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ESTIMATION OF BIOCHEMICAL AND IMMUNOLOGICAL PARAMETERS ALTERATION IN WOMEN WITH POLYCYSTIC OVARY SYNDROME IN BASRAH GOVERNORATE

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ABSTRACT
Polycystic ovarian syndrome (PCOS) is one of the most common endocrine disorder in a reproductive age women around the world. Because of a large number of women infected with PCOS in Basrah city, the present study has been designed to underline some of the causes of PCOS through the changes in biochemical, and immunological parameters. This study was done in basrah governorate since May, 2018 until November, which includes 150 females divided in to two equal groups, PCOS patients and healthy women as control in basrah city. The results showed that AST, ALP, urea, cholesterol, LDL-C, total protein and glucose were significantly increased in PCOS patients than control group ($p<0.05$), while HDL-C was significantly decreased in PCOS patients than control group($p<0.05$), even ALT, TG and VLDL recorded high levels in PCOS patients than control but the difference is not significant ($p>0.05$). Also our study recorded a significant increased in the level of immunological parameters (TNF- α and IL-18) in PCOS patients than control group($p<0.05$). In conclusion the metabolic abnormalities are prevalence in PCOS patients and PCOS may induce the inflammation characterize in these women, also these abnormalities might be involved in the development of PCOS.

KEYWORDS: polycystic ovary syndrome/ PCOS / Total protein/ glucose/ IL-18/ TNF-α.

INTRODUCTION
PCOS was defined as a gynecologic endocrinopathy and as a sort of metabolic disorder.[1] PCOS is a heterogeneous disorder that has both reproductive and metabolic manifestations, which is excited by obesity, however there is a poor understanding of its etiology. The phenotype of PCOS can vary according to race and ethnicity and it is difficult to define PCOS in the perimenarchal and perimenopausal period.[2] PCOS patients have extravagant fats, which it have an crucial role in the cardiovascular disease. These fats present in both obese women with PCOS and normal weight PCOS women and this distribution, adipocyte dysfunction also chronic low grade inflammation could be a narrative mechanisms involved in cardiovascular disease in PCOS.[3]

Many PCOS women have abdominal obesity which it lead to adipose tissue dysfunction, characterized by hypertrophic adipocytes, lipolysis impairments and insulin action. The secretion and expression of adipokines involved in insulin resistance such as adiponectin hormone and dysfunction in the adipose tissue that plays a key role in the metabolic abnormalities of PCOS patients.[4] Many PCOS women showed an increased risk for nonalcoholic fatty liver disease (NAFLD) which is one of the most serious hepatic multiplication of metabolic abnormalities with a wide spectrum ranged from hepatic steatosis, inflammation, fibrosis to hepatocellular carcinoma.[5,6] Obesity, androgen excess, dyslipidemia and insulin resistance are the prime factors related to NAFLD in PCOS patents.[7]

The immune ascendancy cytokines in follicular fluid lymphocytes may be the immunological feature of PCOS ovary, Many evidence shows that immune dysregulation and chronic inflammation may be involved in the etiology of PCOS but the underlying mechanisms still an unclear.[8] The decreasing of dendritic cells percentage and cytokines in follicular fluid of PCOS women indicate a confusion in the immunological microenvironment of the follicles in the ovary, that may be involved in the folliculogenesis dysfunction.[9] Due to the great number of women infected by PCOS in Iraq and in city Basrah in particular, the current study has been designed to highlight some of the causes of PCOS via measure the biochemical, and immunological parameters.

MATERIAL AND METHODS

Current study included 75 PCOS patient group and 75 and healthy women as control both groups are divided into four factions according to their BMI and all women in this study did not get any hormonal therapy and medications for last four months of sample collection and the blood collection was performed during the luteal phase of the menstrual cycle. 10 ml of venues blood samples were collected in Gel/clot activator tubes then left for a short time to form blood clot, serum was separated by using centrifuge (3500 rpm-10minutes).then the serum divided in to 12 eppendorf tubes and kept frozen at (-20 C°)in deep freezer until time of analysis with avoiding multiple freezing. The analysis includes measuring the liver function (aspartate aminotransferase (AST) alanine aminotransferase(ALT) and Alkaline phosphatase (ALP)), glucose and urea by using enzymatic colorimetric method (Randox/ United kingdom) kits. Lipid profile (Cholesterol, Triglyceride (TG), High-Density Lipoprotein (HDL)), creatinine and Total protein were measured by using enzymatic colorimetric method (Biolabo/ France) Kits, while Very Low-Density Lipoprotein(VLDL) and Low-Density Lipoprotein (LDL)) calculated according to Friedewald *et al*.[10] Serum interleukin-18 (IL-18) and tumor necrosis factor-alpha α (TNF-α) levels were measured by using Sandwich ELISA (Al-shkairate/ Jordon and Diclone/ France, respectively) kits. The procedure of kits followed accurately as demonstrated in the leaflet with the kits. The statistical analysis are preformed using SPSS version 20 with P<0.05 at a significant. Data are expressed according to Mann-Whitney Test, Kruskal-Wallis Test and multivariate Anova.

RESULTS

1-Concentration of biochemical parameters: As shown in the Table (1). serum AST and ALP are significantly increased in PCOS patients l compared with control group, while ALT levels are not significant between the two groups. The table(2) showed that the level of serum urea is significantly increased in PCOS patients compared with control group while creatinine level is significantly decreased in PCOS patients compared with control.

Table. 1. Comparison of serum liver profile between control group and PCOS patients. Values was expressed as (median (min- max)).

Liver profile	Control(n=75)	PCOS(n=75)
AST(U/I)	10 (6-13)	11 (6-19)**
ALT(U/I)	8 (4-12)	4 (4-18)
ALP(IU/L)	42 (21-59)	45(21-97)*
*significant at the (P≤0.05) **significant at the (P≤0.01)		

Table. 2. Comparison of kidney profile between control group and PCOS patients. Values was expressed as(median (min- max)).

Kidney profile	Control (n=75)	PCOS (n=75)
Urea(mg/dl)	23 (10-45)	32 (10-53)**
Creatinine(mg/dl)	0.8 (0.4-1.1)	0.6 (0.7-1.2)**
*significant at the (P≤0.05) **significant at the (P≤0.01)		

The current study also showed that the levels of cholesterol, LDL-C are significantly increased in PCOS patients compared with control group and HDL-C is significantly decreased in PCOS patients compared with control group, while The difference in serum TG and VLDL-C levels are not significant between the two groups, table(3). The level of total protein in PCOS patients is significantly decreased compared with control group and glucose level is significantly increased in PCOS patients compared with control group, table(4).

Table. 3. Comparison of lipid profile between control group and PCOS patient. Values was expressed as(median (min- max)).

Lipid Profile	Control (n=75)	PCOS(n=75)
Cholesterol(mg/dl)	144 (79-193)	200 (100-315)**
TG(mg/dl)	98 (53-150)	106 (69-240)
HDL-C(mg/dl)	48 (38-68)	33 (15-65)**
VLDL-C(mg/dl)	19.60(1.0-30.0)	21 (4.8-48.0)
LDL-C(mg/dl)	77 (13.2-120.6)	49 (31.0-250.6)**
*significant at the (P≤0.05) **significant at the (P≤0.01)		

Table. 4. Comparison of total protein and glucose between control group and PCOS patients. Values was expressed as (median (min- max)).

Parameters	Control(n=75)	PCOS(n=75)
Total protein (mg/dl)	74(61-85)	62(38-75)**
Glucose (mg/dl)	85(60-120)	72(84-194)*
*significant at the (P≤0.05) **significant at the (P≤0.01)		

2-Concentration of serum immunological parameters: In the present study, the serum TNF-α and IL-18 levels in the current study showed a significantly increase in PCOS patients when compare with control group, Table (5).

Table. 5. Immunological parameters of control group and PCOS patients. Values was expressed as (median (min- max)).

Proinflammatory Cytokines	Control(n=28)	PCOS(n=60)
TNF-α	2.76 (0.2-12.08)	11.23 (0.12-55.67)**
IL-18	0.73 (0.15-26.97)	45.60 (3.68-159.24)**
*significant at the (P≤0.05) **significant at the (P≤0.01)		

DISCUSSION

Insulin resistance could contribute to the interruption of liver enzymes in PCOS patients. It is involved in the NAFLD pathogenesis and in disease succession from steatosis to nonalcoholic steatohepatitis. Therefore, adjustment of insulin resistance is a probable approach for NAFLD treatment. It was suggested several mechanisms that associated insulin resistance with NAFLD like alternations in rates of adipose tissue lipolysis and lipogenesis, redused oxidation of mitochondrial fatty acid, changes in distribution of fat, changes in the gut microbiome, and alterations adipokines levels and cytokines.[11] Urea found to be higher in association with high testosterone. testosterone effects appears to related with testosterone changes in the internal hemodynamic levels. Testosterone induces both apoptosis and podocyte damage in the kidney and there are the testosterone receptors that found on the afferent arteriole of kidneys.[12,13] It was hypothesized that low serum creatinine could be a good indicator of type 2diabetes multiuse. Because skeletal muscle is one of insulin target tissues, is inversely correlated to type 2diabetes multiuse and creatinine derived from creatine in muscles and is considered as a dependable marker for muscle mass, it was found that.[14] The weakness in HDL-C antioxidant and antiinflammatory function in PCOS women is related to increased oxidative stress, hyperandrogenism status, and abnormalities in HDL-C components.[15] Insulin resistance plays a key role than hyperandrogenaemia in postprandial dyslipidaemia which includes higher cholesterol and low HDL-C in PCOS patients.[16] The elevated serum level of LDL-C in PCOS patients was recorded in many studies and if the insulin resistance is inherent, the lipid abnormalities are mainly weight related in PCOS patients.[17,18] The in protein metabolism changes that caused by insulin may initiate changes in the body tissues compositions. Because lack of insulin leads to turning off protein storage, increases proteins catabolism, stops protein synthesis. Therefore, a large amounts of amino acids are deserted into plasma, and these amino acids are used for energy and for the gluconeogenesis. This amino acids is one of the most severe effects of diabetes mellitus, it can lead to intense weakness also disturb the organs functions[19,20,21,22]

Abnormal glucose dynamics in PCOS adolescents occur because of the severe obesity and the combination of PCOS, whereas the severe obesity has a synergistic effect on glucose dynamics.[23]

Cortisol found to be relate with diabetes multiuse type 2. Because cortisol increases the necessary enzymes for converting amino acids into glucose in the hepatocytes, delays glucose consumption by body cells and moving these amino acids from tissues that were located outside the liver chiefly the muscle which leads amino acids to be obtainable in the plasma for the gluconeogenesis process in the liver then to endorse the glucose formation.[24,25,26]

TNF-α is increases in obesity and have an effect on insulin action in some tissues. In PCOS induces an inflammatory condition worsened when obesity is present, The elevated TNF-α, could effect on glucose absorption in the tissue and may cause fertility collapse in PCOS women.[27] The great existence of proinflammatory genotypes in PCOS including TNF-α receptor and polymorphisms of sequences codifying TNF-α has been suggested. Specially, greater expression of CD11c gene, which is associated with greater proinflammatory macrophage infiltration is visceral adipose tissue and subcutaneous adipose tissue, supporting a transition to decreased secretion of adiponectin also increased TNF-α and leptin secretion from adipocytes.[28,29]

PCOS stimulates high levels of IL-18 that linked with obesity, visceral adiposity and insulin resistance, metabolic syndrome and testosterone level. The increased IL-18 level can be explained by many hypotheses: First, visceral fats produce IL-18 in PCOS women who have visceral adiposity. Second, high levels of IL-18 may be caused by early changes in atherosclerose. Third, genetic defects in IL-18 encoding gene might be linked with insulin resistance, obesity and PCOS.[30,31,32]

CONCLUSION

The current study showed that the metabolic abnormalities are prevalence in women of basrah city and PCOS induce the inflammation characterize that may be responsible for the origin of PCOS.

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