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Comparison of some parameters in urinary tract infection disease patients according to leukocytes count, bacterial type and C-reactive protein in Al-Najaf governorate

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Abstract

This study focuses on using three biomarkers; leukocytes count, bacterial type and C-reactive protein as prognostic indicators for urinary tract infection. Sixty Patients between November 2021 and January 2022 in AL-Najaf province (AL-Sader medical city and private laboratories) were included in the study. The results indicated a significant increase in these biomarkers in UTI patients, when compared to the control group. Also, a significant increase in all biomarkers according to bacterial infection especially in *E. coli* infected patients as compared with *Staphylococcus aureus* patients and *Klebsiella sp*. Patients.

***Key words*:** UTI, leukocytes count, C-reactive protein.

Introduction

Urinary tract infection (UTI) is an infection in any part of human urinary system; kidney, ureters, bladder and urethra and usually causes a significant burden among the individuals and are associated with high health care and social costs.[1] Women are at greater risk than men of developing UTI as it affects half of all women in their lifetime and one-fourth have recurrent infections. These infections can be painful to bladder and serious consequences if occurred and spreads to kidneys. [2, 3] Most of UTI treatment treated with antibiotic due to bacterial infections.

UTI has been the major cause of morbidity and mortality among the Indian population.[1] Moreover, annually 150 million people are suffering worldwide along with a rise in health care cost of at least six million dollars, making it necessary to divert the attention to this disease.[4]

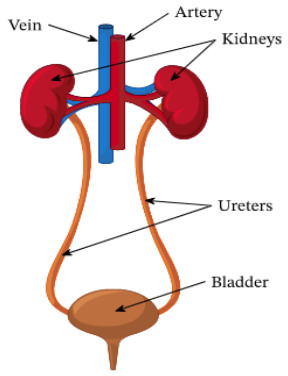

Figure 1: Urinary system in Human body [29]

The main causes of UTI are usually bacteria from poo entering the urinary tract. The bacteria enter through the tube that carries pee out of the body (urethra). Women have a shorter urethra than men. This means bacteria are more likely to reach the bladder or kidneys and cause an infection[5, 6]. If a UTI is not carefully and effectively treated in children, it can lead to renal scarring, which is the major cause of end-stage renal disease in this age.

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On the other hand, Prevention is better than cure, so early treatment of diseases such as UTI avoids renal problems. Many indicators should be studied in each disease to predict its infection of the human body, and a quick test to detect infections is critical, particularly in areas where culture services are unavailable. [7] Quantitative urine culture is the standard diagnosis for UTI, but it is costly, takes a long time, and is not widely available in many health institutions in resource-constrained situations. So, studying another factor to detect UTI is mandatory such as C-reactive protein (CRP) that is an acute inflammatory protein that increases at sites of infection or inflammation. CRP levels that commonly rise within a few hours following tissue damage or the onset of an illness. CRP is generally present in healthy persons at a very low concentration of less than 6 mg/l. Elevated CRP has been used to predict inflammation in patients with infections such as newborn sepsis, fungal infections, and pelvic inflammatory disorders.[8-10] C-reactive protein (CRP) has been utilized as an early biomarker for predicting bacterial infections and as a marker to track antibiotic therapy. CRP blood levels may be used to distinguish acute pyelonephritis (upper UTIs) from asymptomatic bacteriuria in juvenile UTIs, according to recent findings.[11, 12]

Also, white blood cells or leukocytes are human body army and first line of defense with normal number the blood is 4,500 to 11,000 WBCs per microliter (4.5 to 11.0 × 109/L. So, leukocytes account is very important in diseases detections and diagnoses such as infections, allergic reaction, inflammation and blood cancer such as leukemia or lymphoma.[12-14]

Besides, type of bacteria is effective as diagnostic factor in many diseases such as UTI, many investigations in UTI infections have been diagnosed with antimicrobial resistance in common isolated bacteria from UTI as biomarkers.[15, 16]

According to above survey, although there is urinalysis which is often considered to be the single most important diagnostic test in UTI, however, it takes long time for detection the aim of this study is to investigate the three biomarkers; leukocytes count, bacterial type and C-reactive protein as prognostic indicators for urinary tract infection.

Experimental and methods

Sixty clients identified with UTI infection throw four months in AL-Najaf province (AL-Sader medical city and private laboratories) were included, and all patients were subdivided according to age, gender (male and female), types of bacterial infection, total leucocytes count, and concentration of C-reactive protein in serum control group (apparently healthy). Thirty (30) samples had negative urine cultures, normal leukocyte counts, and normal CRP levels, which Two kits from each marker were utilized in this investigation (one for urine and gender, urine and serum samples, bacterial kinds of UTI infection, and several hematological and biochemical parameters such as WBC count, CRP level, and creatinin).

Acute renal failure and chronic kidney failure, sepsis, diabetes, cultures with few fungus or other organisms, and other diseases such as liver, endocrine, and cardiovascular illness were all eliminated.

The following criteria were used to diagnose all of the patients. More than 100,000 colony forming units (CFu / milliliters) of uropathogenic bacteria found in urine; additionally, from 1,000 to 100,000 colony forming units (CFu / milliliters) may contain infections. This study included appositive cultures with ten or more urinary white blood cells per high power field, as well as some clinical signs such as cloudy urine, new back pain, abdominal pain, fever, pain after or during urination, worse incontinence, and appositive cultures without any of the above criteria.

Estimation of total leukocytes count in plasma and urine:

The approach was utilized to detect WBC in urine after centrifugation at 12000 rpm for ten minutes under a microscope with high field power (Sobel, 2014). Total leukocytes were counted in a Neubaure chamber of blood by combining Turks solution (0.4) ml in a test tube with (0.02) of blood, then transferring one drop to the chamber and counting white blood cells in huge four squares under low power field (10 x) using this formula. [17, 18]

WBC mm^3 = Number of cells counted x 50

Results and Discussion

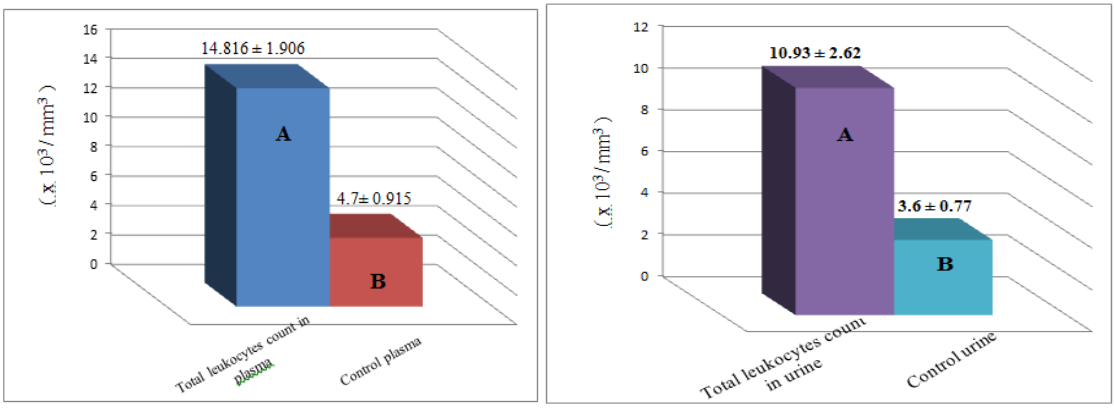
This study focused on using three biomarkers; leukocytes count, bacterial type and C-reactive protein as prognostic indicators for urinary tract infection. Sixty Patients between November 2021 and January 2022 in AL-Najaf province (AL-Sader medical city and private laboratories) were included

in the study. Patients were divided by types of bacterial infection, total leucocyte counts, and C-reactive protein concentration in serum control group (apparently healthy). Thirty (30) samples exhibited negative urine cultures, normal leukocyte counts, and normal CRP levels.

1. Total leukocytes in plasma and Urine:

First, one of the most common indicators of UTI is the presence of leukocyturia, which is defined as a high count of leukocytes greater than 10,000 per milliliter, which indicates urothelial inflammation. Growth of bacteria with leukocytes also provides important signs for UTI diagnosis, so microscopy that shows the presence of leukocytes with bacteria such as (*E. coli*, *S. aureus*, *Proteus mirabulis*, *Klebsiella*).[19, 20]

Total leukocytes account in patients plasma have been done with the routine method [18] to afford this results that depicted in Figure **2a**. The results exhibited a significant increase on leukocytes count ($14.816 \pm 1.906 \times 10^3$ / mm^3) in plasma ($p< 0.05$) in comparison with control group ($4.7\pm 0.915 \times 10^3$ / mm^3). Also, total leukocytes account in urine of patients of UTI was investigated in the current study to reveal a significant increase on leukocytes count ($10.93 \pm 2.62 \times 10^3$ / mm^3) with $p< 0.05$ in comparison with control group ($3.6 \pm 0.77 \times 10^3$ / mm^3) as shown in Figure 2b.



a) **b)**

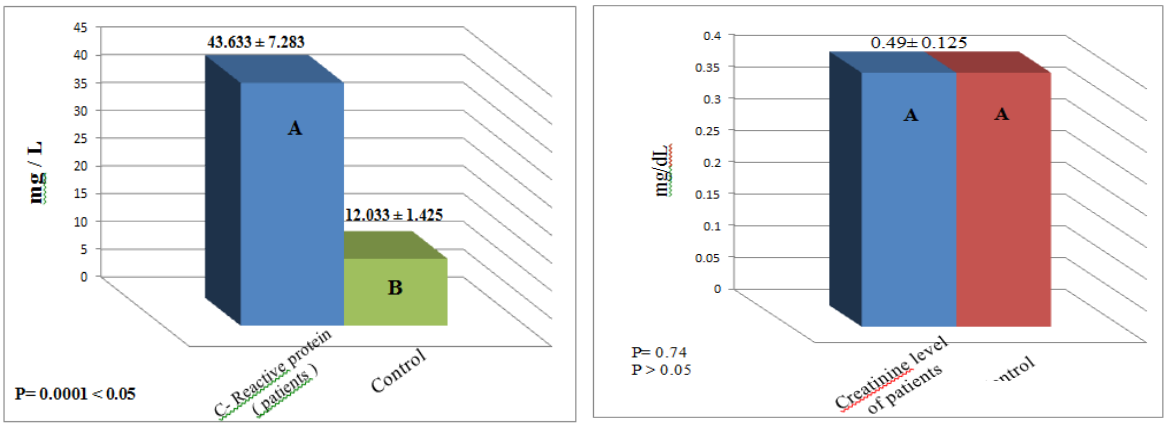
Figure 2: Total Leukocyte Count in a) plasma b) urine in UTI patients ($p\leq 0.05$).

Figure **2a,b** revealed that UTI patients had significantly more leukocytes than the uninfected control group. Several investigations have shown that leukocytosis occurs in UTI patients owing to bacteria, inflammatory tissue, and the second wave of monocyte extravasation [21, 22]. While some studies found that both monocytes and neutrophils migrate in response to chemo-attractants, with cathelicidin, as the most important chemoattractant markers, having the ability to attract neutrophils via specific receptors called formyl-peptide receptor-like-1 (FPRL1) as a receptor activated. During the microbial invasion, monocytes, T lymphocytes, and neutrophils aid in cell attachment and phagocytosis.[23]

2. Level of C-Reactive protein

According above survey and importance of CRP as diagnostic tool in UTI, the results of measuring of CRP level in patient serum were depicted in figure 3. The results revealed a significant increase ($P\leq 0.05$) in patients with urinary tract infection (43.633 ± 7.283) mg/ L in comparison with control group (12.033 ± 1.425) mg/ L. This high result indicated that UTI can be detected during inflammation without needing to urinalysis.

Also, the creatinine level was measured in patients who suffered from UTI as biomarker indictor during inflammation, the results indicated that its level was equal to control specimen ($P\leq 0.05$) in patients with urinary tract infection (0.49 ± 0.125) in comparison with control group (0.49 ± 0.125). This equality between creatinine level and control indicates presence of inflammation of UTI.



a) b)

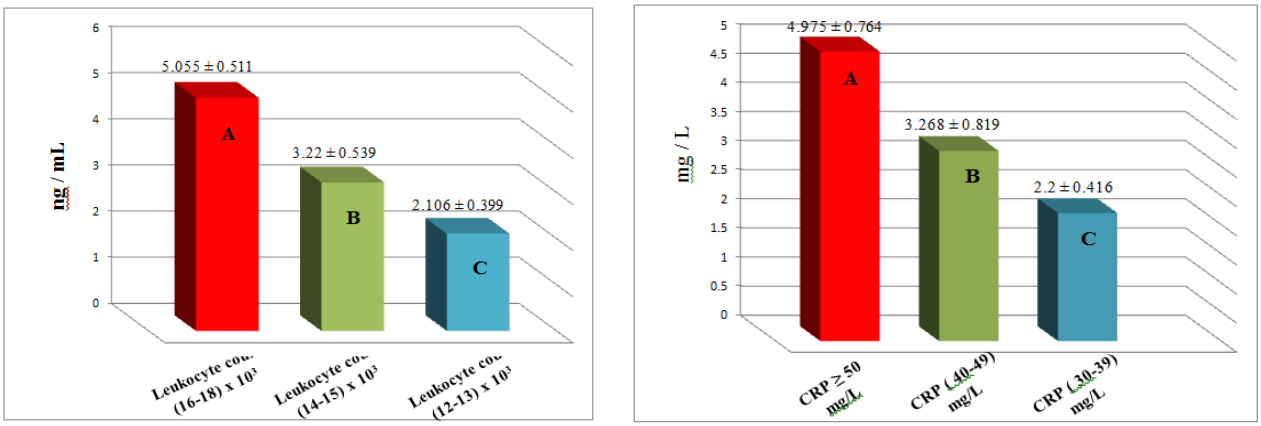
Figure 3: a) concentration of C-Reactive protein in serum with control, b) Creatinine level. Differential letters refer to significant difference between patients and control group.

The current findings support previous research that found creatinine levels were normal and did not change during and after urinary tract infections in patients with kidney disease and obstruction (such as stones or prostate enlargement), and that creatinine levels were between 4.7 and 0.7 in addition to normal creatinine clearance.[24, 25]

According to a previous study, normal creatinine levels in uncomplicated UTI patients as compared to complicated UTI patients with kidney impairment such as injury, loss, failure, and end stage kidney disease show a high creatinine level with low clearance and a decrease in glomerular filtration rate > 25% with a high creatinine level fold from 1.5-2 fold with highly creatinine level fold from 1.5-2 fold with highly creatinine level fold from 1.5-2 fold with highly creatinine level fold from 1.5-2.[25, 26]

3. Comparison among patients according to total leukocytes count in plasma and CRP in serum:

Figure 4 revealed a significant increase ($p< 0.05$) in group that has in urinary tract infection via total Leukocyte count (16-18) x 10^3 (5.055 ± 0.511) in comparison with other groups 14-15 x 10^3 (3.22 ± 0.539) and 12-13 x 10^3 (2.106 ± 0.399) (Figure 4a). While The results proved a significant increase ($p\leq 0.05$) in UTI group as level C-reactive protein ≥ 50 mg/L (4.975 ± 0.764) in comparison with another group 30-39 mg/L and (0-49 mg/L respectively (2.2 ± 0.416, 3.268 ± 0.819) (Figure 4b).



a) b)

Figure 4: a) Means of Urinary tract infection according to total leukocytes count in plasma. B) Means of level of cathelicidin in Urinary tract infection patients according to C-reactive protein (CRP). Different letters refer to significant difference at ($p\leq 0.05$) which $p\leq 0.001$.

Also, CRP level in the serum of UTI patients was significantly higher. Recent research has found a link between some acute inflammatory responses and CRP levels in UTI patients, with positive results of 82.2 percent and negative results of 17.8 percent with highly growth of some gram negative and positive bacteria such as *E. coli*, *S. aureus*, *Proteus*, *Klebsiella*, and *Pseudomonas*, indicating that CRP levels in serum provide a good indicator for lower urinary tract infections. [25, 27]

Comparison between patients group according to types of bacterial infection:

Bacteria type infection was compared between groups of patients and it is depicted in Figure 5. A considerable rise in UTI with infection of Gram-negative bacteria such as *E. coli* in serum and urine (250.84 ± 16.624 Pg/ ml and 272.72 ± 15.528 Pg/ ml), Gram-positive such as *S. aureus* serum-urine (208.15 ± 19.353 Pg/ ml and 237.5 ± 9.230 Pg/ ml), and lower UTI rises in *Klebsiella* as gram negative bacteria in serum- urine (184 ± 11.006 Pg/ ml and 212.13 ± 7.689 Pg/ ml) with p< 0.05. Previous studies have suggested that bacterial infection at the inflammation site produces inflammatory mediators or activates macrophages, resulting in the production of cytokines such as IL-10, IL-6, IL-8, and IL-22. These events have been linked to higher CRP levels in UTI infections.[28]

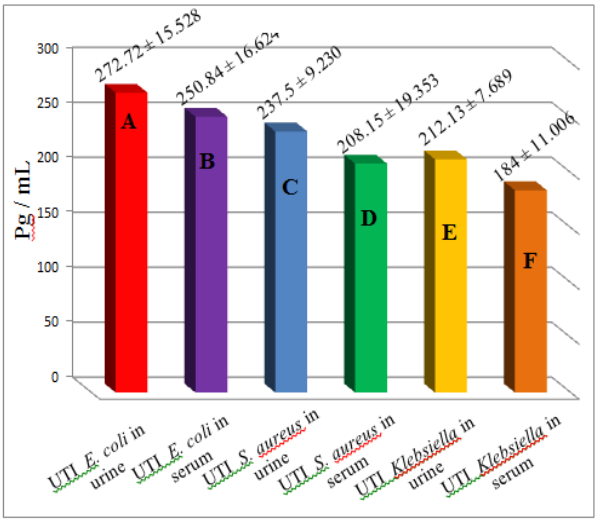


Figure 5: means of level of Urinary tract infection according to types of bacterial infection. Different letters refer to significant difference at p≤ 0.05.

Conclusion

From previous results depicted in this study of measuring the level of three markers such as leukocytes count, bacterial type, and C-reactive protein as prognostic indicators for urinary tract infection can be concluded that using these biomarkers for UTI infection patients is a quick, better way to achieve detection than urinalysis.

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