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Original Research Article

Evaluation Asprosin Level in Polycystic Ovary Syndrome and Its Association with Fetuin a and Some Biochemical Parameter

Balasim J Mahmmoed[1], Nihad N Hilal[2], Entedhar R Sarhat[2*]

[1]University of Northern Technology, Kirkuk, Iraq
[2]College of Medicine University of Tikrit, Tikrit, Iraq

***Corresponding Author:** Entedhar R Sarhat
College of Medicine University of Tikrit, Tikrit, Iraq

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Abstract: An ovarian cyst is a common hormonal condition that affects women of reproductive age and affects the ovaries. Although the precise an etiology is unknown, environmental and genetic variables may play a role in the condition's genesis. Among the most significant symptoms are irregular menstruation, excessive hair growth, and acne. Early diagnosis is crucial since it can help control symptoms and possibly save chronic medical conditions from developing. The aim of this study was to evaluate the levels and relation of asprosin in patients of polycystic ovary syndrome. the relationship between asprosin with fetuin a and some parameter biochemical such as fasting blood sugar, insulin, cholesterol and triglyceride in woman patient's polycystic ovary syndrome. Ninety females were recruited into the study; 60 patients (females) aged between (15-45) years were taken and women that diagnosed with the Polycystic ovaries, by gynecological specialist. The result was a disruption in the hormones responsible for ovulation, such as LH, FSH, as well as an increase in the protein asprosin and fetuin a. On the other hand, 30 people as a control group of (females) were taken and their ages were also and were not infected with polycystic ovary syndrome. Laboratory tests were conducted for both groups to determine the level of asprosin, fetuin a, fasting blood sugar, insulin, total cholesterol and triglyceride. the study conducted a asprosin analysis for patents and a control group. When comparing the results were statistically no significant at P. value =0.115. Also conducted a Fetuin an analysis. When comparing the results of these two groups of patients and healthy controls, the results were statistically highly significant at P. value =0.0002.

Keywords: Asprosin, fetuin a, fasting blood sugar, insulin, cholesterol, triglyceride.

INTRODUCTION

A common endocrine illness called polycystic ovarian syndrome (PCOS) is characterized by hirsutism, anovulation, and polycystic ovaries. These conditions are frequently co-occurring with insulin resistance, dyslipidemia, and obesity [1]. With a prevalence of up to 20%, polycystic ovarian syndrome (PCOS) is the most prevalent endocrine condition in women of reproductive age. PCOS poses a serious public health problem because of its reproductive, metabolic, and psychological characteristics [2]. In addition to irregular menstrual cycles, PCOS patients also struggle with hirsutism, acne, being overweight, and impotence. An important element contributing to PCOS has been identified as long-term, low-grade inflammation. Mononuclear cells (MNC), which ordinarily do not rely on fat, may experience oxidative stress and a negative reaction in females with PCOS when blood glucose levels increase [3]. The disease's cause is still unknown, and the subjective phenomenology makes it challenging for doctors to reach consensus on a diagnosis. It appears to be a hereditary genetic syndrome brought on by a confluence of genetic and environmental variables [4]. The study's focus will mostly be on asprosin and fetuin a as well as a few molecular markers that are associated with polycystic ovaries. Asprosin is a new peptide hormone released from white adipose tissue; it stimulates the G protein camp-PKA pathway to promote glucose production from the liver. Recent research has revealed that people with insulin resistance have higher levels of the asprosin produced from white adipose tissue [5].

Asprosin metabolism may be dysregulated in PCOS individuals because they are more likely to develop dyslipidemia and/or insulin resistance. Therefore, we looked at asprosin levels in serum [6]. One recently identified peptide hormone is asprosin, which is connected to insulin resistance. The peptide encourages the liver to produce more glucose. A metabolic condition known as PCOS is polycystic ovary syndrome. A key part of the disease's development is played by insulin resistance [7]. Fetuin-A is a molecule with a glycoprotein structure that is mostly secreted by the liver Fetuin-A is a multifunctional protein that, through various mechanisms, has a positive effect on unhealthy conditions such as calcification, cardiovascular disease and tumor progression. On the other hand, it has negative effects on processes related to obesity, diabetes and fatty liver [8]. A glycoprotein made by hepatocytes, called fetuin-A, has been implicated in insulin resistance and postnatal bone development. Insulin resistance is a feature of the illness known as gestational diabetes mellitus (GDM) [9]. Obesity and type 2 diabetes have been connected to the Hepatokines fetuin-A (Fet-A) [10]. Humans develop insulin resistance due to fetuin A, a natural inhibitor of the insulin receptor tyrosine kinase [11, 12]. In humans, high Fet-A levels are linked to obesity, metabolic syndromes, and diabetes [13]. Recent research showed that Fet-A is an adipokine, however its expression in adipose tissue is still unknown because it depends on the kind of cells and species examined [14, 15].

PATIENTS AND METHODS

A case Control study was conducted in Mosul in Al Salam field Hospital and AlKuwair health center in Makhmour district and, And the maternity hospital in Erbil from December 2022 to the end of April 2023 on women infected with the polycystic ovary syndrome , 60 patients (females) aged between (15-45) years were taken and women that diagnosed with the Polycystic ovaries, by gynecological specialist .The result was a disruption in the hormones responsible for ovulation, such as LH, FSH, as well as an increase in the protein asprosin and fetuin a . On the other hand, 30 people as a control group of (females) were taken and their ages were also and were not infected with polycystic ovary syndrome. Laboratory tests were conducted for both groups to determine the level of asprosin, fetuin a, fasting blood sugar, insulin, total cholesterol and triglyceride. Fasting blood sugar was measured for patients, as well as this analysis was conducted on a control group. When comparing the results between these two groups, the result was statistically significant at P. value =0.021. Regarding insulin analysis for patients as well as control group. When comparing the results of these two groups, patients and healthy subjects, the results were statistically highly significant at P. value =0.0001. Regarding cholesterol analysis for patients, as well as conducted this analysis on a group of healthy people. When comparing the results of these two groups of patients and healthy controls, the results were statistically highly significant at P. value =0.0003 conducting triglyceride analysis has been done on patients as well as, also conducted this analysis on a group of healthy people. When comparing the results were statistically highly significant at P. value =0.0003. In addition to what was mentioned above, the study conducted an asprosin analysis for patents and a control group. When comparing the results were statistically no significant at P. value =0.115. Also conducted a Fetuin a analysis. When comparing the results of these two groups of patients and healthy controls, the results were statistically highly significant at P. value =0.0002. The blood samples were centrifuged at 3000 g for 10 min. Serum plasma was analyzed using ELISA analyzer, Genotik USA with sandwich Elisa method for the determination of serum insulin. For analyses, Biolabo diagnostic kits used for determination of fasting blood sugar, cholesterol and triglyceride.

Compliance with ethical standards

Before the study began, all participants were given information about the procedure and risks that they may later face as a result of their participation, and they gave their informed permission. The ethical committee of the Director of Health Mosul accepted the study, and all practices conformed to the Declaration of Helsinki.

Statistical Analysis

The GraphPad version 9 and the SPSS statistic programmer version 29 were both used for computerized statistical analysis. Utilizing one-way ANOVA T-Test probability (P value), a comparison was conducted. P values < 0.05 were considered statistically significant, whereas P values > 0.05 were considered non-significant. When using Pearson correlation, the correlation coefficient is used to determine the relationship between the researched markers.

RESULTS

Result the number of Polycystic Ovary Syndrome (PCOs) with Age

Table 1 showed Relation the number of Polycystic Ovary Syndrome (PCOs) with Age Those whose ages ranged between 15-45, where we found that the highest rate of polycystic ovaries was between the ages of 26-35, with a rate of 39% out of a total of 60 people, which numbered 24 women. Also, about 20 women that the ages of 36-45 are infection by rate 35%, (Table 2).

Table 1: Relation the number of Polycystic Ovary Syndrome (PCOs) with Age

Age group(years)	NO	%
15-25	16	26
26-35	24	39
36-45	20	35
Total	**60**	**100%**

Result the number of Polycystic Ovary Syndrome (PCOs) with BMI

Table 2 showed Relation the number of Polycystic Ovary Syndrome (PCOs) with BMI Where the number of women under the mass index was 7 by 11%, which was within the normal limit, their number was 10, by 17%, and those who were above the mass index were 22, by 35%, and those who had obesity were 23, by 37%, (Table 2).

Table 2: Relation number of Polycystic Ovary Syndrome (PCOs) with BMI

BMI (Kg/m2)	Studied group (N)	Polycystic Ovary Syndrome (PCOs) %
Underweight (<18.5)	7	11
Normal weight (18.5 – 24.9)	10	17
Overweight (25– 9.9)	22	35
Obese (≥ 30)	21	37
Total	**60**	**100**

Comparison Serum Level of Asprosin and Fetuin A in women with Polycystic Ovary Syndrome (PCOs) and Control Group

Table 3 showed that the no significant mean of Asprosin was recorded among Polycystic Ovary Syndrome (PCOs) (1.196 ng/ml) as compared with healthy control individuals (1.093) at P. value =0.115, (Table 3), (Figure 1) also, the study showed that the highest significant mean of Fetuin A was recorded among Polycystic Ovary Syndrome (PCOs) (29.8 ng/ml) as compared with healthy control individuals (21.99) at P. value =0.0002, (Table 3), (Figure2).

Table 3: Comparison Serum Level of Asprosin and Fetuin a in women with Polycystic Ovary Syndrome (PCOs) and Control Group

Study groups	No.	Mean ± SD	P. value
Polycystic Ovary Syndrome (PCOs) Asprosin (ng/mL)	60	1.196 ± 0.436	0.115
Control Group	30	1.093 ± 0.178	
Polycystic Ovary Syndrome (PCOs) Fetuin (ng/mL)	60	29.8 ± 10.5	0.0002
Control Group	30	21.99 ± 3.26	

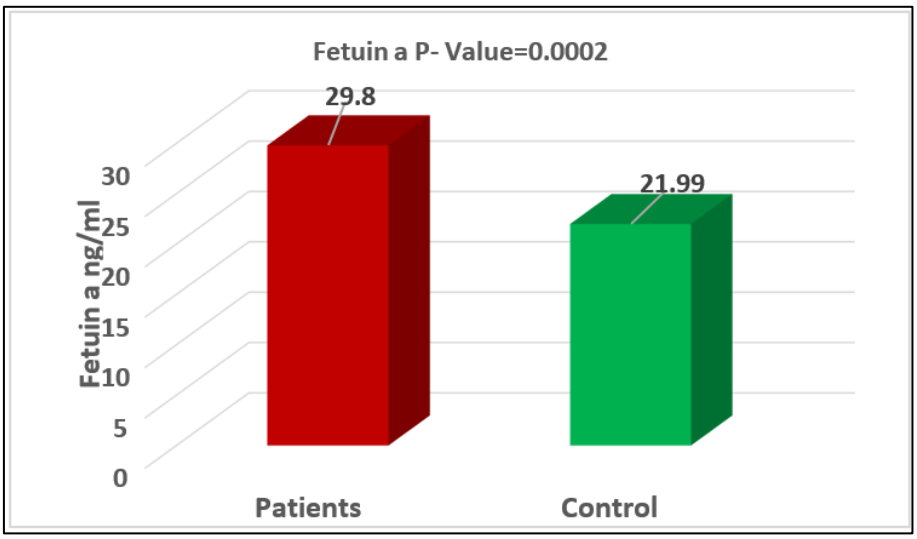

Figure 1: Comparison Serum Level of Asprosin in women with Polycystic Ovary Syndrome (PCOs) and Control Group

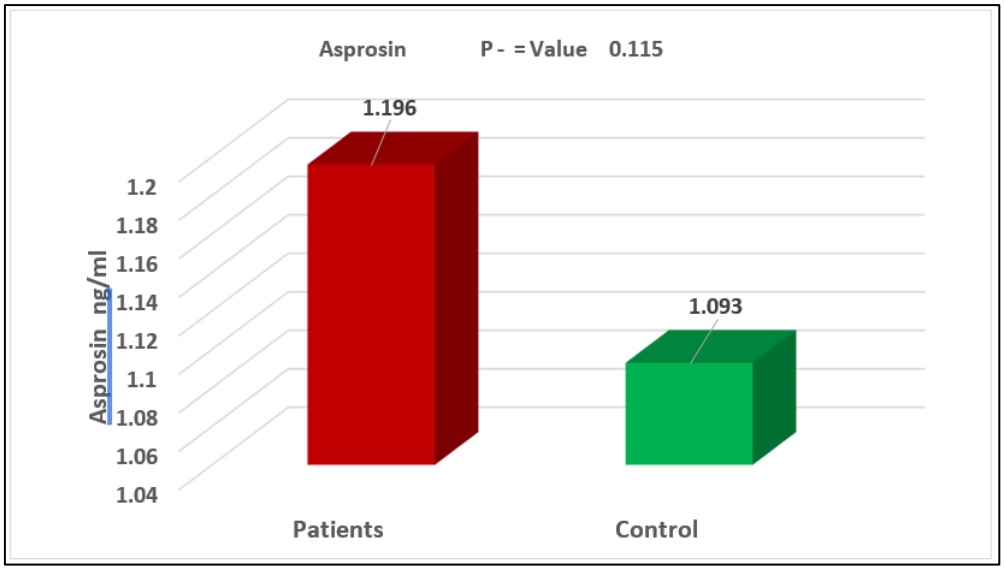

Figure 2: Comparison Serum Level of Fetuin in women with Polycystic Ovary Syndrome (PCOs) and Control Group

Result of Comparison Serum Level of FBS, insulin, cholesterol and (TRI) in women with Polycystic Ovary Syndrome (PCOs) and Control Group

Table 4 show the Comparison Serum Level of FBS, insulin, cholesterol and triglyceride in women with Polycystic Ovary Syndrome (PCOs) and Control Group. The study showed that the significant mean of FBS was recorded among Polycystic Ovary Syndrome (PCOs) (115.1 ng/ml) as compared with healthy control individuals (108.1) at P. value =0.021, (Table 4), (Figure3) and showed that the highest significant mean of Insulin was recorded among Polycystic Ovary Syndrome (PCOs) (26.60 ng/ml) as compared with healthy control individuals (21.24) at P. value =0.0001, (Table 4), (Figure 3). Also showed that the highest significant mean of cholesterol was recorded among Polycystic Ovary Syndrome (215.9 ng/ml) as compared with healthy control individuals (192.3) at P. value =0.0003, (Table 4), (Figure 3) and showed that the highest significant mean of TRI was recorded among Polycystic Ovary Syndrome (PCOs) (205.1 ng/ml) as compared with healthy control individuals (192.3) at P. value =0.0003, (Table 4), (Figure 3).

Table 4: Comparison Serum Level of FBS, insulin, cholesterol and triglyceride in women with Polycystic Ovary Syndrome (PCOs) and Control Group

Study groups	No.	Mean ± SD	P. value
Polycystic Ovary Syndrome (PCOs) FBS (mg/dL)	60	115.1 ± 16.3	0.021
Control Group	30	108.1 ± 11.5	
Polycystic Ovary Syndrome (PCOs) Insulins (mg/dL)	60	26.60 ± 6.82	0.0001
Control Group	30	21.24 ± 5.18	
Polycystic Ovary Syndrome (PCOs) cholesterol(mg/dL)	60	215.9 ± 26.8	0.0003
Control Group	30	192.3 ± 18.0	
Polycystic Ovary Syndrome (PCOs) TRI (mg/dL)	60	205.1 ± 27.2	0.0002
Control Group	30	185.3 ± 19.1	

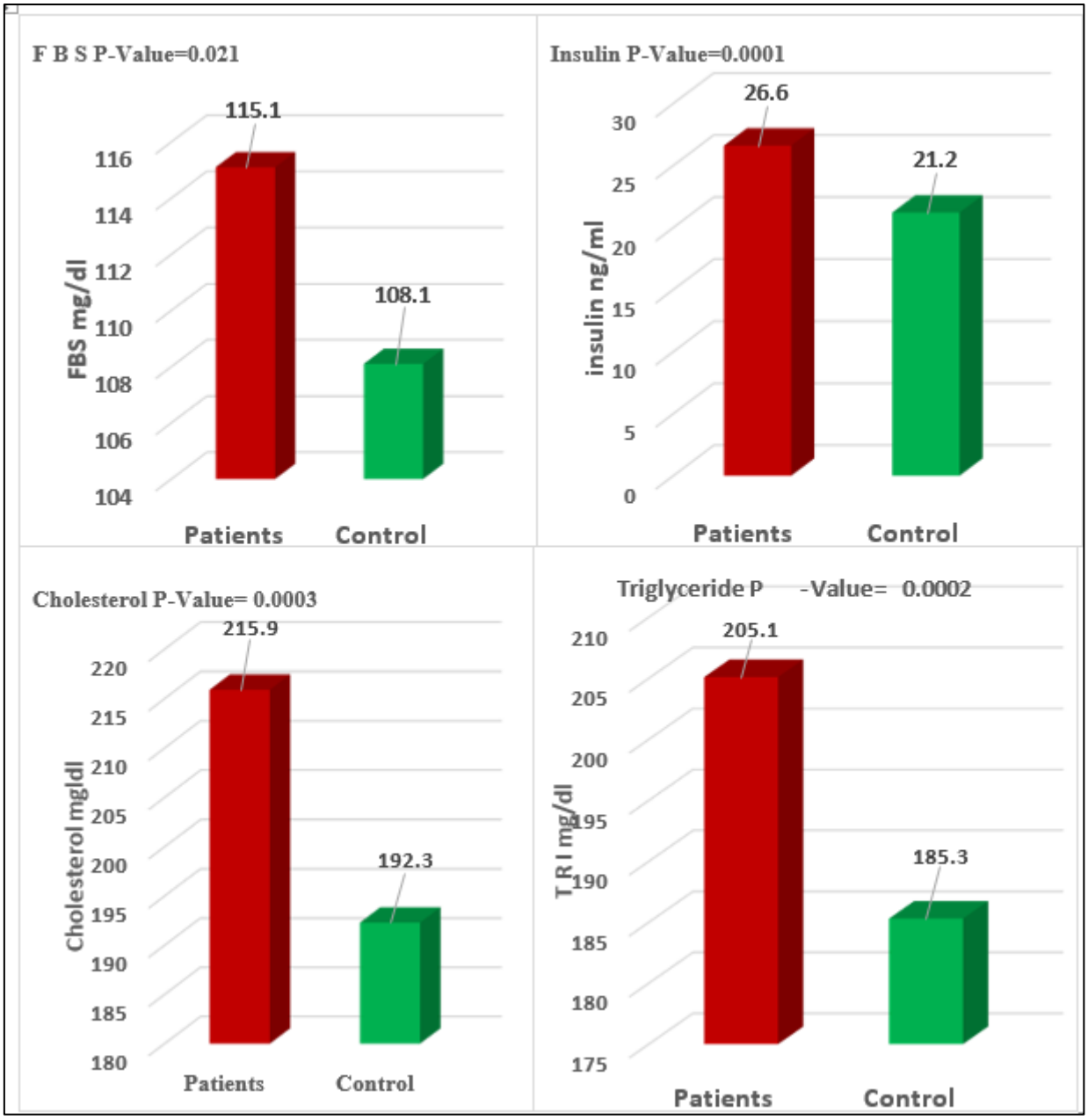

Figure 3: Comparison Serum Level of FBS, insulin, cholesterol and triglyceride in women with Polycystic Ovary Syndrome (PCOs) and Control Group

Result of the Correlation between parameters in women with Polycystic Ovary Syndrome

Table 5 show the correlation between several variables in polycystic ovary syndrome-affected women. We will examine the curve of the table to determine whether or not the correlation is apparent. This table summarizes the interactions between asprosin and fetuin a in PCOS patients with secondary parameters such FBS, insulin, cholesterol, and triglycerides.

Table 5: Correlation between parameters in women with Polycystic Ovary Syndrome

Polycystic Ovary Syndrome (PCOs)		Asprosin	Fetuin	FBS	Insulin	CHO TRIs
P. fetuin	P. value	0.124				
P.FBS	P. value	0.945	0.008			
P. Insulin	P. value	0.163	0.473	0.635		
P.CHO	P. value	0.127	0.024	0.430	0.686	
P.TRI	P. value	0.009	0.128	0.015	0.626	0.816

Result of the Correlation between Patients Asprosin and P.FBS in women with Polycystic Ovary Syndrome.

The study showed significant negative correlation between asprosin and fasting blood sugar (p.value = 0.945), (Figure 4).

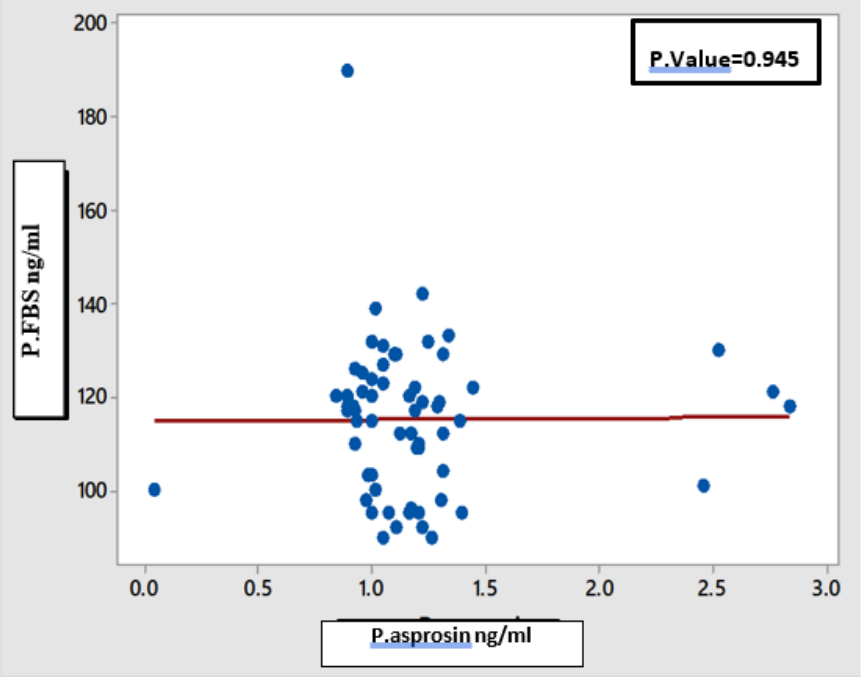

Figure 4: Correlation between Patients Asprosin and P.FBS in women with Polycystic Ovary Syndrome

Result of the Correlation between patients Asprosin and Insulin in women with Polycystic Ovary Syndrome

The study showed significant positive correlation between asprosin and insulin (p.value = 0.163), (Figure 5).

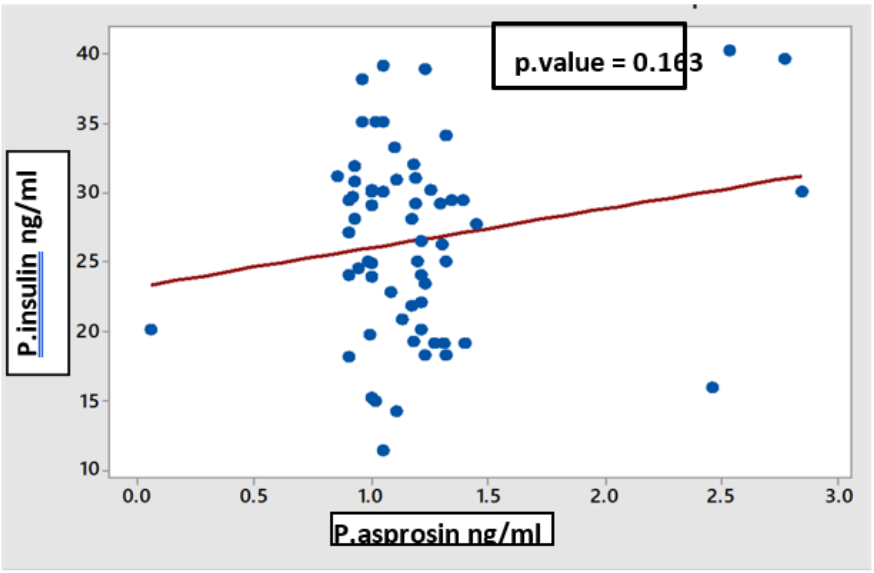

Figure 5: correlation between Patients Asprosin and Insulin in women with Polycystic Ovary Syndrome

Result of the Correlation between Patients Asprosin and Cholesterol in women with Polycystic Ovary Syndrome

The study showed significant positive correlation between asprosin and cholesterol (p. value = 0.127), (Figure 6).

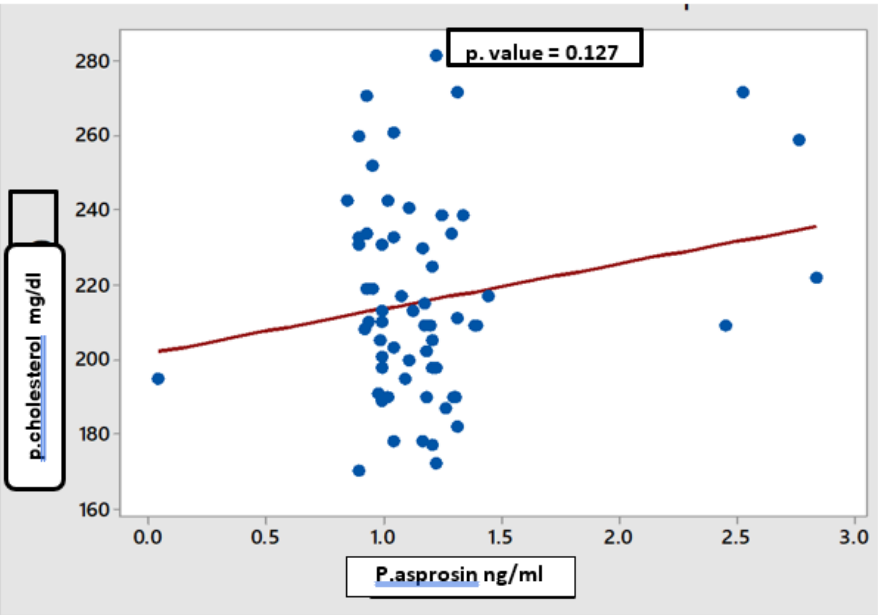

Figure 6: correlation between Patients Asprosin and Cholesterol in women with Polycystic Ovary Syndrome

Result of the Correlation between patients Asprosin and Triglyceride in women with Polycystic Ovary Syndrome

The study showed significant positive correlation between asprosin and cholesterol (p. value = 0.009), (Figure 7).

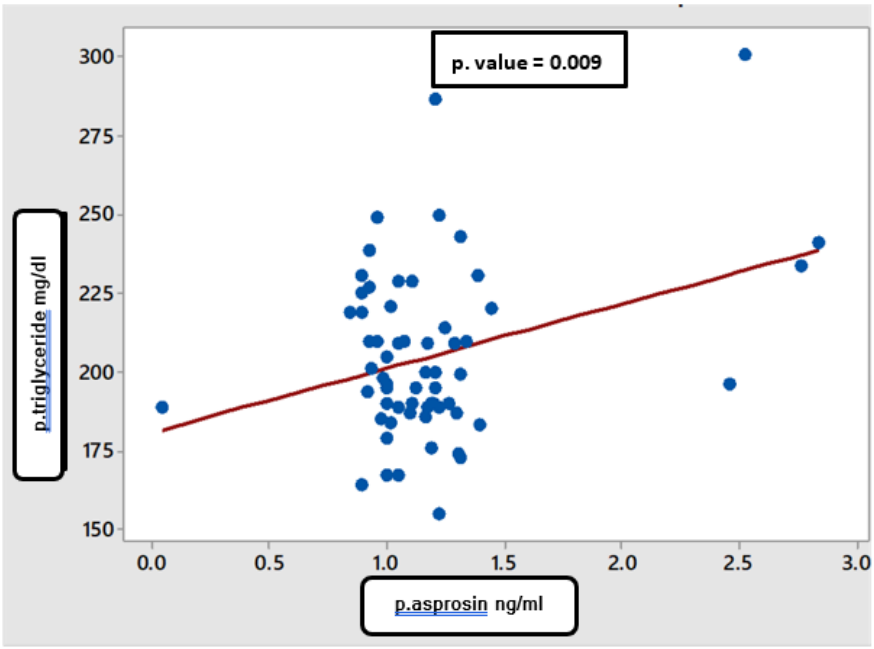

Figure 7: orrelation between Patients Asprosin and Triglyceride in women with Polycystic Ovary Syndrome

DISCUSSION

The study showed positive correlation but no significant the mean of Asprosin was recorded among Polycystic Ovary Syndrome (PCOs) (1.196 ± 0.436 ng/ml) as compared with healthy control individuals (1.093 ± 0.178) at P. value =0.115, (Figure 1). In agreement with our study finding, Yuan, M., *et al.,* [16] found that the late patient with Polycystic Ovary Syndrome had no significantly of asprosin. several studies have highlighted a statistically significant decrease in asprosin levels with polycystic ovary syndrome ; however, the majority of these studies have been conducted in patients with active disease and long-term consequences are still not known and need exploration results also come to an agreement with Jung, T.W., *et al.,* [17] study that reported a high asprosin level in patients with polycystic ovary syndrome in comparison with matched control persons Low asprosin and high fetuin a levels in patients with polycystic ovary syndrome in comparison with age-matched healthy controls were reported also reported by several studies Similarly. On the other hand, these findings were in contrast with another recent Yuan, M., *et al.,* [16] findings patients with polycystic ovary

syndrome which did not observe any significant change in comparison with healthy control participants [18]. This contrast may be explained by different patients' selection regarding ethnicity and disease severity. Few pathogenic mechanisms can explain asprosin deficiency in polycystic ovary syndrome.

According to Alan *et al.,* study's [19], women with insulin resistance are significantly more likely to develop PCOS when their serum asprosin levels are increased. According to Li *et al.,* [20]. They also discovered that asprosin is positively correlated with testosterone and prolactin levels but negatively correlated with estradiol and sex hormone-binding globulin (SHBG) levels. In contrast, asprosin levels in PCOS-affected women did not significantly increase, according to studies by Chang *et al.,* [21]. Also, the study showed that there was a highly significant difference in the correlation means of fetuin a between Polycystic Ovary Syndrome (PCOs) patients (29.8 10.5 ng/ml) and healthy controls (21.99 3.26 ng/ml) with a P value of 0.0002 (Figure 2). In agreement with our study results, Herrmann M, B.A. [22] found positive correlation between Fetuin a level and POCs. Moreover, Kundranda MN, H.M [22] also recorded similar finding. Levels of Fetuin a were high in POCs cases specially belonging to more severe outcome groups. findings of a prospective case control study where patients with POCs have been compared with healthy control individuals Fetuin a was found in almost patients with POCs, are serum Fetuin levels were high significantly correlated. Here, in a large case control study, we provide evidence that POCs is high significantly associated with high Fetuin a level and confirm that POCs correlates with Fetuin a increased level [23]. The inflammation caused by free fatty 7 acids on the beta cells of the pancreas by fetuin-A is another potential link between fetuin-A and insulin resistance [24]. All of these methods make it clear that fetuin-A is necessary for preserving glucose homeostasis. Studies linked serum fetuin-A to Type 2 diabetes risk, insulin resistance, and impaired glucose tolerance (IGT) [25-27]. However, while many studies suggest that higher fetuin-A concentrations may reduce the risk of getting some diseases, other studies address that it could be a sign that something unfavorable is happening. For example, fetuin-A release may increase during tumor development and play a significant role in the development of insulin resistance [28-30].

The study showed no significant no correlation between Fetuin a and asprosin (p.value = 0.124). In agreement with our study's findings, Yuan, M., *et al.,* [16] discovered that asprosin levels were minimal in polycystic ovary syndrome patients. Numerous studies have shown a statistically significant reduction in asprosin levels in patients with polycystic ovary syndrome; however, the majority of these studies were carried out in patients with active disease, and long-term effects are still unknown and need further investigation. The results also concur with a study by Jung, T.W., *et al.,* [31] that found a high asprosin level in patients with recovered polycystic ovary syndrome when compared to matched control in contrast to age-matched healthy controls and other study shows polycystic ovarian syndrome patients had low asprosin and high fetuin a level. In a similar vein, females with polycystic ovary syndrome. Fetuin a level and PCOs showed a positive association, which is consistent with the findings of our investigation, according to Herrmann M., B.A. [22]. In addition, Kundranda MN, H.M [22] also made a comparable discovery. Fetuin A levels were high, particularly in PCOs infection groups with more severe outcomes. Findings of a prospective case-control investigation in which patients with PCOs were compared to healthy controls, blood fetuin levels were found to be very statistically associated in virtually all patients with PCOs. In this work, we establish that PCOs correlate with elevated levels of Fetuin A and give evidence that PCOs patients is strongly linked with high Fetuin A level through a large case-control study [23]. Free fatty acid 7-induced inflammation on the beta cells of Another possible connection between fetuin-A and insulin resistance is because it is produced by the pancreas [24].

The study showed significant negative correlation between asprosin and FBS (p.value = 0.945), (Figure 4). In agreement, Romere *et al.,* [32] reported that the action of asprosin is independent to the stimulation of the glucagon and norepinephrine axis, which is also essential in the release of glucose [33]. By preventing the asprosin-mediated increase in PKA activity and glucose release, high insulin levels oppose the effects of asprosin. These results suggest that asprosin and insulin are functionally antagonistic. Moreover, there is a strong connection between asprosin levels and blood glucose levels, with fasting conditions stimulating asprosin production and non-fasting conditions reducing it (feeding condition). The study showed significant positive correlation between asprosin and insulin (p.value = 0.163), (Figure 5). In agreement with our results According to Alan *et al.,* study's [19], women with insulin resistance are significantly more likely to develop PCOS when their serum asprosin levels are increased. Investigations found that the influence of the insulin resistance diagnostic criteria on PCOS women's ability to determine their insulin resistance is minimal. The main problem with PCOS patients is insulin resistance, and its prevalence and mechanism need to be studied. Previous studies have revealed that a significant number of PCOS women had impaired glucose tolerance and type 2 diabetes (T2DM) [34, 35]. The study showed significant positive correlation between asprosin and cholesterol (p. value = 0.127), (Figure 6).

In agreement with our results Liu, Q., *et al.,* [36] Some of the most prevalent characteristics seen in women with this condition include dyslipidemia. Teede, H.J., *et al.,* [37] PCOS is a chronic, multisystem illness with features that affect fertility and metabolism. All PCOS women who are being watched for hyperlipidemia should have a fasting lipid profile performed, which includes measurements of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglyceride (TG) levels. The study showed significant positive correlation

between asprosin and triglyceride (p. value = 0.009), (Figure 7). In agreement with our results Couto Alves, A., *et al.,* [38] Studies have shown that when PCOS first manifests, abnormal lipid profiles exist in up to 70% of female patients. Body fat percentage rises and lipid abnormalities are important metabolic risk factors for PCOS [38]. Dyslipidemia with high levels of (TG) is frequently present in android-type obesity [39]. The metabolism of TG and CHO has been shown to be influenced by endogenous estrogens and androgens, with estrogens being better known to control lipid metabolism than androgens [40].

CONCLUSION

Asprosin plays a no significant role in diagnosis of polycystic ovary syndrome and its complications. Fetuin a proved to be a highly sensitive marker in estimating the severity and prognosis of polycystic ovary syndrome. Regarding to this study we anticipate that the study we conducted will give doctors useful information and shed light on the connections between the abnormalities in metabolic and hormonal factors seen during PCOS.

Conflict of interest

The authors state no conflict of interest with respect to the research, authorship, and/or publication of this article.

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