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RESEARCH ARTICLE - MEDICAL TECHNIQUES

Concentration of Asprosin Associated with Poor Control of Type 2 Diabetes Mellitus in Diyala Province

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Abstract

A newly secreted adipokine called asprosin is brought on by fasting as well as encourages hepatic glucose release. Its loss of function through immunologic or genetic methods has a significant effect on lowering glucose and insulin as a result of decreased hepatic glucose release. This study aimed to measure the level of asprosin in a group of poor control hyperglycemic patients and compare its level with the control group and find its correlation with obesity and lipid profile. Asprosin level in serum was assessed by enzyme-linked immunosorbent assay (ELISA) technique for 110 Iraqi patients with type 2 diabetes mellitus(T2DM), as well as 70 individual healthy controls. Percentage of glycated hemoglobin (HbAIc), fasting blood glucose (FBG), total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL) and low-density lipoprotein (LDL) concentration were calculated using Roche cobas integra 400 plus. Patients with type 2 diabetes mellitus reported increased levels of asprosin in their blood when compared with controls ($p < 0.001$). A significant positive correlation was seen between asprosin and FBG in patient's ($P< 0.05$). Non-significant correlation was seen between asprosin and body mass index (BMI) or lipid profile. In conclusion, according to the asprosin level in serum, there was a highly significant difference between patients with type 2 diabetes mellitus and control group. BMI and lipid abnormalities were not correlated to asprosin level in the serum of patients.

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Keywords: Asprosin; Poor Control; Type 2 Diabetes Mellitus; BMI.

1. Introduction

One of the major public health issues is diabetes mellitus (DM), has seen an increase in prevalence in latest years [1]. According to some sources, the etiology of diabetes may be influenced by genetic factors, physical and chemical factors, obesity, inactivity, and an unhealthy diet. Adipokines, which are released from adipose tissue, an endocrine organ, have been implicated in the pathogenesis and development of diabetes, according to the latest research [2].

White adipose tissue releases asprosin, a novel secreted adipokine that targets the liver and is induced by fasting. Asprosin activates the G protein–cyclic adenosine monophosphate–protein kinase pathway A to cause hepatic glucose release [3,4]. Additionally, it has been demonstrated to activate the hypothalamic feeding center, causing appetite to increase and fat to be stored [5]. Patients with obesity [6,7], insulin resistance [8,9], type-1 diabetes mellitus (T1DM) [10] and type 2 diabetes mellitus (T2DM) [12], were found to have pathologically elevated asprosin levels.

A risk factor for the onset of DMT2 is elevated asprosin levels, and individuals with the condition also experience abnormal asprosin release as a result of variations in blood glucose levels [11]. Additionally, raised asprosin levels have been linked to both insulin resistance and the atherosclerotic risk factor for cardiovascular disease in DMT2 [12]. Given that asprosin has a prediabetogenic effect [3], it is crucial to keep in mind that hyperlipidemia can also cause asprosin release [13]. Activation of the toll-like receptor 4 (TLR4)/c-Jun N-terminal kinase (JNK) mediated pathway may result in dysfunction of the pancreatic beta-cells, which will impair the release of insulin. [13].

Pathologically elevated plasma asprosin is a sign of human insulin resistance, and its loss of function due to immunological or genetic factors has a significant impact on lowering blood sugar and insulin levels because it causes a reduction in hepatic glucose release [3]. As a result, individuals who have type 2 diabetes may benefit from the therapeutic targeting of asprosin [11]. Therefore, the purpose of this study was to compare asprosin level in the serum of patients and controls and found the relationship between BMI and lipid abnormalities which related to diabetes.

Nomenclature & Symbols			
FBG	Fasting Blood Glucose	T1DM	Type 1 Diabetes Mellitus
DMT2	Diabetes Mellitus Type 2	WHO	World Health Organization
HDL	High Density Lipoprotein	EDTA	Ethylenediaminetetraacetic Acid
LDL	Low Density Lipoprotein	ADA	American Diabetes Association
BMI	Body Mass Index	HbA1c	Hemoglobin A1c
TLR4	Toll-Like Receptor 4	SPSS	Statistical Package For Social Sciences
JNK	Jun N-Terminal Kinase	ROC	Receiver Operating Characteristic Curve
FBG	Fasting Blood Glucose	T1DM	Type 1 Diabetes Mellitus

2. Materials and Methods

2.1. Study design

The study involved one hundred and ten patients suffering from T2DM (38 males and 72 females) age range (40-70) years and seventy apparently healthy individuals (24 males and 46 females) were taken for comparison. Blood samples were collected from the patients at the Specialist Unit for Diabetes and Endocrinology in Baquba Teaching Hospital, Diyala. Iraq during February /2022 to July /2022.

The diagnosis of T2DM and selection of poor controlled hyperglycemic patients without complication related to diabetes was made by specialized consultants, according to the American Diabetes Association (ADA) protocol [14] considering the clinical history, laboratory tests and clinical features of the patients. In addition, all patients are categorized based on BMI by World Health Organization (WHO) guidelines. Patients with T2DM had a mean duration of disease of 8.8 ±4.1 years.

After 8 to 10h of fasting, 5 ml of blood samples were obtained from the patients and control. One ml was placed into Ethylenediaminetetraacetic acid (EDTA) tubes for HbA1c estimations. The remaining blood was separated by centrifugation, the serum was used to estimate FBG, TC, TG, HDL and LDL cholesterol before freezing the serum. The residual serum was kept frozen at -20°C until asprosin analysis is performed on it. The assessment of asprosin was made by enzyme-linked immunosorbent assay (ELISA) technique (My BioSource/USA) by the manufacturer's protocol. Glucose and other tests were assayed by auto analyzer ROCHE COBAS INTEGRA 400 PLUS. Information about the disease duration, age of onset, any treatments received, a person's family history, medical and surgical history were requested.

2.2. Exclusion criteria

T1DM patients, Presence of other autoimmune disease like Hashimoto's thyroiditis, patients with renal or liver disease, and neurological disorders. subjects with a history of acute or chronic infections, any other chronic diseases, under cortisol treatment and pregnant women.

2.3. Statistical analysis

The means of continuous variables were compared between the patient and control groups using a two-tailed independent samples t-test. The correlation between different variables were examined using the Spearman correlation test. Cohen's criterion was applied to assess the strength of the correlations. ROC curve analyses were performed for testing the ability of the study markers to differentiate between patients and control. SPSS version 26.0 (Chicago) and Microsoft Excel v.2016 were used for statistical analyses. Less than 0.05 was considered statistically significant.

3. Results

The research groups characteristics are displayed in Table 1. There was a highly significant elevated in the mean concentration of asprosin in serum of patients with uncontrolled diabetes mellitus (8.84± 2.11ng/ml) in comparison to healthy control (3.91± 0.55ng/ml) ($p < 0.001$), as shown in Fig. 1. The mean difference for the patients according to FBG and HbA1c was significantly higher ($p < 0.001$) in comparison with control individuals. The mean concentration of BMI for patient was higher (29.41± 4.36) than control individuals without significant difference ($p = 0.064$).

Data illustrated in Fig. 2 demonstrated that the mean values of cholesterol, triglyceride and LDL were (196.60± 48.39, 241.11± 108.94, 118.77± 39.05) respectively, while the mean values among control were (164.71± 28.31, 121.86± 39.66, 107.63± 26.17) respectively, with a significant difference between them. The mean value of HDL for patients was (39.27± 8.78) while for control was (43.29± 7.58).

Table 1. Comparison of the studied parameters' mean values between patients and controls

Variables	Groups	Mean± SD	P value
Asprosin ng/ml	Control patients	3.91± 0.55 8.84± 2.11	< 0.001
Glucose mg/ dl	Control patients	101.71± 9.26 275.58± 75.19	< 0.001
HbA1c %	Control patients	5.41± 0.51 10.47± 2.00	< 0.001
BMI kg/m^2	Control patients	28.13± 4.66 29.41± 4.36	0.064

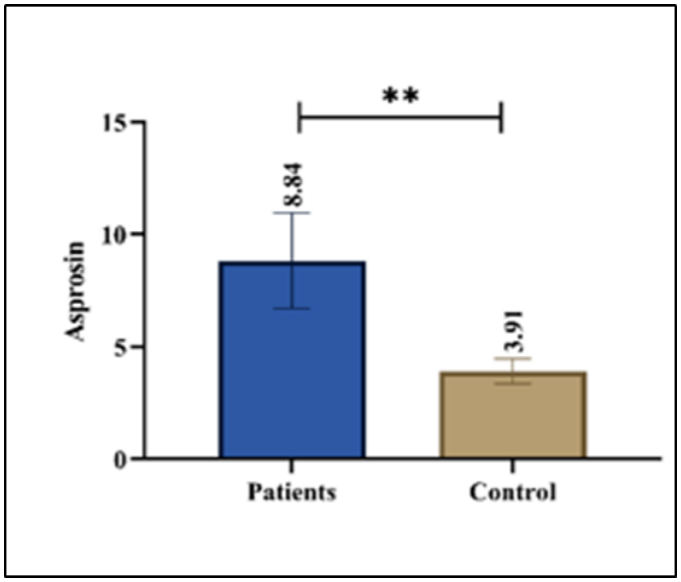

Fig. 1. The average difference between DMT2 patients and normal control according to asprosin

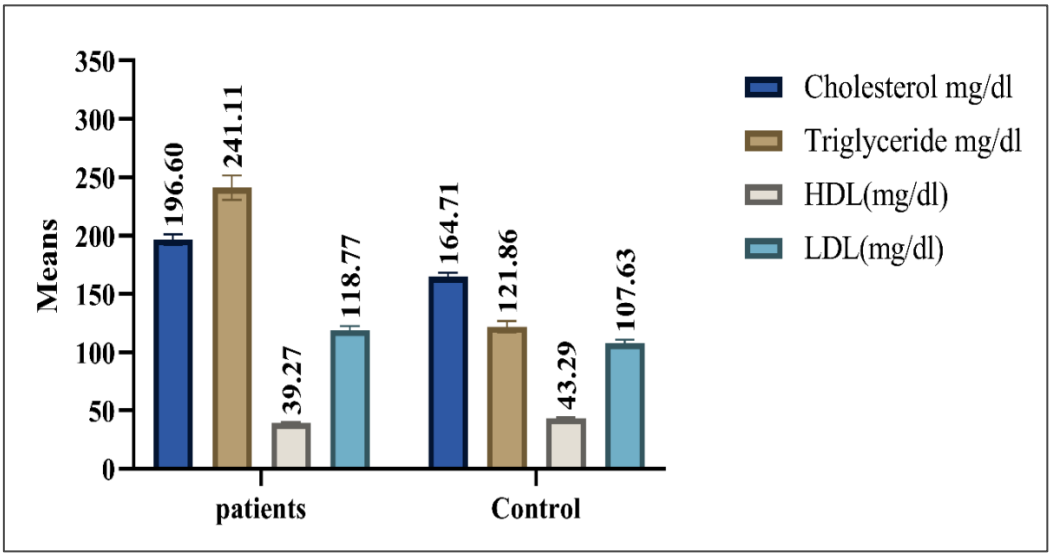

Fig. 2. Summary comparison of the serum lipid levels by groups

The correlation coefficients (r), classified by their P values, are shown in Table 2. A significant positive correlation was seen between asprosin and FBG in patients with T2DM (r =0.21 and p = 0.029), Fig. 3. Non-significant correlation was seen between serum asprosin and BMI,as shown in Fig. 4 . In addition, no significant correlation was seen between asprosin and HbA1c, TC, TG, HDL, LDL, age and duration of disease in patients individual (P> 0.05).

The diagnostic accuracy of asprosin for T2DM was calculated by using receiver operating characteristic curve (ROC) analyses. The area under the curve (AUC) of asprosin for differentiating patients with T2DM and control subjects was 0.990 (95% CI: 0.962 to 0.999). The cut-off value of asprosin for differentiating patients from control subjects was (>4.86). Sensitivity and Specificity of asprosin for distinguishing patients and control were 96.36 and 98.57 respectively, as shown in Fig. 5.

Table 2. Correlation coefficients between asprosin and (Glucose, HbA1c, lipid profile and other factors) in diabetes mellitus patients

		Glucose	HbA1c	BMI	Chol	HDL	LDL	TG	Age	Duration of disease
Asprosin	r	0.21	0.09	0.08	-0.02	0.03	0.01	-0.01	0.18	0.15
	p	0.029*	0.35	0.42	0.82	0.80	0.88	0.94	0.06	0.11

*Significant difference P < 0.05

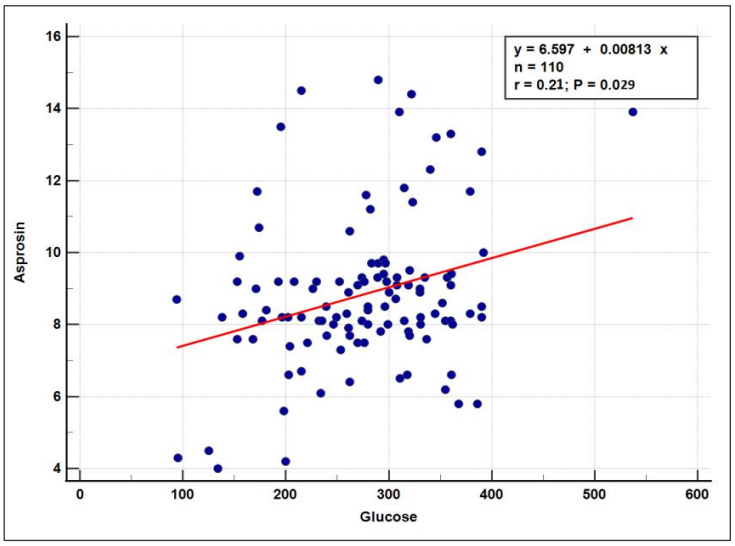

Fig. 3. Scatterplots with the correlation line added for Asprosin and FBG

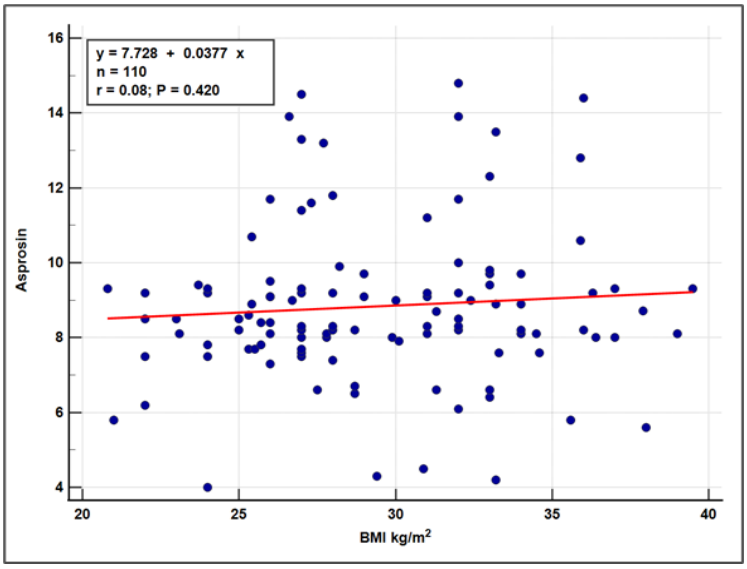

Fig. 4. Scatterplots with the correlation line added for Asprosin and BMI

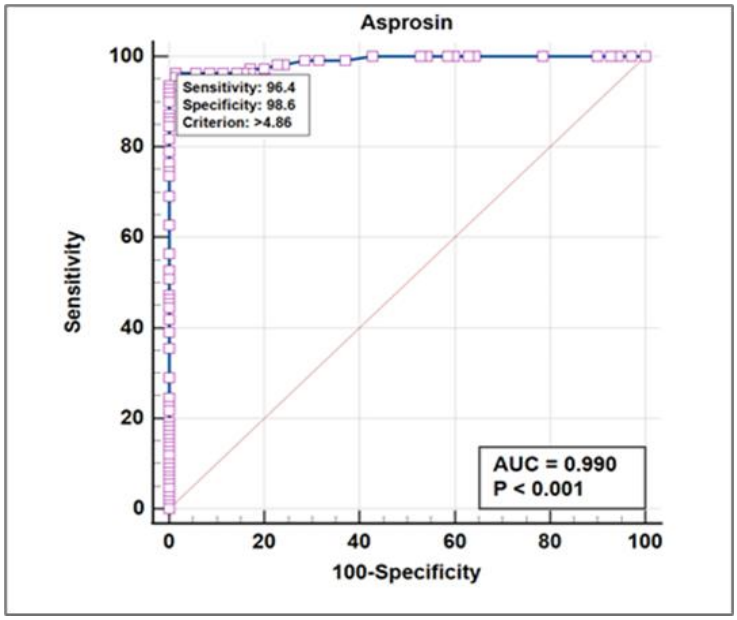

Fig. 5. ROC curve analysis for asprosin as they classifying for distinction between patients and control

4. Discussion

In this research the status of serum asprosin levels been assessed among a group of people with T2DM and their relationships with FBG, HbA1c, lipid profile and BMI. After the results of extensive research by scientists, asprosin is a newly discovered hormone that would significantly improve the health of patients with diabetes mellitus [15].

The current study's findings stated significantly elevated serum asprosin in uncontrolled patients with T2DM than in control group, which may be due to hyperglycemia or insulin resistance [16]. These results agreed with other studies that found the concentration of asprosin increased significantly in patients with T2DM in comparison with healthy control suggesting that the pathogenesis of the disease may be correlated with the hormone level as a risk factor [12], [17].

Glycogenolysis or gluconeogenesis are the mechanisms by which the liver produces glucose. As of now, hyperglycemia or an increase in gluconeogenic precursors like lactate, alanine, and glycerol may be the main causes of the rise in hepatic gluconeogenesis. Finally, fasting hyperglycemia happens. It has been hypothesized that an increase in the production of glucose by the liver is the only cause of fasting hyperglycemia [18]. Asprosin may be the cause of the increased liver glucose production, because it increases in starvation and makes the liver release glucose [19]. Diabetic dyslipidemia is a typical complication. Higher serum triglyceride levels, low HDL cholesterol levels, and an increased level of LDL are hallmarks of diabetic dyslipidemia. Elevated free fatty acid flux as a result of insulin resistance is responsible for the lipid changes linked to diabetes mellitus [20].

In the present study, the significant positive correlation between serum asprosin level and FBG is in agreement with Wang et al. [8]. who found that a significant positive correlation was seen between serum asprosin and serum glucose.

The mean concentration of BMI for patients is higher than the healthy control, hence, with a high percentage of patients with overweight BMI, the absence of correlation between asprosin level and BMI with lipid abnormalities ($P > 0.05$) demonstrate that obesity and other abnormalities correlated to lipids imbalance in T2DM may not be influenced by asprosin imbalance seen in diabetes. The result of this study was in agreement with previous study by Wang et al. [21], who found that there was no correlation between serum asprosin concentration and age, BMI, HbA1c, TC, TG, LDL and HDL. However, this study was incompatible with Naiemian et al. [12] who found a asignificant positive correlation between BMI and asprosin level in a group of patients with T2DM (($r=0.720$, $P < 0.05$).

The diagnostic precision was examined using ROC analyses, it was found that asprosin had high diagnostic precision (AUC =0.990) for distinguishing patients with T2DM from a healthy control. The asprosin cut-off value (>4.86) showed that it has high sensitivity and high specificity for identifying type 2 diabetes mellitus.

5. Conclusion

There was a highly significant difference between T2DM and the control group according to asprosin level in the sera. Due to the direct stimulation of hepatic glucose, asprosin has a positive correlation with hyperglycemia and the progression of type 2 diabetes. Indeed, in the stimulation of appetite by asprosin, no correlation was found between asprosin and obesity or lipid abnormalities in patients with uncontrolled type 2 diabetes mellitus.

Ethical Clearance

The study's goal and procedures were explained to each subject group individually. They gave their approval in order to take part in the study. The study was consented to by the Research Committee of the Diyala Health Department-Training and Human Development Center(no.30887).

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