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Evaluation of the relationship between Fetuin-A level and some biochemical variables in women with PCOS

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Abstract--The current study included the collection of 90 serum samples to assess the relationship between the level of Fetuin-A, and some biochemical variables in women with polycystic ovarian syndrome. The samples were collected from external laboratories in Salah El-Din Governorate for the period from 10/29/2021 to 12/25/2021. 60 samples of women with PCOS and 30 samples representing the control group, their ages ranged between (18-40) years for patients and healthy ones. Fetuin-A level and lipid profile were estimated in the blood serum of groups for both of women with PCOS and healthy women as a control group. The results of the study showed that the level of Fetuin-A was significantly increased at ($P \leq 0.05$) in women with PCOS compared to healthy women as a control group, and the results also showed a significant increase ($P \leq 0.05$) in the cholesterol level, Triglycerides, low-density lipoproteins, with no significant difference in the level of high-density lipoprotein and very low-density lipoproteins in women with PCOS compared to healthy women as a control group.

Keywords--PCOS, Fetuin-A, cholesterol, triglycerides, high-density lipoproteins, low-density lipoproteins, very low-density lipoproteins.

Introduction

Polycystic ovary syndrome (PCOS) is an endocrine and metabolic disorder that is one of the most common diseases in premenopausal women. PCOS is often associated with insulin resistance, abdominal obesity, cardiovascular risk factors,

and metabolic disorders, the main clinical manifestations of which are high androgen levels, Ovarian dysfunction and metabolic disorder ⁽¹⁾. It is a heterogeneous disorder. Approximately (6-20%) of women of childbearing age are affected by this disease, and the symptoms of this syndrome appear during early puberty years ^(2,3). Polycystic ovary syndrome was first discovered by researchers Leventhal and Stein in 1935 AD and the syndrome was known by their names ⁽⁴⁾.

There is strong evidence that proves that it is a genetic disease of genetic origin, because it is known that the syndrome has a strong familial predisposition and that one or more genes may contribute to the heterogeneous phenotype, clinical and biochemical pattern of the syndrome ⁽⁵⁾. There is also evidence confirming the relationship of polycystic ovary syndrome with obesity and insulin resistance, and this is an important cause of systemic complications such as type 2 diabetes, heart disease and skin complications, which are associated with an increase in the level of androgens in the plasma, which leads to hirsutism, acne, baldness, and metabolic syndrome and autoimmune diseases ^(6, 7).

Fetuin-A is a glycoprotein its molecular weight 52 kDa that is predominantly synthesized by hepatocytes and subsequently secreted into the bloodstream. It contains 12 amino acids ^(8, 9). Fetuin-A is also known in humans as α 2-Heremans-Schmid glycoprotein (AHSG) is a large serum glycoprotein secreted primarily by liver tissue, has been identified in both humans and animals and is involved in important cellular physiological functions, including regulation of bone metabolism, vascular calcification, insulin resistance, regulation of acute inflammatory responses, and neutrophil lysis, lymphocyte defense function, and homeostasis of calcium ion. the epidemiological studies have demonstrated significantly elevated prevalence of fetuin-A in obesity and related complications, such as type 2 diabetes, metabolic syndrome, nonalcoholic fatty liver disorder, in addition, fetuin-A has been closely associated with several parameters related to metabolic imbalance, such as insulin sensitivity, lipid biomarker and inflammatory factors interleukin-6 (IL-6) ^(11,10).

Fats are non-polar organic substances that are insoluble in water but are soluble in non-polar organic solvents ⁽¹²⁾. Fat is one of the important nutritional components as it is a source of energy that supplies the body with 9 kilocalories / g, as well as fatty acids such as linoleic acid, which is important in the growth of the children's body, are obtained through food.

Also, fats are important for maintaining the health of human skin and for the production of some hormone-like compounds such as prostaglandins, which are important in regulating some activities in the body ^(13,14). Cell membranes are made of various fats in different proportions and quantities ⁽¹⁵⁾.

Fats are made in the body by the liver and adipose tissue and also obtained through food and then transferred to different tissues and organs for use or storage. Plasma contains the main fats, which are ester cholesterol 36%, phospholipids 30%, triglycerides 16%, free cholesterol 14%, and fatty acids 4% ⁽¹⁶⁾.

Materials and Methods

The samples of the study

The blood samples were 90 which taken, 60 samples were from women with PCOS and 30 blood samples were from healthy women as a control group, their ages ranged between (18-40) and the samples were collected from external laboratories in Salah El-Din Governorate for the period between 10/29/2021 to 12/2021 \25 .

Fetuin-A level estimation

The level of Fetuin-A in the serum was determined by assay kit, ELISA technology, which is a solid phase enzyme-linked immunoassay based on the principle of competitive binding.

Determination the lipid profile in the blood

Blood serum cholesterol concentration

The concentration of cholesterol in the blood serum was measured using kit (kit)⁽¹⁷⁾ .

Determination of the concentration of triglycerides

The concentration of triglycerides in the blood serum was estimated using the Kit⁽¹⁷⁾ .

Determination the concentration of HDL-C in the blood serum

The concentration of high-density lipoprotein (HDL) in serum was estimated using the Kit⁽¹⁷⁾ .

Calculation of the LDL-C concentration in the blood serum

$$LDL - C (mg\ dl) = \text{Total cholesterol} - (\text{HDL} - C + \text{VLDL})$$

Calculation of the VLDL concentration in the blood serum

The value of the VLDL was calculated based on the method of Friedwald et al.,⁽¹⁸⁾.

$$VLDL(mg\ dl) = \frac{TG}{5}$$

Statistical analysis

The statistical program (SPSS) was used, using the T. test to compare between a group of women with PCOS and healthy women as a control group. The significance was calculated when performing a statistical analysis of all data at the probability level ($p \leq 0.05$).

Results and Discussion

Level of serum Fetuin-A

The results of the current study showed that the mean \pm standard deviation of Fetuin-A level was (17.365 \pm 4.476) mg / 100 cm³ in women with PCOS,

compared to (5.375 ± 1.445) mg / 100 cm³ in healthy women as a control group, Table (1).

Parameter	Mean \pm SD
	Fetuin-A mg/dl
Control	5.375 \pm 1.445
Patients	17.365 \pm 4.476
P \leq 0.05	*

*High significant

Table (1) shows that the level of Fetuin-A increase significantly at the ($p \leq 0.05$) in the blood serum of women with PCOS compared to the control, as shown in Figure (1).

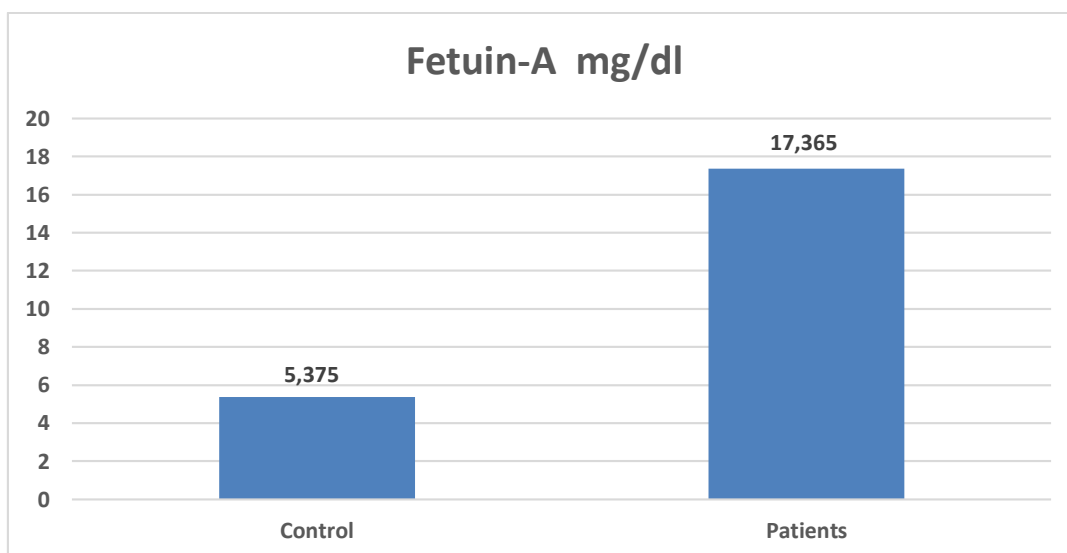


Figure 1 shows the level of Fetuin-A in PCOS groups compared to the control group

The results of the current study agreed with the results of the study of Sak et al.,⁽¹⁹⁾ which showed that the serum Fetuin-A levels were significantly higher in women with PCOS compared to healthy women as a control group. Also, the results of the recent study showed that the levels of Fetuin-A in women with PCOS were higher than that of healthy women as a control group⁽²⁰⁾.

The results also showed a significant increase in the level of Fetuin-A in women with PCOS, and that the cause of the rise may be attributed to metabolic disorders resulting from hyperandrogenism and hyperinsulinemia, which may enhance the synthesis and release of Fetuin-A in vivo, in addition to, the increase in Fetuin-A can be derived at least in part from the low-grade inflammatory state, in which inflammatory cytokines such as CRP are increased in women with PCOS⁽²¹⁾.

Blood lipid profile in women with PCOS

The lipid concentrations (TC, TG, HDL-C, LDL-C, VLDL) were estimated in the blood sera of PCOS and healthy women, and the mean \pm standard deviation of lipids was shown in Table (2).

Table (2) Blood lipid levels in the serum of groups of women with PCOS and healthy women as a control group.

Parameter	Mean \pm SD				
	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	VLDL mg/dl
Control	127.242 \pm 32.740	64.794 \pm 16.990	30.315 \pm 8.356	83.664 \pm 25.903	12.952 \pm 3.626
Patients	149.553 \pm 31.283	78.005 \pm 21.117	35.331 \pm 11.579	98.620 \pm 24.989	15.601 \pm 4.223
P \leq 0.05	*	*	NS	*	NS

NS =Non-significant

The Level of Total Cholesterol

The results of the current study showed that the cholesterol level was 149,553 \pm 31,283 mg/100 cm³ in the blood serum of women with PCOS, while the cholesterol level in the healthy women was (127.242 \pm 32.740) mg/100 cm³ as a control group, as shown in Table (2). It is evident from the above table that the level of cholesterol increased significantly (P \leq 0.05) in the blood serum of women with PCOS compared with the control group as shown in Figure (2).

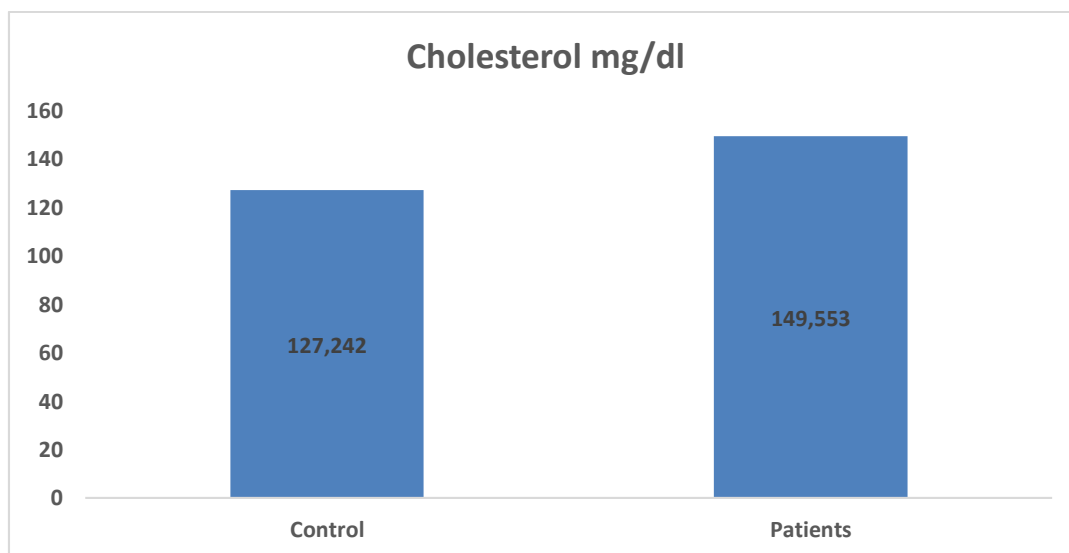


Figure 2 shows the cholesterol level of PCOS groups compared to the control group.

The results of the current study agree with the results of several studies ^(22,19,23,24) that showed a significant increase in blood cholesterol level in women with PCOS

compared to healthy women as a control group. The cause of high blood cholesterol may be due to hyperinsulinemia and androgens. This causes the adipocytes to undergo lipolysis by catecholamine and increase the release of fatty acids ⁽²⁵⁾. Or, the increase in cholesterol levels in the blood may occur for several reasons, including the breakdown of low-density lipoprotein-of LDL-C- or the inefficiency of the receptors for the protein part of LDL-C in the tissues, as well as the activity of the enzyme Acyl Cholesterol transferase which is responsible for the absorption of cholesterol in the intestine, in addition to increasing cholesterol synthesis internally, as well as consuming meals rich in saturated fats ⁽²⁶⁾. The reason for the high cholesterol in the blood serum may be due to the body consuming fats from other sources and using them for energy, and this leads to the accumulation of cholesterol in the blood vessels ⁽²⁷⁾.

The level of Triglyceride

The results of the current study showed that the level of triglycerides was (78.005 \pm 21.117) mg / 100 cm³ in women with PCOS, while its level was 64,794 \pm 16.990) mg / 100 cm³ in healthy subjects as a control group, as shown in Table (2). It is clear from Table (2) that the level of triglycerides increased significantly ($P \leq 0.05$) in women with PCOS compared with the control group, according to Figure (3).

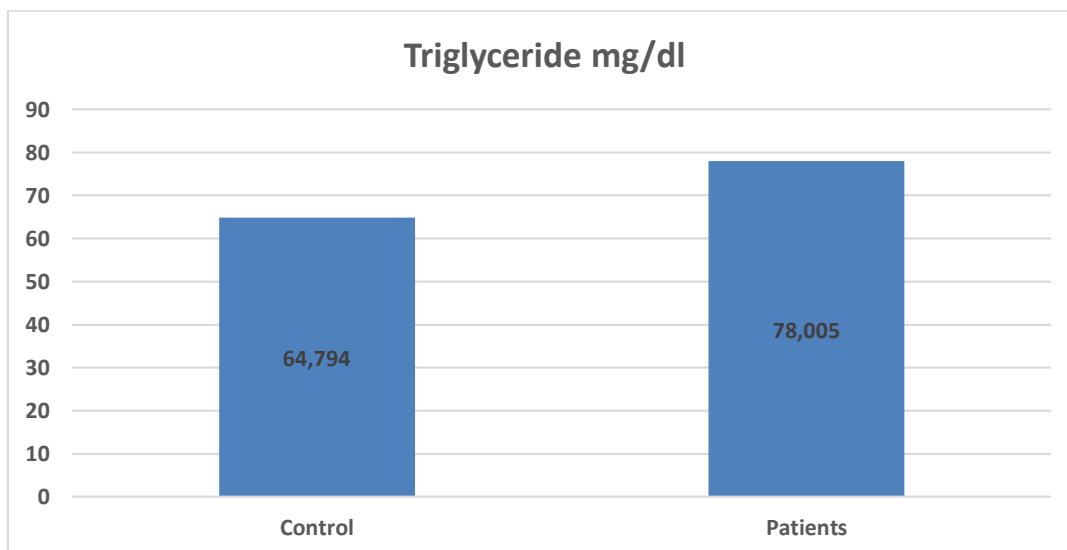


Figure 3 shows the level of triglycerides in PCOS groups compared to the control group

The cause of high triglycerides in the blood may be due to dyslipidemia, hyperinsulinemia or hyperandrogenism ⁽²⁸⁾. Or, the high level of triglycerides in the blood may be caused by a decrease in the activity of the enzyme Lipoprotein lipase -LPL, which leads to the breakdown of triglycerides ⁽²⁶⁾. Or it may be due to an increased intake of large amounts of foods rich in fat, which in turn leads to increasing the production of chylomicrons inside the intestine, which when

decomposing causes the release of fatty acids, and thus the liver cells receive high amounts of fatty acids and thus a rise in the concentration of TG ⁽²⁹⁾ .

The Level of HDL-C

The results of the current study showed that the level of high-density lipoproteins-cholesterol in women with PCOS was $(35.331 \pm 11,579)$ mg/100 cm³, while its level in healthy women was (30.315 ± 8.356) mg/100 cm³ as shown in Table (2). The results showed that there were no significant differences in the level of C-HDL among women with PCOS compared with the control group as shown in Figure (4).

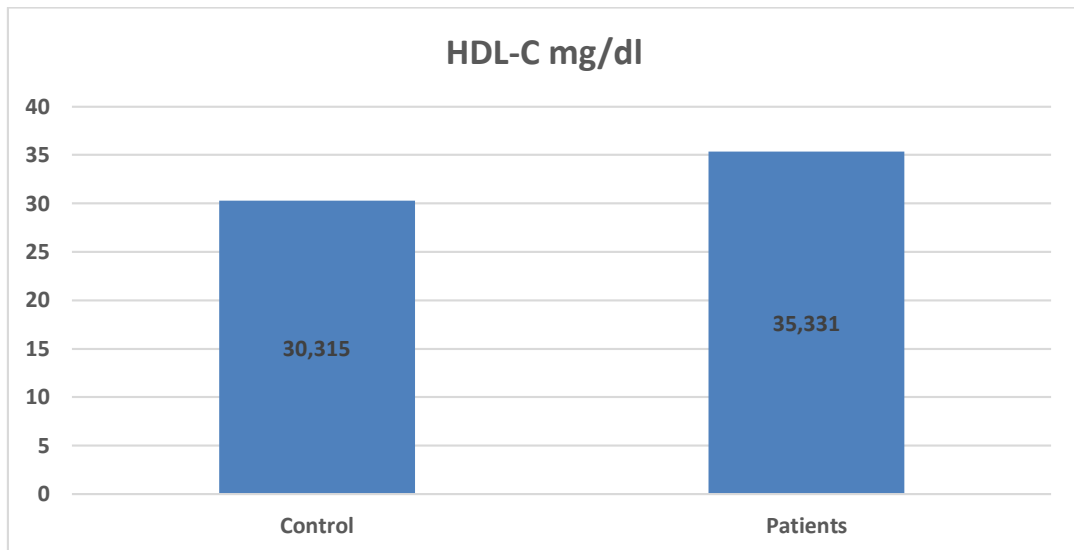


Figure (4) High-density lipoprotein-cholesterol concentration in PCOS groups compared to the control group.

The results of the current study do not agree with the results of the study of Al-Jubouri et al., ⁽²⁴⁾ , which showed a significant decrease in the level of high-density lipoprotein among women with PCOS compared to healthy women as a control group. The results of the current study showed no significant differences in the level of high-density lipoprotein in women with polycystic ovaries.

The level of LDL-C

The results of the current study showed that the level of low-density lipoproteins in women with PCOS was $(98.620 \pm 24,989)$ mg/100 cm³, while the level of it in the blood serum of healthy women was (83.664 ± 25.903) mg/100 cm³ as a control group, as shown in Table (2). It is evident from Table (2) that the level of LDL-C increased significantly ($P \leq 0.05$) among women with PCOS compared with the control group as shown in Figure (5).

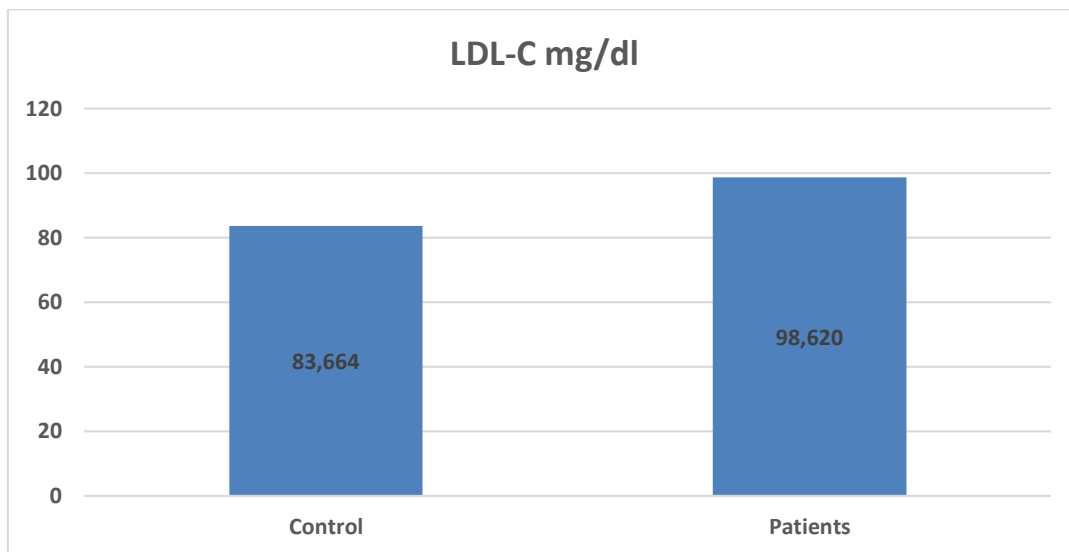


Figure (5) the level of LDL-C in PCOS groups compared to the control group.

The results of the current study agree with the results of several last studies (22,19,23,24) who found higher levels of LDL in women with PCOS compared to healthy women. The reason for the high concentration of LDL-C is due to the fact that hyperlipidemia can lower the level of high-density protein and thus increase the level of low-density protein (30). The high level of LDL-C may be attributed to the low activity of the enzyme Lipoprotein lipase -LPL, which leads to the lack of TG degradation and the conversion of most of VLDL to LDL-C and thus its high level in the blood serum, which is undesirable because it constitutes a risk factor for the development of heart disease (31).

The level of very low density lipoproteins (VLDL)

The results of the current study showed that the level of very low-density lipoproteins was (15.601 ± 4.223) mg/100 cm³ for women with PCOS, while its level was (12.952 ± 3.626) mg/100 cm³ for healthy women as a control group as shown in Table (2). The results showed that there were no significant differences in the level of VLDL among women with PCOS compared with the control group as shown in Figure (6).

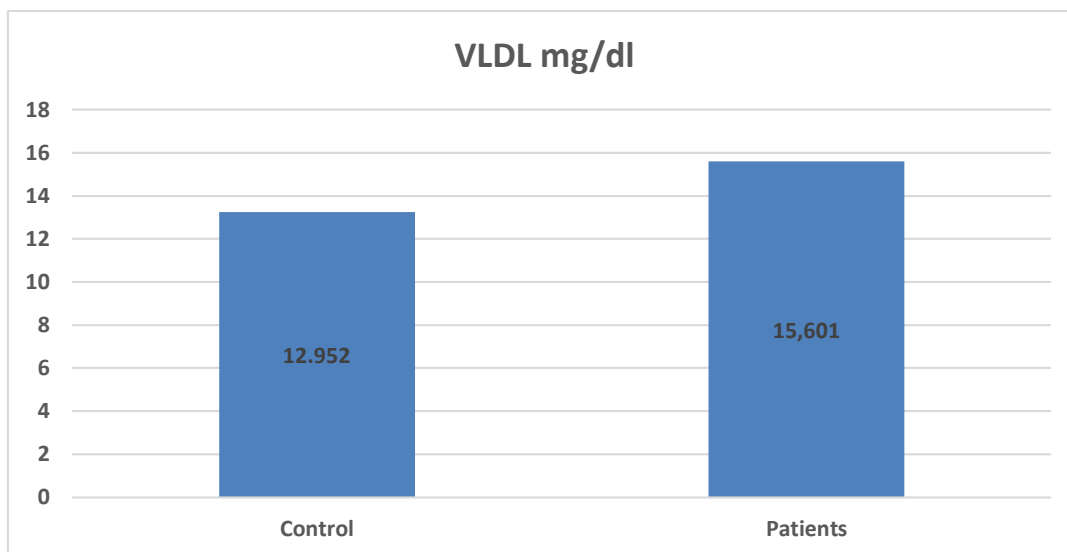


Figure (6) The concentration of very low-density lipoproteins in PCOS groups compared to the control group

The results of the current study do not agree with the results of the study of Al-Jubouri and his group ⁽²⁴⁾, which showed a significant increase in the level of very low-density lipoprotein in women with PCOS compared to healthy women as a control group. The results of the current study showed no significant differences in the level of lipoprotein Low density in women with polycystic ovaries.

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