Bacteriological and Immunological study of kidney failure patients infected with urinary tract infections

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Abstract. Urinary tract infections (UTIs) are one of the most common medical conditions in women and men. They are caused by bacteria that enter the urinary tract through the urethra or the skin around the genitals. In this study, 102 urine samples were collected from 74 patients infected UTIs and 28 patients infected with urinary tract infections with kidney failure (UTIs-KF) admitted to a general hospital in AL-Najaf City, Iraq, between October to 2022 and March 2023 and 30 healthy individuals as control group. Standard laboratory methods were used to culture urine and to diagnose all bacterial isolates that were grown on laboratory media. The levels of cytokines IL-6 and IL-33 were detected by ELISA technique in the serum of control and patients. The results proved that age group 41-50 years old was the most UTIs infected with 31 patients (30.3%) followed by the age group ≤51 with 25 patients (24.5%). Out of total of 102 urine samples, there were 106 bacterial isolates, E.coli was the most dominate bacteria with 50 isolates (47%) followed by K.pneumoniae 18 isolates (17%), P.mirabilis 13 (12.7%), S.saprophyticus 10(9.5%), S.aureus 9(8.5%) and E.faecalis 6(6%). IL-6 and IL-33 were significantly higher in the UTIs and UTIs-KF patients, compared with the control group. Keywords: Bacterial infections, Kidney failure, IL-6, IL-33.

1 Introduction

Urinary tract infections (UTIs) are a common and recurrent health issue that affect millions of individuals worldwide, primarily caused by uropathogenic Escherichia coli (UPEC) bacteria. Urinary tract infections are common infections that affect both the kidneys and urinary tract (bladder and ureters) [1]. UTIs are classified by the area of the body that is affected. Symptoms of a UTI include pain during urination, burning while urinating, frequent urination, discolored urine, frequent feeling of urgency to urinate, nausea, and vomiting [2]. There are many different types of bacteria that cause UTIs [3]. The most common bacteria cause UTIs are Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, and Enterobacter aerogenes. These bacteria are found in the soil and water, but they can also be spread through sexual contact [4]. Other ways of spreading these bacteria include through blood transfusions and through medical equipment that has been

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contaminated [5]. UTIs are most common in young children, women who are pregnant or who have recently given birth, and men who have sexual intercourse with multiple partners. Men also have a higher risk of UTIs than women because they have longer urethras (the tubes that carry urine out of the bladder) [6]. UTIs are more common in people with weakened immune systems, such as people who are sick, people who are malnourished, and people who are in prison. Women are more likely to get a UTI than a man, especially during pregnancy [7]. Risk factors include taking antibiotics, being pregnant or having diabetes. There are more than 200 types of bacteria that can cause a UTI. UTIs cause a lot of discomfort in both men and women [8]. This can lead to delays in work and other activities. It can also have a serious effect on your relationships with others. Different types of UTIs depend on the cause of an infection, where it occurs in the body, and how it is treated. Signs and symptoms of the lower urinary tract disease range from a frequent urge to urinate at night to sudden pain during urination, lower back pain [9]. The immune response against urinary tract infections plays a crucial role in the clearance and prevention of these infections, as it involves various components such as leukocytes, antimicrobial peptides, and cytokines working together to combat the invading pathogens. This intricate interplay of host immune defenses is essential for maintaining urinary tract health and mitigating the potential complications associated with persistent or recurrent infections [10]. Thus, a comprehensive understanding of these immune mechanisms is imperative for the development of more effective treatment strategies and preventive measures against UTIs. In addition to traditional therapies, novel approaches targeting the enhancement of host immunity and promoting a balanced immune response may offer promising opportunities for combating these common infections, ultimately improving the quality of life for affected individuals and reducing the global burden of urinary tract infections [11].

2 Methods

2.1 Total samples, Urine Collection, Culturing and Serum markers measurement

Between October 2022 and March 2023, 102 urine samples were collected from men and women admitted to a general hospital in AL-Najaf City, Iraq with urinary tract infections. Five ml of midstream urine were incubated with brain heart infusion broth for 48 h at 37°C, and a loop of urine was streaked on blood agar and MacConkey agar for 48 h at 37°C [12, 13]. Culture characteristics, biochemical tests, and the VITEK 2 System are used to diagnose all growing bacterial isolates [14, 15]. Two cytokines were detected in serum of all individuals using ELISA technique; IL-6 and IL-33[16, 17].

2.2 Statistically Analysis

Statistics were analyzed using the Grap-pad prism computer software virgin 12 for numbers and percentages to compare between all bacterial isolates and T-test was used to compare between cytokines levels according to mean and slandered divisions [17, 19].

3 Results

3.1 Total men and women infected with UTIs and age groups
Out of total of 102 patients, there were 74 UTIs patients and 28 patients with UTIs-KF, 27 men (26.4%) and 75 women (73.6%). According to the age groups, 41-50 years old was the most infected with 31 patients (30.3%) followed by the age group ≤51 with 25 patients (24.5%). Age group 31-40 was the third age infected with 18 patients (17.6%) followed by age group 21-30 with 17 patients (16.6 %) and there were 11 patients (11%) infected with UTIs in the age group 10-20 years old. The results indicated that out of total of 102 UTIs patients, there were 74 patients (72.5%) infected with urinary tract infections (19 men and 55 women) and 28 patients (27.5%) infected with urinary tract infections with kidney failure (8 men and 20 women) (Table 1).

Table 1. Total men and women infected with UTIs. N=102.

<table>
<thead>
<tr>
<th>Age/year</th>
<th>UTIs patients (74)</th>
<th>UTIs-KF patients (28)</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
<td>Men</td>
</tr>
<tr>
<td>10-20</td>
<td>4</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>21-30</td>
<td>2</td>
<td>14</td>
<td>3</td>
</tr>
<tr>
<td>31-40</td>
<td>3</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>41-50</td>
<td>7</td>
<td>14</td>
<td>2</td>
</tr>
<tr>
<td>≤51</td>
<td>3</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>19</td>
<td>55</td>
<td>8</td>
</tr>
</tbody>
</table>

UTIs: urinary tract infections, KF: Kidney failure.

3.2 Total bacterial isolates

The results of the current study demonstrated that there were 106 bacterial isolates from 102 urine samples distributed as follows; *E.coli* was the most dominate bacteria with 50 isolates (47%) followed by *K.pneumoniae* 18 isolates (17%), *P.mirabilis* 13 (12.7%), *S.saprophyticus* 10 (9.5%), *S.aureus* 9 (8.5%) and *E.faecalis* 6 (6%) (Figure 1).

![Fig. 1. Total bacterial isolates from 102 patients with UTIs.](image)

3.3. Total bacteria isolates according to age groups

The most age group infected with UTIs was 41-50 years with 32 bacterial isolates (30%) followed by age group ≤51 with 31 bacterial isolates (29%), age group 31-40 years with 18
isolates (17%), 21-30 years with 14 bacterial isolates (13.5%) and age group 10-20 with 11 bacterial isolates (10.5%). On the other hand, the results showed that out of total 50 *E.coli*, there were 38 isolates from UTIs patients and 12 isolates from UTIs-KF patients, while, there were 7 and 11 *K.pneumoniae* isolated from UTIs and UTIs-KF patients, respectively. The results documented out of total of 9 *S.aureus* isolates, there were 4 isolates from UTIs patients and 5 isolated from UTIs-KF patients (Table 2).

<table>
<thead>
<tr>
<th>Age / Year</th>
<th>10-20</th>
<th>21-30</th>
<th>31-40</th>
<th>41-50</th>
<th>≤51</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td>M</td>
<td>W</td>
<td>M</td>
<td>W</td>
<td>M</td>
<td>W</td>
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<tr>
<td>W</td>
<td>M</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E.coli</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>50</td>
</tr>
<tr>
<td>K.pneumoniae</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>18(17)%</td>
</tr>
<tr>
<td>P.mirabilis</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>13(12)%</td>
</tr>
<tr>
<td>S.saprophyticus</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>10(9.5)%</td>
</tr>
<tr>
<td>S.aureus</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>6(6)%</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>106(100)%</td>
</tr>
</tbody>
</table>

Table 2. Distribution of bacterial isolates from patients with UTIs.

3.4 Levels of serum cytokines

3.4.1 IL-6

Two cytokines, IL-6 and IL-33 were measurement in serum of 30 patients infected UTIs, 28 patients infected with UTIs-KF and 30 healthy individuals as control group. Figure 2 showed there was a significant increase (P=0.0249) in IL-6 levels in total patients (16.17±4.626 pg/ml) infected with UTIs as compared with control group (2.607±0.732 pg/ml). Also, the results shows (Figure 3) IL-6 levels of UTIs-patients (17.64±11.14 pg/ml) and UTIs-KF-patients (19.29±6.099 pg/ml) were significantly higher than control group (P<0.0001) and the levels of IL-6 in UTIs-patients and UTIs-KF-patients were not significantly different (P=0.4490).

![Serum levels of IL-6](image)

**Fig. 2.** Serum levels of IL-6 in control group and total patients infected with UTIs.
Fig. 3. Serum levels of IL-6 in control group, UTIs-patients and UTIs-KF patients.

3.4.2 IL-33

Figure 4 proved a significant increase (P0.0229) in IL-33 serum levels in total patients (15.72±2.055 pg/ml) infected with UTIs as compared with control group (8.157±1.615 pg/ml). Also, the result shows (Figure 5) IL-33 levels of UTIs-patients (17.03±3.071 pg/ml) and UTIs-KF-patients (13.93±2.481 pg/ml) were significantly higher than control group (P0.0213) and (P0.0373), respectively. On the other hand, the serum levels of IL-33 in UTIs-patients and UTIs-KF-patients were not significantly different (P0.2302).

Fig. 4. Serum levels of IL-33 in control group and total patients infected with UTIs.
Fig. 5. Serum levels of IL-33 in control group, UTIs-patients and UTIs-KF patients.

4 Discussion

Urinary tract infections (UTIs) are common bacterial infections that affect millions of individuals worldwide. They primarily occur when bacteria, usually Escherichia coli, enter the urinary tract and multiply, causing a range of uncomfortable symptoms [20]. Prompt management and appropriate treatment are crucial to prevent complications and ensure a swift recovery. Urinary tract infections (UTIs) are a common medical condition characterized by the presence of pathogenic microorganisms in any part of the urinary system, which includes the kidneys, ureters, bladder, and urethra [21]. The symptoms of UTIs often include frequent urination, a burning sensation during urination, and lower abdominal pain; if left untreated, these infections can lead to severe complications, such as kidney damage and sepsis, ultimately posing a significant threat to an individual's overall health and well-being [22]. Therefore, early diagnosis and appropriate treatment of UTIs are essential in order to prevent further complications and ensure a successful recovery for patients. Furthermore, understanding the risk factors and implementing preventive measures can significantly reduce the incidence of UTIs in susceptible populations [23]. Research in the field of UTIs is crucial for identifying novel therapeutic approaches and improving patient [24]. The prevalence of pathogenic bacteria causing urinary tract infections (UTIs) has been a growing concern in both clinical and public health settings. This underscores the need for developing more effective prevention strategies and advancing our understanding of the underlying mechanisms of bacterial colonization and infection [25]. Additionally, further research into alternative treatments and the role of antibiotic resistance in UTI recurrence is essential to mitigate the global impact of these infections [26]. This is particularly important given that UTIs are one of the most common bacterial infections worldwide and can result in significant morbidity and mortality if left untreated, especially among vulnerable populations such as the elderly, pregnant women, and individuals with compromised immune systems [27]. The immune response against urinary tract infections plays a crucial role in protecting the host from pathogenic invasion,
as it helps to prevent recurrent infections and maintain overall urinary tract health. Thus, understanding the intricacies of this immune response can inform targeted treatment strategies and improve patient outcomes.

One key aspect of this immune response involves the activation of various immune cells, such as neutrophils and macrophages, which work together to eliminate the invading pathogens and facilitate tissue repair at the site of infection [28]. Additionally, the production of cytokines and chemokines aids in recruiting more immune cells to the site of infection, further enhancing pathogen clearance and inflammation resolution [29]. Furthermore, the adaptive immune system generates a robust and specific response through the activation of T cells and B cells, leading to pathogen-specific memory that provides long-lasting protection and facilitates a rapid response upon future exposure to the same pathogens [30]. Consequently, a comprehensive understanding of the immune response against urinary tract infections is essential for the development of novel therapies and preventive measures to combat these common and often debilitating infections [31]. Further research is needed to fully elucidate the immune response against urinary tract infections, including the complex interactions between various immune cells and cytokines, as well as the role of host factors and pathogen characteristics in shaping the overall response.

5 Conclusion

Unraveling the complexity of the immune response against urinary tract infections holds great promise for enhancing our ability to effectively treat and prevent these widespread and burdensome infections, ultimately improving patient quality of life and reducing the strain on healthcare systems globally.

References


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