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PREVALENCE AND ANTIMICROBIAL SUSCEPTIBILITY OF UROPATHOGENS CAUSING URINARY TRACT INFECTIONS(UTI): STUDY OF A TERTIARY CARE CENTER IN CENTRAL INDIA.

Nephrology

Dr Trishala Chhabra*	DM Resident, Nephrology, SAIMS, Indore. *Corresponding Author
Dr Naresh Pahwa	Professor and HOD, Nephrology, SAIMS, Indore.
Dr Shraddha Goswami	Associate Professor, Nephrology, SAIMS, Indore.
Dr Riyaz Asad	Assistant Professor, Nephrology, SAIMS, Indore.
Dr Prachi Saban Shaw	Professor and HOD, Microbiology, SAIMS, Indore.

ABSTRACT

Objective: To study the prevalence, causative organisms, and antimicrobial sensitivity pattern of Urinary Tract Infection (UTI)at a tertiary care center in Central India. **Methods:** The study was undertaken from September 2021 to May 2022 at the Department of Nephrology,SAIMS,Indore. Clean catch midstream urine samples were collected from patients suspected of UTI from patients on OPD basis and inpatients from various departments. The urine samples were processed for Culture and Antibiotic Susceptibility testing after Culture in MacConkey/Blood Agar for 24 hours. The interpretation of the bacterial isolates was carried out by VITEK2 automated system. **Results:** A total of 3241 samples (Females= 1705 and Males=1536) were processed for urine culture and sensitivity. 1022 samples (Females=522, Males=500) were positive for bacterial infection (31.53% positivity rate). Positive isolates were further divided into Outdoor (OPD=315) and Indoor patients (IPD=707) (Wards=480, ICU=227) .E.coli was the most common organism in all groups. However, in ICU most common organism was Pseudomonas. Enterococcus was the most common gram-positive organism. ESBL-producing bacteria among Gram-negative bacteria was 67.4%. Carbapenemase-producing bacteria among Gram-negative bacteria were 60.8%. Among Gram-negative oral drugs sensitivity pattern was: Nitrofurantoin (66.1%), Cotrimoxazole (51.65%), Fosfomycin (48.5%), Amoxycillin+Clavulanic acid(41.15%),Ciprofloxacin(38.25%),Cefixime(20.5%).Pseudomonas was resistant to most oral drugs. Among Intravenous drugs, the sensitivity pattern was: Colistin (89.2%), Amikacin (64.7%), Gentamycin(55.1%), Piperacillin+Tazobactum (44.8%), Tigecycline (43.9%), Meropenam (35.1%), Cefepime (30.1%), Ciprofloxacin (24.71%), Cefoperazone+Sulbactum (20.61%). The sensitivity of Klebsiella was lower than E.coli for most of the drugs. Sensitivity for Fluoroquinolones and Cephalosporins is very low. Among Gram-positive oral medications, the sensitivity pattern was: Linezolid (67.8%) and Nitrofurantoin (65.9%). Among Intravenous drug sensitivity pattern was: Teicoplanin (69.27%), Vancomycin(68.5%), Tigecycline (66.15%), and Linezolid(62.05%). The sensitivity of Enterococcus was higher than Staphylococcus for all drugs. The sensitivity of drugs was higher in OPD patients, followed by wards and least in ICU patients indicating multidrug-resistant strains in ICU are more common. **Conclusion:** Empirical Antibiotics based on regional antibiotic sensitivity patterns should be started and changed as per Culture reports afterwards. It is need of hour to conduct research on the bacteria's culture and sensitivity patterns considering bacterial resistance and multidrug-resistant strains.

KEYWORDS

UTI - Urinary Tract Infection, Gram-positive organism, Gram Negative organism, Culture and sensitivity, Multidrug resistance.

INTRODUCTION

Urinary tract infection (UTI) is one of the most common bacterial infections we see in our routine clinical practice; clinically, it may range from asymptomatic to severe sepsis[1]. Infection of the lower urinary tract includes cystitis, prostatitis and urethritis. Infection of the upper urinary tract includes pyelonephritis. Bacterial colonization of the urinary tract may also occur without symptoms (asymptomatic bacteriuria). UTI also contributes as the most common nosocomial infection in many hospitals and accounts for approximately 35% of all hospital-acquired infections[2]. UTI is treated with broad-spectrum antibiotics to start with, which are de-escalated to specific antibiotics based on urine culture and antimicrobial susceptibility[3]. Overuse and misuse of antimicrobial agents have contributed to the growing problem of resistance amongst uropathogenic bacteria, which is a severe threat to public health. The distribution of urinary microorganisms and their antibiotic sensitivity pattern may vary regionally, so conducting a regional study is necessary. Therefore, we have achieved a study to determine pathogenic organisms causing UTI and antibiotic sensitivity patterns at our center.

MATERIAL AND METHODS

The study was undertaken from September 2021 to May 2022 at the Department of Nephrology,SAIMS,Indore. Clean catch midstream urine samples were collected from patients suspected of UTI from various departments. The urine samples were processed for Culture and Antibiotic Susceptibility testing after Culture in MacConkey/ Blood Agar initially for 24 hours and finally observed for 48 hours. A growth of $\geq 10^5$ colony-forming units/ml was considered significant bacteriuria[4].

Antimicrobial Susceptibility Testing

Interpretation of the bacterial isolates was carried out by VITEK2 automated system[5]. It is an automated microbiology bacterial identification and antimicrobial susceptibility system. A sterile swab was used to transfer a sufficient number of colonies of pure Culture and to suspend the microorganism in 3ml of sterile saline (0.45%NaCl) in a clear test tube. Vortex was used to mix the bacterial suspension until a homogenous suspension was prepared. Densi CHECK plus was used to adjust the suspension turbidity to 0.50 – 0.63 Mac Farland units as per the acceptable turbidity range for bacteria. Tube fixed pipetting (red for Gram-negative and blue for Gram-positive bacteria) from suspension 145mcL for Gram-negative, and 280 mcL for gram-positive bacteria and the above volume was added to 3ml saline. The test suspension tube was placed in the cassette with a reagent card. Identification cards were inoculated with microorganism suspension by vacuum apparatus.

Once the cassette is loaded, the incubation and reading of each card are managed without the operator's intervention. The cards used were different for Gram-negative Lactose fermenting bacilli, Gram-negative non-lactose fermenting bacilli, Gram-negative critically ill, Gram-positive cocci, Gram-positive non-spore-forming bacilli and Gram-positive spore-forming bacilli. Since the panel of antibiotics in each card was different, the antibiotics which were common in cards of all Gram-negative bacteria and similarly common in cards of Gram-positive bacteria were selected for analysis. This data was collected from the Sri Aurobindo Institute of Medical Science Microbiology department and analyzed.

Statistics

Statistical tests(Z-test and Chi-square test) were used to analyze the data using the statistical package SPSS version 22. A P-value<0.05 was considered statistically significant.

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RESULTS

- A total of 3241(Females=1705 and Males=1536) samples were processed for urine culture and sensitivity.
- 1022 samples were positive for bacterial infection (31.53% positivity rate).
- Females were 522(51.07%) and Males were 500(48.92%)
- Positive isolates were further divided into Outdoor (OPD=315) and Indoor patients(IPD=707) (Wards=480,ICU=227).
- Sensitivity of antibiotics was higher in OPD patients followed by wards and least in ICU patients indicating multidrug-resistant strains in ICU were more common. Table 1 shows the various organisms and their distribution in OPD, wards and ICU. The most common organism in OPD, ward and overall was E.Coli but in ICU most common organism was Pseudomonas.

Table 1: Distribution of organisms in OPD, Ward and ICU

ORGANISM	OPD	WARD	ICU	TOTAL
GRAM NEGATIVE ORGANISM				
E.Coli	43.8%	33.8%	17%	33.18%
Klebsiella	24.4%	13.8%	17%	17.8%
Pseudomonas	10.07%	12.8%	18%	13.1%
Acinetobacter	4.31%	2.8%	1%	2.8%
Proteus	0.715%	0.95%	0%	0.66%
GRAM POSITIVE ORGANISMS				
Enterococcus	2.8%	11.4%	7%	7.7%
Staphylococcus	7.9%	5.7%	3%	5.7%

Enterococcus was the most common Gram positive organism. ESBL-producing bacteria among Gram-negative bacteria were 67.4% and the highest was Klebsiella(71.2%).

Carbapenamase-producing bacteria among Gram-negative bacteria were 60.8%, with the highest being Pseudomonas(67.3%). Table 2 shows the percentage of ESBL and Carbapenemase-producing bacteria among Gram-negative bacteria.

Table 2: Prevalence of ESBL producing and Carbapenamase producing Gram Negative bacteria

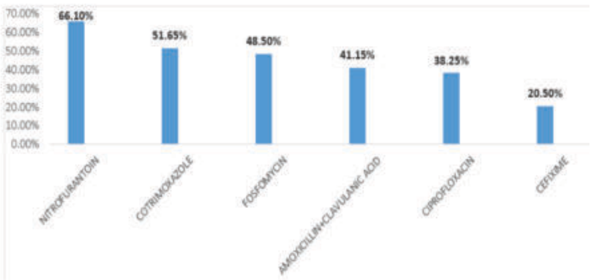
Enterobacteriaceae	ESBL producing	Carbapenamase producing
E.Coli	62.8%	56.4%
Klebsiella	71.2%	58.7%
Pseudomonas	68.4%	67.3%
Overall	67.4%	60.8%

Table 3 shows the sensitivity of E.coli and Klebsiella for oral antibiotics. Pseudomonas was resistant to most of the oral antibiotics.

Table 3: Oral Antibiotic Sensitivity Pattern For Gram Negative Bacteria

ANTIBIOTIC	E.COLI	KLEBSIELLA	P VALUE*
Nitofurantoin	72.2%	60%	0.004
Cotrimoxazole	54.6%	48.7%	0.215
Fosfomycin	51%	46%	0.289
Amoxicillin+Clavulanic acid	44.1%	38.2%	0.141
Ciprofloxacin	44.2%	32.3%	0.128
Cefixime	22.4%	18.6%	0.212

Sensitivity of E.coli was more than Klebsiella for oral Antibiotics. Graph 1 shows the overall sensitivity of Gram-negative organisms for oral antibiotics. Nitrofurantoin(66.1%) was having highest sensitivity among Gram-negative oral antibiotics.



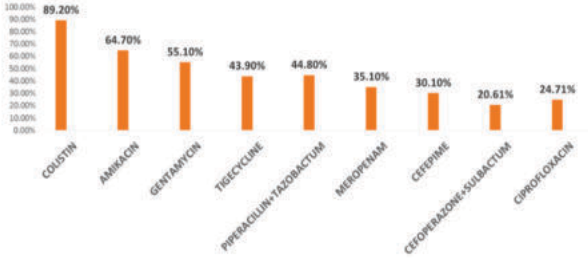
Graph 1: Oral Antibiotic Sensitivity Pattern For Gram Negative Bacteria

Table 4 shows the sensitivity of E.coli, Klebsiella and Pseudomonas for intravenous Antibiotics. E.coli had more sensitivity than Klebsiella for intravenous antibiotics and Pseudomonas had the least.

Table 4 : Intravenous Antibiotic Sensitivity Pattern For Gram Negative Bacteria

ANTIBIOTIC	E.COLI	KLEBSIELLA	PSEUDOMONAS	P VALUE*
Colistin	92.1%	90.4%	85.2%	0.074
Amikacin	76.4%	65.5%	52.3%	0.00001
Gentamycin	62.2%	54.5%	48.7%	0.016
Tigecycline	55.4%	48.8%	27.6%	0.00001
Piperacillin+Tazobactum	51.1%	38.75%	44.6%	0.008
Meropenam	42.2%	40.7%	22.6%	0.00026
Cefepime	34.8%	25%	30.5%	0.31
Cefoperazone+Sulbactum	28.7%	16.25%	16.9%	0.0005
Ciprofloxacin	27.5%	21.25%	25.4%	0.22

Graph 2 shows the overall antibiotic sensitivity of Gram-negative organisms for Intravenous Antibiotics. Colistin (89.2%) was having highest sensitivity among intravenous antibiotics, followed by Amikacin(64.7%).

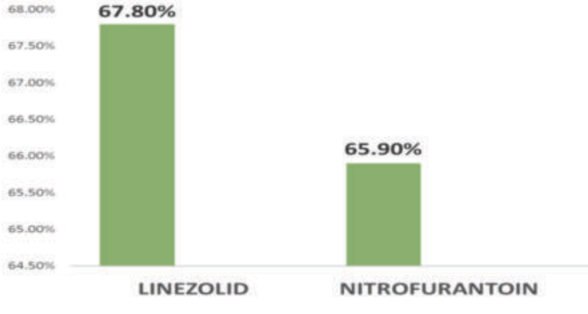


Graph 2: Intravenous Antibiotic Sensitivity Pattern For Gram Negative Bacteria

Table 5 shows the sensitivity of Staphylococcus and Enterococcus for oral antibiotics. Enterococcus has higher sensitivity than Staphylococcus. Graph 3 shows the overall sensitivity of Gram-positive organisms for oral antibiotics. Linezolid was more sensitive than Nitrofurantoin among oral Gram-positive Antibiotics.

Table 5: Oral Antibiotic Sensitivity Pattern For Gram Positive Bacteria

ANTIBIOTIC	STAPHYLOCOCCUS	ENTEROCOCCUS	P VALUE*
Linezolid	64.2%	71.4%	0.379
Nitrofurantoin	65.3%	70.5%	0.503

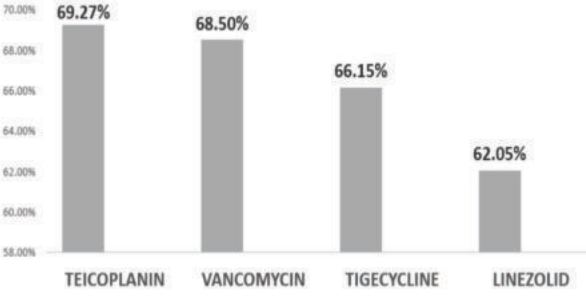


Graph 3: Oral Antibiotic Sensitivity Pattern For Gram Positive Bacteria

Table 6 shows the sensitivity of Staphylococcus and Enterococcus for intravenous antibiotics. Enterococcus has higher sensitivity than Staphylococcus for intravenous antibiotics also. Graph 4 shows the overall sensitivity of Gram-positive organisms for intravenous antibiotics.Teicoplanin(69.27%) was showing higher sensitivity than Vancomycin(68.5%), Tigecycline(66.15%)and Linezolid(62.05%).

Table 6: Intravenous Antibiotic Sensitivity Pattern For Gram Positive Bacteria

ANTIBIOTIC	STAPHYLOCOCCUS	ENTEROCOCCUS	P VALUE*
Vancomycin	65.5%%	71.5%	0.503
Teicoplanin	61.45%	77.1%	0.054
Tigecycline	58.1%	74.2%	0.047
Linezolid	57.8%	66.3%	0.344



Graph 4: Intravenous Antibiotic Sensitivity Pattern For Gram Positive Bacteria

Among Intravenous Gram Negative Antibiotics,increased resistance was observed for Flouroquinolones and Cephalosporins. Resistance to Carbapenems was also high.

Antibiotic Sensitivity as per our study:

Oral Gram-Negative Organisms:
Nitrofurantoin>Cotrimoxazole>Fosfomycin>Amoxicillin+Clavulinic acid> Ciprofloxacin>Cefixime

Intravenous Gram-Negative Organisms:
Colistin>Amikacin>Gentamycin>Piperacillin+Tazobactum>Tigecycline>Meropenam>Cefepime>Ciprofloxacin>Cephoperazone+Sulbactum

Oral Gram-Positive Organisms:-
Linezolid>Nitrofurantoin

Intravenous Gram-Negative Organisms:-
Teicoplanin>Vancomycin>Tigecycline>Linezolid

DISCUSSION

Sri Aurobindo Institute of Medical Sciences, Indore, is one of the largest tertiary care centre in central India.It has 1400 bedded hospital with a daily OPD of about 2700 patients. It caters to the patients of Indore, adjacent peripheral areas, and nearby states. Therefore the study was conducted to determine the antimicrobial sensitivity pattern of UTI-causing organisms at our place.

Among the total OPD and IPD patients attending the hospital with symptoms of UTI, 31.53% had culture positivity which was comparable to many studies. A study by George et al[6] in 2015 had a positivity rate of 32.1%. A study by Yasmeen et al[7]. in 2014 showed positivity of 21% which was lower than ours. This difference could be due to differences in geographical locations. E.coli was the most common isolated organism, but its percentage(33.18%) is significantly reduced compared to other studies. A study by G.Chooramani et al[8]. from Lucknow, India had 53.4% positivity of E.coli in urine samples, and a study by Niranjan V et al[9]. from Puducherry, India, had 56.8% positivity of E.coli in urine samples. Pseudomonas was higher in our study(13.1%), with the highest percentage in ICU(18%). This is in contrast to other studies where the rate of isolation of Pseudomonas was significantly lower. A study by Sohely Sharmin et al[10]. from Bangladesh had 4.7% Pseudomonas in urine samples. Regha et al[11]. from Kerala, India, found 3.5%; Singh et al[12]. from Uttar Pradesh, 6.75%; and Shah et al[13]. From Karachi found 5.4%.

ESBL-producing (67.8%) and Carbapenemase-producing (60.8%) bacteria in our study were significantly high similar to other studies[14,15]. Nitrofurantoin showed 66.1% sensitivity, so it can be used on an OPD basis if a patient with symptoms of UTI comes with creatinine clearance >60 ml/min[16]. So we recommend avoiding Nitrofurantoin in males with a creatinine of >1.6 mg/dl and females with a creatinine of >1.3 mg/dl. Cotrimoxazole showed a sensitivity of 51.65% and can be used in a standard dose if creatinine clearance is>30 ml/min. Dosage is reduced to half if creatinine clearance is between 15 to 30 ml/min and should not be used below creatinine clearance of <15 ml/min [17]. We suggest avoiding Cotrimoxazole in males with creatinine>5 mg/dl and females with creatinine>4 mg/dl. Amoxycillin+Clavulanic acid showed 41.15%sensitivity and Cefixime showed 20.5% sensitivity. These drugs can be considered in pregnancy as they are relatively safe[18,19]. Fosfomycin is deemed a safe and effective drug for UTI. A significant reduction in the sensitivity of Fosfomycin(48.5%) was found in our study. This is in contrast to other studies where the sensitivity of Fosfomycin was high[20]. Colistin showed the most heightened sensitivity(89.2%); we suggest that colistin can be used in ICU settings, preferably with carbapenems, as it offers good synergism with it. But a significant concern is the associated risk of AKI with colistin[21]. So colistin should be used after appropriate dose adjustment as per creatinine clearance. Colistin resistance is increasingly reported in Indian hospitals. Bacterial resistance to all available antibiotics is also increasing, and we are left with no treatment option. In our study sensitivity of colistin was 89.2%, with the lowest for Pseudomonas (85.2%). Similarly, in a study from Northern, India[22] significant colistin resistance was observed. The sensitivity of Meropenam was also significantly reduced in our study(35.2%), similar to the study from Northern India [22]. As far as ward patients are concerned, Piperacillin+ Tazobactum can be used, showing 44.8% sensitivity until the final culture report comes. All the above drugs can be used in children after appropriate dose calculation as per weight and age. Overtreatment and treatment with resistant antibiotics also contribute to the ineffective management of UTIs[23], Carbapenems, Ceftriaxone, and Fluoroquinolones have shown significant reduction in sensitivity which may be due to overuse and misuse in inadequate doses of these antibiotics at primary care centres.

CONCLUSION

Empirical Antibiotics based on regional antibiotic sensitivity patterns should be started and changed as per Culture reports afterwards. It is need of the hour to conduct various regional studies on the culture and sensitivity patterns of the bacteria considering bacterial resistance and multidrug-resistant strains. A strict Antibiotic Policy at the regional level is needed to control widespread misuse and inappropriate use of higher antibiotics at the Primary Health Care System. Community awareness program should commence for adherence to treatment protocol considering bacterial resistance. Every center should prescribe empirical antibiotics based on regional studies.

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