

Trends in Antibiotic Resistance of Major Uropathogens

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Abstract:

Background: Around the world, there is no population clear from urinary tract infection (UTI), particularly among women. UTI is considered the most predominant bacterial infection. This study aimed to detect the incidence of the most common major uropathogens in patients severe from urinary tract infection with antibiotic sensitivity tests that assist urologist doctors for appropriate antimicrobial empirical therapy.

Methods: This study was carried in a private laboratory in Babil city, Iraq from May 2019 to May 2020. Totally 70 individuals suffering from clear symptoms of UTI, as well as, 20 healthy persons participated in this study as a control group. Then, the standard microbiological methods carried out to isolate and identify bacterial species. Antimicrobial susceptibility tests were performed using different antimicrobial discs by applying the Kirby–Bauer disc diffusion method.

Results: Totally, 90 specimens were obtained from them 20 control group, 19 with no growth, and 51 patients with bacterial growth distributed as 43 (83%) females and 8 (17%) males. *E. coli* were the most common predominant organisms. All isolates were showed a high rate of resistance to evaluated cephalosporins 100% and 82% to cefotaxime and ceftriaxone respectively, while very low resistance recorded in Aminoglycosides 20% and 13% to Gentamicin and amikacin respectively. Most age group infected with UTI was 21-40 years old.

Conclusion: The current study showed an increasing burden of urinary tract infection caused by various bacteria implicated in UTI that causes changeable sensitivity to various antimicrobial agents. Therefore, in clinical use appropriate medications should be selected based on the data obtained from antimicrobial susceptibility tests.

Keywords: Urinary tract infection, antimicrobial agents, antibiotic resistance, *E. coli*, uropathogens, aminoglycosides.

Introduction:

Urinary tract infections (UTI) considered the most common bacterial infection globally, every year more than 150 million people severing from acute or chronic UTI caused by various bacteria. ^[1] In the recent few years, bacterial infection as UTI showed terrifying extensive antibiotic resistance by different mechanisms. ^[2]

Urinary tract infection (UTI) is the most continual bacterial infection in females that affect millions of persons yearly. ^[3-5] UTI is responsible for 25% of total infections. ^[4] Females are greatly more susceptible to UTI than males, ^[6] more than 50% of women will suffer from UTI during their life. ^[4] the social cost due to UTI is so expensive that may cost billions of dollars in developed countries. ^[5]

Post-menopausal women have greater rates of UTI due to pelvic prolapse, loss of oestrogen, and little *lactobacilli* in the vaginal flora. Oestrogen helps a generation of *lactobacillus* in the vagina, reduces pH, as well as avoids vaginal colonization by pathogenic bacteria. ^[4]

Resistant pathogens result in decreased morbidity and mortality because this raises the likelihood of inadequate treatment. ^[7-8] This resistance can delay and impede treatment, leading to complications or death. ^[9-10] As well as, the adverse effects associated with these drugs. ^[11-12] Besides, a patient may need more care, as well as the use of alternative and more expensive antibiotics, which may have more severe side effects or may require more invasive treatments to be given in hospitals, such as intravenous injection. ^[8, 13-14]

About 700,000 deaths are recorded annually due to AMR, based on a published survey, and it has been estimated that if appropriate monitoring and preventive steps are not taken, AMR will become one of the major causes of death among hospitalized or non-hospitalized patients in developing and industrialized countries. ^[15]

Implementing an effective treatment has been reduced because of the escalating rate of hospital and community-acquired infections caused by antibiotic-resistant microorganisms. ^[16] Also, as the number of resistant strains in clinical settings increased, broad-spectrum antibiotics became the ultimate choice, but the manifestation of resistance to broad-spectrum antibiotics in multidrug-resistant strains reduces the chances of choosing an effective empirical therapy. ^[17] Because there is not enough data on the profile of antimicrobial resistance towards commonly

used antibiotics in southern Babil City. Therefore, this research was aimed at assessing the trend of antibiotic resistance in major urobacterial pathogens isolated clinically.

Material and methods:

A total number of 90 persons were evolved in this study from May 2019 to May 2020. Numbers of patients with UTI were 70 individuals from theme 51 were with bacterial growth, while other 19 were without growth. Apparent 20 healthy persons also participated in the current study. These patients have attended a private laboratory in Babil city, Iraq. Patients were suffering from clear symptoms as a complaint of frequent urge to urinate and painful, non-repetitive midstream urine samples were included in the study.

Some information related to these patients such as sex, age, and type of specimens was obtained. In the next step, the positive samples were processed at the laboratory, sub-culturing on the specific medium including MacConkey agar, chocolate agar, mannitol salt agar, and blood agar plates, then Gram staining of bacterial colonies were performed. Conventional biochemical tests like catalase test, oxidase test, Indole, Voges Proskauer, Methyl red, Citrate test, Triple Sugar Iron Agar, Kligler Iron Agar, Bile Esculin Agar, 6% NaCl, Motility test, and DNase test have been conducted.

Nine most common prescribed antibiotics such as Ceftriaxone (30 mg), Cefotaxime (30 mg), Amikacin (30 mg), Gentamicin (10 mg), Nitrofurination (300 mg), Ciprofloxacin (5 mg), Tobromycin (10 mg) Trimethoprim and Trimethoprim-sulphamethoxazole (25 mg) were tested on Kirby – Bauer's disc diffusion method.

The study protocol has been approved according to the Ethical Committee in the Babil Health Directorate on May 2, 2019. Besides, verbal approval was taken from the patients before obtaining the sample. Health safety was taken during sampling. Also, this work was done according to the Ethics Committee of the Iraqi Ministry of Health and was performed and agreed with all national regulations. **The proposal was reviewed and approved by Research and Ethical committee of Babil Health Directorate, Babil, Iraq. The Ethics Committee Approval number was IQ. Babil 16440508332414 on May 2, 2019.**

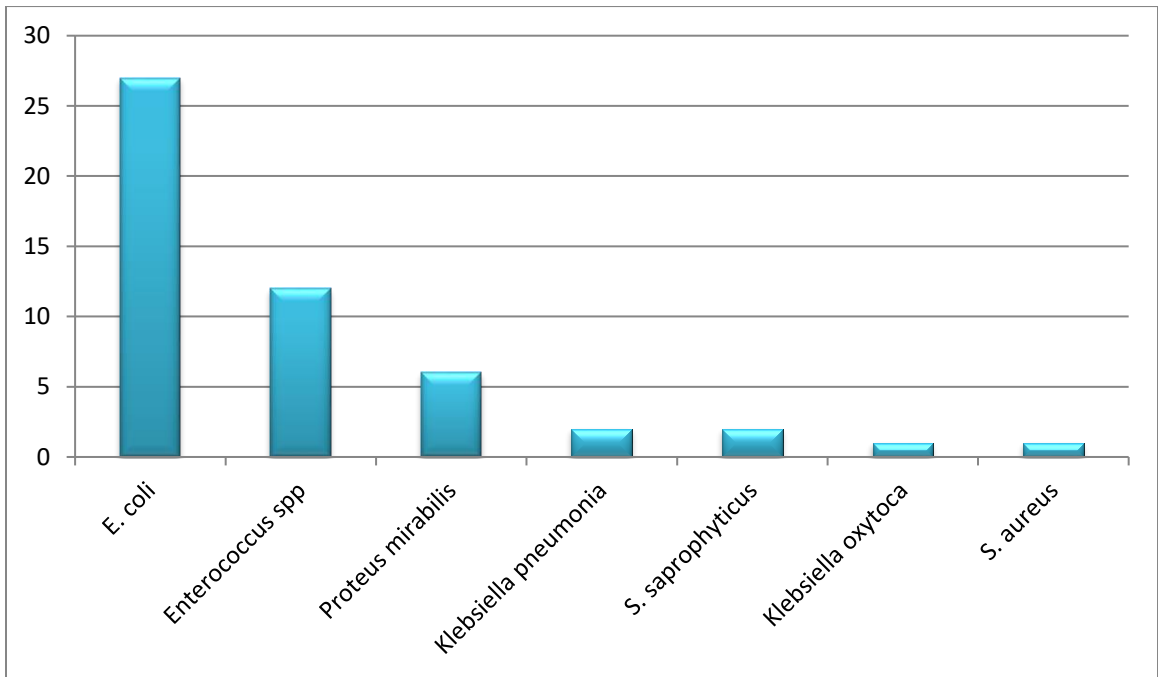
The antibiotic sensitivity results calculated with Microsoft Excel 2010, version 10 software. The rates of resistance for individual antibiotics were analyzed for every bacterial isolate by age and gender of patient, and type of specimen. The mean percentages of the resistance of each isolate to all tested antibiotics were calculated as the number of resistant isolates out of the total number of isolates evaluated to a particular antibiotic in a specimen. Excluded criteria included patients with repeated specimen culture, patients under antibiotics utilization, contaminated or mixed growth.

Results:

The total numbers of specimens that investigated in the current study were 90 urine samples during the period from May 2019 to May 2020 at a private laboratory in Babil city, Iraq. Apparent 20 healthy persons participated in the current study as a control group. Numbers of patients with UTI were 70 individuals from theme 51 were with bacterial growth, while other 19 were without growth.

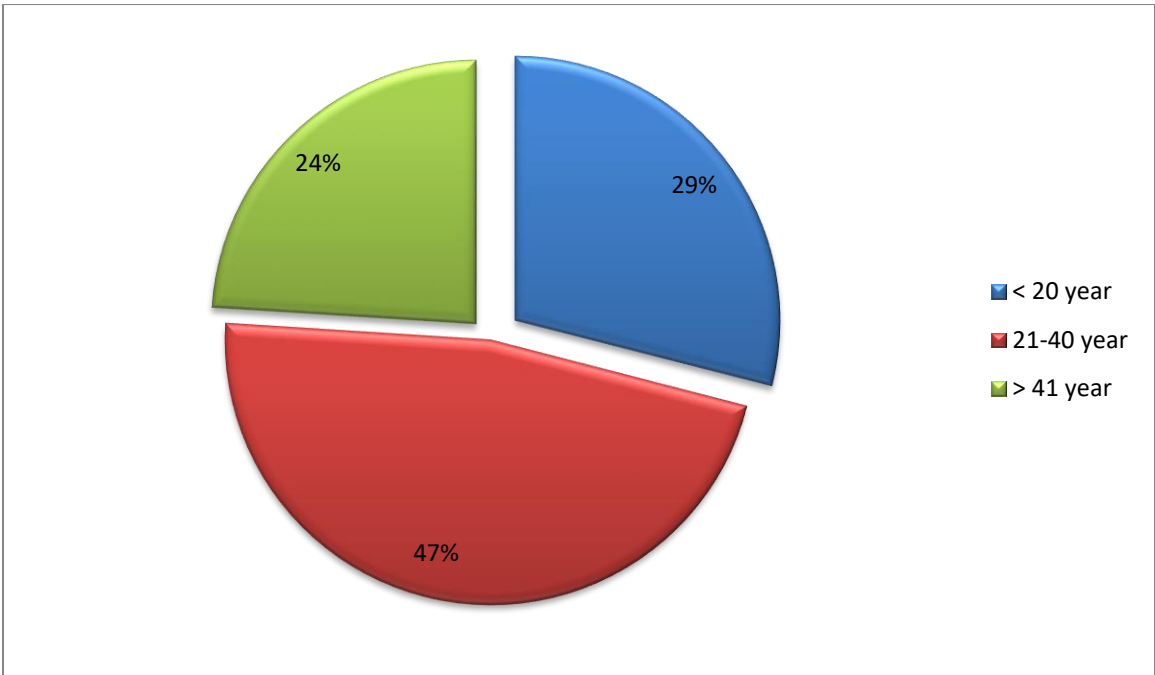
All specimens taken from twenty healthy persons showed no growth on artificial media as a control group. The most common pathogenic bacteria isolates were *E. coli* followed by *Enterococcus spp.* [Figure 1]

Figure 1: Bacteria distribution in urine

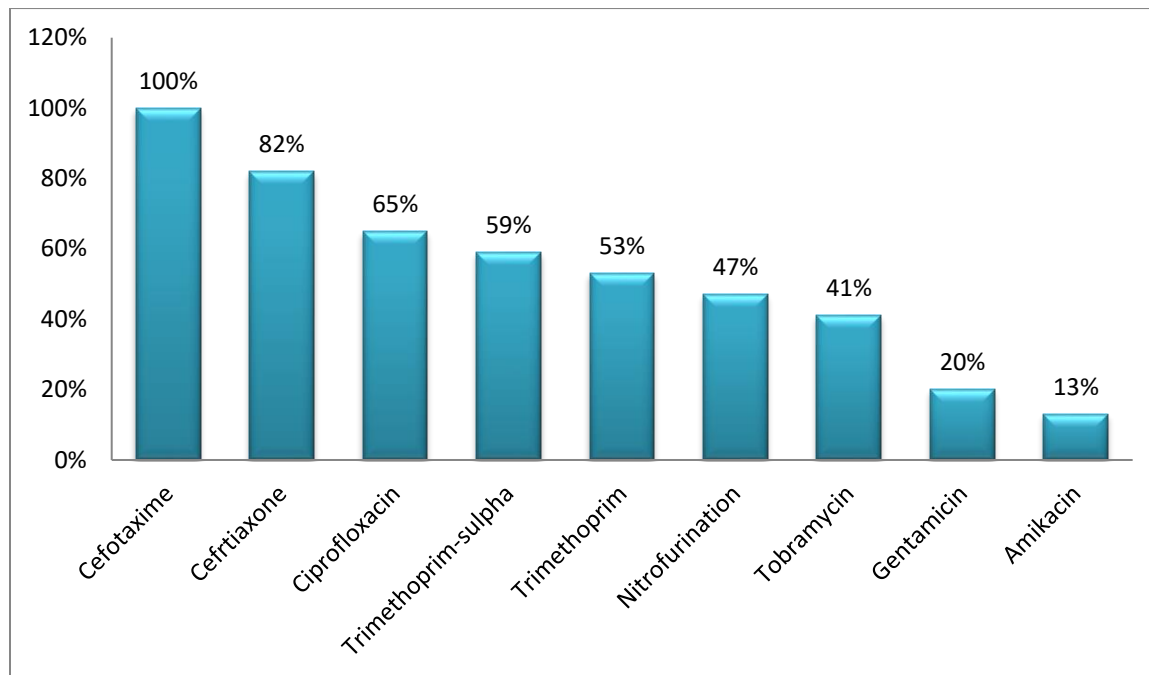


Females were the most common in urine specimens 83% compared with just 17% males. Age group distributions divided into three categories 1-20 years, 21-40 years, and more than 40 years old. In urine specimens, the age group 21-40 years was the most common infected group 47%. [Figure 2]

Figure 2: Age groups of patients participate in the study



Antibiotic sensitivity pattern showed full resistance to cefotaxime 100% among all bacterial isolates in the three specimens' types, followed by ceftriaxone 82%. While gentamicin and amikacin were the less resistance than other evaluated drugs 20% and 13% respectively. [Figure 3]

Figure 3: Antibiotic resistance in uropathogens**Discussions:**

Antimicrobial resistance is a persisting and growing global problem in the 21st century.^[18] It is considered as a main public health threat.^[19-20] In each organism, the number of resistant microbial strains, geographic areas affected by drug resistance, and the extent of resistance are escalating.^[21] Thus, disease-resistant agents once thought to be susceptible to antibiotics are returning to these therapies in new leagues.^[22] The percentages of organisms that exhibit antibiotic resistance, in particular resistance to multiple antibiotics are also continuously increasing.^[23]

Several other aspects contribute to antibiotic resistance, such as incorrect diagnosis, irrational antibiotic use, and possibly irregular antibiotic utilization due to incorrect prescription or poor compliance.^[24-25] Improving these factors can avoid the spread of antibiotic resistance.

Determination or isolation of one or more culturally identified urinary tract pathogen is considered a definitive diagnosis. [26] *E. coli* was the most common prevalent pathogen isolated from UTI patients in the current study, *E. coli* have been implicated in 53 %, this finding accords many studies, [27-28] also agree with [29] that mentioned *E. coli* prevalence was (42,2 %) in patients with UTI. Followed by *Enterobacter species* 23% of total urine samples and these findings were in agreement with other respective studies conducted elsewhere. [30-31] The age group 21-40 years was the most common infected group 47%. [29] followed by the age group less than 20 years 29%.

Females were the most common in urine specimen 83% compared with males just 17%. This finding is agreed with. [32] Many females suffer from recurrent UTI with a high rate that stays a major challenge, this requiring long-term prophylactic therapy to prevent it. [3] In females, rectal flora colonizing the urethral, then ascend to the bladder that causes RUTI, so wiping genital areas from front to back is important to prevent recurrent UTI. [4]

Antibiotic sensitivity pattern showed full resistance to cefotaxime 100% among all bacterial isolates, followed by ceftriaxone 82%. Some studies also showed increased resistance to cephalosporins, analysis of 31 strains of *P. aeruginosa* showed high resistance ceftazidime, Mutation-dependent overproduction of intrinsic -lactamase is considered the main cause of resistance. [33] Another study revealed in 2019 that resistance to ceftriaxone 86%, cefotaxime 80%, and ceftazidime 93 to the *Klebsiella pneumonia*. [34] This high rate of cephalosporins resistance that reaches to 100% resistance may due to prolonged inappropriate administration of these drugs described by doctors, and also few personal education presented by an incomplete full course of antibiotics to eradicate the pathogen to improve infection cure rates and avoid the development of any resistance or treatment failures. [35-36]

In this study, isolated bacteria showed very low resistance to gentamicin and amikacin 20% and 13% respectively. Resistance to ciprofloxacin, Nitrofurination, and TMP were 65%, 47%, and 53%, respectively. Another study found that ciprofloxacin as the most effective drug against uropathogens and chloramphenicol as less sensitive, [37] while another research revealed that cephalosporins as sensitive but not ciprofloxacin and amoxicillin on uropathogens isolated from diabetic patients. [38] The uropathogenic *E. coli* was reported with resistance rates ranging from 51.1%–94.3% to most antibiotics. [39]

Conclusion:

Urinary tract infection (UTI) is a most prevalent bacterial infection worldwide; the increase in multidrug resistance is associated with UTI is considered serious threat to the clinicians and patients. At present, Antibiotic resistance present a global health emergency, antibiotic-resistant bacteria are on the rise and increasing with the time that becoming a crucial problem of all populations, and are being implicated in increasing morbidity among the patients. Infections with resistant species regarding cause to prolonged stays in hospitals; compromised immune persons along with exposures to multiple antibiotics are the main factors that increase the risks for infections and multidrug resistance. The emergence of antibiotic resistance in bacteria from urinary tract is associated with significant adverse outcomes.

Brood spectrum antibiotics' widespread use has led to the emergence of bacterial antibiotic-resistant strains. High resistance levels were observed primarily in bacteria which causes serious health problems. Regular monitoring of the judicious use of antibiotics assists in conserving the effectiveness of sensitive antibiotics and prevents the emergence of further resistance, as well as resistance to multiple antibiotics, limits the therapeutic options for infections.

E. coli was the most common bacteria isolated from urinary tract followed by *Enterococcus spp.* Females were the most common in urine specimens 83% compared with just 17% males. Isolated bacteria showed very low resistance to gentamicin and amikacin 20% and 13% respectively. Full resistance to cefotaxime 100% among all bacterial isolates, followed by ceftriaxone 82% have observed in the current study. The age group 21-40 years was the most common infected group 47%.

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