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ORIGINAL ARTICLE

ASPROSIN AND ITS RELATIONSHIP TO INSULIN RESISTANCE IN METABOLIC SYNDROME

Shaha Abdallha Mohammed [1], Thikra Ali Allwsh [2] ✉

[1] Biochemistry laboratory, Ibn Sina Teaching Hospital, Mosul, Iraq
[2] Department of Chemistry, Collage of Science, University of Mosul, Mosul, Iraq

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Summary

Background: Asprosin is correlated to many pathologic of glucose dysregulation, insulin resistance, β-cell dysfunction, serum lipids, and adiposity.
Objective investigating the role of the asprosin hormone and its relationship to insulin resistance in newly diagnosed metabolic syndrome and clinical parameters.
Methods: The study included measurement of asprosin hormone, insulin, insulin resistance and some biochemical variable levels in metabolic syndrome patients with age matching to the control group (35 - 65 years). The study included the measurement of asprosin hormone. MetS were diagnosed in compliance with the European Group for the Study of Insulin Resistance (EGIR) criteria for patients attending the abdominal consultation unit at the Ibn Sina Teaching Hospital in Mosul, Iraq.
Results: The findings revealed a significant increase in the concertation of asprosin hormone in metabolic syndrome patients compared to the control group. Also, it has been found that was a significant increase in the concertation of glucose, insulin, homeostasis model for insulin resistance (HOMA-IR), Glucose to insulin Ratio(G/I), Triglyceride Glucose index (TyG), and McAuley Index, in addition to decreasing in homeostasis model for β-cell function(HOMA-%β), sensitivity of insulin(HOMA-%S) and Quantitative insulin sensitivity check index(QUICKI) in the metabolic syndrome patients. there is also a significant positive correlation between asprosin hormone with insulin resistance.
Conclusion: Findings indicated that serum levels of asprosin and insulin resistance are increased in patients with metabolic syndrome. Also, they have a relationship with clinical parameters. So asprosin hormone can be used new biomarker of metabolic turbulence.

Key words: Asprosin; insulin; metabolic syndrome; insulin resistance

Introduction

Metabolic syndrome (MetS) is characterised by a number of abnormal physical and laboratory findings that are brought on by the interaction of biochemical, clinical, physiological, and metabolic factors. As a result, atherosclerosis, cardiovascular disease, and overall mortality are significantly increased (1), also The metabolic

✉ University of Mosul, Collage of Science, Department of Chemistry, Mosul, Iraq
thekraaliallwsh@uomosul.edu.iq

syndrome, which comprises hypertension, glucose intolerance, dyslipidemia, and abdominal obesity, is known as a metabolic disease with persistent low-grade inflammation (2). Although there has been much discussion on the definition and concept of the syndrome, there is little doubt that this conglomeration of risk factors is associated with a higher risk of type 2 diabetes and cardiovascular disease (3). Whatever the exact criteria, it is estimated that an increase in people who have MetS (4). A key factor in the development of metabolic syndrome is insulin resistance. Insulin resistance causes an increase in insulin secretion (5). Insulin sensitivity is associated with a healthy weight, moderate activity, a low-fat diet, and the absence of visceral or abdominal obesity (6).

A brand-new adipokine called asprosin was discovered in 2016 by Romere *et al*. (7). Adipokines are cytokines that are released from adipose tissue and have a wide range of biological effects (8). As a result of profibrillin's C-terminal domain breaking down, asprosin is generated in adipocytes in response to hunger (7, 9). By turning on the G protein-cAMP-PKA pathway, it quickly releases glucose from liver cells (9). It is believed that adipokine balance is crucial in controlling insulin sensitivity (10). Additionally, certain research (11, 12) has demonstrated a correlation between asprosin serum levels and insulin sensitivity.

Many types of metabolic illnesses linked to insulin resistance may now be successfully treated by concentrating on how asprosin works and how it relates to this condition (13–15). In both people and mice additionally, asprosin causes pancreatic cells to become inflamed and to die (14). Elevated asprosin levels have been linked to both type 2 diabetes (T2DM) and polycystic ovarian syndrome (PCOS) insulin resistance (15). Additionally, in participants with unstable angina pectoris, a relationship between asprosin levels and the degree of coronary artery disease was described (16). Asprosin also has inflammatory properties (17).

We focused on determining the degree of asprosin change in newly diagnosed metabolic syndrome since there isn't enough information about the relationship between asprosin and the condition of metabolic syndrome. In addition, we sought to determine if asprosin and metabolic parameters in metabolic syndrome were related.

Materials and methods

Ethical approval

This study has received ethical approval from the Iraqi Ministry of Health - Nineveh Health. Before collecting samples, written informed permission was acquired from each participant.

Research Objectives

From the beginning of August 2021 to the end of December 2021, samples from (95) metabolic syndrome patients (49) females and (46) males between the ages of (35 – 65 years) were gathered for this study. All samples were from MetS patients visiting the abdominal consultation unit at the Ibn Sina Teaching Hospital in Mosul, and they were chosen at random. According to the criteria of the European Group for the Study of Insulin Resistance (EGIR) (18), which included fasting glucose, blood pressure, blood lipids, and waist circumference, MetS were identified.

The control group, which included samples from (76) healthy individuals who matched the patient’s age and body mass index and did not have (MetS), diabetes, high blood pressure, or any other medical conditions, as well as no medication, was also included in the study. This group included samples (40) females and (36) males.

Age, gender, and family medical history were among the information gathered. Systolic and diastolic blood pressures were taken twice with an automated device, and the average values were utilized and after the participant had been sitting for at least five minutes, their blood pressure was checked. Weight in kg/height in m2 was used to determine the body mass index (BMI).

Five milliliters of venous blood from each participant was drawn after an overnight fast [of 12 hours], and the serum was extracted by centrifuging the blood for 10-15 minutes at 4000 (rpm) to get the serum that was separated and refrigerated in aliquots at -20°C until utilized.

Laboratory Evaluation

The serum asprosin hormone was measured by using an Enzyme-Linked Immunosorbent Assay (ELISA) kit from SUN LONG Biological Technology Co., Ltd kit (China).

Insulin hormone was measured by using an Enzyme-Linked Immunosorbent Assay (ELISA) technique Sandwich using a Monobind kit (USA).

Fasting glucose, high-density lipoprotein-cholesterol (HDL-C) and triglyceride (TG) were determined by using ready-made assay (kits) from the company (BIOLABS) and using enzymatic colorimetric methods.

HOMA-IR= insulin (μU/ml) × glucose (m mol/L) / 22.5 (19)
HOMA-β (%) = insulin (μU /ml) × 20 / (glucose (m mol/ L)-3.5) (20)
Glucose to Insulin Ratio G/I =Fasting glucose(mg/dl) /Fasting Insulin(μU) (21)
Quantitative Insulin Sensitivity Check index(QUICKI)= 1 / log (fasting insulin, IU/ml) + log (fasting glucose, mg/dl) (22)
Triglyceride Glucose (TyG) Index = In[T.G(mg/dl) × fasting glucose (mg/dl)] /2 (23)
McAuley Index== e2.63−0.28 ln (fasting Insulin μU/ml)−0.31 ln (TG mmol/L) (24)
HOMA-%S =1 / HOMA-IR (25)

Data Analysis: The data is shown as mean ± SE . P values ≤ 0.05 are considered significant while comparing the MetS group to the healthy group for data analysis using the student's t-test. Pearson correlation coefficient (r)-based linear regression analysis was applied to determine the relation between various clinical parameters.

Results

Comparison of Baseline Data

General clinical and anthropometric details of MetS and controls are shown in Table 1. The BMI, waist circumference, TG, systolic blood pressure (SBP), and diastolic blood pressure (DBP) of MetS patients were substantially higher significant at level (P ≤ 0.01) than those of the controls but lower level high-density lipoprotein- cholesterol (HDL-C) in serum of MetS group.

Table 1. Detailed Clinical and Anthropological Features of MetS and Control Groups.

Variables	Controls means ± SE	MetS means ± SE
No. of subjects	76	95
Age (years)	44.3 ± 7. 6	48.1 ± 5. 9*
Gender, M/F	36/40	46/49
SBP (mm Hg)	125.3 ± 13.1	141.2 ± 14.5*
DBP (mm Hg)	78.4 ± 7.9	91.5 ± 6.1*
BMI (kg/m^2)	25.8 ± 1.9	29.7 ± 3.5*
Waist circumference (cm)	88.4 ± 5.5	97.7 ± 7.3*
Smoking	No	No
TC (mmol/l)	4.21 ± 0.4	6.45 ± 0.9*
HDL cholesterol (mmol/l)	1.18 ± 0.1	0.90 ± 0.1*

* Significant at the level (P ≤ 0.01)

The results in Table 2 showed a significant rise in the levels of glucose, insulin, insulin resistance, glucose to insulin (G/L) ratio, McAuley Index, and Triglyceride Glucose Index (TyG), but a fall in homeostasis model

assessment for beta-cell function (HOMA- **β**), (QUICKI), and (HOMA-%S) in serum patients with metabolic syndrome when compared to the control group at the level ($P \leq 0.01$).

Table 2. Glucose, Index of Insulin Resistance and Sensitivity for MetS and Control Groups.

Clinical parameters	Control means ± SE	MetS means ± SE
F.B.S (mmol/L)	4.8 ± 0.47	6.42 ± 0.35*
Insulin	8.23 ± 2.2	14.1 ± 3.7*
HOMA-IR	1.78 ± 0.51	4.02 ± 1.24*
G/I	0.58 ± 3.23	0.45 ± 1.78*
QUICKI	0.35 ± 0.07	0.31 ± 0.06*
McAuley	5.36 ± 1.33	379.9 ± 12.33*
TyG	8.64 ± 1.21	11.1 ± 1.5*
HOMA-β	126.6 ± 12.38	96.5 ± 10.58*
HOMA-%S	0.56 ± 0.031	0.24 ± 0.022*

* Significant at the level ($P \leq 0.01$)

Asprosin hormone and insulin resistance levels in patients with metabolic syndrome and Control Groups

Acording to the results in Table 3, the asprosin hormone's normal level was (53.8± 3.7 ng/L) in the healthy control group, and it was elevated significantly at the probability level ($P \leq 0.01$) for metabolic syndrome patient groups (65.6 ±4.4 ng/l).

Also, the results in Table 3 shown, based on BMI, there is a significant increase in the level ($P \leq 0.01$) of asprosin hormone in the control and metabolic syndrome patient groups with increased BMI.

Table 3 findings showed, insulin resistance (HOMA-IR) levels were (1.78 ± 0.51) in the healthy control group and were significantly higher (3.97 ± 0.63) in the metabolic syndrome patient groups at the probability level ($P \leq 0.01$).

Based on BMI, Table 3 show that there is a significantly higher level of insulin resistance HOMA-IR for the control and metabolic syndrome patient groups depending on BMI at the level ($P \leq 0.01$).

Table 3. Comparison of Asprosin Hormone and HOMA-IR Levels Based on (BMI) for MetS and Control Groups.

Variables	Asprosin (ng/L)		HOMA-IR	
	Control means ± SE	MetS means ± SE	Control means ± SE	MetS means ± SE
Underweight	36.7 ± 3.7	27.2 ± 4.8*	1.52 ± 0.33	3.17 ± 0.59*
Normal weight	45.9 ± 3.2	66.8 ± 4.2*	1.97 ± 0.41	3.88 ± 0.61*
Overweight	58.8 ± 2.7	74.1 ± 5.1*	2.14 ± 0.52	4.09 ± 0.74*
Obese	71.9 ± 3.2	88.9 ± 2.8*	2.87 ± 0.58	5.37 ± 0.86*
TOTAL	53.8 ± 3.7	65.6 ± 4.4*	2.12 ± 0.46	4.12 ± 0.7*

* Significant at the level ($P \leq 0.01$)

Correlation between Asprosin Hormone and Insulin Resistance HOMA-IR for MetS and Control Groups

Serum asprosin and insulin resistance (HOMA-IR) were positively correlated with adiposity-related parameters (BMI and waist circumference) at the level ($P \leq 0.01$) and the results in Table 4 showed that asprosin and insulin

resistance (HOMA-IR) had a positive correlation with fasting glucose,fasting insulin, glucose to insulin (G/L) ratio, McAuley Index, and Triglyceride Glucose Index (TyG), and a negative relationship with beta- cell function, (HOMA-% β), Quantitative Insulin Sensitivity Check index (QUICKI), as well as a negative relationship with a sensitivity of insulin (HOMA-%S), in MetS and control groups at the level ($P \leq 0.01$).

Table 4. Correlation between Asprosin Hormone and Insulin Resistance (HOMA-IR) for MetS and Control Groups.

Clinical Parameters	Asprosin Hormone r-value	Insulin Resistance (HOMA-IR) r-value
Asprosin	1	0.214*
Waist circumference (cm)	+0.171*	0.222*
BMI (kg/m^2)	+0.206*	0.270*
SBP (mm Hg)	+0.102*	0.144*
DBP (mm Hg)	+0.111*	0.172*
TG (mmol/l)	0.251*	0.336*
F.B.S (mmol/L)	+0.302*	0.677*
Insulin	+0.518*	0.435*
HOMA-%β	-0.567*	0.211*
HOMA-%S	-0.522*	0.290*
G/I	+0.468*	0.395*
QUICKI	-0.641*	0.466*
McAuley	+0.446*	0.519*
TyG	+0.254*	0.635*

* Significant at the level ($P \leq 0.01$)

Discussion

For the data in the current study, all participants patients with metabolic syndrome with a baseline information examination were shown to have a high body mass index (BMI) , waist circumference, as well as elevated blood pressure, triglyceride (TG), fasting glucose, fasting insulin, the homeostasis model for insulin resistance (HOMA-IR), glucose to insulin ratio (G/I), triglyceride glucose index (TyG), the McAuley Index, and a decline in HDL-C, homeostasis model assessment for beta-cell function (HOMA- β), (QUICKI), and (HOMA-%S).

All of these findings are consistent with previous research showing that increased waist circumference, elevated hypertension, plasma fasting glucose, TG and reduced HDL-C. Correlates strongly with risk of diabetes, hypertension and dyslipidemia, which are the features of metabolic syndrome (26-27) as well as one high blood pressure is One of the main characteristics of metabolic syndrome (28). The necessity of identifying individuals with metabolic syndrome as a group at high risk for the development of cardiovascular disease is emphasised in the clinical recommendations for managing hypertension published by the European Society of Cardiology (29) metabolic syndrome may intensify the cardiac and renal abnormalities associated with hypertension.

An increase in the levels of fasting glucose, fasting insulin and (HOMA-IR) may be related to cells compensating for insulin resistance by secreting more insulin, which results in hyperinsulinemia, and these tissues are less sensitive to insulin actions because they are full of fat (30-31). Additionally, excessive insulin production causes an imbalance in pancreatic beta cells, which can result in MetS, which result in significant increases in the proportion of glucose in the blood as a response to insulin resistance due to the rise in (FFA) in the blood, which causes hyperlipidemia (27, 32). Dyslipidemia and hyperglycemia are pathological characteristics specific to MetS and are crucial in the onset of the disease in both T2DM patients and healthy controls (33-34).

Serum asprosin levels were higher in MetS than in control groups. Furthermore, all participants control and patients with obesity (high BMI) had significantly higher serum asprosin levels than those without (35-36) they have demonstrated that serum asprosin levels were markedly elevated in MetS and it has evidence for the association between asprosin and MetS (37-38) that corroborated that of recent research done on patients with T2DM (16). Moreover, studies in mice and persons with IR have discovered that plasma asprosin was pathologically raised, but asprosin-specific monoclonal antibodies decreased plasma asprosin and increased insulin sensitivity in these mice (7, 39) the increase in serum asprosin in MetS maybe was a compensatory response to the metabolic load brought on by obesity, hyperglycemia, or hyperlipidemia (32, 35). Hence, we speculated that asprosin may serve as a risk factor associated with the pathogenesis of MetS.

Zhang *et al.* found that serum asprosin concentrations were significantly correlated with adiposity-related variables like BMI, waist circumference, and waist-hip ratio in T2DM. Asprosin and BMI did, however, have favorable correlation in their study's healthy group (12). Patients with obesity (16, 40), insulin resistance (12, 15), and diabetes mellitus type 2 DM2 (12, 41) were also shown to have elevated asprosin levels. Previous research has demonstrated a link between asprosin and insulin resistance (12, 14).

Asprosin serum concentrations were found to be considerably greater in T2DM patients than in healthy control as well as asprosin and the following measurements were positively and significantly correlated in T2DM patients: FBG, HOMA-IR, Glucose to Insulin Ratio (G/I), Triglyceride Glucose Index (TyG), and McAuley Index. Additionally, there was a negative and substantial correlation between asprosin serum concentrations in T2DM patients and QUICKI, HOM-A, and HOMA-S. (42-43).

Insulin resistance occurs in the majority of metabolic syndrome sufferers, to transport glucose into cells for utilisation as energy, the body produces insulin (44). Obesity makes it harder for body cells to react to insulin, which is frequently seen in patients with metabolic syndrome. Age-related declines in exercise cause weight gain, which is often concentrated in the belly, and can make the body more resistant to the hormone insulin.

Metabolic syndrome can increase your risk of developing insulin resistance, which can cause your blood sugar levels to rise. Eventually, can lead to type 2 diabetes.

Conclusion

In both patients with metabolic syndrome and healthy people, there is a clear correlation between the levels of asprosin hormones in the blood and insulin resistance, as well as glucose, insulin, triglycerides, weight, blood pressure, and high-density lipoprotein cholesterol. So, the novel biomarker of metabolic turbulence is asprosin hormone, which could open new horizons for solving metabolic problems.

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Conflict of Interest

The authors have no conflicts of interest regarding the publication of this article.

Adherence to Ethical Standards

This study has received ethical approval from the Medical Research (Research No. 111/21) Ethics Committee in the Iraqi Ministry of Health - Nineveh Health. The study approval number and date)32772 on 14 /9/2021).

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