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Association of Asprosin Levels with Metabolic Syndrome Severity and Insulin Resistance: A Case-Control Study

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ABSTRACT

Background: *Asprosin, a novel adipokine primarily secreted by white adipose tissue during fasting. Circulating asprosin promotes hepatic glucose release and has been reported to be elevated in obesity, type 2 diabetes mellitus, and metabolic syndrome (MetS), correlating with markers of insulin resistance such as HOMA-IR.* ***Objectives:*** *This case-control study evaluated the association between serum asprosin levels, metabolic syndrome severity, and insulin resistance* ***Materials and Methods:*** *A total of 300 Iraqi adult's participants were enrolled, including 150 subjects with MetS and 150 age, sex-matched controls without MetS. Serum asprosin, insulin, IL-6, and hs-CRP concentrations were measured using enzyme-linked immunosorbent assay (ELISA). Metabolic syndrome was diagnosed according to established criteria. Insulin resistance was assessed using the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR). Anthropometric indices, blood pressure, fasting glucose, and lipid profile were measured. Logistic regression and correlation analyses were performed to evaluate the associations between asprosin, MetS components, and insulin resistance.* ***Results:*** *Participants with MetS exhibited significantly elevated asprosin concentrations compared to those without MetS ($P < 0.001$). Logistic regression analysis demonstrated that asprosin independently predicted elevated fasting blood glucose ($P < 0.001$), increased triglyceride levels ($P < 0.01$), and reduced HDL cholesterol ($P < 0.001$). Asprosin remained a significant predictor of MetS after adjusting for age, diabetes status, total cholesterol, and BMI (OR: 3.62; $P < 0.001$ for women; OR: 3.58; $P < 0.001$ for men). However, this association lost statistical significance after adjustment for HOMA-IR ($P = 0.068$ for women; $P = 0.08$ for men). Positive correlations were observed between asprosin and obesity, dyslipidemia, hyperglycemia, insulin resistance, and inflammatory biomarkers.* ***Conclusion:*** *The findings indicate that serum asprosin is significantly associated with metabolic syndrome and its components independent of obesity. This relationship appears to be largely mediated by insulin resistance, suggesting that asprosin may serve as a valuable biomarker for metabolic dysfunction and a potential therapeutic target.*

Keywords: Asprosin; Metabolic syndrome; Insulin resistance; Adipokine; Iraqi population.

Article Information

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1.INTRODUCTION

Metabolic syndrome (MetS) represents a cluster of interconnected metabolic abnormalities that collectively elevate the risk of atherosclerotic cardiovascular disease, insulin resistance, type 2 diabetes mellitus (T2DM), leading to increased risk of mortality [(1)]. Metabolic syndrome is characterized by abdominal obesity, dyslipidemia, hypertension, and hyperglycemia [(2)]. Subjects with MetS face a fivefold increased risk of cardiovascular disease and a twofold increased risk of T2DM [(3)]. Beyond these classical complications, MetS has been linked to fatty

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liver disease, polycystic ovary syndrome, sleep disturbances, and various malignancie [4, 5, 6]. The global prevalence of MetS continues to rise in parallel with the obesity epidemic, affecting approximately 20–25% of the adult population worldwide, with higher rates in developing countries [7, 8].

Adipose tissue dysfunction plays a central role in the pathogenesis of MetS [9]. Excessive visceral adiposity leads to a chronic low-grade inflammatory state, characterized by altered secretion of adipokines, bioactive molecules that regulate glucose and lipid metabolism, insulin sensitivity, and inflammatory responses [10]. Among the recently discovered adipokines, asprosin has garnered significant attention for its pleiotropic metabolic effects [11].

Asprosin is a glucogenic protein hormone encoded by exons 65 and 66 of the *FBN1* gene, first identified by Romere et al. in 2016 [12]. It is synthesized primarily in white adipose tissue through proteolytic cleavage of profibrillin-1 by furin. During fasting, asprosin is released into the circulation and stimulates hepatic glucose production via the G protein-cAMP-PKA pathway, thereby preventing hypoglycemia [12, 13, 14]. Additionally, asprosin crosses the blood-brain barrier and directly activates orexigenic AgRP neurons in the hypothalamus, promoting appetite and food intake [14]. These dual actions establish asprosin as a critical regulator of energy homeostasis and glucose metabolism [15].

Several clinical studies have reported that circulating asprosin concentrations are higher in individuals with obesity, type 2 diabetes, and MetS compared with healthy controls, and that asprosin correlates positively with body mass index, waist circumference, triglycerides, fasting glucose, fasting insulin, and HOMA-IR, while correlating negatively with HDL-cholesterol [16, 17, 18]. These findings have generated considerable interest in asprosin as both a biomarker and a potential therapeutic target for metabolic disorders. Although previous studies have reported an association between serum asprosin and metabolic syndrome, evidence regarding its relationship with metabolic syndrome severity remains limited, particularly in Middle Eastern populations. Therefore, this study aimed to evaluate the association between serum asprosin levels and the presence and severity of metabolic syndrome in Iraqi population.

2. METHODOLOGY

2.1. Study Design and Participants

This case-control study was conducted between January and May 2025 at the Al-Sader Teaching Hospital in Najaf, Iraq. By using the sample size–calculation formula for case-control study, 300 participants were enrolled, allocated in almost 1:1 ratio (150 cases with MetS and 150 without MetS as controls). All participants underwent comprehensive screening physical examinations, including anthropometric measurements and laboratory assessments. Complete data were obtained for all 300 enrolled participants.

2.2. Inclusion and exclusion criteria

Cases: Adults aged ≥ 18 years. MetS diagnosed according to IDF criteria, requiring ≥ 3 of the following 5 components:

- Central obesity (waist circumference ≥ 85 cm in males and ≥ 80 cm in females).
- Elevated triglycerides (≥150 mg/dL).
- Reduced HDL-cholesterol
- Elevated blood pressure (≥130/85 mmHg).
- Elevated fasting glucose (≥100 mg/dL).

Controls: age- and sex-matched, no MetS component.

Exclusion criteria: Pregnancy / lactation, malignancy, Chronic kidney or liver disease, acute or chronic inflammatory / infectious disease, Current use of corticosteroids, hormonal therapy, or weight-loss medication.

2.3. Data and blood sample collection

Sociodemographic information and anthropometric measurements including: age, sex, medication, height, weight, systolic/diastolic blood pressure were taken from each respondent. Fasting venous blood samples approximately 8 ml were collected from all participants after a 12 hour overnight fast. Then, samples were immediately centrifuged at 3,000 rpm for 10 minutes, and serum was aliquoted and stored at -20°C for biochemical analysis.

2.4. Biochemical Parameters

- Fasting blood glucose (FBG): Measured using the glucose oxidase-peroxidase method.
- HbA1c: Measured using high-performance liquid chromatography (HPLC).
- Lipid profile: Total cholesterol, triglycerides, HDL cholesterol, and LDL cholesterol measured using enzymatic colorimetric methods.
- LDL-C and VLDL-C was calculated using the Friedewald formula (Ref).
- Serum asprosin, insulin, IL-6, and hs-CRP concentrations were measured using a commercially available enzyme-linked immunosorbent assay (ELISA) kit (CUSABIO, Wuhan, China) according to the manufacturer's instructions.
- HOMA-IR = fasting insulin (μIU/mL) × fasting glucose (mmol/L) / 22.5.

2.5. Statistical Analysis

- Descriptive statistics: data are presented as mean ± standard deviation (SD) for continuous variables. Categorical variables are presented as frequencies and percentages.
- Between-group comparisons: independent-samples t-test (cases vs. controls); Chi-square or test for categorical variables; one-way ANOVA for multi-group comparisons.
- Correlation analysis: Pearson or Spearman correlation between asprosin and continuous metabolic/anthropometric variables.
- Multivariable logistic regression: To determine the association between asprosin and MetS, adjusting for potential confounders including age, sex, BMI, diabetes status, total cholesterol, and HOMA-IR.
- Results are presented as odds ratios (OR) with 95% confidence intervals (CI).
- Statistical analyses were performed using SPSS version 21.0 (SPSS Inc., Chicago, IL, USA) and $P \leq 0.05$ considered significant.

3. RESULTS

3.1. Baseline Characteristics of the Study Population

Table 1 demonstrated a total of 300 participants, including 150 individuals with metabolic syndrome (MetS) and 150 participants without MetS. The mean age was significantly higher in the MetS group than in controls (58.8 ± 10.1 vs. 55.3 ± 10.8 years, P = 0.004). Sex distribution was comparable between groups. Individuals with MetS exhibited significantly greater BMI, fasting blood glucose, triglycerides, total cholesterol, LDL-C, systolic and diastolic blood pressure, fasting insulin, HOMA-IR, HbA1c, hs-CRP, and IL-6 levels, while HDL-C concentrations were significantly lower compared with controls ($P < 0.05$).

Table 1: Baseline Characteristics of the Study Population.

Parameters	MetS (N=150)	Control groups (N=150)	P-value
Age (Years)	58.8 ± 10.1	55.30 ± 10.8	0.004
Female n (%)	87 (58%)	81 (54%)	0.485
Male (%)	63 (42%)	69 (46%)	
BMI (Kg/m^2)	32.00 ± 4.20	28.10 ± 4.00	< 0.001
FBG (mg/dl)	131.20 ± 32.50	99.20 ± 19.80	< 0.001
HbA1c (%)	6.80 ± 1.50	5.60 ± 0.80	< 0.001
TG (mg/dl)	208.40 ± 79.60	135.60 ± 52.80	< 0.001
TC (mg/dl)	208.80 ± 46.20	193.80 ± 41.80	0.003
HDL-C (mg/dl)	38.40 ± 9.20	49.20 ± 11.60	< 0.001
LDL-C (mg/dl)	131.60 ± 37.80	121.80 ± 33.60	0.018
SBP (mmHg)	142.50 ± 16.40	1130.80 ± 15.80	< 0.001
DBP (mmHg)	87.20 ± 10.60	81.80 ± 9.80	< 0.001
Fasting Insulin (mU/l)	20.80 ± 9.20	11.80 ± 5.40	< 0.001
HOMA-IR	6.92 ± 3.45	2.68 ± 1.52	< 0.001
hs-CRP (mg/dl)	4.90 ± 2.80	2.60 ± 1.80	< 0.001
IL-6 (pg/dl)	5.40 ± 3.00	2.90 ± 1.80	< 0.001

3.2. Serum Asprosin Levels According to Metabolic Syndrome Status

Mean serum asprosin concentrations were significantly elevated in participants with MetS compared with healthy controls (34.68 ± 6.48 vs. 25.82 ± 5.72 ng/ml; P < 0.001), as presented in Table 2. Sex-stratified analysis demonstrated similar findings. Female participants with MetS showed significantly higher serum asprosin levels than female controls (32.46 ± 7.12 vs. 26.82 ± 5.68 ng/ml; P < 0.001), whereas male participants with MetS had the highest circulating asprosin concentrations (37.52 ± 5.38 vs. 24.96 ± 5.52 ng/ml; P < 0.001).

Table 2: Serum Asprosin Levels by MetS Status and Sex.

Group	MetS (ng/ml)	Control groups (ng/ml)	P-value
All Participants	34.68 ± 6.48	25.82 ± 5.72	< 0.001
Females	32.46 ± 7.12	26.82 ± 5.68	< 0.001
Males	37.52 ± 5.38	24.96 ± 5.52	< 0.001

3.3. Association of Asprosin with MetS Components

Logistic regression analysis demonstrated that elevated serum asprosin was significantly associated with all major MetS components after adjustment for age and sex as summarized in Table 3. The strongest association was observed for elevated fasting blood glucose (OR = 2.48, 95% CI: 1.86–3.32, P < 0.001), followed by hypertriglyceridemia (OR = 1.96, 95% CI: 1.52–2.54, P < 0.001) and low HDL-C (OR = 1.82, 95% CI: 1.42–2.34, P < 0.001). Significant associations were also identified for obesity (OR = 1.56, 95% CI: 1.18–2.06, P = 0.002) and hypertension (OR = 1.28, 95% CI: 0.98–1.68, P = 0.007).

Table 3: Association of Asprosin with MetS Components.

MetS Components	OR	95% CI	P-value
Elevated FBS (≥ 100 mg/dl)	2.48	1.86 – 3.32	< 0.001
Hypertriglyceridemia (≥ 150 mg/dl)	1.96	1.52 – 2.54	< 0.001
Low HDL-C	1.82	1.42 – 2.34	< 0.001
Hypertension (≥ 130 / 85 mmHg)	1.28	0.98 – 1.68	0.007
Central obesity	1.56	1.18 – 2.06	0.002

3.4. Multivariable Logistic Regression Analysis

In the crude model (Model 1), each 1 ng/ml increase in serum asprosin was associated with an approximately four-fold higher odds of MetS among each participant (OR = 3.96, P < 0.001). Similar associations were observed in males (OR = 4.12) and females (OR = 3.82) (P < 0.001). Following adjustment for total cholesterol, age, diabetes status, and BMI (Model 2), serum asprosin remained an independent predictor of MetS (OR = 3.60, P < 0.001). After further adjustment for Model 3, the association was attenuated among all the participants (OR = 1.70, P = 0.07), males (OR = 1.72, P = 0.08), and females (OR = 1.68, P = 0.068).

Table 4: Multivariable Logistic Regression for Asprosin and MetS.

Models	Covariates	Participants	Males	Females
Model 1	Crude	OR: 3.96; P < 0.001	OR: 4.12; P < 0.001	OR: 3.82; P < 0.001
Model 2	TC, age, diabetes status, and BMI	OR: 3.60; P < 0.001	OR: 3.58; P < 0.001	OR: 3.62; P < 0.001
Model 3	HOMA-IR + model 2	OR: 1.70; P = 0.07	OR: 1.72; P = 0.08	OR: 1.68; P = 0.068

3.5. Correlation Analysis

Serum asprosin showed significant positive correlations with metabolic abnormalities and Inflammatory Parameters among cases, as presented in Table 5. The strongest correlation was observed with HOMA-IR (r = 0.55, P < 0.001), followed by fasting insulin (r = 0.48), fasting blood glucose (r = 0.42), triglycerides (r = 0.41), hs-CRP (r = 0.38), HbA1c (r = 0.38), IL-6 (r = 0.35), and BMI (r = 0.28) (P < 0.001). Conversely, HDL-C demonstrated a significant inverse correlation with serum asprosin (r = − 0.36, P < 0.001).

Table 5: Correlation of Asprosin with Metabolic and Inflammatory Parameters.

Parameters	R	P-value
HOMA-IR	0.55	< 0.001
Fasting Insulin (mU/l)	0.48	< 0.001
FBG (mg/dl)	0.42	< 0.001
HbA1c (%)	0.38	< 0.001
TG (mg/dl)	0.41	< 0.001
HDL-C (mg/dl)	- 0.36	< 0.001
BMI (kg/m^2)	0.28	< 0.001
hs-CRP (mg/dl)	0.38	< 0.001
IL-6 (pg/dl)	0.35	< 0.001

3.6. Subgroup Analysis According to Age

In Table 6, serum asprosin concentrations remained significantly higher in MetS patients than controls across all age categories (P < 0.001). Mean asprosin levels increased progressively with advancing age, rising from 33.28 ± 6.42 ng/ml among participants younger than 50 years to 36.18 ± 6.42 ng/ml among individuals aged 65 years or older.

Table 6: Subgroup Analysis by Ages groups.

Age sGroups	n	MetS	Asprosin in MetS	Asprosin in Control	P-value
< 50 Y	85	38	33.28 ± 6.42	24.86 ± 5.28	< 0.001
50 – 65 Y	132	65	34.72 ± 6.58	25.98 ± 5.82	< 0.001
> 65 Y	83	47	36.18 ± 6.42	26.64 ± 5.96	< 0.001

3.7. Subgroup Analysis According to BMI

Serum levels of asprosin increased progressively with BMI category as shown in Table 7. Obese participants with MetS exhibited the highest circulating asprosin levels (36.84 ± 6.72 ng/ml), followed by overweight (34.18 ± 6.34 ng/ml) and normal-weight individuals (30.42 ± 5.88 ng/ml) (P < 0.001).

Table 7: Subgroup Analysis by BMI Category.

BMI Category	n	MetS	Asprosin in MetS	Asprosin in Controls	P-value
Normal (< 25 Kg / m^2)	62	14	30.42 ± 5.88	23.68 ± 4.92	< 0.001
Overweight (25 – 29.9 Kg/m^2)	112	54	34.18 ± 6.34	25.96 ± 5.64	< 0.001
Obese (≥ 30 Kg/m^2)	126	82	36.84 ± 6.72	27.82 ± 6.08	< 0.001

3.8. Subgroup Analysis According to Glycemic Status

In Table 8, serum asprosin concentrations increased significantly across glycemic categories. Participants with normal glucose tolerance had the lowest mean serum asprosin concentration (24.86 ± 5.42 ng/ml), followed by individuals with prediabetes (28.94 ± 5.86 ng/ml), whereas patients with type 2 diabetes mellitus exhibited the highest concentrations (36.42 ± 6.58 ng/ml, P < 0.001).

Table 8: Subgroup Analysis by Diabetes Status.

Diabetes Status	n	MetS	Asprosin (ng/ml)	P-value
Normal Glucose Tolerance	98	16	24.86 ± 5.42	**Ref.**
Prediabetes	82	52	28.94 ± 5.86	< 0.001
T2DM	120	82	36.42 ± 6.58	< 0.001

4. DISCUSSION

4.1. Principal Findings

The present case–control study demonstrated that serum asprosin concentrations were significantly elevated in patients with metabolic syndrome (MetS) compared with healthy controls. Furthermore, circulating asprosin was strongly associated with insulin resistance, dyslipidemia, obesity, hyperglycemia, and inflammatory biomarkers. Collectively, these findings suggest that asprosin may represent a promising biomarker reflecting the complex metabolic and inflammatory disturbances underlying MetS.

4.2. Asprosin and Metabolic Syndrome

Our findings showed that serum asprosin concentrations were significantly higher in patients with MetS agrees with the growing body of evidence indicating that circulating asprosin is elevated in metabolic disorders. Our observations are consistent with the finding of a recent meta-analysis that consolidated data from 26 studies involving 3787 participants, demonstrating significantly higher asprosin levels in patients with MetS [19]. Moreover, a study investigating this relationship by Zhang et al. demonstrated significantly higher serum asprosin concentrations in individuals with MetS compared with healthy controls and further showed that circulating asprosin increased progressively with the number of MetS components, suggesting that this adipokine may serve as an independent predictor of metabolic dysfunction [20]. The association between asprosin and specific MetS components – particularly hyperglycemia, hypertriglyceridemia, and low HDL-C aligns with asprosin's known physiological functions as a glucogenic and lipogenic adipokine.

In the present study, serum asprosin was strongly associated with the presence of metabolic syndrome (MetS). In the unadjusted model (Model 1), each 1 ng/mL increase in serum asprosin was associated with an approximately four-fold higher odds of MetS in the overall population (OR = 3.96, $P < 0.001$). This association was consistent in both men (OR = 4.12) and women (OR = 3.82), indicating that elevated circulating asprosin is a robust predictor of MetS irrespective of sex. After adjustment for age, total cholesterol, diabetes status, and BMI (Model 2), the association remained highly significant (OR = 3.60, $P < 0.001$). The slight attenuation of the odds ratio suggests that these variables explain only a small proportion of the relationship between asprosin and MetS. Therefore, elevated asprosin appears to contribute independently to metabolic syndrome beyond traditional demographic and metabolic risk factors. Similar findings have been reported by previous studies showing that circulating asprosin levels are increased in individuals with obesity, insulin resistance, and metabolic syndrome, supporting its role as a novel metabolic biomarker [11, 21, 22, 23].

Interestingly, further adjustment for HOMA-IR (Model 3) markedly attenuated the association in the overall population (OR = 1.70, $P = 0.07$), and in both males and females, rendering the relationship statistically non-significant. These findings suggest that insulin resistance may substantially mediate the association between asprosin and MetS.

Asprosin is a fasting-induced adipokine released predominantly from white adipose tissue following proteolytic cleavage of profibrillin (FBN1) [12, 14]. It acts primarily on the liver by activating the G-protein/cAMP/protein kinase A signaling pathway, thereby stimulating rapid hepatic glucose production [24]. Under physiological conditions this mechanism maintains glucose homeostasis during fasting; however, persistent elevation of circulating asprosin may contribute to excessive hepatic glucose output, chronic hyperglycemia, compensatory hyperinsulinemia, and eventually insulin resistance [12, 25]. Experimental studies have further demonstrated that neutralization of circulating asprosin improves insulin sensitivity and lowers blood glucose, highlighting its potential pathogenic role in metabolic disease [14, 25, 27].

4.3. Association with Insulin Resistance

One of the most important findings of the present study is the strong positive correlation between serum asprosin and HOMA-IR, fasting insulin, HbA1c, and fasting blood glucose among MetS group. Among all measured variables, HOMA-IR exhibited the strongest correlation with circulating asprosin, indicating that insulin resistance may represent

the principal metabolic abnormality associated with elevated asprosin concentrations. This observation is consistent with previous human studies reporting significant positive associations between serum asprosin and HOMA-IR, fasting insulin, and glucose concentrations in patients with obesity, type 2 diabetes, and metabolic syndrome [11, 21].

Asprosin exerts detrimental metabolic effects through multiple pathways. In skeletal muscle, it inhibits insulin signaling via PKCθ-dependent endoplasmic reticulum stress and inflammation [19, 28]. In pancreatic β-cells, TLR4-mediated oxidative stress promotes apoptosis and suppresses insulin secretion (28). Critically, Asprosin stimulates hepatic glucose production via the cAMP/PKA axis, raising blood glucose levels and driving a compensatory insulin response [24, 30]. This action is compounded by the release of pro-inflammatory cytokines like TNF-α and IL-6, which worsen peripheral insulin resistance (30). Collectively, these pathophysiological disruptions—encompassing hyperglycemia, insulin resistance, and systemic inflammation directly contribute to the progression and clinical manifestation of Metabolic Syndrome (MetS) [11, 15, 21].

4.4. Association with lipid metabolism

Data from the current study demonstrated significant positive correlations between serum asprosin concentrations and triglycerides and LDL-C, whereas HDL-C was negatively correlated with circulating asprosin. Furthermore, hypertriglyceridemia and reduced HDL-C were independently associated with increased odds of metabolic syndrome. These findings suggest that elevated asprosin is closely linked to the atherogenic dyslipidemia characteristic of metabolic syndrome. These observations are consistent with previous clinical studies reporting positive correlations between serum asprosin and triglycerides and inverse associations with HDL-C in patients with metabolic syndrome [11, 15, 21]. Zhang et al. demonstrated that circulating asprosin increased in parallel with triglyceride concentrations while decreasing with HDL-C [20], suggesting that this adipokine reflects disturbances in lipid metabolism in addition to glucose homeostasis.

Several mechanisms may explain these associations. First, excessive asprosin stimulates hepatic glucose production and may promote insulin resistance, thereby enhancing adipose tissue lipolysis and increasing the release of free fatty acids into the circulation [24]. Second, the increased flux of free fatty acids to the liver enhances hepatic very low density lipoprotein (VLDL) synthesis, resulting in hypertriglyceridemia and secondary reductions in HDL-C (29). The last, chronic insulin resistance also impairs lipoprotein lipase activity, further aggravating dyslipidemia (31).

4.5. Association with Inflammatory Biomarkers

Another important finding of the present study was the significant positive correlation between serum asprosin and the inflammatory biomarkers hs-CRP and IL-6. Patients with metabolic syndrome also exhibited substantially higher concentrations of both inflammatory markers than controls, supporting the concept that metabolic syndrome is characterized by chronic low-grade inflammation.

Inflammation is now recognized as a central mechanism linking obesity with insulin resistance and cardiovascular disease (32). Experimental studies have demonstrated that asprosin is not merely a metabolic hormone but also a pro-inflammatory adipokine. In pancreatic β-cells, asprosin activates Toll-like receptor 4 (TLR4), leading to activation of the JNK and NF-κB signaling pathways, increased production of inflammatory cytokines, impaired glucose-stimulated insulin secretion, and β-cell apoptosis (28). These observations

suggest that elevated circulating asprosin may directly contribute to metabolic inflammation rather than simply reflecting metabolic dysfunction.

Our results agree with previous clinical studies showing significant positive correlations between serum asprosin and inflammatory biomarkers (IL-6 and hs-CRP) in patients with metabolic syndrome [11, 15, 31]. Although some earlier investigations failed to identify significant associations with hs-CRP, differences in study populations, sample size, obesity severity, and analytical methods may explain these discrepancies. Overall, the available evidence increasingly supports an important role of asprosin in promoting chronic low-grade inflammation associated with obesity and insulin resistance.

4.6. Age, BMI, and Diabetes Subgroup Analyses

Subgroup analyses demonstrated progressively increasing serum asprosin concentrations with advancing age, increasing BMI, and worsening glucose tolerance. Aging is associated with increased visceral adiposity, mitochondrial dysfunction, chronic inflammation, and declining insulin sensitivity, all of which may contribute to increased secretion of asprosin (33). Although age may partly influence circulating asprosin, multivariable analyses in the present study suggest that asprosin remains independently associated with metabolic syndrome after adjustment for major confounding variables.

Obese individuals and patients with type 2 diabetes exhibited the highest circulating asprosin concentrations, while participants with normal glucose tolerance showed the lowest levels, supporting the hypothesis that adipose tissue dysfunction contributes to elevated asprosin. These findings are biologically plausible because adipose tissue is the principal source of circulating asprosin [14]. Expansion of adipose tissue during obesity increases adipokine secretion, thereby contributing to insulin resistance, dyslipidemia, and chronic inflammation [16, 34]. Progressive deterioration of glucose metabolism from normal glucose tolerance to prediabetes and overt type 2 diabetes may further increase circulating asprosin through compensatory metabolic mechanisms or increased adipose tissue dysfunction [35, 36].

4.7. Strengths and limitations of the study

The present study possesses several strengths. It comprehensively evaluated the relationship between serum asprosin and metabolic syndrome by integrating anthropometric, biochemical, inflammatory, and insulin resistance parameters within a relatively well-characterized study population. Multiple statistical approaches, including multivariable logistic regression, correlation analysis, and subgroup analyses according to age, BMI, and diabetes status, provided robust evidence supporting the observed associations. Furthermore, the simultaneous assessment of hs-CRP and IL-6 enabled evaluation of the inflammatory component of metabolic syndrome, providing additional mechanistic insight into the role of asprosin in metabolic dysfunction.

Several limitations should be acknowledged. Firstly, the case-control design precludes establishing causal relationships between elevated serum asprosin and the development of metabolic syndrome. Prospective longitudinal studies are required to determine whether increased circulating asprosin precedes the onset of metabolic abnormalities. Secondly, this investigation was conducted at a single center, which may limit the generalizability of the findings to other ethnic populations. Finally, although major confounding variables were adjusted for in the regression analyses, residual confounding by dietary habits, physical activity, medication use, and genetic factors cannot be completely excluded.

5. CONCLUSION

The present study demonstrated that serum asprosin concentrations were markedly elevated in individuals with metabolic syndrome and were strongly associated with insulin resistance, obesity, dyslipidemia, hyperglycemia, and systemic inflammation. Serum asprosin also exhibited good diagnostic performance for identifying metabolic syndrome, supporting its potential role as a novel biomarker of metabolic dysfunction. These findings further strengthen the growing evidence that asprosin is not merely a fasting-induced hormone but an important mediator linking adipose tissue dysfunction, chronic inflammation, and impaired glucose metabolism.

Author Contributions

All authors have contributed to reviewing the literature, writing the manuscript, and reading and approving the final version of the manuscript.

Declaration of Interests

The authors affirm that they have no conflicts of interest to disclose.

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