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Original Research Article

Antibiotic Susceptibility Pattern of Uropathogens in Urinary Tract Infection in a Tertiary Care Hospital

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Abstract:

Background: Urinary tract infection (UTI) is one of the most frequent infectious illnesses in the population, especially in underdeveloped countries where healthcare and economic resources are limited. The infection of the urinary system is also known as pyelonephritis (kidney infection) or cystitis (bladder infection). Escherichia coli (E. coli), Klebsiella pneumoniae (K. pneumoniae), Citrobacter species, Enterobacter species, Pseudomonas aeruginosa (P. aeruginosa), and Staphylococcus species are examples of UTI bacteria.

Aims & Objectives:

1. To describe the bacteriological profile.
2. To identify the antimicrobial resistance (AMR) pattern.
3. To find the demographic characteristics associated with the presence of bacterial growth and multidrug resistance (MDR) in adult urine samples undergoing culture and drug susceptibilitytesting.

Method of study: This was a hospital-based, cross-sectional research that used normal laboratory information. From 2020 to 2023, the antibiotic sensitivity and resistance pattern of bacteria responsible for UTI at a Tertiary care facility, MGM Hospital Warangal, Telangana, India, were studied to assess the efficacy of empirical treatment. Three years of urine culture findings, biochemical test results, and antibiotic susceptibility test results of isolates were obtained from the medical microbiology laboratory registry using a checklist. Infection reports from persons of all ages and genders were taken into account. To evaluate, enter, and analyze data, SPSS version 23 was utilized. Our results were presented in the form of descriptive tables and graphs.

Results: The most frequent uropathogen was Escherichia coli, with a prevalence rate of 72%, followed by Klebsiella spp. (20%) and Pseudomonas spp. (8%). Penicillin was the least effective against UTI-causing E. coli, with fourth generation cephalosporins being the most vulnerable. Klebsiella spp., another prevalent uropathogen, was most resistant to broad-spectrum penicillin, followed by aminoglycosides and third generation cephalosporins. The infection rate was almost the same in both sexes, but was highest in individuals over the age of 60.

Conclusion: The antibiotic resistance trend of two primary UTI pathogens, E. coli and Klebsiella spp., in our hospital seems to be equivalent to that reported in other parts of the nation. The prevalence of broad-spectrum penicillin resistance was determined to be more than 50%. Fourth generation cephalosporins and macrolides seem to be the medications of choice for treating UTIs in South India. Furthermore, improved infection incidence record keeping in hospitals is essential to allow for regular surveillance of the occurrence of antibiotic resistance patterns, since such levels change.

Introduction

Urinary tract infection (UTI) is one of the most common infectious diseases in the population, especially in developing countries with poor healthcare and economic resources. Urinary tract infection is sometimes known as pyelonephritis (kidney infection) or cystitis (bladder infection). UTI bacteria include Escherichia coli (E. coli), Klebsiella pneumoniae (K. pneumoniae), Citrobacter species, Enterobacter species, Pseudomonas aeruginosa (P. aeruginosa), and Staphylococcus species. UTIs are among the most common illnesses seen in outpatient settings. It is characterized as urinary tract organism proliferation. It is commonly associated with the

presence of polymorphs and 105 organisms in Midstream Urine (MSU) samples. The two types of UTI are lower UTI and upper UTI.

Forms dependent on the location of engagement. Symptoms include dysuria, frequency, urgency, and suprapubic pain. It affects significantly more women than males due to anatomical and physiological factors. Antimicrobial resistance in urinary pathogens has increased as a consequence of antibiotic use. Uncomplicated UTI is one of the most common reasons for antibiotic use in the community. They pose significant challenges to outpatient empiric treatment.

The gram-negative germs that cause UTIs, on the other hand, are growing more resistant to commonly used medications. A few new antibiotics are on the way, and those that have recently been approved are mostly for intravenous use. Every year, an estimated 150 million people globally suffer with UTI, which may reach 75% of the female population by the age of 24, with 15-25% of this group experiencing a recurrence [1, 2, 3, 4]. E. coli showed high resistance to sulfonamide SXT (double-strength trimethoprim-sulfamethoxazole) and fluoroquinolone ciprofloxacin in nine European countries and Brazil, according to the antimicrobial resistance epidemiological survey on cystitis (ARESC), an international survey on antimicrobial resistance of pathogens [5]. SXT resistance seems to be common among urinary infections in the United States, and the Gupta et al. research predicts that SXT will need to be replaced by other drugs sooner or later [6].

Despite the fact that UTI is the third most common illness in India, only a few studies on UTI have been published in this country [7, 8, 9]. In India, UTI is a common ailment that affects individuals of all ages, from babies to the elderly. However, research on UTI and antibiotic susceptibility patterns is still being conducted in India, and there is much debate over antibiotic selection owing to a lack of set guidelines. Understanding the pathogen's aetiology as well as its drug susceptibility pattern is crucial. Uropathogens empirically treated with antibiotics have been recognized as a likely cause of antibiotic resistance in numerous types of bacteria, both worldwide and domestically. Despite the fact that empirical antimicrobial treatment for UTI is clinically authorized, bacteria are developing antibiotic resistance faster than new antibiotic classes are being produced.

Because the causative bacteria have developed resistance to the antibiotic, physicians typically use broad-spectrum antibiotics instead of a specific antibiotic during empirical treatment. Antibiotic misuse, as well as noncompliance or inability to complete an antibiotic course, lead to an increase in antibiotic-resistant bacteria. The present research looks at the trends of antibiotic-resistant uropathogens as well as their susceptibility to various drugs. This research will also help to create recommendations for determining effective empirical therapy for UTIs while waiting for culture sensitivity results.

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Materials and Methods

Design and scope of the study: A cross-sectional investigation was conducted at a hospital utilizing routine laboratory data. To establish the effectiveness of empirical therapy, the antibiotic sensitivity and resistance trend of bacteria responsible for UTI were studied from 2020 to 2023 at a Tertiary care facility, SCB Medical college and Hospital, Cuttack, India. Three years of urine culture findings, biochemical test results, and antibiotic susceptibility test results from the medical microbiology laboratory registry were collected using a checklist. Infection reports from persons of all ages and genders were taken into account. To protect the privacy of patients, all data was obtained retrospectively and de-identified as required. All patients with UTI symptoms who were hospitalized or attended an out-patient department at a hospital or health center throughout the research period and had UTI confirmed by positive urine culture results were included in the study. Patients who received another antibiotic within 48 hours or 24 hours, had just one dosage, and had a positive culture were also eliminated from the study.

Uropathogen Isolation and Identification

To collect a clean-catch midstream specimen, a sterile wide mouth leak-proof container with a capacity of about 50 ml was employed. For isolation, 10 l of uncentrifuged material was streaked without burning the loop on an agar plate, and then incubated at 35-37 C for 24 hours using the calibrated loop method with a loop diameter of 4 mm. When the bacterial density reached 105 colony-forming units (CFU)/ml, a specimen was deemed positive for UTI. Standard microbiological procedures were used to identify the single-colony type cultures up to the genus/species level where they were available.

Antibiotic susceptibility testing

Antibiotic sensitivity was assessed using the Kirby Bauer disc diffusion technique in accordance with Clinical and Laboratory guidelines Institute (CLSI) guidelines. Broad-spectrum penicillin, third generation cephalosporin, fourth generation cephalosporin, quinolones, tetracycline, macrolides, aminoglycosides, and sulphonamides were among the medications examined (Himedia, India). Amikacin, gentamicin, ceftriaxone, and other antibiotics. The panel specifically includes cefepime, ciprofloxacin, nitrofurantoin, cotrimoxazole, and piperacillin tazobactam.

Results

Out of the 1,800 total urine samples obtained, 690 (38.33%) were culture positive, with 662 (96%) being Gramme negative isolates and just 28 (4%) being Gramme positive bacterial isolates. Out of 690 culture positive urine samples, 65% were female and 35% were male. The patients in this research had an average age of 42.3 years and were predominantly young sexually active females.

Table 1: Culture Positive and Culture Negative in the total urine samples

Total Urine Samples	Culture Positive	% CUL. Positive	Culture Negative	% CUL. Negative
1800	690	38%	1110	62%

Of the 1800 urine samples tested for culture sensitivity, 690 (38%) were culture positive, whereas 1110(62%) were culture negative.

Table 2: Gender Wise Distribution of the Culture Positive Cases

Gender Distribution	No.	%
Females	455	65%
Males	235	35%
Total	690	100%

Out of 690 culture positive urine samples, 65% were female and 35% were male.

Table 3: Department Wise Distribution of the Culture Positive Cases

Department	No.	%
OPD	345	50%
IPD	241	35%
EMD	104	15%
Total	690	100%

50% of the samples came from the outpatient department, 35% from the inpatient department, and 15% from the emergency department of the whole hospital, which included patients of various ages and specialities.

Table 4: Gram Staining in the Culture Positive

Type of Isolates	No.	%
Gram Positive	28	4%
Gram Negative	662	96%
Total	690	100%

Only 28 (4%) of the 690 culture positive cases were Gram positive bacterial isolates, whereas 662 (96%) were Gram negative isolates.

Table 5: Age Group Wise Distribution of the Culture Positive Cases

Age Group	No. Culture Positive	% Culture Positive
<1 Year	38	6%
2-10 YRS	28	4%
11-20 YRS	48	7%
21-30 YRS	116	17%
31-40 YRS	180	26%
41-50 YRS	132	19%
51-60 YRS	78	11%
61-70 YRS	42	6%
>71 YRS	28	4%
Total	690	100%

The bulk of samples were positive in the age group 31-40 years, followed by about 40 and 30 years. Approximately 6% were infants and 4% were children.

Table 6: Organisms Isolated

Organism	No.	%
Escherischia Coli	366	53%
Pseudomonas Sp.	138	20%
Proteus Sp.	83	12%
Staphylococcus aureus	10	1%
Klebsiella Sp.	48	7%
Citrobacter Sp.	27	4%
Enterococcus Sp.	18	3%
Total	690	100%

The list of the organisms identified were E. Coli (53%), Pseudomonas Spp. (20%), Proteus (12%), Klebsiella Spp. (7%), Citrobacter (3%), and Staphylococcus (1%).

Table 7: Antibiotics Sensitivity Pattern of Gram-Negative Organisms

Antibiotics Sensitivity Pattern of Gram-Negative Organisms				
Name of the Drug	**Sensitivity**	**Sensitivity %**	**Resistance**	**Resistance %**
Amikacin	510	77%	152	23%
Gentamicin	298	45%	364	55%
Ceftriaxone	180	27%	482	73%
Cefepime	278	42%	384	58%
Nitrofurantoin	582	88%	80	12%
Ciprofloxacin	98	15%	564	85%
Cotrimoxazole	202	31%	460	69%
Piperacillin/Tazobactam	338	51%	324	49%

Amikacin was toxic to the vast majority of Gramme Negative organisms (77%). Nitrofurantoin (88%), Cephalosporins (40%), Cotrimoxazole (31%), Quinolones (15%), and Piperacillin/Tazobactam (35%). In gram-negative organisms, nitrofurantoin outperformed other antibiotics. Resistance to Quinolones (85%), Ceftriaxone (73%), and Nitrofurantoin (12%) was observed, showing the drug's efficacy in Gram-negative UTIs.

Table 8: Antibiotics Sensitivity Pattern of Gram-Positive Organisms

Antibiotics Sensitivity Pattern of Gram-Positive Organisms				
Name of the Drug	**Sensitivity**	**Sensitivity %**	**Resistance**	**Resistance %**
Gentamicin	12	43%	16	57%
Ciprofloxacin	10	36%	18	64%
Erythromycin	11	39%	17	61%
Clindamycin	8	29%	20	71%
Vancomycin	17	61%	11	39%
Nitrofurantoin	23	82%	5	18%
Teicoplanin	21	75%	7	25%
Linezolid	20	71%	8	29%

Nitrofurantoin (82%), Teicoplanin (75%), Linezolid (71%), and Vancomycin (61%), were the most sensitive antibiotics in Gramme positive organisms, followed by Gentamicin (43%), Ciprofloxacin (36%), Erythromycin (39%), and Clindamycin (29%). Clindamycin (71%), Ciprofloxacin (64%), Erythromycin (61%), Gentamicin (57%), and Vancomycin (39%), were shown to have greater resistance patterns, followed by higher antibiotics like Teicoplanin and Linezolid. Nitrofurantoin demonstrated an 18% resistance rate, confirming its efficacy against Gramme Positive isolates in urinary tract infections.

Discussion

Different investigations have shown varying degrees of antibiotic sensitivity in urine isolates. Nitrofurantoin seems to have high clinical and microbiological effectiveness for UTI caused by common uropathogens, with the exception of increased erosion. This is the most effective therapy for a simple E. coli UTI. Also used to treat recurring urinary tract infections, especially in elderly women with poor glomerular filtration rate [10, 11].

Six hundred (38%) of the 1800 urine samples were positive for culture sensitivity, whereas 1110 (62%) were negative. Sixty-five percent of the 690 urine samples that tested positive for culture were female, while 35 percent were male. The bulk of positive samples were identified in the 31-40 year age range, followed by the 40 and 30 year age ranges. There were around 6% babies and 4% children present.

The outpatient department supplied 50% of the samples, the inpatient department 35%, and the

emergency department 15% for the whole hospital, which included patients of all ages and specialisations. Females are more prone to UTIs than men because to their shorter urethra, closer to anus, and usage of diaphragmatic condoms and spermicidal gels. The male-female ratio research conducted by Neelima A and Kiranmai yielded similar findings. Six hundred (38%) of the 1800 urine samples were positive for culture sensitivity, whereas 1110 (62%) were negative. Antibiotic susceptibility testing was performed on culture positive people. Only 28 of the 690 culture positive cases (4% of the total) contained Gram positive bacterial isolates, whereas the remaining 662 (96%) had Gram negative isolates. The results were close to those of a previous research by Brumfitt W et al., which revealed that gram negative bacteria caused 80.3% of illnesses. Another research [12] revealed Gram-positive enterococci as the second pathogenic agent of UTI. Gramme negative organisms are more often linked with lower UTI due to perianal dispersion, while gramme positive organisms are more commonly associated with greater UTI due to haematogenous spread.

The majority of the species discovered in the present study were E. Coli (53%), Pseudomonas Spp. (20%), Proteus (12%), Klebsiella Spp. (7%), Citrobacter (3%), and Staphylococcus (1%). A related research by Al Zarouni M et al. yielded similar results. 14 In another study, Brumfitt W et al. observed comparable findings [13].

As a consequence, the most prevalent bacteria responsible for UTI in most investigations was Escherichia coli. This might be connected to Secreted Autotransporter Toxin (SAT), which has a deleterious impact on the epithelial cell lining of the urinary tract. The latest results for the most prevalent uropathogen are consistent with the previous two investigations.

These isolates were evaluated for antibiotic sensitivity and resistance patterns using a variety of antibiotics. Pathogens associated with UTI are multidrug resistant, and the present study discovered similar resistance. The great majority of Gram-Negative organisms (77% were poisonous to amikacin). Nitrofurantoin (88%), Cephalosporin (40%), Cotrimoxazole (31%), Quinolones (15%), and Piperacillin/ Tazobactam (35%). Nitrofurantoin outperformed other antibiotics in gram-negative organisms. Resistance was demonstrated to Quinolones (85%), Ceftriaxone (73%), and Nitrofurantoin (12%), demonstrating the drug's effectiveness in Gram-negative UTIs.

The gram-negative urine isolates in this investigation were very resistant to the three most widely used antibiotics for UTI therapy in the outpatient setting: ciprofloxacin (85%), ceftriaxone (73%), and cotrimoxazole (69%). Despite the fact that they were largely susceptible to amikacin (77%), piperacillin (35%), and

These drugs, as well as tazobactam (35%), are delivered parenterally and are exclusively used in hospitals. They were 88% responsive to the oral medication nitrofurantoin.

The results agreed with those of Khoshbakht R et al. [15], who discovered that the majority of the isolates (87.12%) were sensitive to nitrofurantoin. They are consistent with the findings of Shalini et al., [16], Kibret M and Abera B [17], and Rijal A et al., [18]. The current findings were comparable to Raja NS 19's research. While the majority of isolates (77% were from female patients), 90% were E. coli, with 93% and 42% sensitivity to nitrofurantoin, respectively.

Nitrofurantoin (82%), Teicoplanin (75%), Linezolid (71%), and Vancomycin (61%), were the most sensitive antibiotics in Gram-positive organisms, followed by Gentamicin (43%), Ciprofloxacin (36%), Erythromycin (39%), and Clindamycin (29%).

Clindamycin (71%), Ciprofloxacin (64%), Erythromycin (61%), Gentamicin (57%), and Vancomycin (39%), were shown to have greater resistance patterns, followed by higher antibiotics like Teicoplanin and Linezolid. Nitrofurantoin demonstrated an 18% resistance rate, confirming its efficacy against Gramme Positive isolates in urinary tract infections.

The rate of nitrofurantoin resistance in this research was higher than in prior studies. This might be due to increased nitrofurantoin usage in recent years compared to previous study.

Routine microbiological testing of urine samples is therefore recommended prior to the administration of medications for UTI therapy. As a consequence, the establishment of atypical resistance among such strains might be discovered early, allowing for more effective treatment and management of patients affected with these illnesses. In an antibiotic resistance epidemiology research on cystitis project in Europe, fosfomycin, nitrofurantoin, and pivmecillinam were identified as useful drugs for the treatment of simple UTIs. Numerous innovative compounds have been licensed, and one such drug that would be appropriate for the treatment of UTI in our nation is nitrofurantoin.

Previous research from India and other countries shown that E. coli is the most common UTI pathogen, followed by Klebsiella spp. The production of extended spectrum-lactamase (ESbL)-producing organisms has been linked to an increase in infection outbreaks on all continents. Resistance determinants to a variety of antibiotic families, including amino-glycosides and

fluoroquinolones, are often discovered in ESbL-producing bacteria, limiting the number of antibiotics that are viable [20].

In recent years, ESbL-producing bacteria have grown increasingly prevalent among clinical Klebsiella isolates, accounting for 6-17% of all nosocomial UTIs [21, 22].

In terms of resistance development, the introduction of various antibiotics in India (http://www.cdsco.nic.in/forms/Default.aspx) for treating microbiological diseases, including UTI, follows a similar trajectory.

From 2008 to 2013, drugs in the penicillin combination were the least effective (had the greatest chance of resistance) against UTI-causing E. coli. MAR enterobacterial strains isolated from West Bengal river waters were shown to transfer R-plasmids to plasmid-free E. coli DH5 cells with ampicillin, cephalexin (first generation cephalosporin), and cefotaxim (third generation cephalosporin) resistance [23]. Drugs from the fourth generation of cephalosporins are the most susceptible. Lesser quinolone resistance may be linked to the fact that E. coli resistance to quinolones was uncommon until recently, when quinolones were frequently used to treat urinary tract infections.

Resistance to the penicillin combination increased significantly from 2008 to 2011, then decreased somewhat in 2012 and 2013. Concerning the use of penicillin combinations (the main components of which included amoxicillin, methicillin, and piperacillin and were introduced into the Indian market from 1978 to 1989), we have reason to believe that these drugs were used in the treatment of UTI until the introduction of quinolones and third generation cephalosporins. Individual exposure to a penicillin combination, such as co-amoxiclav, has been linked to an increase in the occurrence of co-amoxiclav-resistant E. coli urinary tract infections [24]. It should also be highlighted that doctors examined the use of aminoglycosides ranging from gentamicin to amikacin in the treatment of UTI between 1978 and 1986. Only in 1992, when macrolides (azithromycin and clarithromycin) were brought to the Indian market, could they be used to treat UTI. Doctors would most likely prescribe a recently available generic extension within a subgroup or a newly released molecule of a group sparingly based on existing prescription patterns for UTI.

The key issues are either concerns about the availability of a newly introduced medicine in retail outlets or the higher expense of later-manufactured newer generation drugs or antibiotics. Only an antibiotic combination or a single antibiotic, such as fourth generation cephalosporin (which became accessible in India in 2002), could cure a UTI infection that had been resistant to all previous therapies. Cefepime, for example, was first marketed in 2002.

Penicillin/tetracycline resistance is high in compared to other medications, although third to fourth generation cephalosporin resistance is low. Several research have suggested that different antibiotics be used to combat the issue of resistance. One research advised that ofloxacin be used as a first-line therapy for UTI caused by Gram positive or Gram negative bacteria. However, this cannot be supported since only 28 of the 106 patients in our study responded to ofloxacin, and the overall highest response to Ofloxacin group was only 28%. In the same study, gentamicin was also indicated for E. coli. According to our statistics, amikacin would be a preferable option since its sensitivity was 78% greater than that of gentamicin (37%).

Another research conducted in India discovered that hospital-acquired E. coli in UTI was more aggressive and harder to cure, necessitating at least one IV antibiotic, preferably cephalosporin, in addition to an oral antibiotic, confirming the prevalence of resistance in UTI needing inpatient treatment [26]. Shifali and Gupta's investigation on females demonstrated the greatest pathogen sensitivity pattern to Amikacin and Nitrofurantoin, which supported our results [27].

The recommendations that follow are the result of a comparative literature analysis of local and worldwide statistics that may aid in the effort of eliminating resistance in our region.

1. We propose that empirical antibiotic selection be based on local bacterial organism prevalence and antibiotic sensitivities rather than worldwide standards.
2. Culture and sensitivity should be applied when necessary.
3. Floroquinolone use should be restricted because it is the only orally active drug that works against Pseudomonas and other multidrug resistant bacteria, and because resistance is found in more than 50% of hospitalised patients in most published data from our region, this would help relieve resistance pressure on the widely used quinolone class.
4. The use of nitrofurantoin and fosfomycin should be included in our guidelines since they are more effective and have a lower impact on antibiotic resistance. Furthermore, due of its lower risk of adverse reactions, nitrofurantoin has been recommended for usage during pregnancy.

Conclusion

Finally, the antibiotic resistance pattern of the

predominant UTI pathogen, E. coli, in Telangana, India, seems to be similar to that documented in other regions of India and throughout the globe. More over half of the penicillin combinations tested positive for resistance. As a consequence, in India, these medications should not be used as an empirical therapy for UTI. Fourth generation cephalosporins and macrolides seem to be the first-line therapies for UTIs, with a combination of the two perhaps being the most effective. Furthermore, enhanced record keeping and a prospective monitoring system are required in Indian institutions to enable for ongoing observation of antibiotic resistance occurrence as levels and patterns change.

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