

## Serological diagnosis of IL-1 $\beta$ and IL-6 associated with Urinary tract infections among pregnant women in Thi-Qar Governorate

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Received: 2024-04-29, Revised: 2024-05-09, Accepted: 2024-05-15, Published: 2024-06-19

**Abstract-** Urinary tract infections (UTIs) are considered the most prevalent infectious disorders. They can affect the entire urinary tract or specific a portion of it and are mostly brought on by bacteria that are found in the intestine. The present study included 82 pregnant women whom age ranged from 17 to 40 (mean  $\pm$  SD: 27.44  $\pm$  6.66) and divided to 13 in the first trimester, 9 in the second, and 60 in the third. Also, the study included 56 apparently healthy pregnant women as a control, with age (mean  $\pm$  SD: 27.11  $\pm$  5.59). Patients with UTIs had lower mean serum levels of IL-6 (12.08  $\pm$  16.35 pg/ml) compared to control group (42.19  $\pm$  28.0 pg/ml). Also, the same patients showed had lower mean serum levels of IL-1 $\beta$  (6.91  $\pm$  11.78 pg/ml) compared to control group (43.32  $\pm$  34.62 pg/ml). The conclusions, UTIs continues to be one the most socio-health problems that need a lot of care diagnosis and treatment. Both IL-6 and IL-1 $\beta$  in UTIs pregnant women identification may contribute as Diagnostic marker tools for associated infections.

**Keywords:** UTIs, IL-6 and IL-1 $\beta$ , UPEC.

### I. INTRODUCTION

The UTIs are among the most prevalent infectious disorders. They can affect the entire urinary tract or just a portion of it and are mostly brought on by bacteria that are found in the intestine. UTIs are classified as lower urinary tract infections if they affect the bladder or urethra, and upper UTIs if they affect the kidneys and ureter. There are two categories of UTIs, simple and complex [1]. Because of their shorter urethra, which is constantly polluted with infections from the vagina and rectum, women are more vulnerable than men. Because of changes in the urinary system during pregnancy, UTIs

are more prevalent and have been linked to substantial hospital admissions in 20% of pregnant women [2]. Higher progesterone, slower peristalsis, urine retention, uterine expansion, bladder displacement, and higher residual urine volume are among the factors that predispose pregnant women to bacteriuria [3]. Another main cause of UTIs in married pregnant women is that having sex during pregnancy increases the chance that a woman may have urinary tract infections [4]. Major risk factors for UTIs include diabetes, anemia, poor personal cleanliness, and a history of UTIs [5]. Raises the possibility of an upper UTIs as a result of physiological alterations. Urinary retention is caused by the expanding uterus, and progesterone hormone changes in mothers relax the ureteral muscle, accumulating urine in the bladder and raising the risk of UTIs [6]. An increased risk of UTIs during pregnancy is also related to the decreased immune responses that take place during pregnancy [7]. The Interleukin 6 (IL-6) is generated in reaction to an infection or damage to the tissues. It is a pro-inflammatory cytokine that stimulates both adaptive and innate immune responses. When pattern recognition receptors are activated, leukocytes and stromal cells produce IL-6 as part of the innate immune response. The IL-6 then attracts immune cells and initiates the response of B and T cells [8]. The pro-inflammatory cytokine, Interleukin 1 $\beta$  (IL-1 $\beta$ ) is generated in response to necrotic cell death and tissue injury, and it plays a role in the etiology of a number of inflammatory illnesses [9]. Human neutrophils' antimicrobial activity against Uropathogenic *Escherichia coli* (UPEC) is regulated by the release of IL-1 $\beta$  from them when exposed to UPEC[10]. The present study aims to evaluate the role of selected cytokines amongst pregnant women with UTIs by assaying the serum levels of IL-6, and IL-1 $\beta$  using Enzyme-linked immunosorbent assay (ELISA) technique.



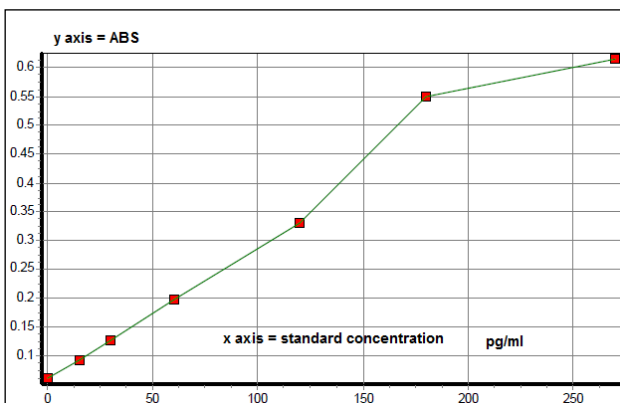
## II. PATIENTS AND. METHOD

**Samples Collection:** A pregnant patient (82) enrolled in the present study, who were aged from 17 to 40, had an age mean  $\pm$  SD ( $27.44 \pm 6.66$ ) and were divided into three groups based on the number of trimesters, as: 13 in the first trimester, 9 in the second, and 60 in the third. Also, the study included 56 apparently healthy pregnant women (mean  $\pm$  SD ( $27.11 \pm 5.59$ )) were considered as a control. A 138 blood samples

were collected from all participants whom visiting Bint Al-Huda Teaching Hospital in Thi-Qar Province during the period between August, 2023 and January, 2024. the following patient data was collected: name, age, months of pregnancy, presence of immunological or chronic disorders, number of births and abortions, antibiotics use, socioeconomic position and educational attainment. All blood samples (5 ml) were collected and brought to the laboratory. The samples were centrifuged for 10 minutes at 3000 rpm. Then, the supernatant was frozen at  $-20^{\circ}\text{C}$  until be used subsequently for ELISA.

### Interleukine-6 and Interleukine-1 $\beta$ Determination:

The serum levels of IL-6 and IL-1 $\beta$  were quantitatively measured among UTIs pregnant women and healthy control subjects by Enzyme Linked Immunosorbent Assay (ELISA) according to the instruction of the manufacturing company (SunLong Biotech, SL100Hu\_1, SLD001Hu). The present study gained the ethical approval via Thi-Qar Health Directorate agreement coded 625/2023. Chi-square ( $\chi^2$ ), T-tests and person correlation ( $r$ ) were applied to statistical reading and comparison of results.  $P$ -value less or equal than 0.01 was considered as significant.



A. Figure 1: Standard curve of IL-1 $\beta$  concentration in serum.

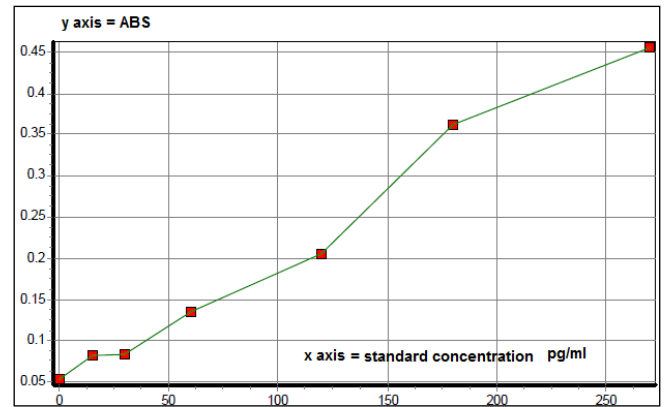


Figure 2: Standard curve of IL-6 concentration in serum.

## III. RESULTS AND DISCUSSION

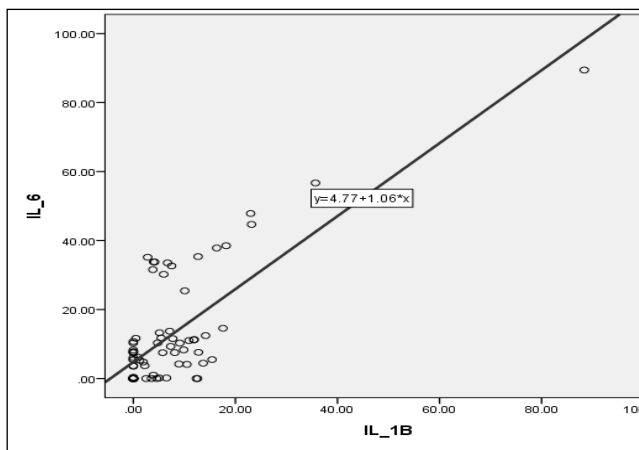
As shown in Table (1), pregnant women with UTIs had lower mean serum levels of IL-6 ( $12.08 \pm 16.35$  pg/ml) than in the control group ( $42.19 \pm 28.0$  pg/ml). This outcome was with high significant differences ( $p \leq 0.002$ ). The current study's findings showed that IL-6 was found in every serum sample, with a concentration range of 0.158–89.425 pg/ml. Also, patients with UTIs had lower mean serum levels of IL-1 $\beta$  ( $6.91 \pm 11.78$  pg/ml) than the control group ( $43.32 \pm 34.62$  pg/ml), as table (1) illustrates. These results were with significant differences between the patient and control groups ( $p \leq 0.001$ ). The current study's findings showed that IL-1 $\beta$  was found in every serum sample, with a mean concentration of  $6.91 \pm 11.78$  pg/ml and a concentration range of 0.486 – 88.359 pg/ml.

Table I: The Mean Levels of IL-6 and IL-1 $\beta$  in Pregnant Women and Control Serum.

Cytokine	group	Mean $\pm$ std. deviation	T-value	P-value
IL-6	patient	$12.08 \pm 16.35$	5.43 <sup>*</sup>	0.0002
	control	$42.19 \pm 28.0$		
IL-1 $\beta$	patient	$6.91 \pm 11.78$	7.15 <sup>*</sup>	0.001
	control	$43.32 \pm 34.62$		

$P$ -value  $\leq 0.01$ .

The present findings founded an positive direct correlation between serum levels of both IL-1 $\beta$  and IL-6 in pregnant women, with an correlation coefficient Of ( $R= 0.76$ ) ( Figure 3).



**Figure III** :Correlation between IL-6 and IL-1 $\beta$ .

It is known now that IL-1 $\beta$  can stimulate the synthesis of IL-6 through a number of signaling pathways, including NF- $\kappa$ B, PI3K, and JNK, it can induce cells to create IL-6. Studies have demonstrated that a complete IL-6 response can be elicited by as little as 0.1 ng/ml of IL-1 $\beta$ . This implies that IL-1 $\beta$  is a strong inducer of IL-6, an essential molecule for the body's defense systems [14]. The present study results showed that pregnant women's mean serum levels of IL-6 and IL-1 $\beta$  were lower than those of the control group. The study finding seems to be in aligned with those other related studies [11-12].

The findings showed that pregnant women's mean serum levels of IL-6 and IL-1 $\beta$  were lower than those of the control group. The study's findings aligned with those of Denney *et al.* (2011), who discovered that pregnant women with UTIs had lower levels of IL-6 and IL-1 $\beta$  in comparison to the control group [15].

Infections are major complications in patients with UTIs after the peak reaction has passed or after the illness is successfully treated with antibiotics or the immune system, which lowers the inflammatory response, that IL-6 levels may be tested. Furthermore, there may be no discernible difference in IL-6 levels between upper and lower UTIs, suggesting that IL-6 may not always accurately reflect the intensity or location of the infection [16]. The impact of IL-6 when a woman gives birth, whether it occurs during a preterm delivery, and how closely linked it is to the fetal tissue damage that results from it [17]. When combined, these adverse systemic conditions may cause maternal fetal tolerance to break down early and result in an early miscarriage. Thus, a healthy pregnancy requires controlled levels of estrogen, progesterone, myeloid derived suppressor cells, and balanced T<sup>H1</sup>/T<sup>H2</sup> cytokines [18]. The use of metformin was also linked to lower concentrations of the inflammatory cytokines TNF $\alpha$ , IL-1 $\alpha$ , IL-1 $\beta$ , and IL-6 in pregnant women's blood, placenta, and omental tissue [19]. In order to prevent severe inflammation and tissue damage, the infection may inhibit the placenta's or the cells producing amniotic

fluid's IL-1 $\beta$  in pregnant women [20]. The infection may cause the release of IL-1Ra, which binds to IL-1 $\beta$  and prevents it from doing its job in order to shield the developing embryo from IL-1 $\beta$ 's detrimental consequences [21,22].The infection might change the vaginal microbiome's equilibrium, which could impact the genital tract's production of IL-1 $\beta$  and other cytokines [23].

#### IV. CONCLUSIONS

UTIs continue to be one the most socio-health problems that need a lot of diagnosis and treatment. Both IL-6 and IL-1 $\beta$  in UTIs pregnant women identification may contribute as accurate diagnostic tools for associated infections.

#### CONFLICT OF INTEREST

Authors declare that they have no conflict of interest.

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