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 common infectious diseases at the community level and particularly in developing countries, overwhelmed with healthcare and economic constraints. Urinary tract infection can be called 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.

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 susceptibility testing.

Method of study: This was a hospital-based, cross-sectional study using routine laboratory records. The susceptibility of antibiotics and resistance pattern of bacteria responsible for UTI at a Tertiary care institution, MGM Hospital Warangal, Telangana, India, were examined from 2020 to 2023 in order to determine the adequacy of empirical therapy. Using a checklist, three years of urine culture findings, biochemical test results, and antibiotic susceptibility test results of isolates were acquired from the medical microbiology laboratory registration. Infection reports from people of all ages and genders were considered. SPSS version 23 was used to examine, input, and analyse data. We provided our findings in the form of descriptive tables and graphs.

Results: With a prevalence rate of 72%, Escherichia coli was the most common uropathogen, followed by Klebsiella spp. (20%) and Pseudomonas spp. (8%). Penicillin was the least effective against UTI-causing E. coli, with fourth generation cephalosporins showing the greatest vulnerability. *Klebsiella* spp., another common uropathogen, was most resistant to broad-spectrum penicillin, followed by aminoglycosides and third generation cephalosporin. The infection incidence was approximately same in both sexes, but was greatest in those over the age of 60.

Conclusion: In our hospital, the antibiotic resistance trend of two major UTI pathogens, E. coli and Klebsiella spp., appears to be comparable to that reported in other regions of the country. Broad-spectrum penicillin resistance was discovered to be greater than 50%. In South India, fourth generation cephalosporins and macrolides appear to be the drugs of choice for treating UTIs. Furthermore, enhanced infection incidence log keeping is required in hospitals to permit frequent tracking of the occurrence of antibiotic resistance patterns, as such levels vary.

Keywords: Urinary tract infection UTI, antibiotic susceptibility, uropathogens, pathogenic bacteria

Introduction

Urinary tract infection (UTI) is one of the most frequent infectious disorders in the population, particularly in underdeveloped nations 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.

UTIs are among the most prevalent infections encountered in outpatient settings. It is defined as organism multiplication in the urinary tract. The presence of polymorphs and 105 organisms in the Midstream Urine (MSU) sample is frequently related with it. Lower UTI and Upper UTI are the two

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 10, 2023

forms based on the place of involvement. Dysuria, frequency, urgency, and suprapubic discomfort are all symptoms. Due to anatomical and physiological causes, it affects far more women than men. Antibiotic usage has resulted in increasing antimicrobial resistance in urinary pathogens. One of the most prevalent indications for antibiotic usage in the community is uncomplicated UTI. They provide considerable obstacles for outpatient empiric therapy. However, the gramme negative organisms that cause UTIs are becoming increasingly resistant to routinely used medicines. A few novel antibiotics are on the horizon, and those that have lately been authorised are largely for intravenous use. An estimated 150 million individuals worldwide suffer with UTI each year, which may climb to 75% in the female population by the age of 24, and 15-25% of this group will have a relapse of this condition [1, 2, 3, 4]. In nine European countries and Brazil, the antimicrobial resistance epidemiological survey on cystitis (ARESC), an international survey on antimicrobial resistance of pathogens, E. coli showed high resistance to sulfonamide SXT (double-strength trimethoprim-sulfamethoxazole) and fluoroquinolone ciprofloxacin [5]. SXT resistance among urinary pathogens appears to be widespread in the United States and Gupta *et al*. study suggests that SXT will need to be replaced by other medicines sooner or later [6].

Despite the fact that UTI is the third most frequent infection in India, various research have only published a few studies on UTI in this nation [7, 8, 9]. UTI is a widespread infection in India, affecting people of all ages, from newborns to the elderly. However, studies on UTI and antibiotic susceptibility patterns are still ongoing in India, and there is substantial discussion on antibiotic selection due to a lack of defined standards. It is critical to understand the pathogen's aetiology as well as its antibiotic susceptibility pattern. Uropathogens treated empirically with antibiotics have been identified as a probable source of antibiotic resistance in various kinds of bacteria, both globally and nationally. Although empirical antimicrobial therapy for UTI is clinically approved, bacteria are gaining antibiotic resistance quicker than new antibiotic classes are being developed.

Due to the causal organism's resistance to the antibiotic, doctors frequently administer broad-spectrum antibiotics instead of a particular antibiotic during empirical therapy. Antibiotic overuse and noncompliance or failure to finish the course of antibiotic medication contribute to a rise in antibiotic-resistant microorganisms. The current study considers the trends of antibiotic-resistant uropathogens and their sensitivity to different antibiotics. This study will also aid in the development of guidelines for setting appropriate empirical treatment for UTIs while waiting for culture sensitivity findings.

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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 susceptibility testing.

Materials and Methods

Study Design and Area: This was a cross-sectional study done at a hospital using standard laboratory data. The antibiotic sensitivity and resistance trend of bacteria responsible for UTI were researched from 2020 to 2023 at a Tertiary care institution, MGM Hospital Warangal, Telangana, India, to determine the efficacy of empirical treatment. A checklist was used to gather three years of urine culture findings, biochemical test results, and antibiotic susceptibility test results of isolates from the medical microbiology laboratory registry. Infection reports from people of all ages and genders were considered.

To ensure patient privacy, all data was collected retrospectively and de-identified as needed. The study included all patients with UTI symptoms who were hospitalised or visited an out-patient department at a hospital or health centre throughout the study period and had UTI confirmed by positive urine culture findings. Patients who got another antibiotic within 48 hours or within 24 hours, had just one dose, and had a positive culture were also excluded from the experiment.

Isolation and Identification of Uropathogens

A sterile wide mouth leak-proof container with a volume of roughly 50 ml was used to capture a clean-catch midstream specimen. For isolation, 10 l of uncentrifuged material was placed on an agar plate and streaked without burning the loop, then incubated at 35-37 C for 24 hours using the calibrated loop technique with a loop diameter of 4 mm. A specimen was considered positive for UTI when the bacterial density reached 105 colony-forming units (CFU)/ml. When available, standard microbiological methods were utilised to identify the single-colony type cultures up to the genus/species level.

Antibiotic sensitivity testing

The Kirby Bauer disc diffusion method was used to assess antibiotic sensitivity in compliance with Clinical and Laboratory criteria Institute (CLSI) criteria. Among the drugs tested were broad-spectrum penicillin, third generation cephalosporin, fourth generation cephalosporin, quinolones, tetracycline, macrolides, aminoglycosides, and sulfonamides (Himedia, India). Amikacin, gentamicin, ceftriaxone,

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 10, 2023

cefepime, ciprofloxacin, nitrofurantoin, cotrimoxazole, and piperacillin tazobactam were particularly included in the panel.

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.

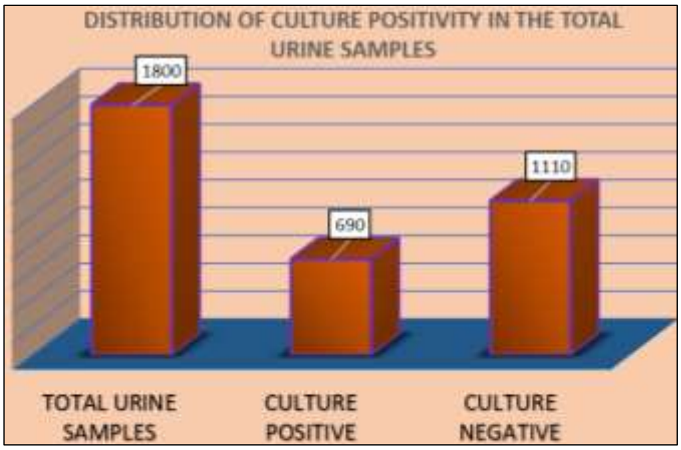

Fig 1: Culture Positive and Culture Negative in the total urine samples

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.

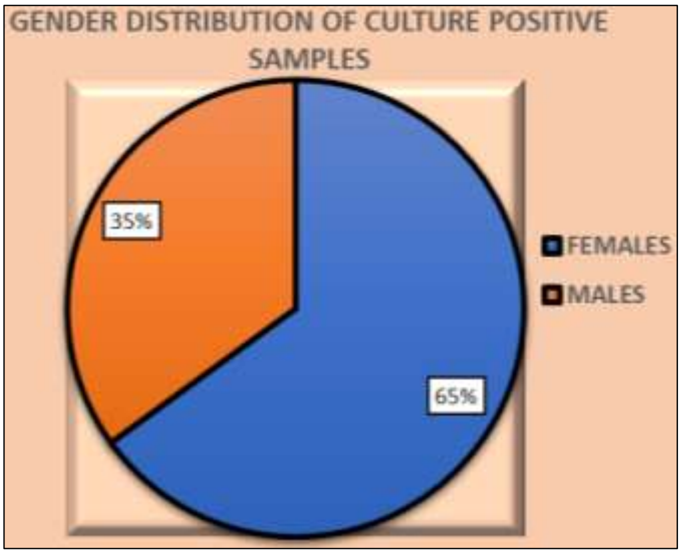

Fig 2: Gender Wise Distribution of the Culture Positive Cases

Table 3: Department Wise Distribution of the Culture Positive Cases

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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.

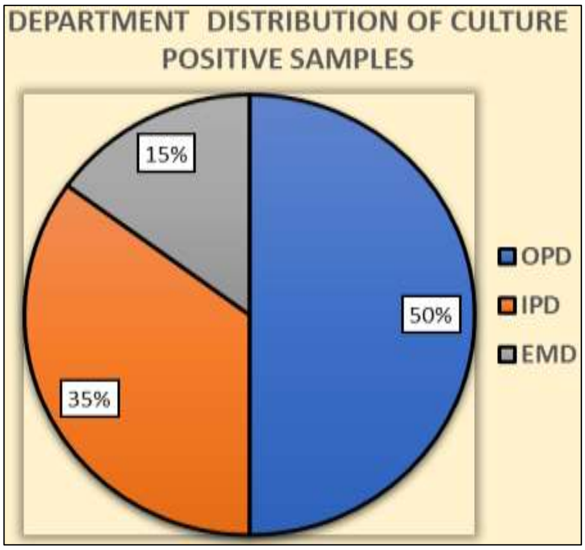

Fig 3: Department Wise Distribution of the Culture Positive Cases

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.

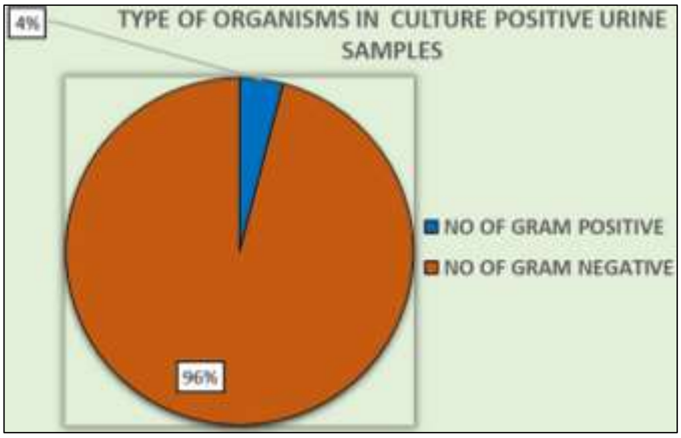

Fig 4: Gram Staining in the Culture Positive

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%

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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.

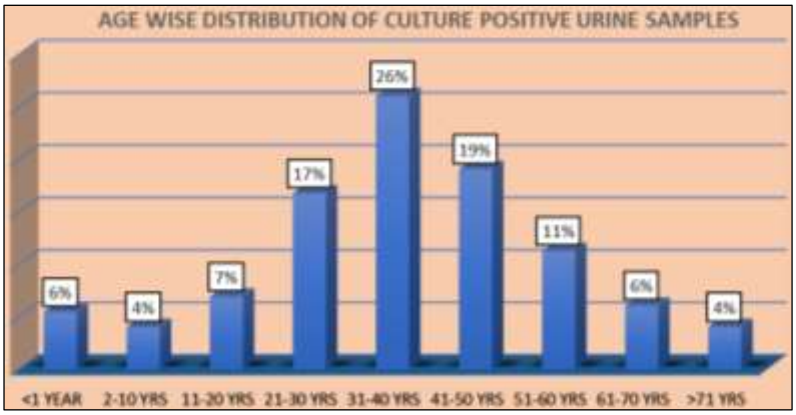

Fig 5: Age Group Wise Distribution of the Culture Positive Cases

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%).

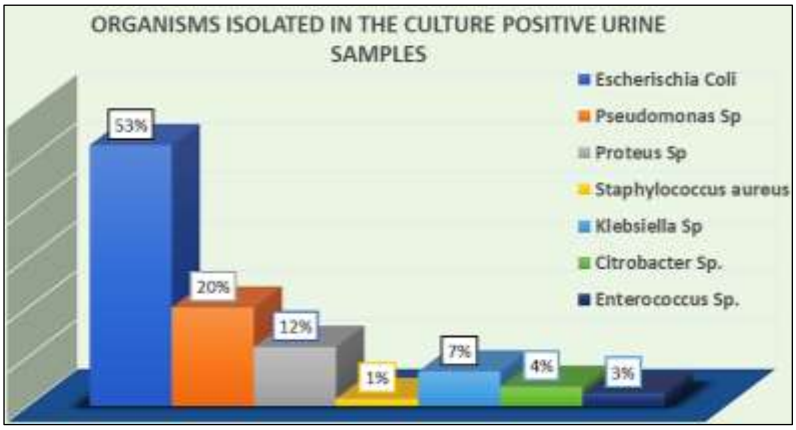

Fig 6: Organisms Isolated

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%

The majority of Gramme Negative organisms (77%) were vulnerable to Amikacin. Gentamicin (45%), Nitrofurantoin (88%), Cephalosprins (40%), Cotrimoxazole (31%), Quinolones (15%), and Piperacillin/Tazobactam (35%). Nitrofurantoin outperformed other antibiotics in gram-negative organisms.
Resistance to Quinolones (85%), Ceftriaxone (73%) and Nitrofurantoin (12%), demonstrating the drug's effectiveness in Gramme Negative UTIs.

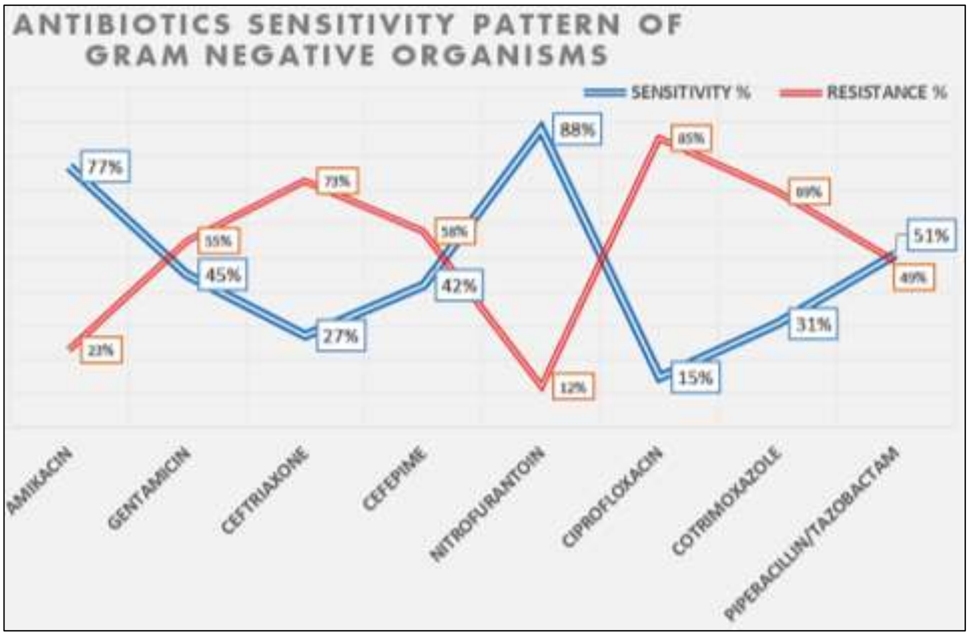

Fig 7: Antibiotics Sensitivity Pattern of Gram-Negative Organisms

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%

Antibiotic sensitivity in Gramme positive organisms was as follows: Nitrofurantoin (82%), Teicoplanin (75%), Linezolid (71%), Vancomycin (61%), followed by Gentamicin (43%), Ciprofloxacin (36%), Erythromycin (39%), and Clindamycin (29%).
Higher resistance patterns were discovered for Clindamycin (71%), Ciprofloxacin (64%), Erythromycin (61%), Gentamicin (57%), and Vancomycin (39%), followed by higher antibiotics like Teicoplanin and Linezolid. Nitrofurantoin had an 18% resistance rate, demonstrating its effectiveness against Gramme Positive isolates in UTIs.

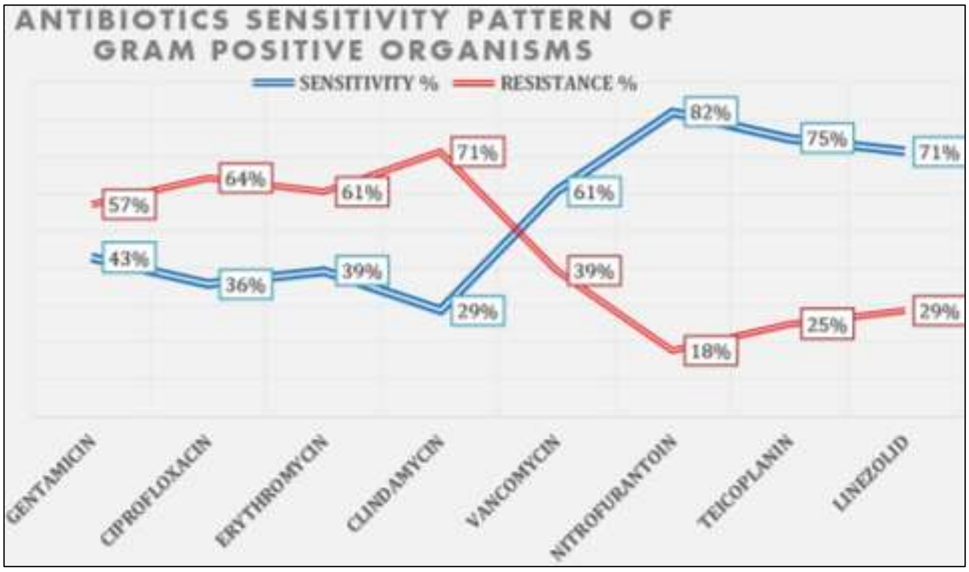

Fig 8: Antibiotics Sensitivity Pattern of Gram-Positive Organisms

Discussion

Various studies have found varied levels of antibiotic sensitivity in urine isolates. Except for the increased erosion, nitrofurantoin appears to have good clinical and microbiological efficacy for UTI caused by common uropathogens. This is the most effective treatment for an uncomplicated UTI caused by E. coli. Also used to treat recurrent urinary tract infections, particularly in older women with low glomerular filtration rate [10, 11].

Six hundred (38%) of the 1800 urine samples evaluated for culture sensitivity were culture positive, whereas 1110 (62%) were culture negative. Sixty-five percent of the 690 culture-positive urine samples were female, whereas 35 percent were male. The majority of positive samples were found in the age group 31-40 years, followed by around 40 and 30 years. There were around 6% newborns and 4% children.

The outpatient department provided 50% of the samples, the inpatient department provided 35%, and the emergency department provided 15% of the samples for the entire hospital, which comprised patients of varied ages and specialisations. Because of their shorter urethra, proximity to anus, and use of diaphragmatic condoms and spermicidal gels, females are more susceptible than males to get UTIs. Neelima A and Kiranmai's study on the male-female ratio showed similar results. Six hundred (38%) of the 1800 urine samples evaluated for culture sensitivity were culture positive, whereas 1110 (62%) were culture negative. On culture positive individuals, antibiotic susceptibility testing was undertaken. Only 28 (4% of the 690 culture positive cases) had Gram positive bacterial isolates, whereas the remaining 662 (96%) had Gram negative isolates. The findings were comparable with another study conducted by Brumfitt W *et al*., which discovered that gramme negative bacteria caused 80.3% of infections. Gram-positive enterococci were identified as the second pathogenic agent of UTI in another study [12]. Gramme negative organisms are more usually associated with lower UTI because of perianal dissemination, whereas gramme positive organisms are associated with higher UTI because of haematogenous spread.

In the current investigation, the bulk of the organisms identified were E. Coli (53%), *Pseudomonas* Spp. (20%), Proteus (12%), *Klebsiella* Spp. (7%), Citrobacter (3%), and Staphylococcus (1%). The findings of a comparable study by Al Zarouni M *et al*. were consistent. [14] Brumfitt W *et al*. discovered similar results in another investigation [13].

As a result, in most studies, Escherichia coli was the most common bacterium responsible for UTI. This might be related to Secreted Autotransporter Toxin (SAT), which has a negative influence on the urinary tract's epithelial cell lining. The most common uropathogen's current findings are consistent with the prior two studies. Using a range of antibiotics, these isolates were tested for antibiotic sensitivity and resistance patterns. Pathogens linked with UTI are multidrug resistant, and the current investigation found comparable resistance.

Amikacin was toxic to the vast majority of Gram-Negative organisms (77%). Nitrofurantoin (88%), Cephalosprins (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.

The gram-negative urine isolates in this study were very resistant to ciprofloxacin (85%), ceftriaxone (73%), and cotrimoxazole (69%), the three most commonly used antibiotics for UTI treatment in the outpatient setting. Although they remained primarily sensitive to amikacin (77%), piperacillin (35%),

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 10, 2023

and tazobactam (35%), these medications are administered parenterally and are only used in hospitals. They were 88% sensitive to nitrofurantoin, an oral drug.

The findings were consistent with a research done by Khoshbakht R *et al*., [15] in which the majority of the isolates (87.12%) were susceptible to nitrofurantoin. They are similar to results documented by Shalini *et al*., [16] Kibret M and Abera B [17] and Rijal A *et al*., [18]. Present results were similar to study by Raja NS [19] Whereas the majority of isolates were from female patients (77%), 90% were Escherichia coli, with 93% and 42% sensitivity to nitrofurantoin, respectively.

Antibiotic sensitivity in Gramm positive organisms was as follows: Nitrofurantoin (82%), Teicoplanin (75%), Linezolid (71%), Vancomycin (61%), followed by Gentamicin (43%), Ciprofloxacin (36%), Erythromycin (39%), and Clindamycin (29%).

Higher resistance patterns were discovered for Clindamycin (71%), Ciprofloxacin (64%), Erythromycin (61%), Gentamicin (57%), and Vancomycin (39%), followed by higher antibiotics like Teicoplanin and Linezolid. Nitrofurantoin had an 18% resistance rate, demonstrating its effectiveness against Gramme Positive isolates in UTIs.

In this study, the rate of nitrofurantoin resistance was greater than in previous investigations. This might be related to greater nitrofurantoin use in recent years compared to past research.

Routine microbiological examination of urine samples is thus suggested prior to the administration of drugs for the treatment of UTIs. As a result, the emergence of atypical resistance among such strains might be detected early, allowing for better treatment and management of those infected with these diseases. Fosfomycin, nitrofurantoin, and pivmecillinam were suggested as helpful medicines for the treatment of uncomplicated UTIs in an antibiotic resistance epidemiology study on cystitis project in Europe. Numerous novel compounds have been approved, and nitrofurantoin is one such medicine that would be acceptable for the treatment of UTI in our country.

Previous studies from India and other countries found E. coli to be the most frequent UTI pathogen, followed by *Klebsiella* spp. Extended spectrum-lactamase (ESbL)-producing organisms have been related to a rise in infection outbreaks across all continents. Resistance determinants to numerous antibiotic families, such as amino-glycosides and fluoroquinolones, are often identified in ESbL-producing bacteria, restricting the number of antibiotics that are viable [20].

ESbL-producing bacteria have become more common among clinical Klebsiella isolates in recent years, accounting for 6-17% of all nosocomial UTIs [21, 22].

The introduction of several antibiotics in India (http://www.cdsco.nic.in/forms/Default.aspx) for treating microbiological infections, including UTI, follows a similar trend in terms of resistance development.

Drugs in the penicillin combination were the least effective (had the highest risk of resistance) against UTI-causing E. coli from 2008 to 2013. MAR enterobacterial strains obtained from West Bengal river waters were discovered to transmit R-plasmids to plasmid-less E. coli DH5 cultures displaying ampicillin, cephalexin (first generation cephalosporin) and cefotaxim (third generation cephalosporin) resistance [23].

The drugs belonging to the fourth generation cephalosporins are the most vulnerable. Lesser quinolone resistance can be attributed to the fact that E. coli resistance to quinolones was unusual until recently, when quinolones were routinely utilised to treat UTIs.

From 2008 to 2011, resistance to the penicillin combination rose substantially, then declined somewhat in 2012 and 2013. Concerning the use of penicillin combinations (the main components, which included amoxicillin, methicillin, and piperacillin, were introduced into the Indian market from 1978 to 1989), we have reason to believe that these drugs were used until the introduction of quinolones and third generation cephalosporins in the treatment of UTI. Individual exposure to a penicillin combination, such as co-amoxiclav, has been connected to an increase in the incidence of urinary tract infections caused by co-amoxiclav-resistant E. coli [24].

It should also be noted that between 1978 and 1986, physicians investigated the use of aminoglycosides ranging from gentamicin to amikacin in the treatment of UTI. Only when macrolides (azithromycin and clarithromycin) were introduced to the Indian market in 1992 could they be given for UTI. According to current prescription trends of physicians treating UTI, doctors would most likely prescribe a recently available generic extension inside a subgroup or a newly introduced molecule of a group sparingly.

The primary factors are either worries about the availability of a newly launched drug at retail outlets or increased cost of newer generation pharmaceuticals or antibiotics manufactured later. Only an antibiotic combination or a single antibiotic, such as fourth generation cephalosporin (which became available in India in 2002), could treat a UTI infection that was resistant to all existing treatments. Cefepime, in example, was initially made available in 2002.

In comparison to other drugs, penicillin/tetracycline resistance is high, whereas third to fourth generation cephalosporin resistance is minimal. Several studies have recommended that various antibiotics be used to fight the problem of resistance. In this regard, one study suggested that ofloxacin be used as first-line treatment for UTI caused by Gramme positive or Gramme negative bacteria. However, this cannot be substantiated because only 28 of 106 patients in our research were responsive to ofloxacin, and the overall greatest response to Ofloxacin group was only 28%.

Gentamicin was also recommended for E. coli in the same research. Amikacin, on the other hand, would be a better choice, according to our data, because its sensitivity was 78% higher than that of gentamicin (37%) [25].

Another study in India found that hospital acquired E. coli in UTI was more aggressive and difficult to control, requiring at least one IV antibiotic, preferably cephalosporin, in addition to an oral antibiotic, confirming the prevalence of resistance in UTI requiring inpatient treatment [26].

Shifali and Gupta's study on females revealed the highest sensitivity pattern of pathogens to Amikacin and Nitrofurantoin, which corroborated our findings [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 pattern of antibiotic resistance of the major UTI pathogen, E. coli, in Telangana, India, appears to be analogous to that described in other parts of India and throughout the world. More than 50% of penicillin combinations were resistant. As a result, these medicines should not be utilised as an empirical treatment for UTI in India. Fourth generation cephalosporins and macrolides appear to be the first-line treatments for UTIs, while a combination of the two may be the best option. In addition, improved record keeping and a prospective monitoring system are necessary in Indian hospitals to allow for continued surveillance of the incidence of antibiotic resistance as levels and patterns change.

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