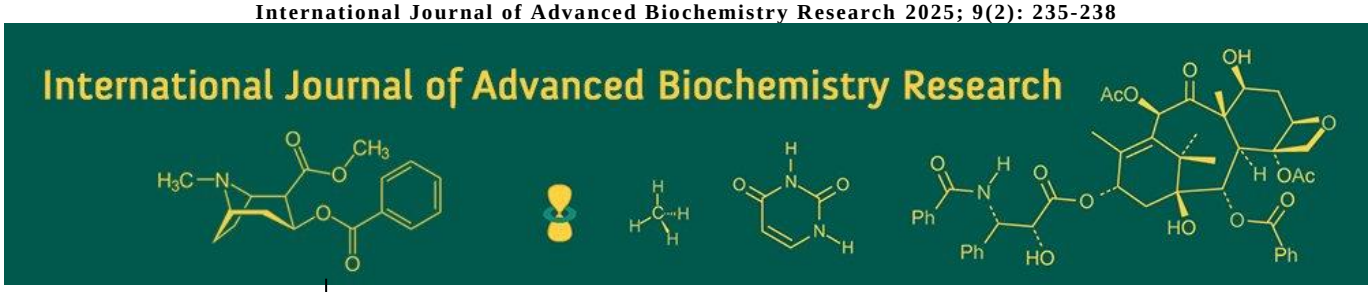


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# Evaluation of asprosin levels in relation to age, gender, BMI, glycemic control, and disease duration in diabetic patients

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**Abstract**
**Background:** Asprosin is a novel adipokine implicated in metabolic regulation, and its levels are thought to be influenced by factors such as diabetes, age, BMI, and glycemic control, potentially reflecting disease severity and progression.
**Objective:** Evaluate the relationship between asprosin levels and factors such as age, gender, BMI, glycemic control, and the duration of diabetes in patients with type 2 diabetes mellitus.
**Methodology:** A case-control study conducted from February to July 2024 in four Basra hospitals included 180 participants: 129 T2DM patients (60 males, 69 females) and 51 healthy controls (28 males, 23 females). Patients were classified into three groups based on urinary albumin to creatinine ratio (UACR): DN0, DN1, and DN2. Exclusion criteria included type 1 diabetes, acute complications, cardiovascular diseases, liver dysfunction, and malignancies. Asprosin levels were measured using the MELSIN Human Asprosin kit (EKHU-3077, China) and ELISA-Human Reader HS (Germany).
**Result:** The study found significant differences in asprosin levels across age, sex, BMI, diabetes duration, and glycemic control ($p$<0.001). Asprosin levels increased with age, disease severity, BMI, and diabetes duration. Females had higher asprosin levels than Males, and advanced stages (DN1, DN2) showed higher levels. Poor glycemic control was associated with elevated asprosin in advanced disease stages.
**Conclusion:** Elevated asprosin levels in advanced stages of diabetic kidney disease (DN1, DN2) suggest its potential role as a biomarker for disease progression. Age, poor glycemic control, and higher BMI contribute to higher asprosin concentrations, indicating their influence on metabolic and inflammatory pathways.

**Keywords:** Asprosin, type 2 diabetes mellitus, diabetic kidney disease, glycemic control, BMI, disease severity

## Introduction
Asprosin, a type of novel adipokine, has recently drawn attention for the regulation of glucose metabolism and rainfall of metabolic diseases such as diabetes. Its main source is adipose tissue where it acts as a key modulator in the regulation of glucose homeostasis by stimulating the liver to release glucose into the bloodstream and has been widely investigated as a potential biomarker for assessing metabolic disorders in particular in patients with diabetes. Until now, association of asprosin levels with age, gender, body mass index (BMI), glycemic control and disease duration have not been studied [1, 2]. Diabetes mellitus (DM) is a chronic metabolic disorder due to a failure of insulin to secrete or work appropriately, which leads to an elevation in blood glucose levels. It is now a growing global health crisis. Diabetes is classified as a chronic disease that is usually complicated by other organs and systems, therefore, early detection and management are of great importance [3]. So the aim of this study how demographic and clinical factors influence the progression of diabetes and asprosin levels. Since age and sex play a significant role in metabolic mechanisms, their association with asprosin may enhance our insight on the disease pathophysiology and the prospect of tailored therapeutic approaches [4, 5]. Cholesterol level and Body Mass Index (BMI) another significant risk aspect of the menace of diabetes disease progression as well as development based on rural research [6]. Overweight and obesity, typically conceptualized as high body mass index (BMI), are strong risk factors for insulin resistance and onset of type 2 diabetes.

Blood glucose levels, indicators of glycemic control,are still key factors in diabetes management and complications. The period of diabetes itself is a contributing factor to the progression of the disease and the development of comorbidities [7, 8].

## Methodology

A case-control study conducted between February 2024 and July 2024 in four hospitals located in Basra, Iraq: Al-Fayhaa Teaching Hospital, Al-Mawani Teaching Hospital, Basra Teaching Hospital and Al-Sadr Teaching Hospital. A total of 180 subjects were recruited into the study, including 129 type 2 diabetes mellitus (T2DM) patients (60 males and 69 females) diagnosed according to the criteria of the American Diabetes Association (ADA) and 51 healthy control subjects (28 males and 23 females). Patients were classified based on urinary albumin to creatinine ratio (UACR) into three groups: DN0 (39 patients; T2DM without diabetic kidney disease, UACR 300 mg/g) The control group included 51 healthy subjects without a history of diabetes or other chronic conditions, matched by sex and age with the patient groups. The exclusion criteria included type 1 diabetes, acute complications of diabetes, severe cardiovascular and cerebrovascular diseases, liver dysfunction, and malignancies. Concentration of Asprosin was determined using MELSIN Human Asprosin kit (EKHU-3077, China), and readings were obtained from the ELISA-Human Reader HS (Germany).

### Statistical analysis

We used SPSS (version 26) and the dependent t-test (two-tailed) and independent t-test (two-tailed) for variables that had a normally distributed distribution. For variables that did not have a normally distributed distribution, we used the Mann-Whitney U test, the Wilcoxon test, and the Chi-square test. $p<0.05$ was seen as statistically significant.

## Results

### Comparison of Asprosin Levels among Different Age Groups in Controls and Cases

The results of the study showed highly significant differences in asprosin levels between the different groups ($p<0.001$). A gradual increase in asprosin concentration was observed with age, with the age group ≥70 years recording the highest levels compared to younger age groups. Asprosin levels were also significantly higher in advanced stages of the disease (DN2 and DN3) compared to early cases (DN0 and DN1) and the control group. These results suggest an association between high asprosin levels and disease severity, in addition to the effect of age on these levels.

**Table 1:** Mean ± SD Values of Asprosin (ng/ml) Across Age Categories and Disease Stages

| Age (Years) | Asprosin (Mean ± SD) (ng⁄ml) | | | | P-value (Between groups) |
|---|---|---|---|---|---|
| | Controls N=51 | Cases N=129 | | | |
| | | DN0 | DN1 | DN2 | |
| 30-39 years | 10.7±0.84 | 14.5±0.52 | 16.51±1.30 | 20.85±0.65 | <0.001 |
| 40-49 years | 10.99±0.83 | 14.36±0.73 | 17.05±1.02 | 21.85±0.63 | <0.001 |
| 50-59 years | 10.36±0.75 | 14.41±0.67 | 17.27±1.50 | 23.0±1.00 | <0.001 |
| 60-69 years | 10.84±1.12 | 14.46±0.91 | 17.71±1.55 | 23.05±1.46 | <0.001 |
| ≥70 years | 10.70±0.28 | 14.58±0.94 | 18.65±0.14 | 24.35±1.06 | <0.001 |

### Comparison of Asprosin Levels between Genders in Controls and Cases

The study results showed highly significant differences in asprosin levels between the sexes and the different groups ($p<0.001$). Asprosin levels were higher in females than in males at all stages (DN0, DN1, DN2) and among the control groups. However, the increase in asprosin levels was associated with the severity of the disease in both sexes, as a significant increase in asprosin levels was observed with the progression of the disease in both males and females, reaching its highest levels at stage DN2.

**Table 2:** Mean ± SD Values of Asprosin (ng/ml) by Gender and Disease Stages

| Gender | Asprosin (Mean ± SD) (ng⁄ml) | | | | P-value (between groups) |
|---|---|---|---|---|---|
| | Controls N=51 | Cases N=129 | | | |
| | | DN0 | DN1 | DN2 | |
| Male | 10.55±0.83 | 14.38±0.73 | 16.98±1.37 | 22.13±1.47 | <0.001 |
| Female | 10.87±0.89 | 14.53±0.74 | 17.34±1.41 | 22.50±1.34 | <0.001 |

### Comparison of Asprosin Levels by BMI Categories in Controls and Cases

The results showed highly significant differences in asprosin levels across BMI categories among the different groups ($p<0.001$). In the normal weight category (18.5-24.9), a significant increase in asprosin levels was observed as the disease progressed from early stage DN0 to advanced stages DN1 and DN2. For overweight (25-29.9) and obese (≥30) individuals, asprosin levels were higher in advanced stages of the disease (DN1 and DN2) compared to the control group. These results suggest that BMI categories influence asprosin levels and their association with disease severity.

**Table 3:** Mean ± SD Values of Asprosin (ng/ml) Across Different BMI Categories and Disease Stages

| BMI | Asprosin (Mean ± SD) (ng⁄ml) | | | | P-value (between groups) |
|---|---|---|---|---|---|
| | Controls N=51 | Cases N=129 | | | |
| | | DN0 | DN1 | DN2 | |
| Normal weight (18.5-24.9) | 10.71±0.87 | 14.77±0.48 | 16.81±1.58 | - | <0.001 |
| Overweight (25-29.9) | - | 14.43±0.78 | 17.29±1.36 | 22.56±1.52 | <0.001 |
| Obese ≥30 | - | 13.86±0.50 | 17.06±1.49 | 22.49±1.41 | <0.001 |

### Comparison of Asprosin Levels Based on Duration of Diabetes Mellitus in Cases

The results showed highly significant differences in asprosin levels between the different groups based on the duration of diabetes ($p$<0.001). In subjects with a history of diabetes less than 5 years, asprosin levels were higher in advanced stages DN1 and DN2 than in early stage DN0. A similar increase in asprosin levels was observed in the groups with a duration of 5 to 10 years. In subjects with diabetes for more than 10 years, asprosin levels were significantly higher in advanced stages of the disease (DN1 and DN2). These results suggest that the duration of diabetes affects asprosin levels and disease severity.

**Table 4:** Mean ± SD Values of Asprosin (ng/ml) Across Different Durations of Diabetes and Disease Stages

| Duration of DM | Asprosin (Mean ± SD) (ng⁄ml) Cases N=129 | | | P-value (Between groups) |
|---|---|---|---|---|
| | DN0 | DN1 | DN2 | |
| < 5 years | 14.36±0.70 | 17.14±1.22 | 22.32±1.48 | <0.001 |
| 5 - 10 | 14.69±0.78 | 17.53±1.48 | 22.51±1.25 | <0.001 |
| ≥ 10 | - | 16.03±0.85 | 22.25±1.79 | <0.001 |

### Comparison of Asprosin Levels Based on Glycemic Control in Cases

The results showed highly significant differences in asprosin levels based on the level of glycemic control ($p$<0.001). In patients with perfect glycemic control (<7), no data were recorded for advanced disease stages (DN1 and DN2). In patients with acceptable glycemic control (7-8), asprosin levels were significantly lower. In subjects with poor glycemic control (>8), asprosin levels were significantly higher in advanced stages DN1 and DN2 compared to early stage DN0. These results suggest that glycemic control significantly affects asprosin levels and disease severity.

**Table 5:** Mean ± SD Values of Asprosin (ng/ml) Across Different Glycemic Control Levels and Disease Stages

| Glycemic control | Asprosin (Mean ± SD) (ng⁄ml) Cases N=129 | | | P-value |
|---|---|---|---|---|
| | DN0 | DN1 | DN2 | |
| Optimal control <7 | 14.55±0.21 | - | - | - |
| Acceptable control 7 – 8 | 4.46±0.77 | - | - | - |
| Poor control >8 | 14.47±0.74 | 17.18±1.38 | 22.32±1.41 | <0.001 |

### Discussion

In this study, the mean serum asprosin variation by age was significantly higher in diabetic patients than in age-group controls ($p$<0.001). That in diabetic patients , asprosin levels were elevated and increased progressively with age and disease progression. Moreover, there was a non-significant positive correlation between the serum asprosin and the age of the study population ($p$>0.05). Similar to Xu L *et al*. findings of a non-significant positive correlation ($p$>0.05) between the research population's age and asprosin levels [9]. The current study's findings demonstrated that, across all stages of DN and control, the mean value of asprosin levels in female participants was greater than that of male participants. A recent study by Long *et al* also reported that serum asprosin was higher in obese girls compared to obese boys, indicating a gender variation in the action and regulation of asprosin [10, 11]. But This finding contrasts with the findings from other studies reporting higher levels in males. Given that there isn't many research that concentrate on gender differences. It is important to investigate these differences and the connection between asprosin and DN, particularly in the female population [12, 13]. Plasma asprosin levels were notably elevated in patients with longer diabetes duration. Interestingly, patients with a disease duration of 5–10 years demonstrated the highest serum asprosin levels compared to those with durations of <5 years and >10 years. Furthermore, a significant positive correlation was observed between asprosin levels and diabetes duration ($p$<0.001). This finding aligns with the results reported by Wang *et al*., who also identified a positive correlation between asprosin and diabetes duration. In addition, diabetes duration was identified as a strong independent predictor of microvascular events [14, 15].

### Conclusion

It was determined from the study that asprosin levels are significantly related to disease severity, age, gender, BMI, duration of diabetes, and glycemic control. Increased asprosin levels were identified in the later stages of diabetic kidney disease (DN1, DN2), suggesting a potential biomarker approach for disease progression. Higher levels were also associated with older age, worse glycaemic control and greater BMI. Asprosin participates in metabolic and inflammatory pathways, and its higher levels correlate with both the severity of the disease and the biological agents that modulate its evolution.

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