Original Article

The Pro-inflammatory IL6 and serum glucose in Polycystic Ovary Syndrome

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Summary:

Background: Polycystic ovary syndrome (PCOS) is one of the most common female endocrine disorders. PCOS produces symptoms in approximately 5% to 10% of women of reproductive age (12–45 years old).
Objective: To detect the level of IL-6 in PCOS patients correlated with their serum glucose.
Patients and methods: This is a prospective study carried out at Baghdad teaching hospital in Baghdad/ Iraq from November 2011 to January 2012. In this study, 80 blood samples (40 untreated women with PCOS cases and 40 healthy control) were collected to investigate their IL-6 levels by using Enzyme linked immunosorbent assay (ELISA) technique and fasting blood sugar (FBS) by enzymatic assay.
Results: Serum IL-6 elevated in PCOS patients mainly those with high blood sugar.
Conclusion: Serum IL-6 levels were significantly higher among PCOS women than in healthy group. PCOS patients had high blood sugar when compared to control group. Significant statistical positive association was seen between serum IL-6 level and FBS among study cases.
Keywords: PCOS, IL-6 & FBS.

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Introduction:

Polycystic ovary syndrome (PCOS) is one of the most common female endocrine disorders (1). PCOS is a complex, heterogeneous disorder of uncertain etiology, but there is strong evidence that it can be classified as a genetic disease(2).
PCOS produces symptoms in approximately 5% to 10% of women of reproductive age (12–45 years old). It is thought to be one of the leading causes of female subfertility and the most frequent endocrine problem in women of reproductive age (3). The principal features are anovulation resulting in irregular menstruation, amenorrhea, ovulation-related infertility, and polycystic ovaries. Excessive amounts or effects of androgenic (masculinizing) hormones resulting in acne and hirsutism. Insulin resistance, often associated with obesity and Type 2 diabetes (4&5). Some, but not all, women with PCOS are overweight or obese, and they are at higher than average risk of developing diabetes(6). The symptoms and severity of the syndrome vary greatly among affected women(7).
Although PCOS is not completely reversible, there are a number of treatments that can reduce or minimize bothersome symptoms. Most women with PCOS are able to lead a normal life without significant complications (8).
There is no single test for diagnosing PCOS. Women may be diagnosed with PCOS based upon their symptoms, blood tests, and a physical examination. Expert groups have determined that a woman must have two out of three of the following to be diagnosed with PCOS: [Irregular menstrual periods caused by anovulation or irregular ovulation. Evidence of elevated androgen levels which can be based upon signs (excess hair growth, acne, or male-pattern balding) or high androgen levels. And lastly Polycystic ovaries on pelvic ultrasound](9).
IL-6 is a protein secreted by T cells and macrophages to stimulate immune response in human. This interleukin acts as both a pro-inflammatory and anti- inflammatory cytokine(10). It is released in response to infection, burns, trauma, and neoplasia, and its functions range from key roles in acute-phase protein induction to B- and T- cell growth and differentiation. IL-6 can have direct effects on cells, can mediate the effects of other cytokines, can be coagonistic or antagonistic in conjunction with other cytokines, and interact with glucocorticoids(11).
IL-6 is also produced by adipocytes and is thought to be a reason why obese individuals have higher endogeneous levels of C-reactive protein (CRP). In the muscle and fatty tissue IL-6 stimulates energy mobilization which leads to increased body temperature. It can be secreted by macrophages in response to specific microbial molecules, referred to as pathogen associated molecular patterns (PAMPs)(12).

Materials and method:

A prospective study conducted in the period between November 2011 and January 2012.Fourty female patients attended Baghdad medical city teaching hospital as newly diagnosed cases of PCOS according to the criteria confirmed by European society of human reproductivity and embryology and American society for reproductive medicine. And 40 apparently healthy fertile women without PCOS with age matched with the patients group ranging from (16-35) years.
Blood samples were obtained from each individual by venous puncture, samples were left to clot at room temperature, centrifuged and serum was collected for the detection of serum IL-6 level by using raybio human IL-6 ELISA kit and serum fasting glucose (FBS) was measured enzymatically. We

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have considered 2 pg/ml and 120 mml/L as the upper limits of normality for IL-6 and FBS respectively.
Statistical analysis was performed, the results were expressed as mean, SD and Chi square. The value of ($p<0.05$) was considered statistically significant.

Results:-
The distribution of all study sample according to the difference in mean of serum IL-6 and serum FBS between PCOS patients and healthy women were shown in table (1).Serum IL-6 were significantly higher in PCOS women who had high blood sugar as compared to control group.

Table (1): Mean changes of IL-6 and FBS in the study individuals

Study group Number=80			
Values	**Patient group**	**Control group**	**P value**
Number	**40**	**40**	
IL-6(pg/ml) Mean ± SD*	**6.45 ± 0.95**	**2.25 ± 0.39**	**p<0.05**
FBS(mmol/L) Mean ± SD	**100.5 ± 15.02**	**89.3 ± 13.92**	**p>0.05**

* SD = standard deviation

Table (2) shows the relation between serum IL-6 and FBS in all women included in this study. A positive association were seen between serum IL-6 and FBS.

Table (2):Serum IL-6 in relation to FBS

		IL-6		
		positive	**negative**	
FBS	**Positive**	**22**	**5**	**27**
	negative	**22**	**31**	**53**
X^2=10.127 P value=0.001		**44**	**36**	**80**

Discussion:-
Although multifunctional proinflammatory cytokine may play a role in the pathogenesis of ovarian cyst, endometriosis and PCOS(10). In the present study, serum IL-6 were significantly higher in PCOS women. This result agreed with other results who showed that IL-6 may be an early low-grade chronic inflammatory marker among PCOS patients(13). FBS in this study were non significantly higher among PCOS patients and this finding goes with previous studies which concluded 30-40 percent of women with PCOS have impaired glucose tolerance, and as many as 10 percent have type 2 diabetes by their fourth decade(14). An enhanced rate of deterioration in glucose tolerance is also evident in PCOS. Most women with the polycystic ovary syndrome are able to compensate fully for their insulin resistance, but a substantial proportion (particularly those with a first-degree relative with type 2 diabetes) have a disordered and insufficient β-cell response to meals or a glucose challenge. Before the development of frank glucose intolerance, defects in insulin secretion may be latent and revealed only in circumstances that augment insulin resistance, as with the development of gestational diabetes in pregnancy, or glucose intolerance associated with glucocorticoid administration(15). The insulin resistance of the polycystic ovary syndrome appears to impart an increased risk of glucose intolerance, diabetes. Hyperglycemia may upregulate the activity of Protein Kinase C (PKC) and Nuclear Factor (NF-kB) leading to increase IL-6 transcription and release, therefore serum IL-6 concentration was positively correlated with obesity and insulin resistance(16). Our study concluded a positive association between serum IL-6 and FBS.

Conclusion:-
Serum IL-6 levels were significantly higher among PCOS women than in healthy group, PCOS patients had high blood sugar when compared to control group,A positive association were seen between serum IL-6 and FBS.

Author Contributions:-
Hayfaa S. AL-Hadithi / acquisition of data analysis, interpretation of data , drafting of manuscript, design and interpretation of data.
Aida R. Al-Derzi / study conception, design, interpretation of data and critical revision

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