

Levels of Interleukine-6 and Interleukin -18 in Iraqi Women with Polycystic Ovarian Syndrome Infected with Urinary Tract Infections

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Abstract

Background: Women with the polycystic ovarian syndrome (PCOS) are among the most common sufferers of endocrine abnormalities, so Urinary tract infections were the most prevalent sickness for women worldwide, Elevated levels of interleukins are presumably part of the pathogenesis of this clinical manifestation, for this reason, this study intends to examine the levels of interleukin-6 and interleukin-18 in PCOS Iraqi women who have been diagnosed with UTIs. **Patients and Methods:** 159 blood and urine specimens were collected from Iraqi women visiting Al-Yarmouk teaching hospital in Baghdad with the control group. The urine specimen was cultured on MacConkey and blood agar, and interleukin (IL-6 and IL-18) levels were measured using the ELIZA technique. **Results:** Results current showed no significant variance ($P>0.05$) mean of age between PCOS with and without UTI, and UTI patients were (24.94 ± 4.14 , 25.84 ± 4.89 , 27.00 ± 2.12) respectively compared to control (28.70 ± 7.88). According to BMI, a non-significant difference was noticed between the studied groups, so level of IL-6 in the study groups (PCOS with and without UTI) (8.93 ± 10.29 ; 19.35 ± 5.08 pg/mL) was more than UTI group (7.36 ± 5.52) pg/mL, as well as levels of IL-18 in (PCOS with and without UTI) (9.36 ± 2.18 ; 9.27 ± 1.47 pg/mL) more than UTI (8.58 ± 1.28 pg/mL), and control (5.30 ± 0.49 pg/mL). the current study showed levels of IL-6 were increased significantly ($p<0.01$) in women infected with UTIs caused by *E. coli* (20.0580 ± 14.85921), *Klebsiella pneumoniae* (16.4148 ± 5.31959), *Staphylococcus aureus* (19.2518 ± 7.04125), *Pseudomonas aeruginosa* (16.9500 ± 2.75482), respectively. **Conclusion:** No significant variance for age and BMI between PCOS with UTI and without UTI, and UTI patients, So both (IL-6 & IL-18) levels in groups (PCOS with and without UTI) were more than UTI group.

Keywords: Interleukins (IL-6&IL-18), Polycystic Ovarian Syndrome (PCOS), Urinary Tract Infections (UTIs) Iraqi Women.

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INTRODUCTION

The PCOS is a prevalent endocrine condition in reproductive-age women⁽¹⁾. PCOS describes as a heterogeneous endocrine disorder that impacts many women of reproductive age worldwide⁽²⁾. This syndrome is often associated with enlarged and dysfunctional ovaries, excess androgen levels, and resistance to insulin⁽³⁾. Although the cause of PCOS is still unknown, there is growing evidence that the condition has a significant genetic component due to its strong familial propensity. The diverse phenotypic and clinical and biochemical presentation are caused by several genes.⁽⁴⁾ PCOS is a pro-inflammatory condition characterised by persistent low-grade inflammation, an increase in cytokines and inflammatory mediators, malfunction of the ovaries, abnormalities in individuals' metabolisms, and effects on endometrial implantation.⁽⁵⁾ PCOS may be linked to low-grade chronic inflammation and may elevate serum IL-18 levels.⁽⁶⁾

Urinary tract infections (UTIs) are among the most common bacterial infections in women and the elderly.⁽⁷⁾ The

infection occurs more commonly in women than in men this is primarily because of anatomic differences, considering the female urethra (short urethra), its proximity to the anus, the moist periurethral environment in women, and hormonal activity⁽⁸⁾.

Interleukin-6 (IL-6), and other cytokines are involved in the cytokine response to UTIs. There are several types of cells that release IL-6, including macrophages and fibroblasts as well as endothelial cells⁽⁹⁾. Women with active UTIs generate the inflammatory cytokine IL-18, which is implicated in the development of inflammasomes⁽¹⁰⁾. Of the most prevalent infections globally is UTI and one of the main and common causes of this infection is the bacterium Uropathogenic *Escherichia coli* (*UPEC*)⁽¹¹⁾. In comparison to their contemporaries, women with polycystic ovarian syndrome, a prevalent hyperandrogenic disorder, may experience an elevated rate of UTI.⁽¹²⁾ IL-6 is one of the many cytokines that fat cells in the body, called adipocytes, let out. In turn, IL-6 levels in the body are kept in check by how close they are to other cytokines. The significance of IL-6 in PCOS is being researched because of its involvement in a wide range

of other pathological illnesses, including rheumatoid arthritis, cardiovascular disease, asthma, colon cancer, and many more⁽¹³⁾. So Interleukin-18 (IL-18) belongs to the IL-1 family due to signal transduction pathways, structural homology, and receptor use⁽¹⁴⁾.

MATERIALS AND METHODS

159 blood and urine specimens from Iraqi women were divided into four groups, PCOS with and without UTI, and UTI without PCOS, and apparently healthy women who don't suffer from UTI or PCOS, the specimens collected from women in Al- Yarmouk teaching hospital at Baghdad from October to December 2021, in term of age the women from 17-45 years. and measuring the body mass index (BMI)= weight (Kg)/tall(cm²). measuring the level of interleukins in the serum by enzyme-linked immunosorbent assay (ELIZA) technique. Urine specimens were detected for the presence of UTI by general urine examination, urine culture, and using the traditional biochemical test with VITEK 2 compact system for bacterial diagnosis.

RESULTS

Table (1) illustrates in case of age, there is no significant variance (P>0.05) mean of age between PCOS with and without UTI, and UTI patients were (24.94±4.14, 25.84±4.89, 27.00±2.12) respectively compared to control (28.70±7.88). According to BMI, a non-significant difference was noticed between the studied groups, BMI in PCOS without UTI, PCOS with UTI, and UTI patient groups were (29.51±5.63, 29.64±6.12, and 29.12±7.06) Kg/m², respectively, and compare with control 26.19±3.38 Kg/m².

Table (1): Distribution of study groups with control according to age and BMI

Parameter	PCOS & UTI	PCOS	UTI	CONTROL	P-value
Age	25.84±4.89	24.94±4.14	27.00±2.12	28.70±7.88	N.S
BMI	29.64±6.12	29.51±5.63	29.12±7.06	26.19±3.38	N.S

Table (2): The levels of interleukins (IL -6, IL -18) in patient groups' study

Interleukins levels	PCOS with UTI	PCOS without UTI	UTI	CONTROL	P-value
	M± S.D				
IL-6	18.93±1.029	19.35±5.08	17.36±5.52	15.69±1.45	0.01
IL-18	9.36±2.18	9.27±1.47	8.58±1.28	5.30±0.49	0.01

Mean± Std. Deviation, N. S= non-significant.

The level of IL-6 in the study groups (PCOS with and without UTI) (8.93±10.29; 19.35±5.08 pg/mL) was more than UTI group (7.36±5.52) pg/mL, compared to the control group (15.69±1.45), as well as levels of IL-18 in (PCOS with and without UTI) (9.36±2.18; 9.27±1.47) more than UTI (8.58±1.28), and control (5.30±0.49).

Table (3): The levels of interleukine-6 and interleukine-18 with the bacterial types isolated from urine for women infected with PCOS&UTI

Interleukins levels	<i>Escherichia coli</i>	<i>Klebsiella pneumoniae</i>	<i>Pseudomonas aeruginosa</i>	<i>Staphylococcus aureus</i>	P-value
	M± S.D				
IL-6	20.0580±14.85921	16.4148±5.31959	16.9500±2.75482	19.2518±7.04125	0.01
IL-18	9.4667±2.29733	10.0900±3.58822	8.7095±.61380	8.7775±.16689	0.01

Table-3 showed levels of IL-6 were increased significantly (p<0.01) in women infected with UTI caused by *E. coli* (20.0580±14.85921), *Klebsiella pneumoniae* (16.4148±5.31959), *Staphylococcus aureus* (19.2518±7.04125), *Pseudomonas aeruginosa* (16.9500±2.75482). on the other side, the *Klebsiella pneumoniae* shows the highest IL-18 (PCOS with and without UTI) (9.4667±2.29733; 10.0900±3.58822; 8.7095±.61380; 8.7775±.16689) the (PCOS with and without UTI) of IL-18 with *E. coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus* respectively.

DISCUSSION

The current findings agreed with^(15,16), who concluded that there were no significant differences in age between the PCOS and control, as well as^(17,18,19,20). The lack of a significant difference between groups indicates neutrality in the results because age is related to immunity, hormone factors, hormone secretion, and other factors. a substantial incidence of symptomatic bacterial UTIs according to women's ages, with the highest incidence found in those between the ages of 21 and 30.^(21,22) The highest women's age range at the reproductive age of 16-30 years were more susceptible to urinary tract infections⁽²³⁾. In the case of BMI, the current results agreed with^(15,18,16,19,24,25) who concluded that non-significant difference in BMI between PCOS and the control group. A higher risk of urinary tract infections appears to be linked to a higher BMI.⁽²⁶⁾ The existing study found that women with PCOS in Iraq have a higher upper body weight than their counterparts in other countries⁽²⁷⁾, which could be due to our country's different dietary habits and the lack of exercise among Iraqi women. Studies have

shown that adopting a healthier lifestyle improves the hormonal health of PCOS patients who suffer from weight gain which will lead to decreased testosterone levels, which increases insulin sensitivity⁽²⁸⁾.

Serum interleukin levels are altered in polycystic ovarian syndrome⁽²⁹⁾. The result of a local study of the interleukin-6 (IL-6) level was significantly greater in PCOS patients in comparison with a control group^(30,31). It is a condition that causes an increase in the production of several inflammatory cytokines, including IL-6, as a result of the polycystic ovarian syndrome. IL-6 levels were mostly based on obesity⁽³²⁾. The other study linked UTIs with IL-6⁽³³⁾. According to our findings, the levels of IL-6 in the UTI and control groups were significantly different from the control. In both cases, interleukin serves as a helpful indication. Our findings are supported as well⁽³⁴⁾.

Serum level of IL-18 in total patient groups compared with control groups. This results in agreements⁽³⁵⁾. Serum Interleukin-18 levels are greater in women with PCOS than in healthy women⁽³⁶⁾. The PCOS group had greater IL-6 and IL-18 levels than the control group⁽³⁷⁾. There was a significant difference in IL-18 levels between the PCOS and control groups, while IL-6 levels were significantly higher in the PCOS group⁽³⁸⁾. PCOS was related to considerably higher IL-18 levels than in healthy women, and these elevated levels of cytokines were found to be associated with PCOS even in the absence of obesity. Serum IL-18 may serve as a good indicator of the inflammatory process linked to obesity and IR⁽³⁹⁾. Furthermore, there was a positive correlation between IL-18 and IL-6, which are both associated with inflammation⁽⁴⁰⁾, which is consistent with our current study.

The study demonstrates a rise in IL-6 levels in *E. coli* and *S. aureus*. Given the function of IL-6 in the immune response to *E. coli* infection, *E. coli* produced the greatest proportion of interleukin-6^(41,42). When bacteria reach the mucosal surface of the urinary system, cytokine responses occur, and attachment to epithelial cells initiates a cascade of cytokines including IL-6, IL-1, IL-8, and other chemokines⁽⁴³⁾. The levels of IL-6 in the serum of women with an acute UTI caused by *E. coli*, in comparison to the control group were significantly greater⁽⁹⁾. Patients with UTI who have elevated levels of urine IL-6 may be returning their urinary tract epithelial cells to normal production, especially if they have been infected with gram-negative bacilli. A rise in body temperature and a boost in the generation of CRP, an indicator of illness, can be attributed to an increase in blood IL-6 concentrations⁽⁴⁴⁾. There is no doubt that the cell-wall components of Gram-positive bacteria, such as peptidoglycan and teichoic acid, play a significant role in the activation of monocytes and macrophages, which ultimately results in the release of cytokines; however, exotoxins may also play a role in this process⁽⁴⁵⁾. Gram-negative bacteria can cause host cells, especially monocytes and macrophages, to make a lot of cytokines. Endotoxin (lipopolysaccharide), which is a big part of Gram-negative bacteria's cells, is one of the most

powerful triggers of inflammatory cytokines. The complement and coagulation systems are also activated by endotoxins^(46,47).

CONCLUSION

1. No significant variance in age between PCOS with and without UTI compare to UTI patients
2. No significant difference in BMI was noticed between the studied groups.
3. Levels of both levels of (IL-6 & IL-18) in groups (PCOS with and without UTI) were more than UTI group.

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