Original Research Article

Evaluation of serum asprosin levels in women with metabolic syndrome in Duhok City-Kurdistan Region/Iraq

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ABSTRACT

Background: Serum asprosin, a recently discovered hormone as a new adipocytokine, which has been associated with the regulation of both glucose and lipid metabolism, and insulin resistance. Metabolic syndrome considered as a disorder of lipid and glucose metabolism, with impairment in insulin function, which might be associated with serum asprosin, therefore, new researches focused on the role of asprosin in the pathogenesis of metabolic syndrome to clarify such relationship. This study aimed to evaluate serum asprosin levels in women with metabolic syndrome and compared with a woman without metabolic syndrome.

Methods: This study was performed at Obstetrics and Gynecology Hospital, and Mazi medical clinics in Duhok, Kurdistan Region-Iraq, the study was established from June, 2020 to January, 2021. In this cross-sectional study, serum asprosin concentration in 40 women with metabolic syndrome were compared with a 131 women without metabolic syndrome. The demographic data were collected, serum asprosin levels, lipid profile, fasting blood glucose, fasting insulin were biochemically analyzed by using the autoanalyzer machine COBASS series 6000 and ELISA technique.

Results: The mean age of women with metabolic syndrome was (24.36±3.23) and women without metabolic syndrome was (23.18±3.87), serum asprosin in women with metabolic syndrome was (18.34±5.4) ng/ml, while in women without metabolic syndrome was (7.48±5.82) with significant difference (p<0.001). In study population, there was a positive correlation between asprosin and body mass index, waist circumference, triglyceride, total cholesterol, fasting blood glucose, fasting insulin, and HOMA-IR (p<0.0001), while serum asprosin was negatively correlated with high density lipoprotein- cholesterol (p<0.01).

Conclusions: The study confirms that serum asprosin in women with metabolic syndrome was higher than in the control group.

Keywords: Insulin resistance, Asprosin, Metabolic syndrome, White adipose tissue

INTRODUCTION

Metabolic syndrome is considered as a cluster of disorders which are occurring collectively together, resulting in increasing the risk for cardiovascular disease, cerebrovascular accident and type 2 diabetes. The main biochemical findings seen in Metabolic syndrome represented by low serum high density lipoprotein-cholesterol, elevated triglyceride, high blood pressure as well as increased fasting plasma glucose which are in direct relation to the increase of adipogenesis, weight gain and increased waist circumferences. The prevalence of metabolic syndrome now a day is rapidly increasing problem worldwide which is ranges from 20 to 25% in the adult population. Further studies are demanding to be done on metabolic syndrome to demonstrate its predictive factors and pathogenesis. Adipocytokine excreted by white adipose tissue play a significant role in the
metabolism of energy in the entire body and are central component in the pathogenesis of the constellation of diseases associated with obesity. Changes in adipocytokine levels may make a major contribution to the occurrence of metabolic disorders. Recent researches have shown the importance of a fibrillin-1-derived hormone, and asprosin, which plays a role in Neonal Progeroid Syndrome and obesity, further more new studies revealed that adipocytokine might play an important role in the pathogenesis of Metabolic syndrome.

Asprosin consists of 140-amino-acids protein. The receptors of asprosin lie mainly in arcuate nucleus of hypothalamus, which contribute to the promotion of appetite and regulation of energy balance. While liver, pancreas, skeletal muscle and heart are other main target organs and tissues for action of asprosin. In fasting status asprosin act as fasting-induced glucagonetic hormone, that leads to glucose production and release from hepatocytes. In normal physiological conditions elevated serum insulin levels antagonize the action of asprosin, meanwhile in pathological conditions as seen in the case of obesity and insulin resistance a different situation was observed, as levels of asprosin are dramatically elevated, which, in turn result in enhancing appetite activity and disturbance in the energy homeostasis of body. Hence, as reported by Duerrschmid et al, which concluded that administration of anti-asprosin antibodies significantly suppressing food intake and decreased pathologically elevated asprosin levels in insulin-resistant (IR) and obese mice. On the basis of these findings, as Metabolic syndrome is significantly associated with lipid homeostasis, glucose and insulin resistant, asprosin seems to be a promising factor for understanding the pathophysiology of patient with metabolic syndrome and related diseases, so that we hypothesized that serum asprosin levels were altered in metabolic syndrome and its necessary to confirm this possibility. Therefore, a cross-sectional study was done in order to measured serum asprosin levels in women with metabolic syndrome and to demonstrate its association with different component of metabolic syndrome.

METHODS

This cross-sectional study was conducted to determine serum asprosin levels in women with and without metabolic syndrome. The study was established from June, 2020 to January, 2021. A total of 171 women (with ages ranging from 18-34 years) from Duhok city, Kurdistan Region-Iraq, attended Obstetrics and Gynecology Hospital, Mazi Private Laboratory and Mazi medical clinics were involved in the study. 40 (23.4%) women of study population were enrolled in this study as metabolic syndrome group, while 131 (76.6%) women were participated as a control group (women without metabolic syndrome). For collecting the necessary information from participants, a questionnaire type was used and they were informed about the aims and methods of the study, the privacy of their information. Informed written consents were subsequently obtained. Study variables within the questionnaire form included personal details (phone number, age, work and address), pregnancy history, height, weight, body mass index (BMI), waist circumference (WC), any history of any chronic diseases, oral hypoglycemic drug history or insulin therapeutic drugs. The National cholesterol education program adult treatment panel III guidelines was used for the diagnosis of metabolic syndrome, so that if three or more of the following criteria are available they were diagnosed as metabolic syndrome: waist circumference (>88 cm), serum triglycerides (≥150 mg/dL), HDL-C (<50 mg/dL), blood pressure (≥130/85 mm Hg), fasting blood glucose (≥100 mg/dL). Age-matched healthy women without features of metabolic syndrome and any clinical evidence of major diseases were involved in this study as control group. Measurement parameters, including height (cm), weight (kg), BMI, waist circumference (centimeter), blood pressures were measured by using standard methods. Participants were given directives to attend the lab for blood sampling in the morning after overnight fasting for about 10 hours. Serum samples were biochemically analyzed using the Autoanalyzer biochemical machine named COBASS series 6000 and ELISA technique at Mazi Private Laboratories in Duhok City. Fasting blood glucose, Total cholesterol, serum triglyceride, HDL-Cholesterol and fasting insulin were measured. The insulin resistance for each participant was calculated by utilizing homeostasis model assessment of insulin resistance (HOMA-IR) = fasting insulin (µU/ml) * fasting glucose (mg/dl)/405. The quantitative detection of serum asprosin concentrations were determined by using the commercial ELISA kits Human Asprosin ELISA kit (96 T) with the catalog No.:MBS7606420, sensitivity: 0.938 ng/ml (from My BioSource, Inc. San Diego, USA). The Scientific Committee and the Ethical Committee of the General Directorate of Health in Duhok have reviewed and approved the study protocols (Code of Ethics: 22062020-2).

Statistical analysis

Through the Statistical package for social sciences (SPSS) software version 25 the data were analyzed and indicated as the normal and mean standard division (±SD). In comparison with proportions, T-test was used. In addition, one-way variance analysis (ANOVA) was used to compare different groups. Pearson correlation was used for the estimation of the relationship between variables. ROC curve analysis was used to found the cut-off point of serum asprosin for prediction of metabolic syndrome. A p value of less than 0.05 has been statistically important in all experiments.

RESULTS

Demographic and biochemical parameters of study population

Demographic and Biochemical parameters of study population are elucidated in (Table 1).
Women with metabolic syndrome presented significantly higher mean values of BMI, waist circumference (WC), systolic blood pressure (SBP), diastolic blood pressure (DBP), total cholesterol, serum levels of TG, FBS, fasting insulin, HOMA-IR and serum asprosin, in comparison to women without metabolic syndrome (p<0.001). Except HDL-C which were higher in women without metabolic syndrome in comparison to women with metabolic syndrome (p<0.01). On the contrary, there was no significant variation in age across the groups (p>0.05).

**Association of asprosin concentration with demographic and biochemical parameters in study population**

According to Pearson correlation coefficient (r), there was a significant positive correlation (p<0.001) between serum asprosin and age, BMI, Waist circumference, T. Cholesterol, Triglyceride, FBS, Insulin, and HOMA-IR (p<0.05) in both groups. In contrary, serum asprosin was negatively correlated with HDL-C in both groups (p<0.001) (Table 2).

**Table 1: Comparison of the demographic and laboratory characteristics of the study population.**

| Variables                | Women with metabolic syndrome (n=40) | Women without metabolic syndrome (n=131) | p*  |
|--------------------------|--------------------------------------|----------------------------------------|-----|
| Age (years)              | 24.36 ± 3.23                        | 23.18 ± 3.87                          | NS  |
| BMI (kg/m2)              | 34.94 ± 5.82                        | 24.74 ± 4.97                          | <0.001 |
| Waist circumference (cm) | 100.85 ± 9.46                       | 75.48 ± 10.61                         | <0.001 |
| SBP (mmHg)               | 120.35 ± 13.37                      | 112.35 ± 11.37                       | <0.001 |
| DBP (mmHg)               | 82.03 ± 11.21                       | 75.82 ± 5.21                         | <0.001 |
| Cholesterol (mg/dl)      | 170.68 ± 34.62                      | 138.86 ± 24.74                       | <0.001 |
| Triglyceride (mg/dl)     | 157.28 ± 63.97                      | 84.07 ± 32.49                        | <0.001 |
| HDL-Cholesterol (mg/dl)  | 40.33 ± 8.10                        | 52.90 ± 10.63                        | <0.01 |
| FBS (mg/dl)              | 116.38 ± 27.68                      | 96.11 ± 9.65                         | <0.001 |
| Insulin (μU/mL)          | 17.81 ± 9.53                        | 13.76 ± 7.49                         | <0.001 |
| HOMA-IR                  | 5.28 ± 3.75                         | 3.33 ± 2.01                          | <0.001 |
| Serum asprosin (ng/ml)   | 18.34 ± 5.40                        | 7.48 ± 5.82                          | <0.001 |

According to components of metabolic syndrome, women with metabolic syndrome were divided into three groups (women with three, four and five components of metabolic syndrome). Levels of serum asprosin, were significantly increased as the components of metabolic syndrome increased, one-way ANOVA test demonstrated statistically significant difference among all groups (p<0.001). (Table 3).

**Table 2: Pearson correlation analysis between serum asprosin concentrations and possible affecting factors of the study population.**

| Variables                | Women with metabolic syndrome (n=40) | Women without metabolic syndrome (n=131) |
|--------------------------|--------------------------------------|----------------------------------------|
| Age (years)              | r 0.248 P value 0.001                 | r 0.525 P value 0.001                 |
| BMI (kg/m2)              | 0.423 0.005                           | 0.622 0.001                            |
| Waist circumference (cm) | 0.469 0.001                           | 0.592 0.001                            |
| SBP (mmHg)               | 0.249 0.01                            | 0.211 0.001                            |
| DBP (mmHg)               | 0.179 0.06                            | 0.198 NS                                |
| T. Cholesterol (mg/dl)   | 0.419 0.005                           | 0.502 0.001                            |
| Triglyceride (mg/dl)     | 0.410 0.007                           | 0.602 0.001                            |
| HDL-Cholesterol (mg/dl)  | -0.310 0.031                          | -0.396 0.001                           |
| FBS (mg/dl)              | 0.388 0.007                           | 0.652 0.001                            |
| Insulin (μU/mL)          | 0.392 <0.001                          | 0.301 0.001                            |
| HOMA-IR                  | 0.495 <0.001                          | 0.436 <0.001                           |

According to serum asprosin levels, all subjects were divided into three tertiles (T1: <4 ng/mL, T2: 4–13.5 ng/mL and T3: >13.5 ng/mL). The demographic and biochemical parameters for each category are listed in (Table 4). Parameters such as age, waist circumference, BMI, FBG, fasting insulin, T. Cholesterol, TG, and HOMA-IR increased in correspondence to tertiles. Parameter such as HDL-C decreased in correspondence to tertiles. One-way ANOVA test demonstrated statistically significant difference among all groups (p<0.001). The receiver operating characteristic (ROC) analysis showed that the cut-off value for serum asprosin to predict women with metabolic syndrome was (6.40 ng/ml) (p<0.001).
Table 3: Distribution of serum asprosin concentrations among different groups of women with metabolic syndrome.

| Variables               | Women with three components of metabolic syndrome (n=17) | Women with four components of metabolic syndrome (n=14) | Women with five components of metabolic syndrome (n=9) | P value |
|-------------------------|--------------------------------------------------------|--------------------------------------------------------|-------------------------------------------------------|---------|
| Serum asprosin (ng/ml)  | 13.23± 4.57                                            | 20.37± 5.01                                            | 21.07± 4.94                                           | <0.001  |

Table 4: Distribution of demographic and laboratory characteristics in different tertiles according to serum concentrations of asprosin in study population.

| Variables               | T1 Serum asprosin (< 4 ng/mL) N=47                  | T2 Serum asprosin (4–13.5 ng/mL) N=75                  | T3 Serum asprosin (> 13.5 ng/mL) N=49                  | P value |
|-------------------------|-----------------------------------------------------|-------------------------------------------------------|-------------------------------------------------------|---------|
| Serum asprosin (ng/ml)  | 2.39 ± 0.26                                         | 8.27 ± 2.66                                           | 19.62 ± 5.18                                          | <0.001  |
| Age (years)             | 21.91 ± 4.02                                        | 27.23 ± 8.14                                         | 28.19 ± 7.85                                          | <0.001  |
| BMI (kg/m2)             | 22.26 ± 3.52                                        | 26.60 ± 5.59                                         | 32.71 ± 6.91                                         | <0.001  |
| Waist circumference (cm)| 74.68 ± 8.68                                        | 77.99 ± 12.37                                      | 94.837 ± 16.274                                     | <0.001  |
| SBP (mmHg)              | 111.95 ± 10.01                                      | 114.42 ± 11.71                                      | 115.83± 14.80                                       | NS      |
| DBP (mmHg)              | 75.64 ± 6.36                                        | 76.50 ± 7.30                                         | 80.46 ± 11.583                                      | < 0.05  |
| Cholesterol (mg/dl)     | 131.45 ± 22.54                                      | 142.58 ± 25.34                                      | 168.25 ± 34.76                                     | <0.001  |
| Triglyceride (mg/dl)    | 67.95 ± 21.12                                       | 94.79± 37.11                                         | 146.46± 66.85                                      | <0.001  |
| HDL- Cholesterol (mg/dl)| 57.97 ± 6.85                                         | 51.59 ± 10.75                                       | 38.86 ± 7.22                                       | <0.001  |
| FBS (mg/dl)             | 91.64± 5.14                                         | 100.00 ±13.35                                     | 112.54 ± 26.64                                     | <0.001  |
| Insulin (μU/mL)         | 9.84± 3.01                                          | 14.19 ± 7.26                                         | 20.49 ± 9.82                                         | <0.001  |
| HOMA-IR                 | 2.23 ± 0.70                                         | 3.55 ± 1.95                                          | 5.79 ± 3.71                                          | <0.001  |

Figure 1: ROC curve analyses were done for serum asprosin in the study population.

It had an area under the curve (AUC) of 0.92, a sensitivity of 0.99, and a specificity of 0.71 (Figure 1).

DISCUSSION

The present research is one of the few studies that descriptively investigated serum asprosin levels in women with metabolic syndrome and its related factors. The results of this study showed that the mean serum concentrations of asprosin in women with metabolic syndrome were significantly higher than women without metabolic syndrome. There was a significant positive correlation between serum asprosin and age, BMI, Waist circumference, T. Cholesterol, Triglyceride, FBS, Insulin, and HOMA-IR in both groups. In contrary, serum asprosin was negatively correlated with HDL-C in both groups. We found that regardless the metabolic syndrome situation serum asprosin concentrations, were significantly increased as the components of metabolic syndrome increased.

Recently some researchers identified that asprosin secreted from Adipose tissue, as one of the novel adipokines, and elevated concentrations of it has been documented to be raised in patients with type two diabetes mellitus (T2DM).
and those with obesity.\textsuperscript{13,15} Regarding evidence for association of asprosin and metabolic syndrome components, tell now its obscure and not well studied.\textsuperscript{16} In this study, it was elucidated that women with metabolic syndrome were had markedly elevated serum asprosin concentrations, similarly to a finding conducted from newly established study done in patients with T2DM.\textsuperscript{17-19} However, the exact causes for an excessive production of asprosin in this condition is uncertain.\textsuperscript{20} Nevertheless, data from previous studies show that pathologically elevated serum asprosin concentrations were be found in mice and humans with IR, in addition improving in insulin resistant and reduction in serum asprosin levels were be seen in mice treated by asprosin-specific monoclonal antibody.\textsuperscript{9,11,21} So that, in this study it was suppose that asprosin might be considered as one of the risk factors that associated with the pathogenesis of metabolic syndrome.

Data from the current research clearly revealed a significant positive association between serum asprosin and fasting blood sugar, fasting insulin, and HOMA-IR in both study group. Insulin resistance in metabolic syndrome may have been caused by a high level of asprosin, which mediates the excretion of glucose from the liver into the blood stream, resulting in an accumulation of glucose in the blood and an excessive secretion of insulin to get rid from increased glucose levels and bringing it to normal physiologic status.\textsuperscript{8,20,22,23} As a result, in current research, increasing of the circulating asprosin levels of women with metabolic syndrome could be in order to neutralize the hyperinsulinemia observed in these patients.

In the current study, the serum asprosin was a positively correlated with BMI and waist circumference in both study group. As an increase in BMI and waist circumference indicated there were excessive fatty tissues deposit in the body, especially in the abdominal area. Consequently, the accumulation of these fats leads to an increase in asprosin secretion.\textsuperscript{2,24,25} The results of our study supported by many researchers, they found a positive correlation between serum asprosin and BMI in the women with T2DM and poly cystic ovarian syndrome (PCOS).\textsuperscript{16,23,25,27} In contrast with these findings, a cross-sectional study of Jiang et al revealed that in the PCOS women, serum asprosin was negatively correlated with body mass index.\textsuperscript{28}

Lipid abnormalities are characteristics and pathological status seen in person with metabolic syndrome and play a great role in the pathogenesis of the disease.\textsuperscript{19} Data from this study demonstrated that there was a strong positive association between serum asprosin and total cholesterol and triglyceride levels in women with metabolic syndrome. The findings, however, demonstrated the existence of a significant positive association between HDL-C and serum asprosin in women with metabolic syndrome. Similarly, serum asprosin had a significant positive association with total cholesterol and triglycerides in women without metabolic syndrome. Nonetheless, there was a strong negative association between HDL-C and serum asprosin in women without metabolic syndrome. This research discovered a significant correlation between dyslipidemia and increased asprosin levels in women with metabolic syndrome.

The effect of asprosin on metabolic parameters was most likely due to asprosin's appetite-stimulating effects, as it was previously stated that increased asprosin in T2DM patients impaired appetite and resulted in metabolic changes.\textsuperscript{15,23,29,30} Additionally, several metabolic hormones regulate the release of glucose from the liver into the circulation.\textsuperscript{31} Besides this, asprosin is one of a molecule that facilitates the release of liver glucose, and resulting in hyperglycemia.\textsuperscript{9} The current study's results corroborated to those of Li et al, Alan et al and Deniz et al.\textsuperscript{2,23,27}

In the current study, ROC curve analysis shown that asprosin might be a useful indicator for the discrimination of women with metabolic syndrome from those without metabolic syndrome in the studied population. The crude AUC of the ROC curve of asprosin for detecting metabolic syndrome was 0.92 and it was statistically significant.

Though our study had some limitations; firstly, the study was a cross sectional study and it was done in a single city. Secondly, sample size was small and could be one of the obstacles for creating general knowledge about the conclusion in this study. Finally, the present study contained only one ethnic group from Iraqi-Kurdish women.

**CONCLUSION**

The results from this research showed that serum asprosin increased in women with metabolic syndrome and was positively correlated with BMI, waist circumferences and SBP. Moreover, it was found out that serum asprosin positively correlated with fasting insulin, fasting blood sugar, HOMA-IR, total cholesterol and triglyceride in the study population. However, high density lipoprotein – cholesterol was negatively correlated with serum asprosin in both groups of the study population.

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**Ethical approval: The study was approved by the Institutional Ethics Committee**

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