



INTERLEUKIN-6 LEVELS IN IRAQI WOMEN WITH POLYCYSTIC OVARY SYNDROME

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ABSTRACT

BACKGROUND: The change of serum Interleukin-6 (IL-6) levels in women with polycystic ovary syndrome (PCOS), as well as the relations between IL-6 levels PCOS patients and healthy control group.

OBJECTIVE: The aim of this study was to evaluate serum concentrations of interleukin-6 (IL-6) in PCOS patient's relation with healthy control group. **MATERIAL AND METHODS:** In this study, 250 Iraqi women aged between 20-50 years were studied. The patients were divided into two groups: study group (n=125, PCOS women) and age-matched controls group (n=125 normal women). The blood sample was obtained on the 2nd day of menstruation cycle. IL-6 concentrations were determined in both groups. **RESULTS:** Women with PCOS exhibited higher body mass index (BMI) and serum concentrations of IL-6 levels more than controls ($p < 0.05$); however, levels of IL-6 were not significantly increased when compared with BMI-matched controls ($p > 0.05$). IL-6 levels were significantly correlated positively with BMI and low anti-mullerian hormone (AMH) levels. **CONCLUSION:** The data of this study suggested that serum IL-6 levels were found to be higher in women with PCOS as compared to controls. Raised serum IL-6 levels may be related to high BMI and low AMH levels.

KEYWORDS : IL-6, inflammation, anti-mullerian hormone, body mass index, polycystic ovary syndrome.

INTRODUCTION

The human IL-6 gene is located at chromosome 7p21-24 and has an upstream 303 bp promoter. A SNP, which results in exchange of G-C at position -174 in the promoter region of the IL-6 gene, has been found to influence its transcription rate⁽¹⁾. Correlation of circulating inflammatory markers with obesity and insulin resistance are common findings in PCOS⁽²⁾.

Interleukin -6 expression in adipose tissue correlates with obesity. It is still not known whether these parameters of chronic inflammation are primary or secondary to obesity and/or insulin resistance especially since short term administration of IL-6 in humans failed to impair insulin sensitivity⁽³⁾. A high IL-6 level is not an intrinsic characteristic of PCOS, but may be a useful monitoring biomarker for the treatment of PCOS^(4,5).

Most women with polycystic ovary syndrome have insulin resistance, hyperinsulinemia, and elevated serum IL-6 levels. These elevated IL-6 levels may have links with insulin resistance and hyperandrogenism. Considering the relationship between IL-6 levels and insulin resistance, treatment such as metformin has the potential to affect serum IL-6 levels in PCOS patients⁽⁶⁾.

Low-grade chronic inflammation in women with PCOS is involved in the pathogenesis of T2DM and cardiovascular disease. Interleukin-6 (IL-6), a major pro-inflammatory cytokine in chronic inflammation, has been shown to be closely associated with insulin resistance and cardiovascular abnormalities. Early research *in vivo* showed that infusion of human recombinant IL-6 could induce gluconeogenesis, subsequent hyperglycemia, and compensatory hyperinsulinemia. Obesity, a major risk factor for T2DM, was reported to be associated with elevated IL-6 levels⁽⁷⁾.

In contrast, IL-6 levels decreased in PCOS patients after they reduced their level of IR and body mass. IL-6 might play a key role in the development of cardiovascular disease through

metabolic, endothelial, and coagulant. Elevated levels of IL-6 were reported to be associated with an increased risk of future myocardial infarction and athero thrombosis⁽⁸⁾.

Interleukin -6 may be a useful as a biomarker for the diagnosis of PCOS and the treatment of T2DM and cardiovascular diseases in women with PCOS. However, the findings of recent studies of changes in IL-6 levels in PCOS patients are inconsistent. Although some studies reported significant elevations in IL-6 levels in women with PCOS compared with controls^(9,10).

The change of serum interleukin-6 (IL-6) levels in women with polycystic ovary syndrome (PCOS), as well as the relations between IL-6 levels and body mass index (BMI), insulin resistance (IR) and androgen status of PCOS patients, are not fully understood⁽¹¹⁾.

MATERIALS AND METHODS

The study was conducted from February 2019 to January 2020. A total of 250 women with and without polycystic ovarian syndrome (PCOS) who were collected from the high Institute of infertility diagnosis Assisted reproductive technology (ART) / Al-Nahrain University. The history and all data taken for each PCOS patients. The study was approved by the Institutional Review Board (IRB) of Baghdad University. Control: The control group was collected from healthy normal women.

SAMPLES COLLECTION

The first step was the collection of information from the patients, and then the second step was blood samples collection. Blood samples were collected from all the patients and controls, two milliliters of venous blood were collected in sterile screw cap plastic gel tubes.

SERUM SEPARATION

Serum was obtained from the blood samples were left for 30 minutes at room temperature, then centrifuge at 3000 rpm. For ten minute, then serum for each sample was collected in

appendrof tubes and stored in deep freeze at -20 °C until the time for using in ELISA technique for detection of IL-6 level.

RESULTS

The level of IL-6 showed significant difference in PCOS patients and healthy control. The level was $2.88E2 \pm 166.57$ (Pg /ml), $1.36E2 \pm 105.06$ (Pg /ml) in PCOS patients and healthy control respectively. Rang of serum interleukin-6 (IL-6) level were from 0 to 627 Pg/ml, table 1.

Table 1: Serum Interleukin-6 (IL-6) Value Of The PCOS And Control Groups Involved In The Study

Serum IL-6 (Pg /ml)	Number	Mean	Std. Deviation	P-value
Patients	125	2.88E2	166.57	<0.0001
Controls	125	1.36E2	105.06	

*E2: $\times 100$

DISCUSSION

The current study suggested that Proinflammatory cytokines may play a role in the pathogenesis of polycystic ovarian syndrome. In the present study, serum IL-6 was significantly higher in PCOS women. This result agrees with that of another study which showed that IL-6 may be an early low-grade chronic inflammatory marker among PCOS patients⁽¹²⁾.

IL-6 is an adipokine that is produced by adipocytes and stromal cells of the fat tissue and evidence show that IL-6 may play a role in insulin resistance⁽¹³⁾. Moreover, mediators of chronic low-grade inflammation such as IL-6 are predictors of risk of type 2 of diabetes⁽¹⁴⁾. It has been presented that in PCOS women, IL-6 levels are increased⁽¹⁵⁾. Several studies have suggested that IL-6 increment may be related to hyperandrogenism and insulin resistance in PCOS patients. However, the findings on effects of IL-6 on insulin resistance are different. Some evidence has shown that insulin resistance in PCOS patients is due to defects in insulin signaling pathway and in PCOS, adipocyte-derived factors such as free fatty acids and IL-6 affect insulin signaling in the skeletal muscles⁽¹⁶⁾.

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