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Assessment of Drug Resistance Patterns of Organisms Isolated From Urinary Tract Infections At Agartala Government Medical College, Agartala State Tripura, India

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Abstract

Objective: This study was conducted to assess the pattern of uro- pathogens causing urinary tract infections (UTIs) and to determine their pattern of antimicrobial resistance.

Methods: It was an institution based cross-sectional study and conducted on 2630 urine samples. The clinical samples were cultured and bacterial strains were identified by Routine biochemical tests for primary identification of uro-pathogens in the department of microbiology. The antibiotic susceptibility profile of different bacterial isolates was studied according to Clinical and Laboratory Standards Institute (CLSI) guidelines to detect MDR, XDR and PDR bacteria. Statistical package for the social sciences (SPSS) 16 and Microsoft excel were used to analyse data.

Results: 421 samples were culture growth positive out of 2630 samples received from different department accounting 16% of growth positive . Escherichia coli was the predominant organism isolated from urine (37.07%) followed by enterococcus spp 24.94% klebsiella spp 21.61% . More XDR than MDR and 60.95% of the Enterococcus isolates were XDR followed by Esch coli and Klebsiella spp respectively . 26.19% isolates of staphylococcus were found to be MRSA strain and all are Vancomycin and Linezolid sensitive. Pseudomonas spp isolated very few but maximum isolates were XDR and ESBL producers .

Conclusion; Escherichia coli , Enterococcus and Klebsiella were the predominant pathogens causing urinary tract infection and have different resistant pattern. Pseuodomonas , although isolated infrequently, demonstrates high resistance and ESBL producers. These findings underscore the importance of emphasizing infection control measures and judicious antibiotics use to prevent the development of resistance strains in bacterial isolates .

Keywords : Antimicrobial resistance , Pseudomonas aeruginosa, Methicillin Resistant Staphylococcus aureus *(*MRSA), Enterococci especially Vancomycin Resistant Enterococci (VRE), multidrug-resistant (MDR), extensively drug-resistant (XDR), and pandrug-resistant (PDR

Introduction

Urinary tract infection and antimicrobial resistance is one of the major problem, with significant health and socioeconomic burden, particularly in developing countries[1]. Due to recent dramatic change in

antimicrobial activity spectrum, we are trying to evaluate the current spectrum of antimicrobials activity in UTIs in our institution.

The bacterial causes of UTI include Escherichia coli (E. coli) (which causes 80% of theUTI), Klebsiella,pneumoniae(K. pneumoniae), Citrobacter species, Enterobacter species, Pseudomon as aeruginosa (P. aeruginosa), and Staphylococcus species[2-3] . The mechanism of pathogenesis of the urinary tract infection by pathogens include adhesion to the host cell epithelium, invasion, immune evasion via cell wall lipopolysaccharide, capsule, and fimbriae [4]. As the infection is higher in females due to biological factors such as the short urethra, ano-genital proximity, and use of spermicides [5] . Urinary tract infection is mostly associated with increased resistance to antimicrobial agents like multidrug resistance (MDR) with substantial medical and a financial burden[6-7].

Antimicrobial resistance is a major medical problem where microorganisms used varied resistance mechanisms such as horizontal gene transfer (such as plasmids and bacteriophages), genetic recombination, and mutations[8]. In addition, self-medication[9], empirical therapy, misuse, and overuse of antimicrobials which are highly practiced everywhere hasten antimicrobial resistance (AMR) end up in prolonged illness, disability, increased health care costs, and death[1,10,11]. In the era of rising antimicrobial resistance, current longitudinal studies revealing the prevalence and AMR trend of uropathogens are crucial to come up with this problem [12]. In 2011, WHO declared "combat drug resistance: no action today, no cure tomorrow[13].

The clinical isolates such as Pseudomonas aeruginosa, Methicillin Resistant Staphylococcus aureus (MRSA), Enterococci especially Vancomycin Resistant Enterococci (VRE), and members of Family Enterobacteriaceae, for example, Klebsiella pneumoniae, E. coli, and Proteus sp rapidly develop antibiotic resistance and spread in the hospital environment. Actually, the health care planners have declared "Health for All by the year 2000."[14] -[15] In the last two decades, it was observed that there were so much increase of infectious diseases that the standard of public health in many parts of the world is equivalent to preantibiotic era [16]. As per standardized international terminology created by European Centre for Disease Control (ECDC) and Centre for Disease Control & Prevention (CDC), Atlanta, the multidrug-resistant (MDR), extensively drug-resistant (XDR), and pandrug-resistant (PDR) bacteria have been well defined [17]. Multidrug resistant (MDR) was defined as acquired non susceptibility to at least one agent in three or more antimicrobial categories. Extensively drug resistant (XDR) was defined as nonsusceptibility to at least one agent in all but two or fewer antimicrobial categories (i.e., bacterial isolates remain susceptible to only one or two antimicrobial categories). Pandrug resistant (PDR) was defined as nonsusceptibility to all agents in all antimicrobial categories.

The present study was undertaken to assess and up-to-date evidence of prevalence of isolates and their pattern of antimicrobial resistance which will support clinicians to identify the etiology of UTI, ensure appropriate empirical treatment for a reasonable period and an affordable cost. Moreover, it will help to health policymakers in implementing locally efficient therapy and preventive guidelines or adevise effective measures to control the occurrence of multidrug-resistant infections in future.

Material and Methods

This short term institutional based cross-sectional study was conducted in the department of microbiology at Agartala govt medical College and GBP Hospital from 1st January2023 to 30th june of 2023. The bacterial strains were isolated from urine samples of the suspected case of UTI from all the departments and were identified by conventional methods [18]. The clinical specimens received from both

indoor patient departments (IPD) and out door patients were included in the study. After the reception of the samples, we inoculated the samples on Cystine Lactose Electrolyte-Deficient agar and incubated for 24 h. After incubation, the culture plates were inspected for bacterial growth and results were recorded.

Case definition

Significant bacteriuria: Significant bacteriuria is defined as the presence of a significant quantity of bacteria in the urine, typically indicating UTI. The presence of a specific threshold of bacteria is considered significant (generally $> 10^5$ CFU/ml for a single bacterium). However, the threshold was considered lower than 10^5 for certain populations such as elderly age groups, males, symptomatic individuals, urinary catheters, low immune status, and urine collected via bladder aspiration[19].

Antibiotic susceptibility test of bacterial strains was done by Kirby Bauer disc diffusion method [20] as per Clinical Laboratory Standard Institute (CLSI) guidelines [21].

Antibiotics used for Gram positive cocci (GPC) were Amoxi-clavulanic acid, Ciprofloxacin, Doxycycline, Gentamycine, Vancomycin, Cefotaxime and linezolid and for Gram negative bacilli (GNB) were Amikacin, Cefotaxime, Amoxi- clavulanic acid, Ciprofloxacin, Meropenem, Tazobactum-piperacillin , Nitrofurantoin , Levofloxacin and Colistin and polymaxin B for Pseudomonas spp as they are reserved drugs , respectively. Linezolid and Colistin were used as supplemental drugs. For routine Quality Control of antibiotic susceptibility test, S. aureus ATCC 25923, E. coli ATCC 25922, and Pseudomonas aeruginosa ATCC 27853 were used.

MDR, XDR, and PDR strains were detected as per criteria described by ECDC and CDC [21].

Methicillin Resistant Staphylococcus aureus (MRSA) strains were detected by mecA-mediated oxacillin resistance using cefoxitin disk (30 µg) on Mueller Hinton (MH) agar plate inoculated with test strains as per standard disk diffusion recommendations and incubated at 33–35°C for 16–18 hours. Inhibition zone ≤21 mm with cefoxitin disk was interpreted as mecA positive according to CLSI guidelines [22] Cefoxitin is used as a surrogate marker for mecA-mediated oxacillin resistance. S. aureus ATCC 43300 was used as Quality Control for mecA positive strains.

Extended Spectrum β-lactamases (ESBL) producing strains were detected by combined disk method using ceftazidime (30 μg) and ceftazidime plus clavulanic acid (30 μg plus 10 μg) [23]. An increase in diameter of ≥5 mm with ceftazidime plus clavulanic acid as compared to ceftazidime disk alone was considered positive for ESBL detection.

Inclusion and exclusion criteria: We have included the records of patients' data which contains the patients' age, sex , department of collection including indoor and out door patients department , type of sample quality (collected aseptically) and those samples lacking of at least one of the variables mentioned above were excluded..

Ethical approval letter was obtained from ethical review committee (ERC).

Data analysis

We used SPSS and Microsoft Excel to analyze the data and generate figures.

Results and observations: In the present study, we have first arranged the results based on department, indoor , outdoor and gender of the patients whose samples were processed for culture from suspected UTI. All age groups were included in the study. A total of 2630 number of clinical samples were included in the study, out of which 1764 samples were from indoor patients and 866 samples from out

door patients from different specialities . Samples received from indoor (67.07%%) were more than the samples received from the outpatient department (32.93%). In the indoor the maximum samples were from the gyanecology department followed by medicine and surgery. There were predominantly female samples received in both cases .

In present study UTI cases were more in female as compared to male i.e. female 2015 (80.04%) and Male : 615(23.38%) isolates were more in female than in males. Moreover, cumulatively 72% were females.

We observed that 421 samples showed growth out of 2630 samples received for cultures accounting Overall 16% samples of growth positive.

Among 2015 submitted samples of females, 356 (17.67%) were infected in female and 615 out of male , 65 (10.67%) males were suffering from UTI. Thus, explains comparatively greater risk of UTI in females.

Similarly, 1764 IPD samples , out of which 289 (68.65%) were positive and 866 OPD samples , 132 (32.12%) were suffering from UTI, thus showing higher rate of infection in indoor patients.

In present study E coli was the predominant organism isolated from urine accounting 37.07% of total isolates followed by Enterococcus spp 24.94% , klebsiella spp 21.61% , Staph aureus , Citrobacter spp , Pseudomonas spp 1.

Enterococcus was the leading predominant isolate in IPD accounting 30.80% followed by E coli , klebsiella spp , staphylococcus aureus , citrobacter and at last Pseudomonas spp. In present study the isolate of Pseudomonas was very less but showed highly resistance to multiple drugs.

In OPD, E coli (51.52%) was the predominant isolate followed by Klebsiella ssp , Enterococcus, Staph aureus and Citrobacter spp.

E coli was more isolated in gyanes/obs followed by medicine and pediatric department .

Enteroccus sp which was second most important isolates recovered mostly in obs and gyane department followed by klebseilla spp , Staph aureus and citrobacter spp.

Beside obs and Gyanea department , Enterococcus spp was predominant isolate in Pediatric , ICU , casualty , orthopedic , surgery and chest department respectively .

Isolates were more XDR than MDR and among them 60.95% of the Enterococcus isolates were XDR followed by Esch coli and Klebsiella spp respectively . 26.19% isolates of staphylococcus were found to be MRSA strain and all the isolates are Vancomycin and linezolid sensitive. 50.49% of Enterococcus were high level Gentamycin resistance . Among MDR isolates Esch coli were more predominant isolates.

Pseudomonas spp isolated very few but maximum isolates were XDR and ESBL producers .

Antibiogram of Escherichia coli :156

Name of Antibiotics	Sensitive	Resistant
MRP	149 (95.51 %)	7 (4.49 %)
CXM	75 (48. 08 %)	81 (51.92 %)
NIT	133 (85.26 %)	23 (14.74 %)
AMC	81 (51.92 %)	75 (48.78 %)
PIT	127 (81.41 %)	29 (18.59 %)
AK	137 (87.82 %)	19 (12.18 %)
LE	98 (82.82 %)	58 (17 .18 %)

Esch coli showed highly resistance to CXM 51.91% followed by AMC (48.78%) and LE (37.18%).

Antibiogram of klebsiella ssp.: 91

Name of Antibiotics	Sensitive	Resistant
MRP	85 (93.41 %)	6 (6.59 %)
CXM	51 (56.04 %)	40 (43.96 %)
NIT	51 (56.04 %)	40 (43.96 %)
AMC	53 (56.24 %)	38 (41.56 %)
PIT	78 (85 .71 %)	13 (14.29%)
AK	73 (80.22 %)	18 (19.78%)
LE	67 (73.63 %)	24 (26.37 %)

Klebsiella spp were highly resistance to CXM and NIT which is 43.96% both followed by AMC 41.56 % and LE 26.37% respectively .

Antibiogram of Citrobacter spp :16

Name of Antibiotics	Sensitive	Resistant
MRP	15 (93.75%)	1 (6.25%)
CXM	10 ((62.5%)	6 (37.5%)
NIT	12(75%)	4((25%)
AMC	10 (62.5%)	6 (37.5 %)
PIT	12 (75%)	4 (25 %)
AK	14 (87.5%)	2 (12. 5%)
LE	10 (87.5%)	6 (37.5 %)

Citrobacter spp were highly resistance to 37.5% to CXM and AMC and highly sensitive to MRP , AK and LE .

Antibiogram of Pseudomonas spp :8

Name of the Antibiotics	Sensitive	Resistant
MRP	3 (37.5%)	5 (62.5%)
CXM	3 (37.5%)	5 (62.5%)
NIT	0	8 (100%)
AMC	2 (25%)	6 (75%)
PIT	6 (75%)	2 (25%)
AK	2 (25%)	6 (75%)
LE	5 (62.5%)	3 (37%)

Pseudomonas were highly resistance to MRP and CXM (62.5%) both and 100% resistance to NIT . Out of 8 ,5 isolates were ESBL producers. And maximum are XDR .

Antibiogram of Enterococcus spp:105

Name of antibiotics	SENSITIVE	RESISTANT
AMC	51 (48.57%)	54 (54.43%)
CIP	32 (30.48%)	73 (69.52%)

DOX	29 (27.62%)	76 (72.38%)
CXM	21 (20%)	84 (80%)
VAN	105 (100%)	00
NIT	87 (82.86%)	18 (17.14%)
HGEN	52 (49.52%)	53 (50.48%)

Enterococcus spp were highly resistance to CXM (80%) followed by DOX (72.38%) , CIP (69.52%) and AMC (54.43%). All the isolates were sensitive to VAN 100%.

Antibiogram of Staphylococcus aureus : 42

Name of antibiotics	Sensitive	Resistant
AMC	27 (64.29%)	15 (35.71%)
CIP	27 (64.29%)	15 (35.71%)
DOX	29 (69.05%)	13 (30.95%)
CXM	30 (71.43%)	12 (28.57%)
VAN	42 (100%)	00
NIT	39 (92.86%)	3 (7.14%)
HGEN	39 (92.86%)	3 (7.14%)

Staph aureus showed higher resistance to AMC and CIP . all the isolates were 100% to van and LZ.

	MDR	**XDR**	**MRSA/PAN/HGN/ESBL**
E coli 156	**18 (11.54%)**	**28 (17.95%)**	**(17.95%)**
Klebsiella spp 91	**8 (8.79%)**	**13 (17.95)**	**13(17.95)**
Pseudomonas 8	**1 (12.50)**	**4 (50%)**	**4 (50%)**
Citrobacter 16	**3 (18.75%)**	**1 (6.25%)**	**1(6.25%)**
Enterococcus 105	**7 (6.67)**	**64 (60.95%)**	**53(50.48%)**
Staphylococcus 42	**3 (7.19%)**	**7 (16.67%)**	**11 (26.96%)**
	40 (9.50%)	117 (27.29%)	

Frequency distribution of MDR , XDR , PAN DRUGS , MRSA AND ESBL

Discussion

This study is mainly giving the present scenario of prevalence of MDR organisms causing UTI as there is emerging threat of MDR among uropathogenic organisms which is a major public problem, prolongs the treatment ,imposes disabilities and also reduces the life expectancy.

MDR are common in urinary pathogens due to environmental factors, host behavioral factors which dramatically changes the antimicrobial susceptibility of organisms. Therefore in present study, we evaluated the current spectrum of activity among uropathogenic organisms which will strengthen the knowledge of AMR through surveillance. In present study we have seen that the positive growth rate was 16 % which is much lower as compared to various other studies as for examples previously reported in Uttar Pradesh 43.61% (Ruchi Mishra, Jayesh, Singh, & Jasuja, 2016), 40–50%, and 39.6% (Rodríguez-Baño, Navarro et al., 2008). But, it was higher than the infection rate of 13.9% (Mohammed,

Alnour, Shakurfo, & Aburass, 2016). These findings advocated that the prevalence of UTIs varies greatly in different areas with time periods.

Our study reported that the infection rate was predominantly higher in admitted patients than outdoor and similar study was reported by Patel Soni, Bhagyalaxmi & Patel et in their study on 2019 were stated 30.23% from OPD and 51.26% from IPD. On the other hand , 16% IPD and 17% OPD was reported in which was lower than our present study.

In our study , from indoor patient department predominant isolates was enterococcus which was 30.80% of total isolates followed by Esch coli ,Klebsiella spp , Staph aureus , Citrobacter, Acinetobacter and Pseudomonas . (shown in table).

Common non-fermenters isolated were P. aeruginosa and A. baumannii, which were mostly involved in hospital-acquired infection rather than community-acquired. Though isolated very less numbers but P. aeruginosa had a greater prevalence than A. baumannii among the non-fermenters and they all were highly multi drugs resistant . Prevalence of P. aeruginosa exceeding A. baumannii has been documented in several studies.

Present study also shown a higher infection rate of (84.56%) in female than males of (15.44%). The number of females infected with UTI is 5.48 times more as compared with males which was much higher than the studies done by Mohammed et al. who reported 1.5 times higher risk of infection than males ,3.75 times in Muhammad Imran Khan et al which is bit similar but still lower than our study and others reported that females had 1.21 times more infection than males (Ruchi Mishra et al., 2016). Their findings are not similar to our findings. A study stated that there were predominantly females with a ratio of 13:7 (Pérez Heras, Sanchez-Gomez, Beneyto-Martin, Ruano-de-Pablo, & Losada-Pinedo, 2017) which was much higher than our present study . Although the rates of prevalence are different in several other studies.

In present study , out of 421of total isolates where 37.05% was Esch coli followed by 24.94% of Enterococcus spp ,Klebseilla spp 21.61% and 9.98% of Staph aureus respectively. Similar sequence of results of isolates were observer in several studies like by Muzammi et al were Ecoli was 39.6%, Enterococcus 33.9% , Pseudomonas spp 13.2%, MRSA 5.7% and in Sohail et al study 65% was E coli , Enterococcus ssp 15% , Pseudomonas 6% and Staphylococcus aureus 1% which was not similar to the present study .

In our study enterococcus spp was the second most predominant isolate from urine and Klebsiella spp was the third followed by Staph aureus. There were few isolates of citrobacter spp , Pseudomonas spp, Acinetobacter and Candida spp and Serratia spp in our study.

But in study by Muhammad Imran Khan et al showed that Klebsiella spp was second most common isolate followed by Pseudomonas spp and in another study by Orrett, 2001 showed Proteus spp as second most common isolate . Our results are in agreement with the results reported in study (Muzammil , 2020) , where Enterococcus spp was the second most common followed by klebsiella spp , Staph aureus and Citrobacter spp. So these patterns of results in various studies are suggestive of prevalence in different countries , and places and even vary from institutions .

In present study susceptibility pattern of Esch coli shown much better than previous strains published before and compared to other studies. Esch coli showed sensitivity to meropenam , nitrofurantoin , levofloxacin and pipperecilin-tazobactum , Amikacin were 95.51%,85.26%,,82.82% and 81.41%, 87.82 and maximum resistant was observed with ceftriaxone and amoxi-clavulanic acid . A study in 2016 reported that E. coli was completely sensitive to Amikacin, Imipenem, and Meropenem (Mohammed et

al., 2016) which is bit similar to our results and indicates that *E. coli* has not been developed much resistance to these drugs.

Sensitivity rates of Amikacin 61.46%, Ceftazidime 25.89%, Ciprofloxacin 18.97%, Cotrimoxazole 32.02%, Imipenem 91,69%, Meropenem 91.89%, Nitrofurantoin 72.33%, Piperacillin+Tazobactam 51.77% in *E. coli* as per studied by (Patel et al., 2019). *E. coli* showed resistant to oral drugs like Amikacin 8.21%, Cotrimoxazole >67%, Ciprofloxacin >74%, Nitrofurantoin>5–6%, and 6.19% in Tazobactam+Pipperacillin (Sood & Gupta, 2012).

A study reported the sensitiveness of *E. coli* for Amikacin was 65%, Ciprofloxacin 15.61%, Ceftriaxone 20.81%, Cefotaxime 21.1%, Ceftazidime 21.1%, Nitrofurantoin 63%, Imepenem 92.77%, and Piperacillin+Tazobactam 70.80% (Ruchi Mishra et al., 2016).

Another reported the susceptibility of *E. coli* was Augmentin was 80%, Amikacin 60%, Piperacillin+Tazobactam was 90.66%, Ciprofloxacin 54.66% Ceftazidime and Ceftriaxone 33.33%, Cefotaxime 28%, Imipenem 100%, and Nitrofurantoin was 66.66% (Kumar, Singh, Ali, & Chander, 2014). A study in Saudi Arabia reported that 96.7% showed complete resistance to >5 antibiotics and moreover 16 isolates even to 10 tested the antibiotics showing dramatic multidrug resistance (Yasir et al., 2018). The drugs they tested included Amikacin.Amikacin,Ceftazidime, Cefepime,Ciprofloxacin, Cefalotin, Cefoxitin,Ceftriaxone, Gentamycin, Imipenem, Meropenem, Tigecycline.

These studies shows that E. coli *is* evolving very quickly, sensitivity rates are decreasing and resistivity rates are booming very fast and the multidrug resistance may vary with the variation of geographical location and some other factors as several has reported previously.

Enterococci was the second most predominant isolates in present study as it is a notorious pathogen because of its intrinsic resistance/tolerance to different group of antibiotics and is a main causative agent of gram positive UTI. By observing the various parameters of present study it can be concluded that enterococci which was thought to be a commensal organism is now emerging as a potential pathogen, particularly among hospitalised patients. In our study enterococcus was 24.94 % of total isolates . enterococcus still were 100% sensitive to Vancomycine as well as linezolid too. (100%) Resisistance mostly seen with cephalosporin groups of drugs whish is similar with sohail et al study where all 18 (15.0%) cultures were resistant to cefotaxime, ceftriaxone, and cefuroxime and also decreasing sensitivity with fluoroquinolone and aminoglycoside group of drugs . like ceftriaxone 20%, doxycycline 27.62% sensitive . Sohail et al. observed that the Enterococcus species were detected in 18 (33.9%) of all the positive cultures and 18 (100.0%) were sensitive to vancomycin; 15 (83.3%) were sensitive to linezolid;13(72.2%)were sensitive to ampicillin, amoxicillin, co-amoxiclav, teicoplanin, and penicillin G; and five (27.8%)were sensitive to ciprofloxacin which was quite similar to our study .

Among MDR enterococci, three dangerous resistance mechanisms are spreading: VRE (Vancomycin-Resistant *Enterococcus*), GRE (Glycopeptide-Resistant *Enterococcus*), and even LRE (Linezolid-Resistant *Enterococcus*) . The use of glycopeptides and linezolid in empirical therapy may increase enterococcal resistance to these antibiotics and lead to the spread of super-resistant bacteria with no chance of treatment.

In present study have been observed 50.48% enterococcus isolates were Aminoglycoside resistant and was detected by Gentamicin 120 µg disc show considerably high resistance to Gentamicin the result is similar to study of Sanal C. Fernandes et al.

Natural intrinsic tolerance to Aminoglycosides has been shown by enterococci. This property is due to two main factors, poor entry of antibiotic and inactivation of antibiotic by covalent modification of the hydroxyl or amino groups by naturally occurring enterococcal enzymes. In addition to this enterococci can modify the ribosomal target by the action of ribosomal RNA (rRNA) methyltransferase known as EfmM.

In present study have shown highest resistance to Fluoroquinolone like ciprofloxacin 69.52%, and most effective are Aminoglycosides, Nitrofurantoin, Ampicillin, Vancomycin and Linezolid which was almost similar to Sohail et al study .

observed the prevalence of Enterococci to be more than that of S. aureus, results similar to those seen in the current study .

Third important isolate was klebsiella spp showed better results from previous study and mostly were sensitive to drugs like meropenem 93.41%, tazobactum-pipperacillin 85.71% , Amikacin 80.22% , and levofloxacin 73.63% , respectively . A study conducted by Mohammed et al., 2016 shown Amikacin 100%, Imipenem 100% meropenem 92.3%, Ceftazidime 75.4%, Ceftriaxone 71.5%, Augmentin 71.5%, Piperacillin+Tazobactam 76.9%, Nitrofurantoin 46.2% and Ciprofloxacin 69.2%. but our study resistance mostly seen in drugs like ceftriaxone 43.96% , nitrofurantoin 43.96% , amoxi-clavulanic acid 41.56% and levofloxacin in fluoroquinolone group 26.27%. as reported by Patel et al in their study on 2019 Sensitivity rates of Amikacin 44.66%, Ceftazidime 19.76%, Ciprofloxacin 22.13%, Cotrimoxazole 27.27%, Imipenem 75.89%, Meropenem 75.49% in Klebsiella . A study reported the sensitiveness of K. pneumoniae for Amikacin 62.84%, Ciprofloxacin 17.48%, Ceftriaxone 13.11%, Cefotaxime 12.56%, Ceftazidime 13.66%, Nitrofurantoin 61.20%, Imepenem 90.71%, and Piperacillin+Tazobactam 65.51% by Ruchi Mishra et al., 2016. Another reported that K. pneumoniae susceptibility rates were 89.5% for Augmentin, 94.7% for Amikacin, 87.3% for Cefotaxime, 89.3% for Ceftazidime, 85% for Ciprofloxacin, 97.5% for Imipenem, 99.3% for Meropenem, and 91.3% for Piperacillin+Tazaobactum by Lin et al., conducted on 2016 . Further, the antimicrobial activities of Ciprofloxacin and Moxifloxacin against K. pneumoniae were 75% and 67.5%, respectively by Grillon, Schramm, Kleinberg, & Jehl, on 2016 . Thus , these shows sensitivities reported very different from our studies and represent a big change in the spectrum of activities of antibiotics against K. pneumoniae. That is again an alarming situation for treatment .

In present study Pseudomonas aeruginosa isolated very less but were highly drugs resistance . All isolates were completely resistant to Nitrofurantoin , 75% stains were resistant to Amikacin and Amoxi-clavulanic acid , 62,50% isolates were resistant to Meropenem and ceftriaxone , only tazobactum – piperracillin and Levofloxacin were effective drugs for treatment of pseudomonas aeruginosa associated UTI . Colistin and polymaxin B are the reserved drugs for Pseudomonas spp which are still 100% sensitive to pseudodonas isolates in our present study . While Mohammed et al., 2016 and Patel et al. previously reported sensitivities for Amikacin, Imipenem, Meropenem, Ceftazidime, Ceftriaxone, Augmentin, Piperacillin+Tazobactam, Nitrofurantoin, and Ciprofloxacin were 88.9%, 88.9%, 77.8%, 88.9%, 0.00%, 0.00%, 100%, 0.00%, and 100%, respectively which have shown much similarity with our study .

A study reported by Ruchi Mishra et al. on 2016 that the sensitiveness of P. aeruginosa for Amikacin was 46.15%, Ciprofloxacin was 23.07%, Ceftriaxone was 11.54%, Cefotaxime was 11.54%, Ceftazidime was 19.23%, Nitrofurantoin was 3.84%, Imipenem was 80.76%, and Piperacillin+Tazobactam was 73.07%.

In our study also P. aeruginosa expressed strong resistance against Cephalosporin group of drugs and Nitrofurantoin. Our findings are also different from previously reported some studies and agree with some previously published findings. these findings indicate that susceptibility patterns also differ in different setups.

We have isolated very few 3.80% of Citrobacter spp from total isolates which showed much significance about citrobacter in causing UTI. Sensitivity patterns showed much better results than other oraganisms causing UTI . 93.75% of citrobacter sensitive to Meropenem , 875 to Amikacin ,75% to Nitrofurantoin and Tazobactum-piperacillin , 62,5% to levofloxacin , Amoxi-clavulanic acid , ceftriaxone . maximum resistance seen with Beta-lactum groups of drugs and fluoroquinolones. Sami et al on 2017 studied shon that 100% sensitive to imipenem , 66.2% Nitrofurantoin , 82.2% to Amikacin andleast sensitivity was observed in tazobactum-piperacillin 23.1%.

Of the S. aureus isolated, 24% were methicillin-resistant S. aureus (MRSA). Susceptibility to vancomycin, teicoplanin, and linezolid was 100%, while susceptibility to erythromycin, clindamycin, gentamicin, trimethoprim-sulfamethoxazole, fusidic acid, and tetracycline, was 86%, 93%, 97%, 91%, 68%, and 87%, respectively.

In present study 9.98% were staphylococcus aureus isolated in urine which is slightly higher than the usual prevalence rate .2-4% in urine causing UTI. Antimicrobial susceptibility pattern of staphyloccus aureus shown were, 100% sensitive to Vancomycin , and Linezolid . Sensitivity to others drugs were much better than the previous study as 92.86% sensitive to Nitrofurantoin and high level gentamycin ,64.29% were sensitive to Amoxi-Clavulanic acid and Ciprofloxacin , 71.43% to Ceftriaxone , 69.05% to Doxycycline . Mohammad K Alshomrani et al on 2023 studied showed that susceptibility to Vancomycin, Teicoplanin, and linezolid was 100%, while susceptibility to erythromycin, clindamycin, gentamicin, trimethoprim-sulfamethoxazole, fusidic acid, and tetracycline, was 86%, 93%, 97%, 91%, 68%, and 87%, and Of the S. aureus isolated, 24% were methicillin-resistant S. aureus (MRSA) respectively and in our study we have 26.96% were MRSA which was quite similar with our study .

High prevalence of XDR followed by MDR shown in our study and among them 60.95% of enterococcus were XDR which was quite unusual from others study followed by Pseudomonas spp which were isolated very few but 50% were XDR and 12.50% MDR . Isolates of ESch coli and klebsiella were 17.95% XDR both /11.54% MDR/ 8.79% MDR and staphylococcus aureus 16.67% XDR and 7.19% MDR .

In a study by Chowdhury et al on 2022 shown that MDR organism was identified in 23 patients (55%). *Escherichia coli* was the most common organism, found in 23 (59%) of the cultures, with the next being *Klebsiella* spp. 12 (30.8%), *Enterococcus* spp. 2 (5.1%), *Pseudomonas aeruginosa* 1 (2.6%), and *Staphylococcus aureus* 1 (2.6%).28% exhibited of MDR pattern, 18% XDR and 1.9% PDR among E coli by Wajid M et al .

The MDR Gram-negative isolates accounted for 105 (83.3%), and Gram-positive isolates 21 (16.7%). The predominant MDR bacterium was *E. coli* 60 (47.6%), followed *by* K. pneumoniae 24 (19.1%), S. aureus 13 (10.3%), P. mirabilis and S. saprophyticus 8 (6.4%), Pseudomonas spp. 6 (4.8%), P. vulgaris 4 (3.2%) and K. rhinos 3 (2.4%). Extensive (XDR) and pan-drug resistant (PDR) isolates were 63 (24.8%) and 6 (4.8%), respectively and Escherichia coli was the most common MDR and XDR bacteria, while Pseudomonas was the only PDR isolate by Getachew Bitew et al . In study by Silpi et al, among 202 *E. coli* isolates, 28% are MDR strains, 8% are XDR, and 1.9% are PDR. This is similar to the study conducted by Silpi et al.

Conclusion

In conclusion , our study highlights that the Escherichia coli , Enteroccocus and Klebsiella are the predominant pathogens exhibiting distinct resisitance patterns. Notably , Pseuodomonas , although isolated infrequently, demonstrates high resistance and ESBL production. These findings underscore the importance of emphasizing infection control measures and judicious antibiotics use to prevent the development of resistant strains in bacterial isolates . Now , time has come to use alternative therapeutic strategies in combination with drugs . For example combining two therapies, i.e. Near-infrared red radiations could sensitize the microbes first (Ha & Kang, 2015) and then antibiotics could easily kill the microbes. Moreover, recently it has been reported that metal organic frameworks (nanomaterial used in several disciplines) have also increased the activity of vancomycin against Staphylococcus aureus. (Iqra Ghaffar et al., 2019)and use of Cefazolin loaded chitosan nanoparticles to cure multi drug resistant Gram-negative pathogens Exposure of MDR pathgens to the chitosan nanoparticles led to the disruption of cell membranes and the leakage of cytoplasm.

This indicates that use of nanomaterials could have promising applications in therapeutics as well in future to combit MDR pathogens .

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