

## Estimation of Interleukin -6 and Tumor Necrosis Factor-Alpha Levels in Menopausal Women with Urinary Tract Infections

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### ABSTRACT

Urinary tract infections (UTIs) are very common, especially among women of reproductive age, and affect people of both sexes.

This research was out to quantify cellular Interleukin levels in postmenopausal women experiencing UTIs. Results: The results of the results of the most recent research shown both IL-6 and TNF- $\alpha$  were very high in women with urinary tract infection ( $P>0.01$ ) and that levels of these cellular motility were positively correlated.

Conclusions: The current study found a relationship between increased levels of IL-6 and TNF- $\alpha$  in serum of postmenopausal woman patient with urinary tract infection.

**Keywords-** Urinary Tract Infections (UTI), IL-6, TNF- $\alpha$ , Menopause.

### I. INTRODUCTION

The most frequent kind of bacterial infection is an infection of the urinary tract (UTI), as they are prevalent in a large proportion at different ages and for both sexes, but they are more prevalent in females due to several reasons, the most important of which are the proximal of the urethral opening between vaginal opening and the anus, urethral length and pregnancy (Stefaniuk et al., 2016).

Urinary tract infection (UTI) occurs when bacteria or fungi invade any part of the urinary system (urethra, bladder, ureter, kidney). The most common pathogens factors were Escherichia coli, Klebsiella pneumoniae, Enterococcus faecalis, and Proteus mirabilis. (Neugent et al., 2020).

The effect of urinary tract infection ranges between Moderate symptoms to renal scarring, hypertension, chronic kidney disease and acute sepsis of blood (Das, 2020).

Cytokines are small proteins secreted in response to the antigen response, and they play a role in inflammation similar to that of hormones, which is why

they are so important in the host's defenses against infection. (Klein and Hultgren, 2020).

IL-6 is a soluble cellular cytokines that plays a major role in many biological processes and inflammatory response share in host defense mechanisms, antigen-specific immune response and production of C-reactive protein (CRP) (Ataie-Kachoe et al., 2013).

Numerous cell types, such as B-cells, T-cells, fibroblasts, monocytes, and endothelial cells, generate IL-6. (Fujihara et al., 2020).

IL-6 play a protective role during bladder infection, on the other hand in deficiency of IL-6 lead to increases the number of intracellular bacterial communities (IBC) that allow Uropathogenic Escherichia Coli (UPEC) to evade the innate immune system and contribute in urinary tract infection (Edwards et al., 2023).

TNF- is a kind of cytokine that is mostly produced by T and B cells and monocytes. Dendritic cells, glomerular cells, and endothelial cells in the kidney can all produce TNF- (Rizk et al., 2013), so it's not like the kidneys don't have immune systems. Among TNF-'s many effects is the induction of cytotoxicity,

apoptosis, and necrosis (Vazquez-Huerta et al., 2014). Additionally, TNF- contributes to the utilization of connective tissue cells and the reduction of glomerular filtration rate (GFR) by modifying endothelial permeability to blood vessels. An increase in TNF-levels also indicates the existence of bladder inflammation and UTI (Jiang et al., 2013 demonstrate the connection between UTI and TNF-).

Increased concentration of TNF- $\alpha$  has been observed in women with urinary tract infection.

The natural biological transition known as menopause occurs when estrogen levels in women naturally decline. After menopause, this hormone levels drop, causing immune system changes that boost cellular cytokines like IL-6 and otherwise aid in innate immunity. To reduce the prevalence of urinary tract infections, estrogen hormone promotes the growth of lactobacillus in the vaginal epithelium (Metcalf et al., 2021) and inhibits the spread of Enterobacteriaceae inside the vagina (Raz and Naber, 2011). As a result, the elderly are more likely to get infectious illnesses, such as UTIs. This may be because to age-related functional changes in the immune system, such as the alterations in the urinary epithelium that result in decreased resistance to infection. (Kim et al., 2012).

## II. MATERIALS AND METHODS

This research was conducted by the Department of College at the University of Tikrit. Patients provided samples for analysis.

### Study Design:

Blood samples of 90 patients (study group) were collected (60 patients) and control group (30 control healthy women) for the period (1/12/2021 – 28/2/2022), with personal interview was done for each

woman, through which a questionnaire form was filled out that includes several questions including housing, chronic diseases diabetes and blood pressure. UTI was confirmed by a general urine test in the laboratory.

### Blood Samples:

Blood samples were collected from the vein using sterile medical syringes and blood samples were placed in gel tubes and left at 24C° for about 30 min until coagulation occurred, then centrifuge was done at 3000 cycles / minute for 10 minutes to obtain serum that was distributed on appendroff tubes and then kept at a temperature of -20C° until used.

### Immuno Assays:

ELISA technique was used to estimate IL-6, TNF- $\alpha$  levels in the serum of current study, the test was done using a kit manufactured by the SUNLONG Chinese company and the serum test was done based on information provided by the manufacturer.

### Statistical Analysis:

Statistical testing was conducted. by using the statistical program- 17 Minitab by applying the analysis of variance test (ANOVA) and the averages value were compared with a significant at  $p < 0.05$ .

## III. RESULTS

Figure (1) and table (1) reveal that IL-6 levels were higher in women with urinary tract infections than in the control group, with the former having levels of 9.91150.80 ng/L and the latter having levels of 12.4840.78 ng/L. Figure (2) and Table (1) from the present research demonstrate that the mean and standard deviation of TNF- levels for the experimental group were 37.50375.70 and 5.2730.08, respectively; this difference is statistically significant at the  $P < 0.01$ .

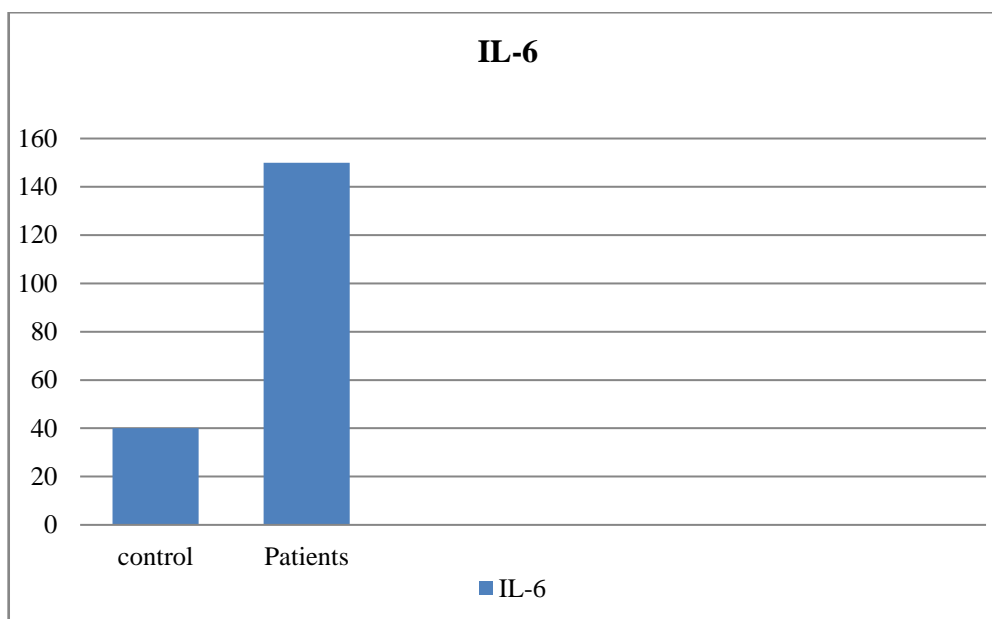


Figure 1: IL-6 levels in study group and control group.

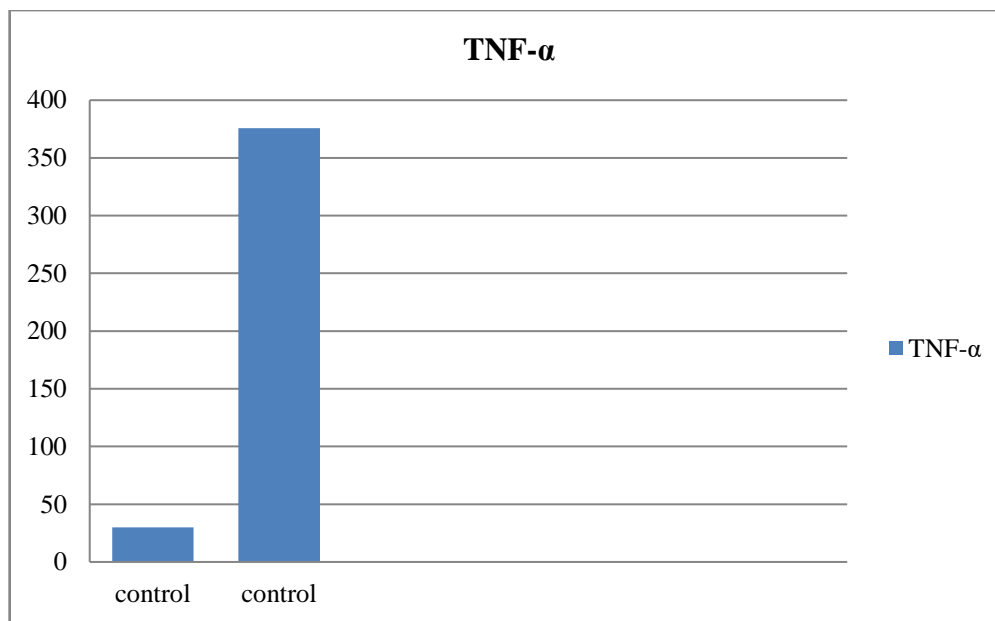


Figure 2: TNF-α levels in study group and control groups.

Table (1): shows the value of IL-6 & TNF- α in Study groups & Control group on level P < 0.05

TNF-α (pg/ml)	IL-6 (ng/l)	Study groups
30.08±5.27	40.78±12.48	Control group
375.70±37.50	150.80±9.91	Study group
0.00002	0.00004	P-value

#### IV. DISCUSSION

In general, during infection, which induced immune response represented by and inflammation, many and inflammation cells begin to secreted a cellular cytokine, which are soluble proteins that are enable communication in between cells as an immune response which increased post infection, including Other inflammatory markers besides C-reactive protein include interleukin-6 (IL-6) and tumor necrosis factor (TNF-). (CRP) (Al-Khafaf., 2012).

The results obtained from current study agreed with study Stepan et al., 2019 conducted an increase in concentrations of inflammatory cellular cytokines in serum such as (TNF-α, IL-6, CRP, IL-1) in postmenopausal urinary tract infection where the low level of estrogen affects on monocytes and lymphocytes. and also, our results agreed with the study (Ching et al. 2020).

They pointed the major roles of IL-6 in the immune response by response in production of antibodies and differentiate of T- cells and contributes to the regulation of the balance between regulatory T- cells and T- helper cells (Tanaka et al. 2012), the results of current study also agreed with (Ali and Jaafar.,2022), which found an elevation in the level of IL-6 in patients with urinary tract infection as it is involved in regulating the migration of white blood cells to the site of infection

and control the acute phase of immune responses (Zarkesh et al., 2015).

In postmenopausal women, IL-6 levels are positively associated with those of TNF- and IL-1; both of these cytokines serve to increase IL-6 production, while IL-6 itself may alter their synthesis. therefore, levels of these cellular cytokines are directly related (Gameiro et al., 2010) This agreed the results of the current study that showed an increase in the level of TNF-α which is a type of pre-inflammatory cytokines and it's role in inflammation. Our study was also agreed with the Al-Kaabi and Al-Khalidi.,2020 study, which indicated a clearly elevated level of TNF-α in patients with urinary tract infection.

#### REFERENCES

- [1] Neugent, M. L., Hulyalkar, N. V., Nguyen, V. H., Zimmern, P. E., & De Nisco, N. J. (2020). Advances in understanding the human urinary microbiome and its potential role in urinary tract infection. *MBio*, 11(2), e00218-20.
- [2] Stefaniuk, E., Suchocka, U., Bosacka, K., & Hryniewicz, W. (2016). Etiology and antibiotic susceptibility of bacterial pathogens responsible for community-acquired urinary tract infections in Poland. *European Journal of Clinical Microbiology & Infectious Diseases*, 35(8), 1363-1369.

- [3] Das, S. (2020). Natural therapeutics for urinary tract infections—a review. *Future Journal of Pharmaceutical Sciences*, 6, 1-13.
- [4] Klein, R. D., & Hultgren, S. J. (2020). Urinary tract infections: microbial pathogenesis, host–pathogen interactions and new treatment strategies. *Nature Reviews Microbiology*, 18(4), 211-226.
- [5] Edwards, G., Seeley, A., Carter, A., Patrick Smith, M., Cross, E. L., Hughes, K., ... & Hayward, G. (2023). What is the diagnostic accuracy of novel urine biomarkers for urinary tract infection?. *Biomarker Insights*, 18, 11772719221144459.
- [6] Ataie-Kachoei, P., Pourgholami, M. H., & Morris, D. L. (2013). Inhibition of the IL-6 signaling pathway: a strategy to combat chronic inflammatory diseases and cancer. *Cytokine & growth factor reviews*, 24(2), 163-173.
- [7] Fujihara, K., Bennett, J. L., de Seze, J., HARAMURA, M., Kleiter, I., Weinshenker, T. (2020). Interleukin-6 in neuromyelitis optica spectrum disorder pathophysiology. *Neurology-Neuroimmunology Neuroinflammation*, 7 (5).
- [8] Rizk, A. H., El-Shishtawy, M., & Al-Kholy, A. F. (2013). Tissue extract fluid cytokine levels as markers for wound vitality: an experimental comparative study. *J Am Sci*, 9, 188-93.
- [9] Kallioliass, G. D., & Ivashkiv, L. B. (2016). TNF biology, pathogenic mechanisms and emerging therapeutic strategies. *Nature reviews rheumatology*, 12(1), 49-62.
- [10] Raz, R., & Naber, K. G. (2011). Urinary tract infection in postmenopausal women. *Korean journal of urology*, 52(12), 801-808.
- [11] Gameiro, C. M., Romão, F., & Castelo-Branco, C. (2010). Menopause and aging: changes in the immune system—a review. *Maturitas*, 67(4), 316-320.
- [12] Stepan, J. J., Hruskova, H., & Kverka, M. (2019). Update on menopausal hormone therapy for fracture prevention. *Current Osteoporosis Reports*, 17, 465-473.
- [13] Kim, O. Y., Chae, J. S., Paik, J. K., Seo, H. S., Jang, Y., Cavaillon, J. M., & Lee, J. H. (2012). Effects of aging and menopause on serum interleukin-6 levels and peripheral blood mononuclear cell cytokine production in healthy nonobese women. *Age*, 34, 415-425.
- [14] Ali, A. J., & Jaafar, N. A. H. (2022). Role of IL-6 in urinary tract infection among diabetic and non-diabetic patients. *Tikrit Journal of Pure Science*, 27(5), 7-11.
- [15] Al-Kaabi, H. K. J., & Al-Khalidi, B. A. H. (2020, November). Investigation of IL-6, IL-8 and TNF- $\alpha$  among patients infected with *Proteus mirabilis* in UTI Cases. In *Journal of Physics: Conference Series* (Vol. 1664, No. 1, p. 012124). IOP Publishing.
- [16] Al-Khafaf, D. M. R. (2012). Study of some microbial and Immunological parameters in patients with Urinary Tract Infection in Al-Diwanyia city; *QMJ VOL . 8 No . 13 : 28 – 38 .*
- [17] Tanaka, T., Kishimoto, T. (2012). Targeting interleukin-6: all the way to treat autoimmune and inflammatory diseases. *Int J Bio Sci*; 8 : 1227 – 1236 .
- [18] Zarkesh, M., Sedaghat, F., Heidarzadeh, A., Tabrizi, M., Moghadam, K. B., & Ghesmati, S. (2015). Diagnostic value of IL-6, CRP, WBC, and absolute neutrophil count to predict serious bacterial infection in febrile infants. *Acta Medica Iranica*, 408-411.
- [19] Metcalf, C. A., Johnson, R. L., Freeman, E. W., Sammel, M. D., & Epperson, C. N. (2021). Influences of the menopause transition and adverse childhood experiences on peripheral basal inflammatory markers. *Brain, Behavior, & Immunity-Health*, 15, 100280.
- [20] Jiang, Y. H., Peng, C. H., Liu, H. T., & Kuo, H. C. (2013). Increased pro-inflammatory cytokines, C-reactive protein and nerve growth factor expressions in serum of patients with interstitial cystitis/bladder pain syndrome. *PloS one*, 8(10), e76779.
- [21] Vazquez – Huerta, D. I., Alvarez – Rodriguez, B. A., Topete – Reyes, J. F., Munoz – Valle, J. F., Parra – Michel, R., Fuentes – Ramirez, F., & Brennan – Bourdon, L. M. (2014). Tumor necrosis factor alpha – 238 G/A and – 308 G/A polymorphism and soluble TNF- $\alpha$  levels in chronic kidney disease: correlation with clinical variables. *International journal of clinical and experimental medicine*, 7 (8), 2111 .
- [22] Ching, C., Schwartz, L., Spencer, J. D., & Becknell, B. (2020). Innate immunity and urinary tract infection. *Pediatric nephrology*, 35, 1183-1192.