Role to Interleukin-17 levels in Urine in UTI Patients

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Abstract
In order to determine whether Interleukin-17 levels in urine specimens for patients with urinary tract infections (UTI) caused by *E. coli* and *S. aureus* in Iraqi patients are related, a case control study was proposed. Around 200 clinical specimens of midstream urine were collected from Iraqi patients suffering from UTIs from Al-Salam teaching hospital. An extra only 10 of mid-stream urine specimens were collected from apparently healthy Iraqi individuals; hence considered as the control group. All specimens were collected from November 2021 to February 2022. The IL-17 was estimated by enzyme linked immunosorbent assay from urine samples in patients with *E. coli* and *S. aureus* as well as control group. The results revealed that IL-17 levels were highly significant at $P < 0.05$ higher in UTI patients infected with *E. coli* and *S. aureus* infections than in controls (670.21 ± 67.7, 506.85 ± 44.8 vs 308.51 ± 9.12 pg/ml respectively). Simultaneously, significant differences in IL-17 levels in patients with *E. coli* and *S. aureus* infections were noticed as well. The results also noted a non-significant increase of IL-17 in female patients and control than male group
Keywords: IL-17, UTI, E. coli

1. Introduction

The most frequent illnesses seen in clinical practice around the world are urinary tract infections (UTIs). Despite several efforts, over 150 million people globally experience UTIs each year, with significant morbidity and huge medical expenses in the United States, UTIs are responsible for over 10 million office visits, over 2 million visits to emergency rooms, and 100,000 admissions to hospitals each year (Flores-Mireles et al., 2015). Acute, chronic, and recurrent infections, as well as asymptomatic and symptomatic bacteriuria are all disorders that can be brought on by UTIs (Klein et al., 2020). The most prevalent etiological agent, uropathogenic E. coli (UPECs), is responsible for more than 75% of UTI infections (Flores-Mireles et al., 2015). Prior to colonizing the urinary tract, UPECs keeps urea, unstable pH levels, urine flux (which is challenging due to adhesiveness and persistence), and low levels of oxygen availability in the environment (Neugent et al., 2020). E. coli consist of various groups as described below. The IL-17 family contains six isoforms of 20–30 kDa molecular weight and is a group of secreted and glycosylated proteins, The cytokine IL-17 pro-inflammatory effect in the presence of autoimmune and inflammatory disorders was the main focus of early scientific investigations, however, it is becoming more and more clear that IL-17 roles are far more complicated. Recent study has shown that the protective and pathogenic properties of IL-17 are delicately balanced, and that these properties are very tissue- and context-dependent. Where it has been demonstrated that IL-17 acting a significant function in the immune response triggered via fungi, bacteria, and viruses that is associated with protection but also with inflammation (Bagri et al., 2022). also, IL-17-mediated downstream pathways induce the production of inflammatory molecules, chemokines, antimicrobial peptides (AMPs), and remodeling proteins. IL-17A elicits crucial impacts on host defense, cell trafficking, immune modulation, and tissue repair

The current study aims to detect the main strains that cause urinary tract infection and estimate the levels of IL-17 in urine samples and then classify E. coli into intestines and extra intestines strains.

In the past decade, IL-17A (IL-17), a proinflammatory cytokine, has received considerable attention for its pathogenic role in autoimmune diseases. Although protective in infectious settings, overproduction of IL-17 promotes inflammation and autoimmunity. IL-17 recruits and stimulates different cells to drive chronic inflammation. Regulating IL-17 levels or action by using IL-17 or IL-17R blocking Abs has shown remarkable efficacy in attenuating experimental autoimmune diseases. In this review, we will overview IL-17 induction and function in relation to host defense and autoimmune diseases in the kidney (Gaffenm 2011).

Due to the shortage of studies concerning the relationship between IL-17 in urine and UTI in Iraqi population, the purpose of the current investigation was chosen to identify whether a correlation exists between them.

2. Materials and Method

Ethical statement

All of the people participating agreed to give the researcher urine samples. In accordance with the Helsinki Declaration, all participants gave their informed consent.

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Specimen collection

The mid-stream urine samples of patients with UTIs were collected. By telling patients to clean their genitalia first before collecting urine and to throw away the first and last samples they collected, mid-stream urine samples might be obtained. As a result, midstream urine was isolated in the top of a sterile container and collected. The IL-17 was estimated by enzyme linked immunosorbent assay from urine samples.

Statistical Analysis

The current data were analyzed by statistical program SPSS, based in using One-way ANOV, LSD and independent t test at p. value < 0.05.

3. The Results and Discussion

Concentration of IL-17 among study groups

In the current investigation, IL-17 levels in sera of the study group were shown to be significantly (P 0.05) higher in cases than in controls for both E. coli and S. aureus infections (699.48±37.63 vs 308.63±11.68 pg/ml, and 506.86 ± 66.92 vs 308.63±11.68 pg/ml respectively). According to Table 4-2, the results illustrate highly significant between patients with S. aureus and *E. coli* compared to control group.

Table (4.2): IL-17 urine concentration among study groups			
Studies Groups	Cases No.	mean ± SD	*P*-value
Infected with S. aureus	10	506.85 ± 44.8b	P< 0.0001 (high sig.)
Infected with E. coli	20	670.21 ± 67.7a	
Control group	10	308.51 ± 9.12c	LSD = 42.0

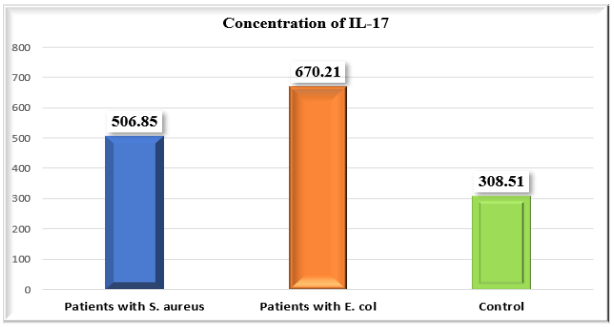

Figure (3.1): IL-17 concentration in the case (patients with S. aureus and E. coli infections) and control groups

Concentration of IL-17 among study groups according gender

The current study recorded the high concentration of IL-17 in UTI patients infected with E. coli, followed by patients infected with S. aureus, while the lowest concentration was recorded in control group in both male and female. According to gender with same group the results noted a non-significant difference at p. value < 0.05.

Concentration of IL-17 among study groups according to gender

Studies Groups	IL-17 Mean ± DS		P. value
	Male	Female	
Infected with *S. aureus*	492.0 ± 57.7[b]	521.7 ± 25.2[b]	0.323 non-sig
Infected with *E. coli*	671.4 ± 80.1[a]	669.0 ± 57.1[a]	0.993 non-sig
Control group	304.2 ± 8.41[c]	312.7 ± 8.46[c]	0.152 non-sig
p. value	< 0.0001 high-sig	< 0.0001 high-sig	
	74.9	50.3	

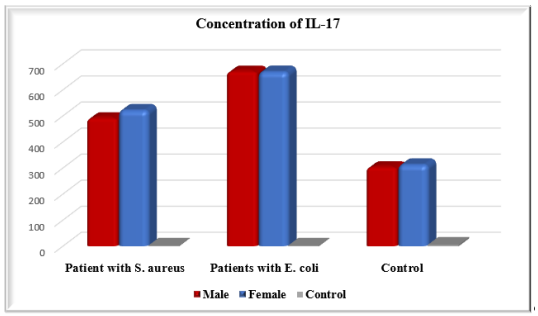

Figure (3-2): IL-17 concentration in the case (patients with S. aureus and E. coli infections) and control groups according to gender.

The significant difference between the mean IL-17 concentration of cases and control is illustrated in Table 3-1 and 3-2. On the other hand, the findings depicted in Figure 3-1 and 3-2 suggested no existence of interference between two cases group with control group. According to the current research, this interleukin can therefore be used as a differential marker for UTI. Additionally, the control group's data appear to be less flexible than those of the case group. Additional likely, the results would show more interpretations if the sample size was larger.

The current findings are comparable to those of Ahmadikia et al. (2018) who found that candiduric patients had significantly higher levels of IL-17 in their urine than non-candiduric controls and that IL-17 levels were also significantly correlated with candiduria. E. coli is the bacterium that causes kidney infections the most often. It is responsible for around 80 % of instances of pyelonephritis, which is another name for kidney infections, as well as urinary tract infections & bladder infections (cystitis). Another common example of gram-positive bacteria is S. aureus, which is also a major contributor to the development of urinary tract infections (Stamm and Norrby, 2001).

Sivick et al. (2010) perform thorough analysis of the function of IL-17 in both the innate and adaptive immune responses to UPEC in a mouse model of transurethral infection. The adaptive immune response that takes place in the bladder in this

system has been proven to be completely independent of IL-17. In contrast, the removal of microorganisms from an infected bladder is brought on by the IL-17 that is initially generated by + T cells. The capacity of IL-17 to produce cytokines and chemokines that are essential to allow the entrance of neutrophils as well as other innate signaling pathways in the bladder was determined to be the cause of its protective action. In keeping with this finding, animals lacking γδ+ T cells demonstrated an increased propensity to develop urinary tract infections (Jones-Carson et al., 1999).

After (IL-17) was neutralized, the load of Staphylococcus in the kidney increased by 15 fold. This preliminary research suggests that IL-17 plays a crucial role in protecting against widespread infection (Chan et al., 2015). A previous investigation into the concentration of IL-17 in patients with urinary tract infections caused by E. coli showed that the maximum mean level of IL-17 was documented in UTI patients infected with E. coli positive for virulence genes when compared with patients infected with E. coli negative to these genes. This finding was based on the observation that patients with UTIs who were infected with E. coli positive for virulence genes had significantly higher levels of IL-17 (Mohammed Al-Warmeziary et al., 2020). This indicated that IL-17 play role in response to severe infections caused by high virulent bacteria.

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