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Overview of Urinary Tract Infection Caused by Bacteria

Abdulkarem AT[1], Khudhur HR[2]* and Abed SM[3]

[1]Ministry of health, Iraq

[2]College of Education for Pure Science, Al-Muthanna University, Iraq

[3]Department of Medical Laboratories, College of Medical and Health Techniques, Sawa University, Iraq

Review Article

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***Corresponding author:** Hasan Raheem Khudhur, College of Education for Pure Science, Al-Muthanna University, Iraq, Email: hassanraheem1990@gmail.com

Abstract

Urinary tract infections (UTIs), a significant public health concern, can be brought on by a wide variety of bacteria, including Escherichia coli, Proteus mirabilis, Enterococcus faecalis, Klebsiella pneumoniae, and Staphylococcus saprophyticus. The high recurrence rates and evolving antibiotic resistance of uropathogens constitute a serious threat to the financial burden of these disorders. Pathogens in urine can be detected using a variety of diagnostic approaches, which are broadly divided into laboratory-based and point-of-care (POC) detection methods. Many research institutions and companies working in this subject have strived to establish rapid and accurate pathogen identification because traditional approaches may be time-consuming. The indications and symptoms are further divided into the following three groups: (1) General signs and symptoms like fever; (2) lower urinary tract symptoms including urgency, frequency, and dysuria; (3) non-specific signs and symptoms such nausea and malaise. Additionally, the prevalence of UTIs brought on by multidrug resistance (MDR) is rising, which has a considerable negative impact on the propagation of antibiotic resistance as well as the financial burden of these infections.

Keywords: UTI; In Iraq; Different Diagnostic; Multidrug Resistance

Abbreviations: UTIs: Urinary Tract Infections; POC: Point-of-Care; MDR: Multidrug Resistance; CAUTIs: Catheter-Associated Urinary Tract Infections; UPEC: Uropathogenic Escherichia Coli; GBS: Group B Streptococcus; AST: Antibiotic Susceptibility Testing; PCR: Polymerase Chain Reaction; MALDI-TOF: Matrix-Assisted Laser Desorption/Ionization-Time of Flight; FISH: Fluorescence in Situ Hybridization; ESBLs: Extended-Spectrum–Lactamases.

Introduction

Every year, 150 million individuals throughout the world suffer from urinary tract infections (UTIs), one of the most prevalent bacterial illnesses1. According to reports, there were 10.5 million office visits for UTI symptoms in the United States alone in 2007 (0.9% of total ambulatory visits), and 2-3 million emergency room visits, according to Schappert and Rechtsteiner [1]. The same bacteria that cause UTIs in non-pregnant persons also cause UTIs in pregnant people. *E. coli* is the root cause of 70–80% of infections, according to Barr, et al. [2]. Two further typical GNBs are Proteus mirabilis and *Klebsiella sp*. [3]. Fastidious pathogens and anaerobic bacteria have been detected in large numbers of urine samples from pregnant women, but it is yet unknown how these germs may impact newborn outcomes. The pressure of the gravid uterus on the bladder, which restricts urine flow, as well as other hormonal and immunological changes that take place throughout a typical pregnancy, raise the risk of UTI in pregnant women [4]. As a result, throughout pregnancy, women should periodically check their urine [5]. Clinically, UTIs can be categorized as basic or complicated. Uncomplicated UTIs most frequently afflict individuals who are in general good health and do not have any anatomical or neurological abnormalities of the urinary system [6]. The Pyelonephritis and the cystitis are two different classifications of these illnesses. Some of the risk factors associated with cystitis include female gender, a history of UTI, sexual activity, obesity, diabetes vaginal infection and genetic susceptibility [7]. According to Tien, et al. [8], complex UTIs include the following: calculi, indwelling catheters, or other drainage devices; urinary obstruction; urinary retention brought on by neurological conditions; immunosuppression; renal failure; renal transplantation; pregnancy; and diseases that affect the host's capacity to protect the urinary tract. Sofyan, et al. [9] research, indwelling catheters are to blame for 1 million cases of complex UTIs each year. Catheter-associated urinary tract infections (CAUTIs), which are the most common cause of future bloodstream infections, are linked to higher rates of morbidity and death. According to Rizwan, et al. [10], long-term catheterization, being a woman, being older, and having diabetes are all risk factors for developing a CAUTI.

Both Gram-positive and Gram-negative bacteria, as well as some fungi, are responsible for UTIs. The most frequent cause of both simple and complex UTIs is Uropathogenic Escherichia coli (UPEC), which is highly widespread. According to Foxman [11], UPEC is followed in prevalence among the bacteria that cause simple UTIs by *K. pneumoniae*, *S. saprophyticus, E. Faecalis*, group *B streptococcus* (GBS), *P. mirabilis, P.aeruginosa, S. aureus, and Candida spp, Enterococcus spp. and staphylococcus spp*are the most prevalent causal agents for complex UTIs, after UPEC, which is the most frequent [12].

Prevalence of UTI in Iraq and Other Countries

Salman, et al. [13] found that 14.7% of school-age children in Al Imamein Kadhimaein Medical City had urinary tract infections. This rate is lower than that found in a different Iraqi study conducted in Tikrit city in 2012, which found that the culture positive rate in school-age children was 42.9% [14], but similar to those found in a descriptive cross-sectional study conducted in Iraq by Kareem and Issa [15], which discovered that 18.3% of kids from Basra city's five hospitals had positive urine cultures, and the findings of a cross-sectional study conducted on 2,511 schoolchildren in Turkey by Zincir, et al. [16], which revealed a prevalence of (7.1%), which was lower than the findings of a study carried out in Nigeria by Isa, et al. [17], which revealed that 31.7% of primary school-aged kids had positive urine cultures for bacterial growth. There may be differences in socioeconomic level, culture, personal cleanliness, health infrastructure, and school health services among various communities that contribute to these variations in UTI rates among school-age children. The rate found in the current study is also typical for symptomatic UTI, while the rate of asymptomatic UTI in our sample was 1.6%, which is lower than the results of the 2003 Al-Rawi study in Iraq, which found a prevalence of (6.6%) for schoolchildren with an asymptomatic UTI. Hasan [18] and associates discovered in 2022 While tigecycline, amikacin, ciprofloxacin trimethoprim/sulphomethoxizole, levofloxacin, meropenem, and tetracycline showed lower resistance to these illnesses' drug resistance, all gram-negative bacterial isolates were found to be highly resistant to ampicillin and cefotaxime. This is concerning because it limits clinical practitioners' options for treatment and forces them to choose drugs with low resistance. In 2022, Nahab, et al. [19] found that E. coli was the most prevalent pathogenic bacteria. These results support those of a 2009 study by Al-nasrawi A [20], who named E. coli as the uropathogen in charge of UTI. The findings of females with UTI in other Iraqi cities, such as Baghdad and Al-Mosul were supported by this discovery [21].

Pathogenesis of UTI

UTIs (urinary tract infections), which are brought on by uropathogens that reside in the gut, can travel to the urethra and bladder thanks to a group of adhesins. The bacteria start to multiply and produce poisons and enzymes that help them survive when the host's inflammatory response cannot entirely eradicate all of the bacteria. If the bacterium succeeds to get beyond the kidney epithelial barrier, further colonization of the kidneys could lead to bacteremia. Catheterization in cases of complete UTIs causes uropathogens infection, which is followed by bladder dysfunction. The strong immunological response brought on by catheterization frequently causes fibrinogen to build up on the catheter. Fibrinogen-binding proteins made by uropathogens enable them to attach to the catheter According to McLellan and Hunstad [22], UTIs are the most common bacterial infection in humans worldwide and the most common sickness picked up in a hospital. Infections can progress to pyelonephritis and bacteremia if they are left untreated because bacteria also thrive as a result of biofilm protection. According to Lewis, et al. [23] the success of various uropathogen invasion and adhesion techniques is directly related to the spread of UTIs. The infection may not initially appear to be very severe, especially in the early stages, but if aggravating conditions are present, it may get much worse Zagaglia, et al. [24] 2022 Biofilms, urinary stasis from blockage, and catheters are complicating variables that contribute to the development of UTI. UTIs are a diverse set of clinical illnesses that differ in their genesis and degree of severity. Numerous inherent and acquired variables, including urine retention, vesicoureteral reflux, frequent sexual activity, prostate gland enlargement, vulvovaginal atrophy, and familial history, might increase the risk of UTI. Women who take spermicides may get more UTIs. Asymptomatic bacteriuria is defined as a urine culture with 105 colony-forming units/mL without any particular UTI symptoms since it typically cures on its own and doesn't need to be treated [25]. Only some individuals, such as those who are pregnant, have neutropenia, or are having genitourinary surgery, should get therapy for asymptomatic UTIs since doing so increases the risk of bacterial resistance developing [26]. Contrarily, antibiotics are frequently used to treat symptomatic UTIs, which increase the likelihood of the development of multidrug-resistant microbes by altering the intestinal and vaginal microbiota [27].

Signs and Symptoms

Most UTI criteria used in the studies that were included required signs and symptoms to be present. It's interesting to note that 15% of research did not clarify which symptoms or indicators had to be present in order to identify UTIs, and even more studies did not indicate which symptoms or signs had to be present at all. The mainstay of UTI diagnosis continues to be symptoms and indications. By precisely identifying specific symptoms, the risk of classification mistake may be decreased. In study including older patients with UTI, symptom characterization is particularly crucial due to the high background prevalence of asymptomatic bacteriuria and pyuria [28]. Classic UTI-associated symptoms like dysuria, frequency, and urgency were commonly mentioned in studies that did not specify which symptoms were included in the UTI criteria. But we also found a wide range of non-specific symptoms, especially in trials that failed to isolate the specific UTI subtype under research. The fact that only a small percentage of the included studies employed the same collection of symptoms to diagnose UTI supports the theory that, despite the ambiguous clinical importance of nonspecific symptoms in UTI, this diversity of symptoms contributes to study heterogeneity. Furthermore, no minimum number of symptoms (for diagnosis) was specified in more than a third of the reports that were included. A minimum number of symptoms should be stated because even the normal lower urinary tract symptoms are not 100% specific for UTIs and because the likelihood of UTI increases when numerous symptoms are present [29].

Types of UTI and Definitions

Adult UTIs can be diagnosed as either pyelonephritis or cystitis. Men and women who have urethritis, a sexually transmitted disease, are included in the differential diagnosis. Males are susceptible to both acute and chronic bacterial prostatitis, which are all parts of the UTI spectrum. Men can suffer from the associated disorders epididymitis, orchitis, and epididymo-orchitis.

A-Uncomplicated Cystitis

A healthy, premenopausal female with normal urinary system, non-pregnant has a bladder infection [30].

B-Complicated Cystitis

A bladder infection accompanied with elements that either lessen the effectiveness of treatment or raise the danger of unfavorable effects. This includes vesicoureteral reflux, cystitis, a foreign item (such a catheter or urinary tract stone), and recent instrumentation. It also covers cystitis in men, pregnant women, those who have had kidney transplants, and those with various immunocompromised situations. These UTIs are brought on by unique organisms or bacteria that are resistant to numerous medications [31].

C-Uncomplicated Pyelonephritis

A healthy, non-pregnant patient with a healthy urinary system develops a kidney infection [32].

D-Complicated Pyelonephritis

An infection of the kidneys that develops during pregnancy or in a patient who has additional aggravating circumstances (as mentioned above under complex cystitis), and that often necessitates hospitalization [33].

E-Recurrent UTI (rUTI)

After the first infection, up to 25-32% of women may experience recurrent episodes, which are classified as 3 episodes within a year or 2 episodes within a 6-month period. The real rate, however, could be considerably higher given that a sizable portion of UTIs go undetected [34]. The most frequent organisms known to cause UTIs are *Escherichia coli* (E. coli), Klebsiella pneumoniae, Proteus mirabilis, Enterococcus faecalis, and Staphylococcus saprophyticus [35].

F-Asymptomatic Bacteriuria

On clean catch urine culture, 100,000 cfu/mL of bacteria are found without any illness-related signs or symptoms [36].

Risk Factors

Females

Females are more prone to get a UTI than men, perhaps as a result of the urethral opening's proximity to the bacteria-rich vagina and rectum, as well as the fact that there is less space between it and the bladder. In healthy premenopausal females, the probability of periurethral E. coli colonization is increased for both acute cystitis and recurrent UTI in the presence of recent or frequent sexual activity, the use of spermicide, or both [37].

Older Age

Older age for both women and men, getting a UTI rises with age (especially after 65 and especially after 80). According to Schaeffer and Nicolle [38], UTI is uncommon in men under the age of 60, but the rate rises significantly after that. By the age of 80, both men and women had comparable rates of UTI.

Decreased Estrogen Levels

Decreased estrogen levels also in the postmenopausal women are a risk factor.

Incontinence

The urethral aperture is made vulnerable to germs by fecal incontinence, although most of these bacteria are quickly eliminated from the urinary system unless they are uropathogenic strains [39].

Family History and Genetics

Family history and genetics also influence risk a woman's chance of developing UTIs is 2-4 times higher if her mother had them. In addition, it appears that genetic predisposition affects the severity of UTIs [40]. According to Li, et al. [41], catheterization significantly raises the risk of a urinary tract infection. Over 70% of UTIs in patients being treated in hospitals are caused by catheters. An indwelling catheter is not as safe as clean intermittent catheterization. UTIs are more common when there are conditions that call for catheterization, such as neurogenic bladder, insufficient bladder emptying, and genitourinary tract structural abnormalities [42].

Procedure

The risk of UTI increases after a urinary tract operation, such as a flexible ureteroscopy for the treatment of bladder cancer or the management of kidney stones. According to a Cochrane analysis, giving patients undergoing cystoscopy antibiotic prophylaxis may lower their likelihood of developing a symptomatic UTI [43]. Urogynecologic surgery patients are more likely to get UTIs. According to Thomas-White, et al. [44], between 7% and 24% of women who have surgery for pelvic organ prolapse or stress urine incontinence will get a postoperative UTI.

Recurrent UTIs can be brought on by kidney or bladder stones, which often harbor the same type of bacteria. According to Ripa, et al. [45] ureteral stones enhance the probability of urosepsis in pyelonephritis patients. UTI risk is increased by half in those with diabetes [46]. Although obesity has statistically been linked to a higher incidence of UTI, it is not known if obesity is the root of the problem [47].

Immunocompromised Status

Immunocompromised status, one research found that solid organ transplants, namely kidney transplants, increase the risk of UTI by showing that 28% of 417 patients had a UTI within 13 days of getting the transplant [48]. Human immunodeficiency virus (HIV) infection is not thought to affect the frequency of symptomatic UTI even in those with low CD4 levels [49].

Laboratory Detection Methods

Midstream urine sampling is one of the most frequent ways to diagnose a UTI, followed by microbiological investigation (urine culture) for pathogen isolation, identification, and antibiotic susceptibility testing (AST) [50]. This type of diagnosis frequently takes two to three days, delaying treatment and promoting the spread of the infectious disease. Due to this restriction, many empirical decisions are made and unnecessary antibiotics are used. Microorganisms can be recovered and concentrated while testing times are decreased using separation and filtration techniques (chemical, physical, and antibody-based procedures). These procedures are not optimal since they make use of potent chemicals that could harm cells and affect how well bacteria retain their surface characteristics during recovery and concentration [51]. The quantity of an antigen in a solution can be determined using a variety of immunoassays that depend on the precise interaction between an antibody and an antigen. According to Gan and Patel [52], the ELISA test is an enzyme-linked immunosorbent assay, is a biochemical test that identifies antigens, antibodies, and proteins in a sample using antibodies and enzyme-mediated colour change. The use of recently developed methods such as polymerase chain reaction (PCR), matrix-assisted laser desorption/ionization-time of flight (MALDI-TOF) , fluorescence in situ hybridization (FISH), and forward light scattering has been beneficial for the diagnosis of UTIs Mo, et al. 2019 [53]. These methods have significantly shorter detection times and better sensitivity and specificity than culture-based tests. Combining them also enables a precise identification and assessment of the pathogen's medication susceptibility. However, a clinical microbiology laboratory, as well as pricy reagents and equipment, are all necessary in order to carry out the tests for these p8 Shi, et al. [54,55].

Antimicrobial Resistance in UTIs

Due to their ability to obtain genes that coding for extended-spectrum –lactamases (ESBLs) , which are located on transferable plasmids, Gram-negative bacteria, which are the main cause of UTIs, pose an increasing threat to the public's health [56]. These enzymes are unable to hydrolyze carbapenems, but can do so with third-generation cephalosporins and monobactams [57]. ESBLs are also a public health problem since they are frequently found on plasmids that also carry additional resistance genes against several other classes of antibiotics (such as sulfonamides, aminoglycosides, and quinolones) Shaikh, et al. [58]. Bacteria that take up these plasmids therefore acquire multidrug resistance. Although the mechanism by which all ESBLs function is the amide bond of the -lactam ring, the genes that code for these enzymes are diverse and broken down into several groups [59]. These methods significantly shorten detection times while improving sensitivity and specificity when compared to culture-based assays. Combining them also makes it easier to accurately identify and assess the pathogen's drug susceptibility. But to carry out the tests for these p8 Shi, et al. [54], a clinical microbiology laboratory, as well as expensive reagents and equipment, are all needed [55,60]. The majority of ESBLs are of the CTX-M type, which is found in P. aeruginosa and Acinetobacter species as well as other members of the order Enterobacterales [61]. Cefotaxime resistance is increased in isolated isolates harboring CTX-M, and they are less susceptible to ceftazidime [62]. Other significant drug resistance mechanisms include drug target alteration, drug efflux activity, and drug absorption restriction. Antimicrobials target certain bacterial proteins. One frequent method of resistance is to alter these bacterial proteins such that the antibiotic binds ineffectively or not at all. The efflux of medicines from cells via membrane transporters is the most frequent route of bacterial resistance. These transporters are proteins that are members of the ATP-binding cassette (ABC) gene superfamily. Because it enhances the efflux of many medications from cells and lowers the intracellular concentration of pharmaceuticals, overexpression of ABC transporters is a key factor in multidrug resistance [63]. Because uropathogens are becoming more and more resistant to medicines, there are more and more urinary tract infections that people get in hospitals and the general public. As a result of rising fluoroquinolone-resistant Enterobacteriaceae isolation rates, first-choice empiric treatment are no longer advised [64].

Antimicrobial Therapies

Medical practitioners are familiar with the medication nitrofurantoin, and its side effects are controllable. The well-known antimicrobial nitrofurantoin is less effective against Klebsiella and Pseudomonas than it is against other Gram-negative rods. In especially in patients who are prone to these disorders, such as those with chronic obstructive pulmonary disease, ordering clinicians must be aware of the possibility for serious but relatively uncommon hazards of pulmonary fibrosis and interstitial pneumonitis [65]. UTIs are effectively eradicated with TMP-SMX. The restriction on using this drug in clinical practice is that it is only advised when the resistance rate is less than 20% based on the antibiogram and resistance pattern identified in a particular location or institution [66]. Because of the SMX component, this medication cannot be given to anyone with sulfa allergies.

Although fosfomycin is suitable for treating a uncomplicated UTI [67] suggest that it may not have as potent an antibacterial effect. Quinolones have a lengthy history of use in the management of UTIs. However, because to rising community resistance rates and the necessity to save it for more serious UTIs, experts recommend not to use it for simple UTIs [68-73].

Conclusion

Because of the closer proximity of the urethral opening to the bladder, females are more likely than males to get urinary tract infections (UTI). UTIs have a negative effect on a person's quality of life and are associated with serious morbidity and mortality. The length of the ailment is shortened as a result of antibiotic therapy's efficacy. The development of antibiotic resistance, adverse effects, and other associated problems necessitated the development of alternative management strategies for UTIs. Natural treatments have been used to successfully manage a variety of illnesses to ease symptoms and improve general health.

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