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Antimicrobial susceptibility pattern of uropathogens in urinary tract infections (UTI) patients of Punjab, Pakistan

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Abstract---The prevalence, antimicrobial susceptibility pattern, and associated factors of urinary tract infections among Punjabi patients attending Tertiary Care Hospitals of Punjab were the objectives of this study. Participants were selected by systematic random sampling in a cross-sectional study at Tertiary Care Hospitals of Punjab. 988 participants provided clean catch midstream urine samples, which were then cultured and tested for antimicrobial susceptibility. We inoculated n=988 urine samples in which 255 samples were found positive for bacterial growth. Among them 126 were *E. coli*, 66 *Klebsiella pneumoniae*, 4 *Enterobacter cloacae*, and 21 were *Pseudomonas spp*. The frequency of Uropathogens was observed for Gram negative E. coli 49.02% and Gram positive bacteria were 7.78%. The prevalence of urinary tract infections was 16.4%. *Pseudomonas aeruginosa* (19, 7.3%), *Pseudomonas spp.* (2, 0.7%), *Enterobacter cloacae* (4, 1.5%), and Gram positive bacteria such as Methicillin resistant *staphylococcus aureus* (3, 1.1%), Methicillin sensitive *staphylococcus aureus* (15, 5.8%),

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and *Enterococcus faecalis* (20, 7.7%) were the most common bacteria. Ampicillin and tetracycline were both resistant to Gram-negative bacilli (96%) and Gram-positive cocci (72%), respectively. In the study area, a culture and susceptibility test is essential for effective urinary tract infection management.

***Keywords*---**antibiogram panel, resistant pattern, CLSI panel, Enterobacteriaceae, hospital, urine tract infection.

Introduction

Urinary tract infections (UTI) can be defined as presence of bacteria in urine. It is among the most frequent infectious diseases encountered in clinical practice, especially in poor nations, with a high incidence of financial costs and morbidity (Zahra et al., 2021). Insufficient hygiene habits and urinary system disorders have been identified as some of the major variables that predispose to urinary tract infection Urinary tract disease causes vary by location, as do their vulnerability and antibiotic susceptibility. Different microbial pathogens are responsible for UTIs (Ahmed et al., 2020).

The presence of microbial pathogens in the urinary system is referred to as a urinary tract infection (UTI), and this is typically categorized according to the site of infection bladder, kidney (pyelonephritis) and can be symptomless or simply a symptom percussion is classified as "uncomplicated," whereas "intricate" diseases are identified in urogenital territories with functional or structural malformations. The word cystitis has been used to designate the lower UTI infection, which is characterized by symptoms such as dysuria, frequency, urgency, and suprapubic pain. UTI can affect both the lower and upper urinary tracts (Yusof et al., 2022; Zeshan et al., 2021).

The bacteria that cause complex UTI are significantly more diverse than those that cause simple urinary tract infection (Ahmed et al., 2022a). Gram negative bacteria, such as *E. coli*, *Klebsiella pneumoniae*, and *Pseudomonas* are the most often seen microorganisms, whereas Gram positive bacteria, such as Enterococcus faecalis and Staphylococcus aureus, are detected relatively seldom (Ahmed et al., 2022b). In developing countries, urinary tract infection (UTI) is one of the most frequent bacterial illnesses encountered by doctors. Area-specific monitoring studies aiming at learning more about the bacteria that cause urinary tract infections and their response to therapy may aid clinicians in selecting the most appropriate approach which data base presumption (Mustafai et al., 2023).

Neighborhood surveillance research suggests the bacteria that cause UTIs as well as resistance trends, giving doctors with a wealth of information for selecting the best empirical therapy. Because the female urethra is physically less efficient at blocking bacterial entrance, UTI is more prevalent in females than in males. It might be because the urethra and genital canal are so close together (Rabaan et al., 2022b; Rasool et al., 2022).

The frequency of bacteria that are resistant to at least three different treatments is one of the characteristics of the increase in the incidence of UTIs that is one of the most alarming aspects (Zeb et al., 2022). The Infectious Disease Society of America (IDSA) has determined that certain bacterial strains present excellent opportunities for the development of new drugs. We referred to the microorganisms and viruses that caused illness in people and other animals as "ESKAPE pathogens," and these included Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumonia, Acinetobacter baumannii, Pseudomonas aeruginosa, and several species of Enterobacter. Because of the rise in antibiotic resistance, urinary tract infections (also known as UTIs) are becoming ever more challenging to cure (Sohail et al., 2023; Tariq et al., 2020).

In order to obtain correct data on sensitivity, it is necessary to take into consideration a number of different criteria, such as the patient's UTI categorization (complicated versus uncomplicated), gender, age, and treatment history with drugs (Ramzan et al., 2022; Rizvi et al., 2022). There is a wide range of variability in the antibiotic susceptibility profiles of the bacteria that are responsible for urinary tract infections across time and space. Empirical selection of biocides for the treatment of urinary tract infections (UTIs) is possible with the assistance of sensitivity statistics made available by regional microbiological facilities (Ahmad and Abdullah, 2020).

Urine tract infection (UTIs) are an overall medical problem that influences a greater number of females than males. Imipenem and meropenem are more compelling against uropathogens. Piperacillin-tazobactam, amikacin, cotrimoxazole and netilmicin were the following most famous substitutes for treating Urine Tract Infection brought about by (Gram negative bacteria) followed by (piperacillin-tazobactam, nitrofurantoin, cotrimoxazole and netilmicin). Making wary determination of right antimicrobial medications helps in decreasing the rise and extended of fostering the Resistance (Parveen et al., 2020; Rabaan et al., 2022a).

Aims and Objectives

1. To isolate Uropathogens from UTI patients and to characterize them morphologically and biochemically.
2. To check the antibiotic susceptibility of individual Uropathogens.
3. To check the prevalence of Multiple Drug Resistant (MDR) and extensively drug resistant (XDR) isolates.

Material and Methods

Study Area

The current study was design in Lahore Garrison University and conducted in the Department of Microbiology Laboratory, Pakistan Kidney and Liver Institute & Research Centre, Lahore (PKLI&RC) Samples were collected from February 2021 to September 2021.

Sample collection

Total 988 samples were collected in Pakistan kidney and Liver institute from both indoor and outdoor patients in sterilize urine container (20ml) and transported to the microbiology Laboratory via Sample transport box.

Storage of Samples

All the samples were stored in urine container (20ml) at 2-80C in Biobase refrigerator for three days as per policy of CLSI (urinalysis Approved guidelines third edition) Weinstein and Lewis, (2020).

Sample Inoculation

CLED agar (Cystine–Lactose–Electrolyte-Deficient) is recommended for Urine specimen. Urine was collected from the patients and used to inoculate cysteine-lactose-electrolyte-deficient (CLED) agar plates. CLED stands for cysteine-lactose-electrolyte-deficient. Following the application of the inoculum, the plates were kept in an incubator at 37 degrees Celsius for a period ranging from 18 to 24 hours (Ahmed et al., 2019).

Growth isolation
Colony Morphology

Urine culture is a kind of quantitative bacterial culture in which number of colonies forming units (CFU) are very much important, in this regard 1 microliter lumen loop is used to inoculate urine sample and in 1 microliter urine sample there must be more than 50 bacterial units present. If colony number is less than 50 its means it is not UTI but simple bacteria. Remaining decision is as the clinician demand (Grimes et al., 2020). Different types of colonies were observed on the inoculated plate. Different types of colonies include dry colonies mucoid colonies, different in shapes and color were observed (Ahmed et al., 2022c).

Lactose fermentation

Lactose fermenter on CLED agar change the color of agar due to presence of "Andrade Indicator" in CLED agar when lactose fermenter organism produces lactic acid so this lactic acid reacts with CLED indicator and changed the pH of CLED into Pinkish or Orange color. Most prevalent lactose fermenter having small round pink color colonies as shown in figure 3.1 and with mucoid large pink color colonies as shown in (figure 3.2) (Ahmed et al., 2022d).

Results

Isolation of bacteria on CLED agar

After sample inoculation, culture plates were observed after 24hrs to check the bacterial growth. Culture plates with no bacterial growth were excluded and positive cultures i.e., culture plates with and above 50 colonies (10^5) were processed for further identification. Total 998 samples were collected. Out of 998 samples, only 255 sample were positive for bacterial growth. Among these 255 positive samples, 217 were affected with Gram negative bacteria and 38 were affected with Gram positive bacteria.

Different types of colonies on media

After inoculation if bacteria different types of bacterial colonies were seen on CLED agar. They were different in color, shape and density.

Lactose fermenter bacteria

Different types of colonies were observed on CLED Ager which showed the characteristics of lactose fermentation

Gram negative lactose fermenter

Lactose fermenter on CLED agar changed the color of agar due to presence of “Andrade Indicator” in CLED agar when lactose fermenter organism produces lactic acid so this lactic acid reacts with CLED indicator and changed the PH of CLED into pinkish or orange color. Most prevalent lactose fermenter is *E. coli* having small round pink color colonies and *Klebsiella* with mucoid large pink color colonies (figure 1 & 2).

Gram positive lactose fermenter

Gram positive were found lactose fermenter but their colony morphology was found different from Gram negative in appearance they were non-mucoid and in size their colonies were significantly small as shown in (figure 1 & 2).

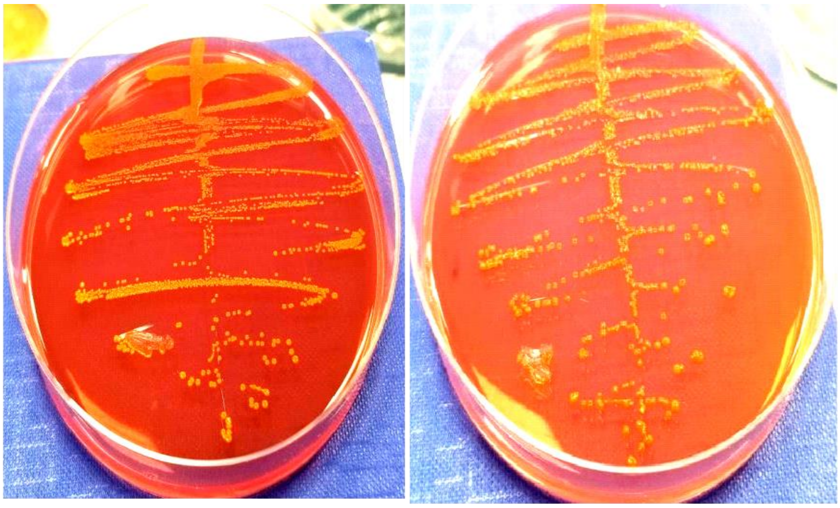


Figure 1 shows the densdry pink colonies. Figure 2 shows the lightsmall colonies

Gram-negative

Non lactose fermenters

Non-lactose fermentation, they did not produce lactic acid react. The colonies of *Pseudomonas* become darkish or greenish in color. Combination of CLED agar with colonies of *Pseudomonas* on agar. The colonies of *Pseudomonas* showed in dark color. Their colony morphology size and density are different from lactose fermenter as shown in (figure 3.3)

Gram staining

Gram staining was performed to differentiate between Gram positive and gram-negative bacteria. Gram positive stained purple and Gram negative appear pink, when observed under microscope as shown in figure 3.6 & 3.7

Biochemical characterization of bacterial isolates
Biochemical tests for Gram positive bacterial isolates
Catalase Test

The gram-positive were first tried for catalase test to separate (Staphylococcus from Streptococcus). The S. aureus showed the positive results for catalase test while Streptococcus showed negative results for catalase test.

Coagulase

All the catalase positive *Staphylococcus* were further tested through coagulase. The further identification test specifically for *S. aureus* were coagulase. The reaction was found positive as shown in figure 3.9.

Biochemical tests for Gram negative bacterial isolates
Indole test

All *E. coli* bacterial isolates were found positive for Indole test. While *Klebsiella pneumoniae* isolates were found to negative for Indole test.

Triple sugar iron test

All *E. coli* isolates gave acidic butt and acidic slant on TSI. All *Klebsiella* isolates also gave acidic butt (yellow color) and acid slant on TSI.

Oxidase test

For non-lactose fermenter, oxidase test was performed. *Pseudomonas* spp showed positive reaction for oxidase test.

API results

For further specie level identification of the bacterial colonies. APIs were used. Score for positive test results were added and the resulting seven-digit code was entered in an online API software to get the results as shown in figure 3.

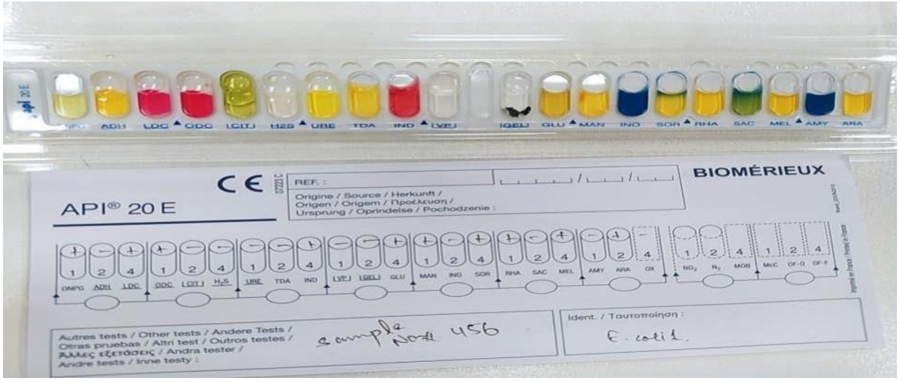


Figure 3: API 20E results for *E. coli*

Antibiotic susceptibility testing

All isolated bacteria were evaluated for antimicrobial susceptibility profile, for antibiotics depicted by CLSI rule 2017. After the procedure and analysis of plates and incubation at (37°C for 48 hours), bacteria were set apart as (Resistant or Sensitive) according to the zone of inhibition in (mm) portrayed in CLSI rules.

Enterobacteriaceae

Antibiotic susceptibility pattern for all gram-negative isolates including *E. coli*, *Klebsiella spp* and *Pseudomonas spp* were noted after identification of each isolate. Pictures of growth and antibiotic susceptibility pattern of *Enterobacteriaceae.*

Staphylococcus aureus

Antibiotic susceptibility pattern for all gram-positive isolates were noted after identification of each isolate. Pictures of growth and antibiotic susceptibility pattern of *Staphylococcus aureus* .

Frequency distribution of uropathogens

Out of 998 samples, only 255 sample were positive for bacterial growth. Among these 255 positive samples, 217 were affected with Gram negative bacteria and 38 were affected with Gram positive bacteria.

Gram negative bacterial frequency

In Gram negative 126 colonies show the characteristics of *E. coli*, 66 colonies show the characteristics of *Klebsiella pneumoniae,* 4 colonies show the characteristics of *Enterobacter cloacae,*21 shows the characteristics of *Pseudomonas spp.* The comparative frequency of each organism causing urinary diseases are given in the table 4.1 and graph 4.1. It was observed that *E. coli* comprised of 49.02% of all the uropathogens isolated from urine samples. Among Gram positive bacteria, *Enterococcus faecalis* was on the top of the list 7.78% responsible for causing urinary diseases as shown in table 4.2. The overall Mean was observed as 43.4 while, standard deviation was observed as 47.318. the probability was observed as more significant (p=0.01).

Table 1: Frequency distribution, of Gram negative uropathogens in Urinary tract infection.

Isolates	Frequency(n =217)	%	Mean ± SD	P=value
Gram-negative bacteria isolates			43.4(47.318)	0.01**
Escherichia coli	126	49.02%		
Klebsiella pneumoniae	66	25.68%		
Enterobacter cloacae	04	1.55%		
Pseudomonas aeruginosa	19	7.39%		
Pseudomonas spp.	02	0.77%		

*Mean (SD), P= Probability, %= percentage, more Significant (**)

Gram positive bacterial frequency

Among Gram positive bacteria, *Enterococcus faecalis* was on the top of the list of organisms responsible for causing urinary diseases as shown in table 4.2. The overall Mean was observed as 12.6 while, standard deviation (7.133) was observed as. The probability was observed as less significant (p=0.02).

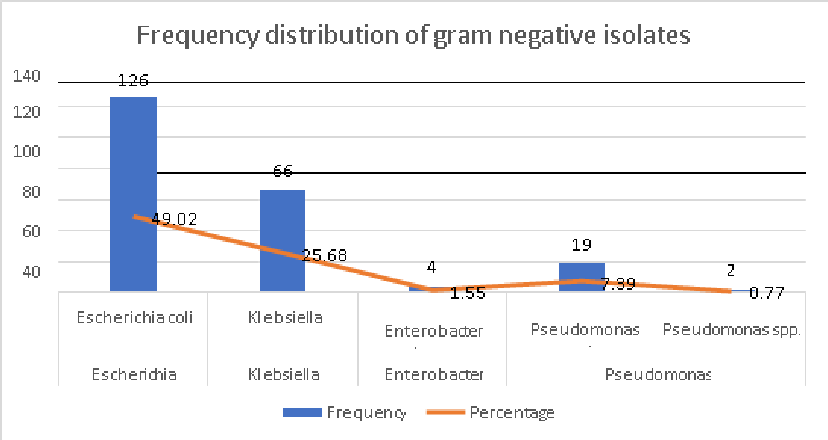
Table 2: Frequency distribution, of Gram positive uropathogens in Urinary tract infection

Gram-positive Bacterial isolates (n=38)				
Isolates	Frequency(n=38)	%	Mean ± SD	P=value
Enterococcus faecalis	20	7.78%	12.6 (7.133)	0.02*
Methicillin resistant *staphylococcus aureus (MRSA)*	03	1.16%		
Methicillin sensitive *staphylococcus aureus (MSSA)*	15	5.83%		
Total	38			

*Mean (SD), P= Probability, %= percentage, Less Significant (*)

Gram negative Bacterial Percentage

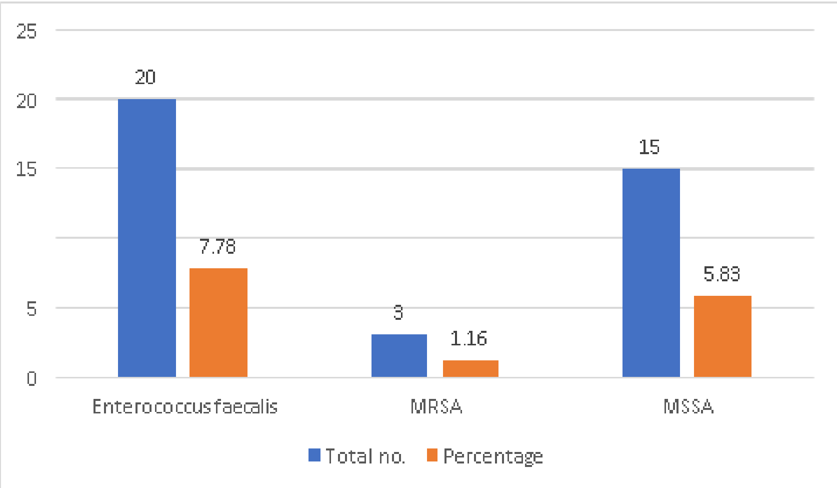
Out of 998 samples, only 255 sample were positive for bacterial growth. Among these 255 positive samples, 217 were affected with Gram negative bacteria and in which 49.0% colonies show the characteristics of *E. coli*, 25.68% colonies show the characteristics of *Klebsiella pneumoniae,* 1.55% colonies show the characteristics of *Enterobacter cloacae,*8.16% shows the characteristics of *Pseudomonas spp.*



Graph 1: frequency distribution of gram-negative isolates

Gram positive Bacterial Percentage

Out of 255 there were 38 affected with Gram positive bacteria. In which 20 colonies show the characteristics of *Enterococcus faecalis* 7.78%, *Methicillin resistant staphylococcus aureus (MRSA)* 1.16% and 5.83% colonies show the characteristics of *Methicillin sensitive staphylococcus aureus (MSSA)*.



Graph 2: frequency distribution of gram-positive isolates

Antibiotic susceptibility pattern of gram-negative isolates

When susceptibility pattern of antibiotics was studied against Gram negative bacteria, it was observed that among all antibiotics, sensitivity to Carbapenems (Imipenem and Meropenem) was higher sensitive than Cephalosporins (Cefuroxime, Cefepime, Cefixime, Ceftriaxone and Ceftazidime) and Aminoglycosides (Tobramycin, Amikacin and Gentamycin). However, lowest susceptibility percentage was recorded against quinolones (Ciprofloxacin and Levofloxacin)

Table 3: Antibiotic susceptibility pattern of gram-negative bacteria

Antibiotics	No of Sensitive isolates	No of Resistant isolates	%
Imipenem	198	19	91.24
Meropenem	198	19	91.24
Cefepime	186	31	85.71
Ceftazidime	185	32	85.25
Cefuroxime	43	174	19.81
Cefixime	43	174	19.81
Ceftriaxone	45	172	20.73
Tetracycline	48	169	22.11
Aztreonam	41	176	18.89
Amikacin	188	29	86.63
Gentamicin	184	33	84.79
Tobramycin	193	24	88.94
Ciprofloxacin	28	189	12.90
Levofloxacin	30	187	13.82

Antibiotic susceptibility pattern of gram-positive isolates

The comparative susceptibility pattern of different gram-positive isolates against different antibiotics is given in the table below. Antibiotics like Amikacin, Fuscidic acid, Teicoplanin, Linezolid and Vancomycin showed 100% effectivity against *MSSA* and *MRSA*. It is important to note that Vancomycin and Linezolid showed 100% efficacy against *Enterococcus faecalis* as well.

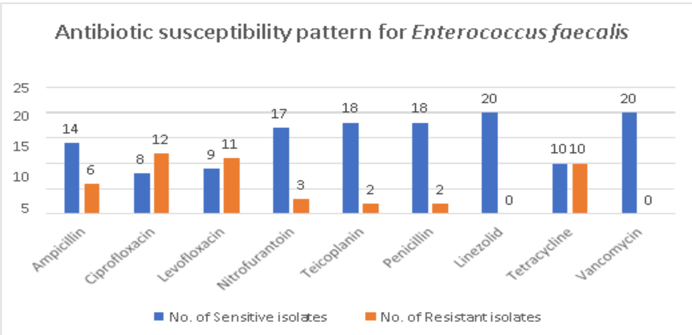
Table 4: Antibiotic susceptibility pattern of gram-positive isolates in Urinary tract infection

Antibiotics	*Enterococcus faecalis*		*MSSA*		*MRSA*	
	No. of sensitive isolates	%	*No. of sensitive isolates*	%	*No. of sensitive isolates*	%
Ampicillin	14	70	N/A		N/A	
Amikacin	N/A		15	100	03	100
Gentamycin	N/A		13	86.67	01	33.34
Tobramycin	N/A		12	80.00	00	00
Ciprofloxacin	8	40	09	60.00	00	00

Levofloxacin	9	45	09	60.00	00	00
Nitrofurantoin	17	85	11	73.34	01	33.34
Teicoplanin	18	90	15	100	03	100
Erythromycin	N/A		09	60.00	02	66.67
Penicillin	18	90	12	80.00	02	66.67
Azithromycin	N/A		13	86.67	03	100
Fusidic Acid	N/A		15	100	03	100
Linezolid	20	100	15	100	03	100
Clindamycin	N/A		11	73.34	02	66.67
Tetracycline	10	50	11	73.34	02	66.67
Vancomycin	20	100	15	100	03	100
Total no. of isolates	20		15		03	

Antibiotic susceptibility pattern of gram-positive isolates

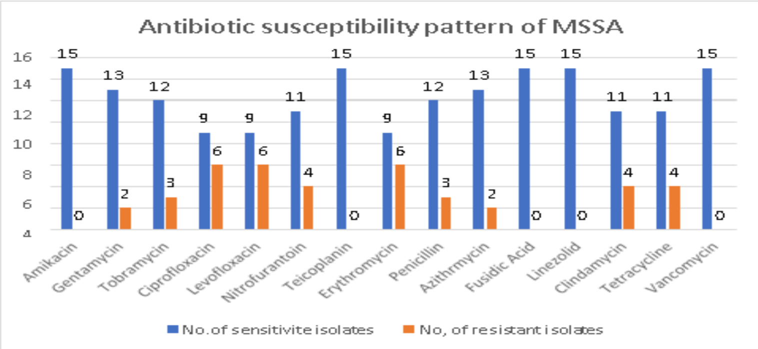
In case of gram-positive isolates, it was observed that all gram-positive isolates showed highest sensitivity towards Linezolid, Vancomycin and Teicoplanin. However, lowest sensitivity was recorded for quinolones (Ciprofloxacin and levofloxacin). The graph below shows comparative susceptibility pattern of *Enterococcus faecalis* against different drugs.



Graph 3: Antibiotic susceptibility pattern for *Enterococcus faecalis*

Antibiotic susceptibility pattern of MSSA

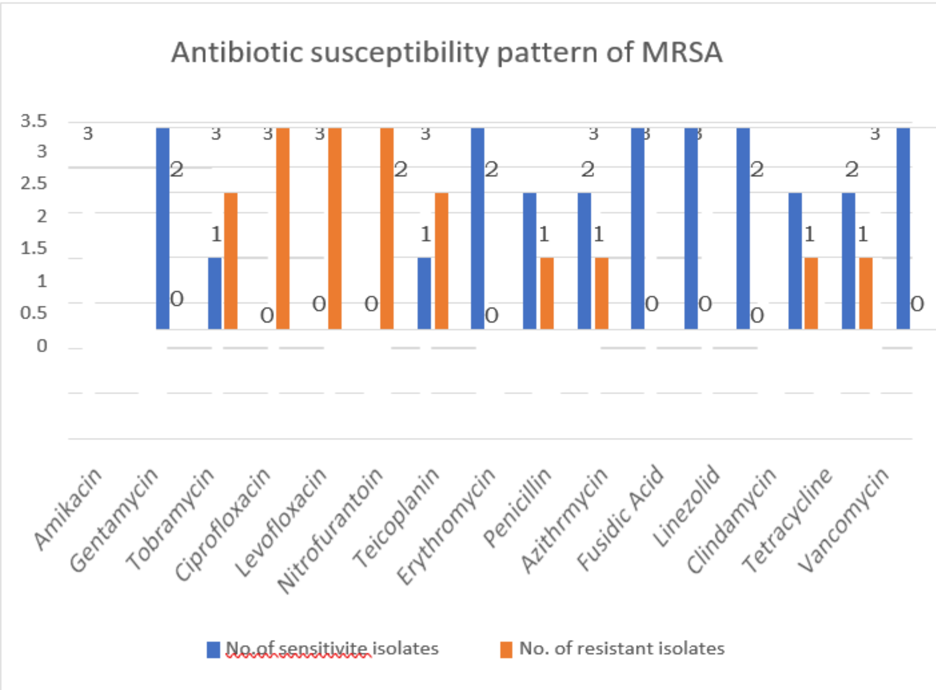
The observed the antibiotic susceptibility pattern of MSSA like 15 isolates were sensitive against Amikacin, 13 gentamycin, 12 Tobramycin, 9 Ciprofloxacin, 9 Levofloxacin, 11 Nitrofurantoin, 15 Teicoplanin, 9 Erythromycin, 12 Penicillin, 13 Azithromycin, 15 Fuscidic acid, 15 Linezolid, 11 Clindamycin, 11 Tetracycline and 15 Vancomycin showed 100% effectivity against *MSSA*. While, the study observed the antibiotic susceptibility pattern of MSSA like 0 isolates were resistive against Amikacin, 2 gentamycin, 3 Tobramycin, 6 Ciprofloxacin, 6 Levofloxacin, 4 Nitrofurantoin, 0 Teicoplanin, 2 Erythromycin, 3 Penicillin, 2 Azithromycin, 0 Fuscidic acid, 0 Linezolid, 4 Clindamycin, 4 Tetracycline and 0 Vancomycin showed 100% effectivity against *MSSA*



Graph 4: Antibiotic susceptibility pattern of MSSA

Antibiotic susceptibility pattern of MRSA

The observed the antibiotic susceptibility pattern of MRSA like 3 isolates were sensitive against Amikacin, 1 gentamycin, 0 Tobramycin, 0 Ciprofloxacin, 0 Levofloxacin, 1 Nitrofurantoin, 3 Teicoplanin, 2 Erythromycin, 2 Penicillin, 3 Azithromycin, 3 Fuscidic acid, 2 Linezolid, 2 Clindamycin, 2 Tetracycline and 3 Vancomycin showed 100% effectivity against *MRSA*. While, the study observed the antibiotic susceptibility pattern of MRSA like 0 isolates were resistive against Amikacin, 0 gentamycin, 2 Tobramycin, 3 Ciprofloxacin, 3 Levofloxacin, 3 Nitrofurantoin, 3 Teicoplanin, 2 Erythromycin, 1 Penicillin, 0 Azithromycin, 0 Fuscidic acid, 0 Linezolid, 1 Clindamycin, 1 Tetracycline and 0 Vancomycin showed 100% effectivity against MRSA



Graph 5: Antibiotic susceptibility pattern of MRSA

Discussion

Due to the high prevalence, the wide spectrum of isolated uropathogens and the diversity of antibiotic resistance profiles, the need to develop local research is evidenced to guide actions in health and epidemiological surveillance is a real focus of this present study. In Hospital setups when a septic patient has very little time to wait for therapy so on the basis of research clinicians can go with presumptive antibiotics by suspecting MDR and XDR they can with empirical therapy and this practice is adopted worldwide (Hussain et al., 2022; Naveed et al., 2022a; Naveed et al., 2022b). The research area had a high prevalence of urinary tract infection, and all uropathogens identified had developed resistance to the most common antimicrobial agents and there was a statistically significant association between uropathogens and certain UTI risk variables (Ahmed et al., 2019).

Gentamicin, chloramphenicol, and nitrofurantoin were the most efficient drugs against the majority of the isolates cephalexin, Amoxicillin and vancomycin (Ahmed et al., 2022e). On the other hand, were the antibiotics to which the majority of the strains acquired resistant while in this study carbapenem is most affective drug for Gram negative and vancomycin is most affective in Gram positive (Ahmed et al., 2022c). Many investigations have found a high frequency of uropathogens and elevated rate of multi- drug resistance (Abdallah and Abdulla, 2009; Andrade et al., 2003; Colgan et al., 2006).

As a result, ongoing observation of uropathogens prevalence and resistance rates is required in order to provide suitable empirical therapy recommendations, establish reasonable prescription programs, and make policy choices. As in our research there are many MDRs isolated as well that can help clinicians to make decision to go empirical therapy (Maheen et al., 2014). As described pathogens of urinary tract were shown to be strongly linked to type 2 diabetes and a history of urinary tract infections (Najeeb et al., 2015).

Most antibiotics examined demonstrated resistance in both Gram positive and gram-negative bacteria. 81.1% of bacterial isolates had antibiotic resistance to two or more medications. Same in this study most of the Gram negative bacteria were ESBL (Extended-spectrum –beta lactamase) positive and also resistant to fluoroquinolone (Mehboob et al., 2021). Antibiotic resistance to amoxicillin (83.8%) and clindamycin (100%) was greatest in Gram negative and positive bacteria, respectively (Esposito et al., 2021). In addition, *E. coli* and *Klebsiella* produced 69.2% and 30.8 % of extended spectrum beta lactamase (ESBL) respectively. And in this study quinolones are least sensitive in both Gram negative and Gram positive (Parveen et al., 2020).

Because of the high prevalence of ESBL development and drug resistance, the effectiveness of third-generation cephalosporins has been decreased. These data advise the clinician on which antibiotics to prescribe for the patient, as well as urine culture reports and monitoring the patient's clinical response, so that community-wide antimicrobial resistance does not emerge. In current study most of gram negatives were ESBL positive that indicates how increased resistant of Cephams is present in this community (Chouchani et al., 2013). An ongoing epidemiological investigation of UTI in health facilities across the country is warranted, based on the observation of various bacterial species causing UTI in earlier research. The high prevalence of drug resistance to frequently given medications requires a search for alternative treatments. This study also showed misuse of antibiotics can lead to serious consequences of antibiotic resistant increase in hospital set-up (Basu and Mukherjee, 2018). Approximately one amongst three individuals having a urinary tract infection were positive for culture for a variety of bacterial uropathogens. Bacterial infections were more likely to occur in inpatients and hypertensive individuals. Different percentages of susceptibility to the tested drugs were found in bacterial isolates. Given pattern is also applied in this study as from 998 samples we got 253 positives which are about ¼ of total samples and all have different sensitivity pattern (Boroumand et al., 2012).

In a recent research of urine isolates, it was determined that antimicrobial resistance among uropathogens has grown, and there is significant heterogeneity in antibiotic susceptibility patterns of uropathogens. Meropenem is an antibiotic that can be used to treat UTIs caused by Gram-positive bacteria. These findings suggest that future research should concentrate on the origins of antibiotic resistance in order to discover solutions to the problem, as well as the adoption of primary care to prevent drug misuse in societies while in this study resistance of Meropenem is about 9 to 10 percent (Agarwal et al., 2015).

To avoid therapeutic failures and antibiotic abuse, UTI treatment should be based on current local antimicrobial susceptibility patterns of uropathogens. The 45.69 percent positive culture rate or isolation rate reported in the previous study was similar to that observed in similar studies done throughout Bharat. This is one of major issue in case of UTI because positivity rate in this study is less than 30 percent which is not so good as per clinical signs symptoms, this leads to wrong diagnosis and misuse of antibiotics with antibiotics resistant as end result (Vieira et al., 2020).

According to data from a prior study, the range of organisms that cause UTI is comparable to what has been found in other studies across India. However, the rates of diverse species being isolated differed from one research to the next. The findings of this study differed from those of prior investigations. Because number of isolates and area wise positivity can be different due to many reasons (Garau and Gomez, 2003).

On the basis of clinical signs, symptoms, and urine microscopy, UTI might be over diagnosed and overtreated. Effective counselling and delaying antibiotic start or empirical therapy with a short course of nitrofurantoin is strongly advised in the era of growing antimicrobial resistance. Empirical treatment recommendations should be revised on a regular basis to reflect changes in uropathogens antimicrobial resistance. this is how this study is so important to identify the flaws of medical set-up and force or implement to make sure correct diagnosis of UTI (Ranjan et al., 2010).

The much more frequent uropathogens is still *E. coli.* For the treatment of UTIs, nalidixic acid, ampicillin, co-trimoxazole, and first-generation fluoroquinolones are ineffective. Amikacin and imipenem sensitivity is still present, and these antibiotics may be given for complex UTIs. Monitoring medication resistance patterns on a regular basis will aid in identifying regional resistance trends. This will aid doctors in the empirical management of UTIs. And in this study we also have *E.coli* is most prevalent pathogen among all UTI patients (Shakil et al., 2008).

As in this study most of *E. coli* were ESBL positive and showed how much increase in resistance is present in society against *E. coli* (Struelens et al., 2010). The majority of uropathogens seen in patients presenting to the emergency department with urinary complaints are susceptible to Fosfomycin, Nitrofurantoin, Gentamycin, and Imipenem, which might be used as empirical treatment in ICU settings. Including *E. coli* some other gram negatives also showed resistance to fosfomycin and nitrofurantoin. And these are two primary drugs used to treat UTI (Tam et al., 2010).

It was also discovered that 90% of the participants were between the ages of 16 and 30, while 78 percent were between the ages of 46 and 60. The presence of ESBL was detected in 33.5 percent (63/188) of *E.coli* and 15.25 percent (9/59) of K. pneumonia, with a significant relationship (p =0.007) (Abbasi et al., 2018). The most effective treatment choices were determined to be amikacin, fosfomycin, imipenem, and tazobactam/piperacillin. The resistance to ciprofloxacin, enoxacin, and amoxicillin/clavulanic acid was revealed to be significantly associated with ESBL-producinguropathogens (P >0.05). It was determined that, rather than empiric therapy, adequate ESBL and culture sensitivity tests should be used for successful UTI therapy. But empirical therapy got much importance in some tertiary care hospitals as the patients have a little time to wait while having sepsis (Agarwal et al., 2020).

In a previous study it shows that pathogens Cefixime (83 percent), ceftriaxone (81 percent), and amoxicillin-clavulanic acid resistance was particularly high in *E. coli* (69 percent). The bacteria *Acinetobacter baumanni* was discovered to be the most resistant. The most effective antibiotics were meropenem, amikacin, and piperacillin-tazobactam. Multidrug-resistant organisms are causing UTI in children in our area, according to the findings. Local surveillance studies to test for antibiotic resistance should be conducted on a regular basis, according to the authors (Brink et al., 2011; Capparelli et al., 2005). A conclusion of previous study is multiple drug-resistant *E. coli* caused a significant proportion of urinary tract infections in study participants. From 2012 to 2015 the sensitivity trend continued to deteriorate with Imipenem being the most effective antibiotic at the time (Dubey et al., 2013).

The research was carried out regionally at microbiology lab of a tertiary care hospital, the homogenous and consistent pattern in the collection of samples, testing for antibiogram and patient information provision eliminates a number of errors. But as the data was collected from indoor and outdoor patients, actual drug sensitivity patterns of uropathogens may differ in community and even in a single set-up. We suggest studies in specific groups of community subjects, and in hospitals, to further elucidate the factors associated with drug resistance in uropathogens in our community and to identify and isolate the MDRs and XDRs. Moreover, molecular and genetic factors causing critical drug resistance needs urgent research. Research can be helping a meaningful way to treat suspected UTI patients empirically with most sensitive antibiotic in community. As in case of severe symptoms patient can barely survive a hard-hitting infection prior mistreat or untreated.

Conclusion

The study concluded that the higher frequency of uropathogens like *E. coli* while, Gram positive bacteria like *Enterococcus faecalis* was directed to top in cause of urinary diseases**.** The susceptibility pattern of antibiotics was studied higher efficacy against Gram negative bacteria, sensitivity to carbapenems (Imipenem and Meropenem) was notably higher than cephalosporins (cefuroxime, cefepime, cefixime, ceftriaxone and ceftazidime) and aminoglycosides (Tobramycin, Amikacin and Gentamycin). However, lowest susceptibility percentage was recorded against quinolones (Ciprofloxacin and Levofloxacin). Study recommended that follow all the above suggested results of antibiotics susceptibility patterns against Gram positive and Gram negative in Uropathogenic UTIs of patient.

Recommendations

- The resistant pattern of uropathogens causing urinary tract infections to common antimicrobial agents is changing and must be taken into account when selecting treatment strategies. Therefore, antibiotic policy should be made according to local surveillance data.
- Moreover, studies in specific groups of community subjects, and in hospitals, to further elucidate the factors associated with drug resistance in uropathogens in our community and to identify and isolate the MDRs and XDRs. Moreover, molecular and genetic factors causing critical drug resistance needs to be explored.

Currently, members of Medical Microbiology and Infectious Diseases of Pakistan (MMIDSP) from all over the country, have joined forces to fight against antimicrobial resistance (AMR). AMR data from different hospitals of Pakistan is being collected and compiled, which soon will be available for everyone.

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