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ASPROSINA: RELAÇÃO COM O ESTRESSE OXIDATIVO EM PACIENTES COM SÍNDROME METABÓLICA EM MOSUL/IRAQUE

ASPROSIN: RELATION TO OXIDATIVE STRESS FOR METABOLIC SYNDROME PATIENTS IN MOSUL/IRAQ

الأسبروسين: العلاقة مع الإجهاد التأكسدي لدى مرضى المتلازمة الأيضية في الموصل/العراق

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RESUMO

Introdução: A asprosina é um hormônio proteico importante na regulação do apetite; glicose e metabólitos lipídicos são secretados durante o jejum. **Objetivos**: O presente estudo investiga a relação entre o nível de asprosina e o estresse oxidativo na Síndrome Metabólica (MetS). **Métodos**: O estudo incluiu 171 participantes com idade entre 35-65 anos, divididos em dois grupos: um grupo controle, que incluiu 75 participantes, e um grupo de pacientes, que incluiu 95 participantes em tratamento no Hospital Educacional Ibn Sina na cidade iraquiana de Mosul. A aprovação ética foi obtida do Ministério da Saúde do Iraque - Saúde de Nínive. Cinco mililitros de sangue venoso foram coletados após jejum durante uma noite inteira para realizar testes de fatores oxidativos e antioxidativos, bem como avaliações clínicas. **Resultados**: Os níveis do hormônio asprosina na MetS aumentaram significativamente, mas houve uma diminuição significativa dos antioxidantes (glutationa, capacidade antioxidante total e arilesterase), além de um aumento substancial na malondialdeído, lactoperoxidase e peroxidase. Foi encontrado através do coeficiente de correlação linear (R) que havia uma correlação positiva significativa entre asprosina e fatores oxidativos e uma correlação inversa com variáveis antioxidantes. **Discussão**: Esses achados sugerem que a asprosina é um indicador de distúrbios metabólicos e está associada à MetS e aos indicadores de estresse oxidativo. **Conclusões**: Portanto, pode ser considerada um novo indicador e uma ferramenta promissora para diagnóstico e tratamento para iniciar e desenvolver MetS

Palavras-chave: *Hormônio Asprosina, Estresse Oxidativo, Síndrome Metabólica, Resistência à Insulina, Capacidade Antioxidante Total.*

ABSTRACT

Background: Asprosin is a protein hormone important in regulating appetite; glucose and lipid metabolites are secreted during fasting. **Aims**: The present study investigates the relationship between asprosin level and oxidative stress in MetS. **Methods**: The study included 171 participants persons aged 35–65 years who were divided into two groups: a control group, which included 75 participants, and a patient group, which included 95 participants from patients getting treatment at the Ibn Sina Educational Hospital in the Iraqi city of Mosul. Ethical approval was obtained from the Iraqi Ministry of Health - Nineveh Health. Five milliliters of venous blood were taken following a fast for an entire night. To perform oxidative and antioxidative factor tests as well as clinical evaluations. **Results**: Asprosin hormone levels in MetS significantly increased, but a significant decrease of antioxidative (glutathione, total antioxidant capacity, and arylesterase) also A substantial rise in malondialdehyde, lactoperoxidase, and peroxidase. It was found through the linear correlation coefficient (R) that there was a significant positive correlation between asprosin and oxidative and an inverse correlation with antioxidative variables. **Discussion**: These findings imply that asprosin is an indicator of metabolic disorders and is associated with MetS and oxidative stress indicators. **Conclusions**: Therefore, it can be considered a new indicator and a promising tool for diagnosis and treatment to initiate and develop MetS .

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Keywords: *Asprosin Hormone; Oxidative Stress; Metabolic Syndrome; Insulin Resistance; total antioxidant capacity*

الملخص

الخلفية : الأسبروسين هرمون بروتيني مهم لتنظيم الشهية، وايض الكلوكوز والدهون ويتم إفرازه أثناء الصيام. تبحث الدراسة الحالية في العلاقة بين مستوى الأسبروسين والإجهاد التأكسدي في متلازمة الايض , **طرق العمل**: شملت الدراسة 171 مشاركاً تتراوح أعمارهم بين 35-65 سنة تم تقسيمهم إلى مجموعتين: مجموعة ضابطة الاصحاء التي ضمت 75 مشاركاً، ومجموعة المرضى التي ضمت 95 مشاركاً من المرضى الذين يتلقون العلاج في مستشفى ابن سينا التعليمي في مدينة الموصل العراقية. تم الحصول على الموافقة الأخلاقية من وزارة الصحة العراقية – صحة نينوى. تم أخذ خمسة ملليترات من الدم الوريدي بعد صيام ليلة كاملة لإجراء اختبارات العوامل المؤكسدة ومضادات الأكسدة وكذلك التقييمات السريرية. **النتائج**: مستويات هرمون الأسبروسين زادت بشكل ملحوظ في مرضى متلازمة الايض ولكن هناك انخفاض كبير في مضادات الأكسدة (الكلوتاثيون ، القدرة الكلية لمضادات الأكسدة، والأريل استريز) بالإضافة إلى ارتفاع كبير في المالونديالدهيد، اللاكتوبيروكسيديز، والبيروكسيديز. وقد وجد من خلال معامل الارتباط الخطي علاقة معنوية موجبة بين الأسبروسين والمواد المؤكسدة كذلك وجدا ارتباط عكسي بين الأسبروسين والمواد المضادة للأكسدة. **الاستنتاج:** تشير هذه النتائج إلى أن الأسبروسين هو مؤشر على الاضطرابات الأيضية ويرتبط بمؤشرات متلازمة الايض والإجهاد التأكسدي. ولذلك يمكن اعتباره مؤشرا جديدا وأداة واعدة لتشخيص وعلاج بدء وتطوير متلازمة الايض .

الكلمات المفتاحية. *هرمون الاسبروسين.الاجهاد التاكسدي؛ متلازمة الأيض؛ مقاومة الأنسولين ؛ القدرة الكلية لمضادة الاكسدة*

1. INTRODUCTION:

Asprosin is a protein hormone that is produced in mammals. It was discovered for the first time in 2016 during a study on a rare genetic disease known as neonatal progeroid syndrome (Romere *et al.,* 2016; Duerrschmid *et al.,* 2017). White adipose tissue is the main source of asprosin in humans and mice, and it is considered an adipokine (Zhang *et al.*, 2020). It was found that asprosin has multiple effects, including regulating appetite, glucose metabolism, insulin resistance, and programmed cell death in pancreatic cells (Yuan *et al.,* 2020; Jung *et al.,* 2019). Asprosin also impairs the sensitivity of muscle cells to insulin by promoting inflammation and oxidative stress, which leads to insulin resistance (Yuan *et al.,* 2020).

Metabolic Syndrome (MetS, MetSy) has been described and became widely used at the end of the twentieth century (Alberti *et al.,* 2009; Catharina *et al.,* 2018). It isn't a disease in itself but rather an umbrella term for risk factors for individuals at increased risk of developing vascular diseases, high blood sugar, and lipids. MetS is characterized by a disorder of oxidative stress levels (Šebeková *et al.,* 2023; Rezzani *et al.,* 2021). Several mechanisms of oxidative stress processes have been suggested in the MetS, including changed metabolism of lipids and glucose, chronic inflammation, and ROS production (Colak *et al.,* 2021; Vona *et al.,* 2019).

The current study intends to examine variations in the hormone asprosin in MetS patients, determine what factors influence it, and investigate its link to oxidative stress.

2. MATERIALS AND METHODS:

2.1. Materials

The hormones (asprosin and insulin), total antioxidant capacity, glucose, triglyceride, and high-density lipoprotein cholesterol levels were assayed using kits. Malondialdehyde (MDA), glutathione (GSH), arylesterase, lactoperoxidase, and peroxidase levels were assayed using Chemical methods using high-purity chemicals from Sigma-Aldrich companies.

2. 1.1.Study design

2.1.1.1.Patient group

Inclusion of 95 participants with MetS, (49) were females and (46) males ages (35–65 years), all patients of Arab origins from the city of Mosul / Iraq review the Ibn Sina Education Hospital, noting that the patients were diagnosed by specialized doctors and were chosen according to the criteria of (AHA/NHLBI) (Fahed *et al.,* 2022). The patient's information was recorded according to the questionnaire paper, noting that the patient has no family history of the disease.

2.1.1.2. Control Group:

The study included 76 healthy participants (36 males and 40 females) whose ages matched those of the patient group.

2.2. Methods

2.2.1. Estimation of demographic and clinical parameters:

Blood pressure (Brunström and Carlberg 2016), Body mass index (BMI), and waist circumference (Ross *et al*., 2020) were estimated for participants in control and patient groups.

2.2.2. Blood Sample Collection

Five milliliters of blood were taken from all participants after an overnight fast, and the blood was centrifuged for 20 minutes at 4000 rpm to produce the serum. The serum was stored in the freezer at -20 °C (Haque *et al*., 2019).

2.2.3.Hormone Evaluation

Hormones of Asprosin and insulin levels were tested using an Enzyme-Linked Immunosorbent Assay (ELISA) kit from S. B. T. Co. (China) (Acara *et al*., 2018).

2.2.4. Total Antioxidant Capacity Measurements

The total antioxidant capacity(T-AOC) concentration, which represents the total amount of antioxidants in the serum, was measured using a colorimetric technique kit from the Chinese firm Solarbio (Munteanu *et al*., 2021).

2.2.5.Clinical Evaluations

Glucose, triglyceride, and high-density lipoprotein cholesterol levels were measured using enzymatic colorimetric techniques (kits).

Using mathematical equations, it was estimated that HOMA-IR and HOMA -β (%) (Jasim *et al*., 2021).Glucose to Insulin Ratio (G/I) and Triglyceride Glucose (TyG) Index (Wang *et al*., 2021).

HOMA-IR=insulin(µU/ml)×glucose (mmol/l) /22.5

HOMA-B = [(Insulin (µU/ml)×20)/glucose (mmol/l)]-3.5

G/I= Fasting glucose(mg/dl)/Fasting Insulin (µU/ml)

TyG = ln[T.G(mg/dl) ×fasting glucose(mg/dl)]/2

2.2.6. Estimation of oxidative stress markers

Serum concentrations of oxidative stress markers, namely malondialdehyde (MDA) and glutathione (GSH), as well as the effectiveness of the following enzymes, arylesterase, lactoperoxidase, and peroxidase, were estimated using chemical methods described previously (Allwsh, 2013).

2.3. Data Analysis:

The statistical analysis of the study results was conducted through the following:

- Found the mean ± SE
- Used the t-test to compare two groups
- Found the Pearson correlation coefficient (r) to determine a linear relationship between variables
- The result is considered significant at P values ≤ 0.05

3. RESULTS AND DISCUSSION:

3.1. Results

3.1.1. Criteria approved to diagnose metabolic syndrome:

The clinical and anthropometric Baseline Data of control groups and MetS and Criteria approved to diagnose MetS are shown in (Table 1).

The results showed a significant rise in BMI, waist circumference, blood pressure (BP), glucose, and TG but lower (HDL-C) in the Mets group when contrasted to controls at (P ≤ 0.01).

Table 1: *Features of Clinical and Anthropological*

Indicators	Control group means ± SE	MetS group means ± SE
BMI (kg/m^2)	25.8 ± 1. 9	29.7± 3.5*
Waist circumference (cm)	85.3 ± 6.4	98.3 ± 8. 1*
BP (mm Hg)	125/78 ± 13/7	141/91± 14/6*
Glucose (mmol/L)	4.8±0.47	6.4 ± 0.3*
HDL (mmol/L)	1.21± 0.2	0.8 ±0.3*
TG (mmol/L)	1.13 ± 0.6	3.54 ± 0.5*

* significant at P values ≤ 0.01

3.1.2. Indicators of Insulin Resistance for MetS

Table 2 shows a significant rise in insulin, (TyG) Index, HOMA-IR, and (G/I) ratio but a significantly lower (HOMA-β) (P ≤ 0.01) in the MetS group when contrasted to controls.

Table 2: *The Indicators of Insulin Resistance and Sensitivity for MetS and Control Groups.*

Indicators	Control group means ± SE	MetS group means ± SE
Insulin (I)	8.23±2.2	14.1 ± 3.7*
HOMA-IR	1.78± 0.51	4.0 ± 1.2*
HOMA-β	126.6±12.38	96.5±10.58*
Triglyceride Glucose (TyG) Index	8.64±1.21	11.1±1.5*
Ratio Glucose to Insulin (G/I)	0.61 ±0.2	0.51±0.1*

* significant at P values ≤ 0.01

3.1.3. Asprosin Hormone for MetS

The results in Table 3 showed a 13.6% significant increase of asprosin hormone in the MetS group when contrasted to the control group (53.8± 3.7 ng/L).

Table 3: *ASPROSIN Hormone for Control Groups and MetS.*

Asprosin hormone (ng/L)			
Variables	Control group means ± SE	MetS group means ± SE	%
TOTAL	**53.8±3.7**	65.6± 4.4*	13.6

* significant at P values ≤ 0.01

3.1. 4. Oxidative and Antioxidant Variables for MetS

Table 4 shows a significant reduction (P≤0.01) in glutathione, antioxidant capacity, and arylesterase activity in MetS serum compared to the control group. MetS showed significantly higher levels of peroxidase, lactoperoxidase activity, and malondialdehyde compared to the control group (P≤0.01).

Table 4: *Oxidative and Antioxidant Variables for MetS and Control Groups*

Asprosine		
Oxidative and Antioxidant Variable	**MetS r-value**	Controls r-value
Glutathione (µmol/l)	-0.433*	- 0.518
Total Antioxidant Capacity (µmol/g)	- 0.611*	- 0.656
Aryleasterase(U/ml)	-0.668*	-0.735
Peroxidase(U/ml)	+0.583*	+0.521
Lactoperoxidase(U/ml)	+0.436*	+0.320
Malondialdehyde (MDA) (µ mol/l)	+0.760*	+0.589

*significant at P values ≤ 0.01

3.1.5. The Relationship between Asprosin Hormone and Oxidative and Antioxidant Variables for MetS

Table 5 showed that there was an inverse correlation significant at (P≤0.01) between the level of asprosin hormone with glutathione, the total antioxidant capacity, and aryleasterase activity, also a positive correlation significance at (P≤0.01) between asprosin hormone with peroxidase, lactoperoxidase activity and malondialdehyde in MetS and control groups.

Table 5: *Asprosin Relation to Oxidative and Antioxidant Variables for MetS and Control Groups.*

Oxidative and Antioxidant Variables	Controls Mean± SE	MetS Mean ± SE
Glutathione (µmol/l)	13.71±1.75	8.55±1.09*
Total Antioxidant Capacity(µmol/g)	0.66±0.0 4	0.44±0.08*
Aryleasterase (U/ml)	132.48±4.99	96.41±8.59*
Malondialdehyde (µmol/l)	5.57± 0.42	8.65±0.63*
Peroxidase (U/ml)	158.60±11.42	194.9±15.75*
Lactoperoxidase (U /ml)	80.58±9.48	106.83±10.49 *

* significant at P values ≤ 0.01

3.2. Discussion

In the present study, all individuals who have MetS were shown to have an increase in the levels of (BMI), waist circumference, blood pressure, (TG) and glucose, also decline in HDL-C which are the features of diagnosed MetS

(Yasein *et al*., 2010; Grundy *et al*., 2005), this is due to an excessive increase in adipose tissue, especially in the abdomen, which has an important role in energy metabolism and causing obesity-related diseases, including high blood pressure and cardiovascular disease (Abdallha and Allwsh 2023).

The cells and tissues that are full of fat cause low sensitivity to insulin activity, a flaw in beta cells, and increased secreting of insulin, which results in a rise in glucose and is related to insulin resistance, which are characteristics of metabolic syndrome (Yasein *et al*., 2010; Abdallha and Allwsh 2023). TyG and (G/I) are new markers for the development of Mets because it is associated with a risk factor for heart disease, diabetes, and hyperlipidemia, which is due to it representing the relationship between fat and glucose metabolism (Wang *et al*., 2021; Quon *et al*., 1994).

The results revealed a rise of the hormone asprosin in MetS group, and the reason is that asprosin is an adipokine that regulates appetite, glucose balance, and insulin resistance and that the role of asprosin in the central nervous system is on neurons that lead to anorexia Proopiomelanocortin (POMC) and peptide neurons agouti-related peptide (AgRp) lead these the mechanisms leading to increased food intake, regulated energy balance, and the tendency to accumulate fat and increase body weight (Romere *et al*., 2016; Duerrschmid *et al*., 2017). Perhaps this is because the asprosin hormone is affected by the level of cholesterol and triglycerides, and the high level of fat leads to a rise in the asprosin hormone with an increase in blood pressure. (Aguilar *et al*., 2015) Found that high blood pressure is one of the important criteria in determining the MetS, and dyslipidemia is one of the most important characteristics that appear in people with MetS and plays an important role in high blood pressure (Wang *et al*., 2018).

Oxidative stress is described as an imbalance between the generation of oxidative substances, including reactive nitrogen compounds and reactive oxygen compounds, and the defending antioxidant mechanism, enzymatic and non-enzymatic (Masenga *et al*., 2023). It was found that the concentration of glutathione decreased in people with metabolic syndrome, where glutathione acts as an antioxidant that scavenges free radicals and protects the heart muscle, reduces fat oxidation, and reduces the percentage of oxidized LDL, so its concentration decreases (Bajic *et al*., 2019; Jasim and Allwsh 2021). Perhaps the reason for the decrease in glutathione concentration is a decrease in the activity of the glutathione peroxidase (Jasim and Allwsh 2021).

Also, a decrease was found in the concentration of the total antioxidant capacity of the group of MetS due to a defect in the oxidation mechanism and the action of antioxidants resulting from high levels of free radicals. MetS is due to high levels of free radicals due to fat oxidation, as the aryl esterase connects with HDL subunits to exercise its antioxidant activity (Ravi Kiran *et al*., 2016). The reason for its decrease is attributed to the association of fats with the free sulfhydryl group, which then becomes ineffective (Sabah and Allwsh, 2021).

The elevated malondialdehyde in MetS is produced by an increase in oxidative stress processes, which raises the amount of lipids and free radicals peroxide, increasing malondialdehyde (Sankhla *et al*., 2012). The elevated lactoperoxidase and peroxidase activity in MetS may be attributed to the effect of oxidative stress in the metabolic syndrome, as both of these enzymes belong to the oxidative variables whose efficacy rises in the context of oxidative damage, leading to a rise of resistance to insulin, malfunction in the activity of pancreas for beta cells, malfunction of the mitochondria, and complications of diabetes (Newsholme *et al*., 2019).

The inverse correlation between the hormone asprosin and each of glutathione and the total capacity of antioxidants and aryl esterase may be due to the decrease in antioxidant factors due to their consumption in the processes of oxidative stress, which causes a defect in the function of pancreatic beta cells, insulin secretion and the metabolism of sugars and fats (Masenga *et al*., 2023).

The direct correlation between The level of the hormone asprosin with peroxidase and lactoperoxidase activity and malondialdehyde may be due to elevated free radicals as a result of the effect of oxidative stress by the high concentration of glucose, lipid, and insulin in the metabolic syndrome.

These enzymes work to increase the products of oxidation processes, such as free radicals, malondialdehyde, and peroxides (Magacz *et al*., 2019; Vona *et al*., 2019).

4. CONCLUSIONS:

Asprosin hormone is a new biomarker correlated with metabolic syndrome and is also related to oxidative stress, and perhaps this is owing to the elevated levels of metabolic factors in the blood such as sugar, lipid, insulin, and insulin resistance in the metabolic syndrome. Hence, it is believed that the hormone asprosin plays a significant role in limiting oxidative stress by regulating metabolic factors.

5. DECLARATIONS

5.1. Study Limitations

This research is limited to the Model size, and the analyses were conducted under experimental circumstances.

5.2. Acknowledgements

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5.3. Funding source

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5.4. Competing Interests

There is no potential conflict of interest in this publication.

6. HUMAN AND ANIMAL-RELATED STUDIES

6.1. Ethical Approval

This study received ethical approval from the Medical Research Ethics Committee of the Iraqi Ministry of Health - Nineveh Health (Research No. 111/21, approval No. 32772, dated September 14, 2021). Before sample collection, each participant provided written informed consent.

6.2. Informed Consent

All participants provided written informed consent for both study participation and subsequent publication of research findings.

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