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Research Paper

Antimicrobial Resistance Profile of Uropathogenic Gram Negative Bacteria

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Abstract
UTIs are one of the common illness in the worldwide, affecting people of all ages, with females having the highest prevalance. The study investigate the drug resistance profile of the uropathogenic bacterial isolate from study region antibiotic. The study aims to describe guidelines for empiric UTI treatment in the current context, when antibiotic resistance patterns are shifting.
Aim: *The Aim of this study is to identify gram negative pathogen associated with UTI in certain districts of UP and Bihar with the help of retrospective data from referral lab in the districts having no or very low microbiological lab facilities.*
Method: *This study was carried out in the department of microbiology's bacteriology laboratory from January 2019 to December 2020. (Pathkind, NABL Accrediated lab).To attain the stated goals, the investigation employed a retrospective study design. All urine cultures are included in the research. Use SPSS software to analysis data. Urine cultured positive, organism isolates and their antibiotic resistance profile for UTI included as variables*
Results: *Overall, 19546 urine samples were received in 2019 and 29785 samples received in 2020.Out of which 2521 urine samples were isolates in 2019.Out of which 202 sample were gram positive whereas 2319 samples were gram negative Among the bacterial isolates all were gram-negative. The most common bacteria isolated were E.coli*
Conclusion: *Antibiotic therapy for infections should be based on local experience of sensitivity and resistance patterns since bacterial resistance to specific antibiotics evolves over time and in various regions. Antibiotic resistance is prevalent, especially to ampicillin, cefuroxime, ampicillin sulbactam, and cefuroxime.*
Keyword: *Uropathogens; antibiotic resistance.*

Introduction

The kidneys, renal pelvis, ureters, bladder, and urethra are all parts of the urinary system. Urine is produced, stored, and excreted by these organs in concert. The urinary system maintains equilibrium by eliminating waste such as urea, excess salt, excess water, and other substances that the body does not require. These organs control urine production, storage, and excretion. Urinary tract infections (UTIs) are one of the most frequent illnesses in the world, and they're a severe health issue in primary care, general practice, and emergency rooms. People of various ages are affected. UTI infects an estimated million people each year. UTIs are a severe health condition that affects millions of individuals each year, and their treatment is expensive, both directly and indirectly.[1]

It's one of the most widespread infections, especially among women.[2] A UTI episode will affect approximately 50-60% of all women at some point in their lives. It is also typical for UTI episodes to recur if the predisposing factors responsible for the incidence of UTI are not identified, diagnosed, and treated promptly. Untreated urinary tract infections can lead to

major problems such as kidney damage, renal scarring, and renal failure.[3] For improved management and prognosis, it is critical to identify the likely site of infection, whether the infection is simple or complicated, re-infection, relapse, or treatment failure, as well as the etiology and risk factors.[4]

E.coli is the most frequent uropathogenic bacteria.[5] Escherichia coli, Proteus species, Pseudomonas aeruginosa, Acinetobacter species, Klebsiella species, Enterococcus species, and Citrobacter species are all Gram-negative bacteria. Gram-positive bacteria include Staphylococcus saprophyticus, Enterococcus species, Coagulase-negative Staphylococcus are a common predictable spectrum of bacteria that are responsible for causing UTI.[6]

The goal of this study was to identify gram-negative bacteria linked to UTI in various districts of Uttar Pradesh and Bihar, as well as their medication resistance profiles. The study aims to describe guidelines for empiric UTI treatment in the current context when antibiotic resistance patterns are shifting.

Material and Method

The study was carried at path kind lab, Gurugram, and employed a retrospective study design. The Details of the isolated organisms, antimicrobial resistance profile, and information of ESBL and Carbapenemase producer were collected from Path kind (NABL Accredited) lab. This study includes all the samples with positive urine culture isolated in the years 2019 and 2020 in 9 districts of UP and 2 districts of Bihar.

Isolation of uropathogens

To determine the presence and quantity of uropathogen, urine is cultured on CLED (Cystine lactose electrolyte deficient) agar. 0.001 ml urine is cultured on a CLED agar plate by using the steaking technique. Incubate cultured plate at 37°C. If a single organism was cultured at a concentratio of >105 colony-forming units/ml, the specimen was considered as positive for UTI. Gram stain was performed if there is any growth on the plates.

Identification and Antibiotic sensitivity testing

The BD Phoenix M50 "Automated Microbiological System" was used for antimicrobial susceptibility testing and identification of bacteria. After the confirmation of the gram stain result, a suitable BD Phoenix panel for inoculation was selected. Dry substrates for bacterial identification and an AST with varying antimicrobial drug concentrations are included in the combo panel. On the ID side, there are 51 wells, whereas, on the AST side, there are 85 wells. The BD Phoenix M50 "Automated Microbiological System" automatically detects ESBL producers, prospective carbapenemase producers, and carbapenemase producer classes.

Statistical Analysis

The study was carried out using the SPSS statistical software. Urine culture positive, organism isolates, and their antibiotic resistance profile for UTI included as variables. The categorical data were summarized using percentages.

Result

Overall, 19546 urine samples were received in 2019 and 29785 samples were received in 2020.Out of which 2521 urine samples were isolates in 2019. There were 202 gram-positive samples and 2319 gram-negative negative samples out of the total.

In 2020, 1982 urine samples were isolates, out of which 250 samples were gram-positive whereas 1732 samples were gram-negative.

In this investigation, only gram-negative bacteria (E.Coli, Klebsiella, and Pseudomonas) were used. Among the bacterial isolates, all were gram-negative E.coli (72.2%), Klebsiella pneumonia (19.6%), and Pseudomonas aeruginosa (4.9 percent) [TABLE 1] [Fig.1]. The antibiotic susceptibility pattern has changed over time. The findings of the present study were also discussed with the study conducted by Dash M, Padhi S,

Mohanty I, Panda P, Parida B (2013) to identify the causative uropathogens.

The most common bacteria isolated were E.coli (72.2%) (2919 in 4048) and Klebsiella pneumonia (19.6%) (792 in 4048) [Table 1]. The isolation of pseudomonas aeruginosa was 4.9% (201 of 4048), which is comparable to earlier research.[8]

In 2019, E.coli show high resistance to cefazolin (100%), and ampicillin (85%) and very low resistance to tigecyclin (2%), nitrofurantoin (16%), imipenem (16%) and piperacillin tazobactam (24%). [Figure 2,Table 4]Where as in 2020 high resistance to Cefazolin (100%), cefotaxime (100%) colistin (100%) and tetracycline (100%) and low resistance to tigecyclin (2%), nitrofurantoin (15%) and imipenem (17%).[Figure 5]

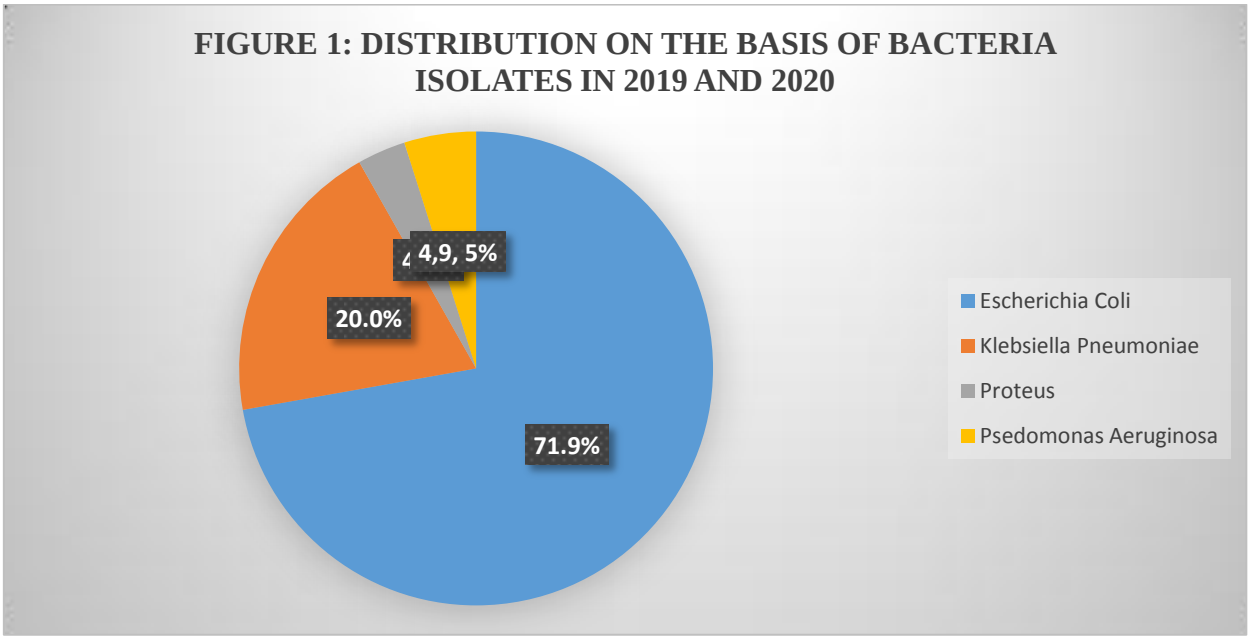
In 2019 High resistance of Klebsiella pneumonia was observed in ampicillin (100%), cephalexin (100%), and cefazolin (100%) and low resistance to tigecycline (18%), gentamicin (28%), and piperacillin-tazobactam. (33%).[Figure 3]Whereas in 2020 high resistance to cefazolin (100%), Colistin (100%), and tetracycline (100%). Low resistance to tigecycline (17%) and gentamicin (26%) [Figure 6]

Pseudomonas aeruginosa shows 100% resistance to several antibiotics such as amoxicillin-clavulanate, ampicillin, cefazolin, cefoxitin nitrofurantoin, and trimethoprim-sulfamethoxazole that is observed in the year 2019. Low resistance to piperacillin tazobactam (31%).[Figure 4]Where as in 2020 high resistance to amoxicillin-clavulanate, ampicillin, cefazolin, cefoxitin nitrofurantoin with 100 %. Low resistance to piperacillin tazobactam (34%). [Figure 7]

In the present study, most of the uropathogens show resistance to cefazolin (100%), ampicillin whereas piperacillin-tazobactam, gentamicin ceftazidime-avibactam and imipenem and tigecycline were least resistant. [Table 4]

Table 1: Organism Incidence

Bacteria Isolates	Total No.	Percentage (%)
Escherichia Coli	2919	72.2
Klebsiella Pneumoniae	792	1.6
Pseudomonas Aeruginosa	201	4.9
Proteus	136	3.3
Total	4048	100



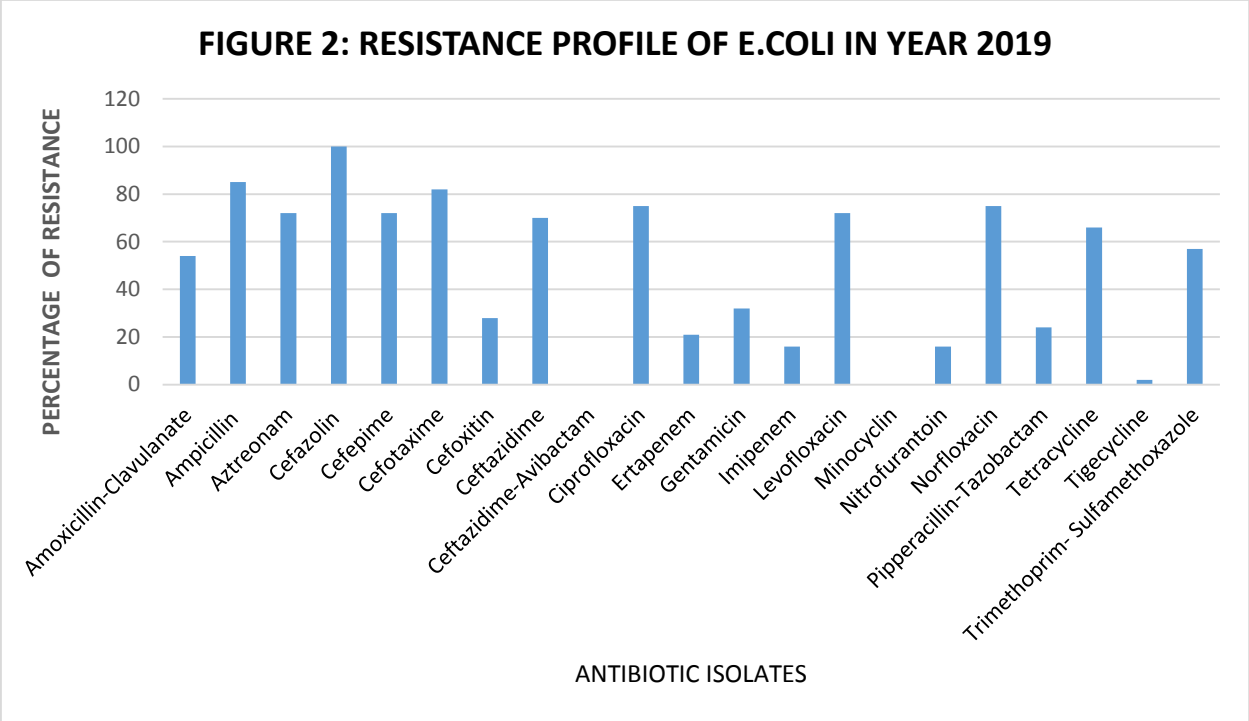


FIGURE 2: RESISTANCE PROFILE OF E.COLI IN YEAR 2019
PERCENTAGE OF RESISTANCE
120
100
80
60
40
20
0
Amoxicillin-Clavulanate
Ampicillin
Aztreonam
Cefazolin
Cefepime
Cefotaxime
Cefoxitin
Ceftazidime
Ceftazidime-Avibactam
Ciprofloxacin
Ertapenem
Gentamicin
Imipenem
Levofloxacin
Minocyclin
Nitrofurantoin
Norfloxacin
Pipperacillin-Tazobactam
Tetracycline
Tigecycline
Trimethoprim- Sulfamethoxazole
ANTIBIOTIC ISOLATES

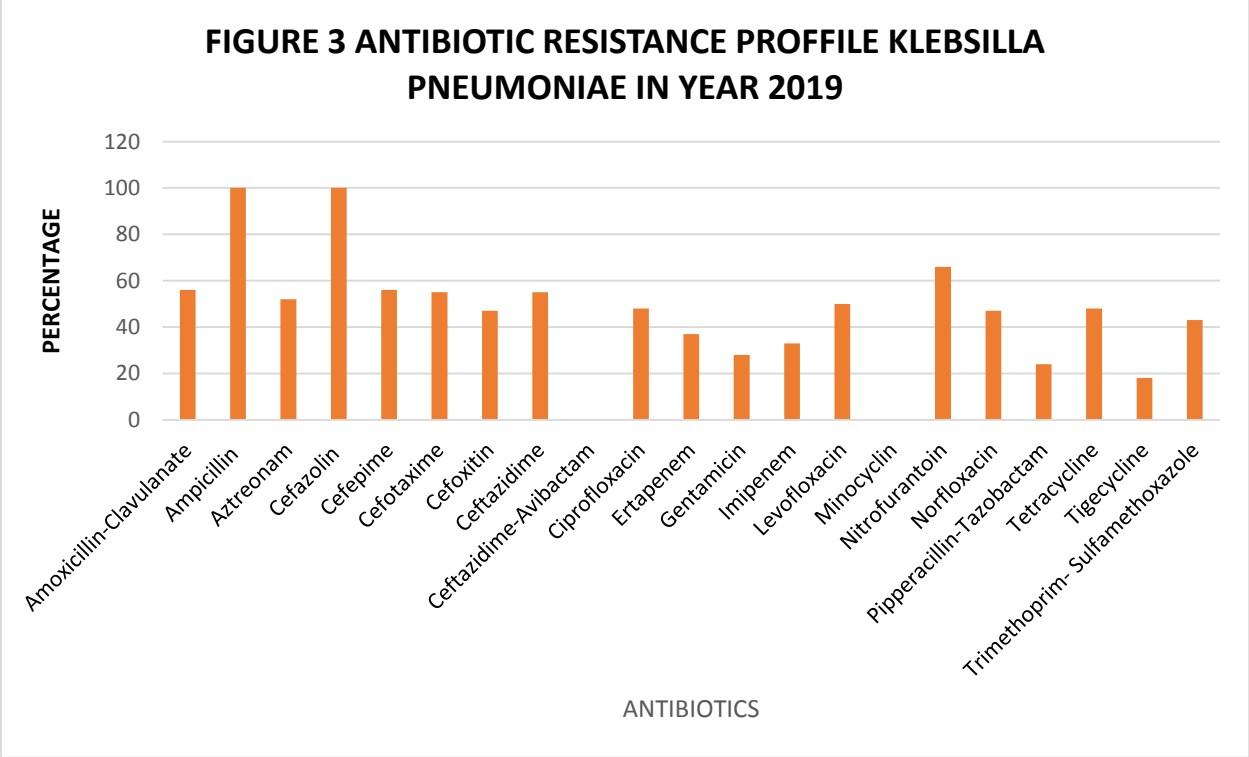


FIGURE 3 ANTIBIOTIC RESISTANCE PROFFILE KLEBSILLA PNEUMONIAE IN YEAR 2019
PERCENTAGE
120
100
80
60
40
20
0
Amoxicillin-Clavulanate
Ampicillin
Aztreonam
Cefazolin
Cefepime
Cefotaxime
Cefoxitin
Ceftazidime
Ceftazidime-Avibactam
Ciprofloxacin
Ertapenem
Gentamicin
Imipenem
Levofloxacin
Minocyclin
Nitrofurantoin
Norfloxacin
Pipperacillin-Tazobactam
Tetracycline
Tigecycline
Trimethoprim- Sulfamethoxazole
ANTIBIOTICS

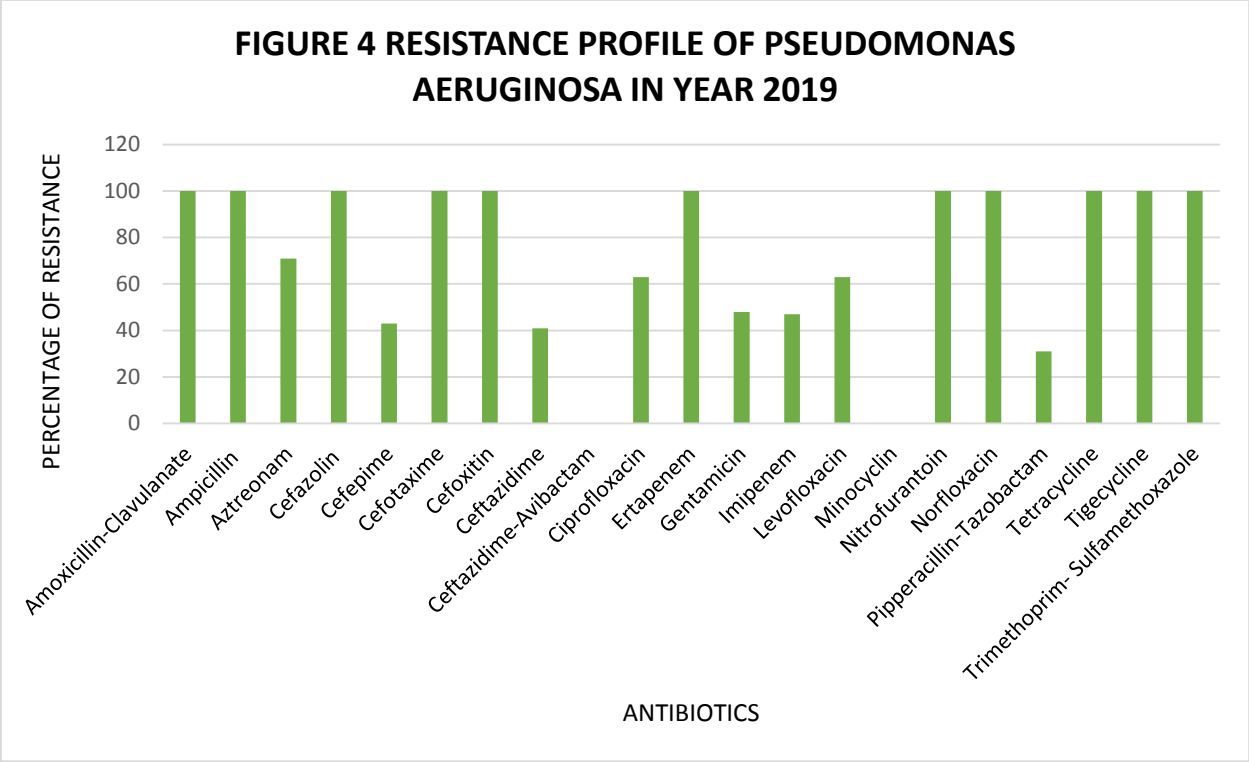
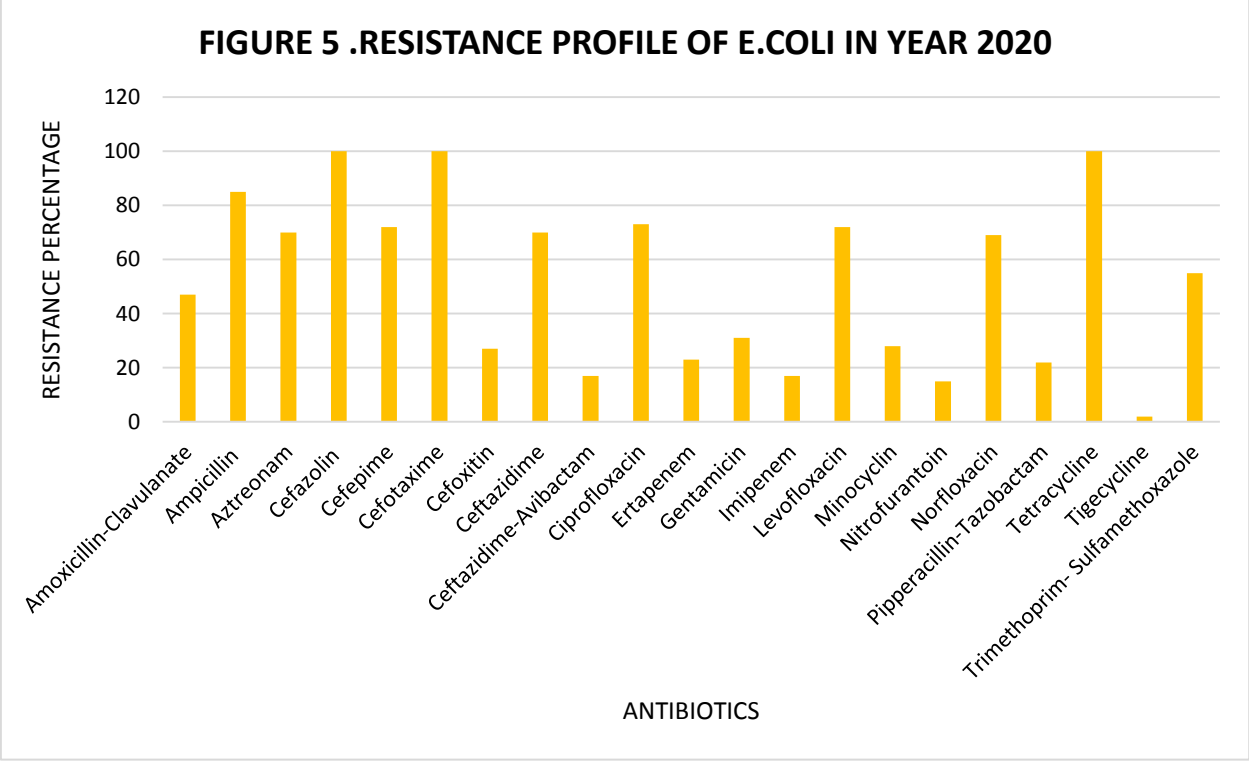
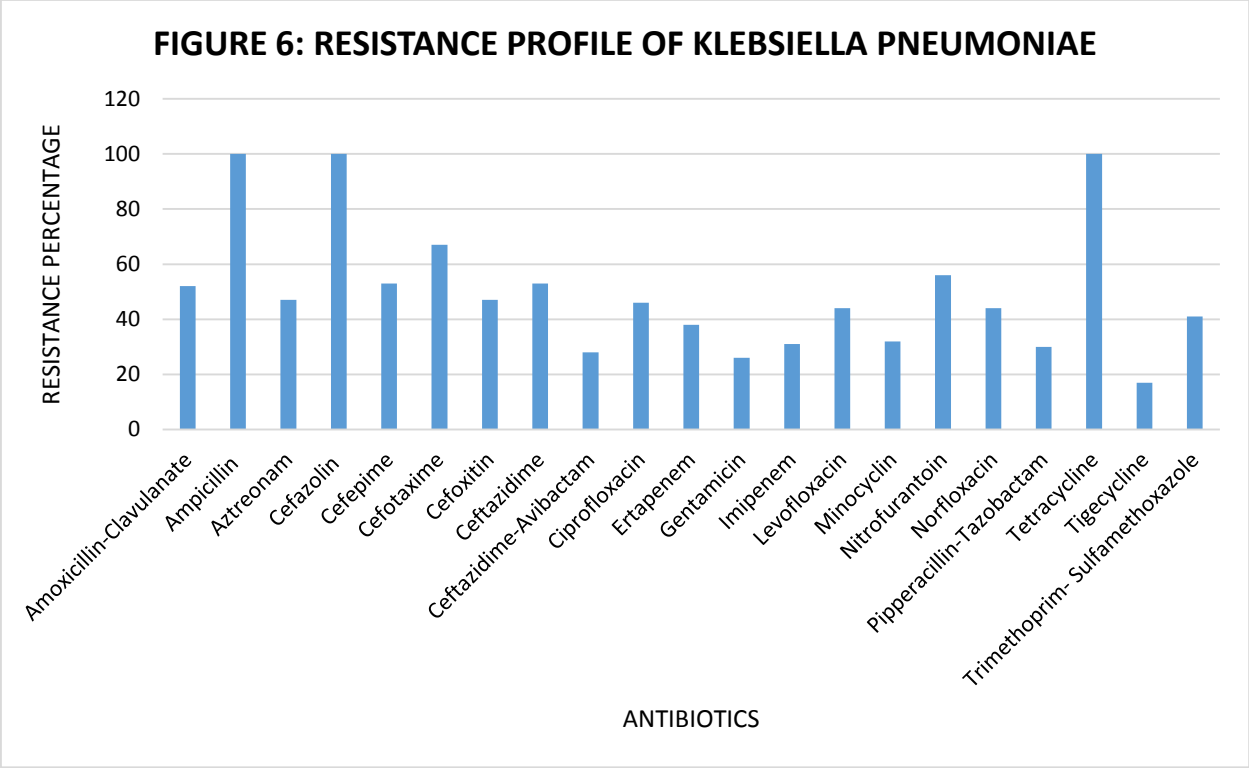


Table 2: Resistance Marker in year 2019

Isolate		Alert 1	ESBL	ESBL Alert	Total
E.coli	524	109	797	292	1722
K.pneumoniae	168	57	75	131	431
P.aeruginosa	105	-	-	-	105
TOTAL	797	166	872	423	2258





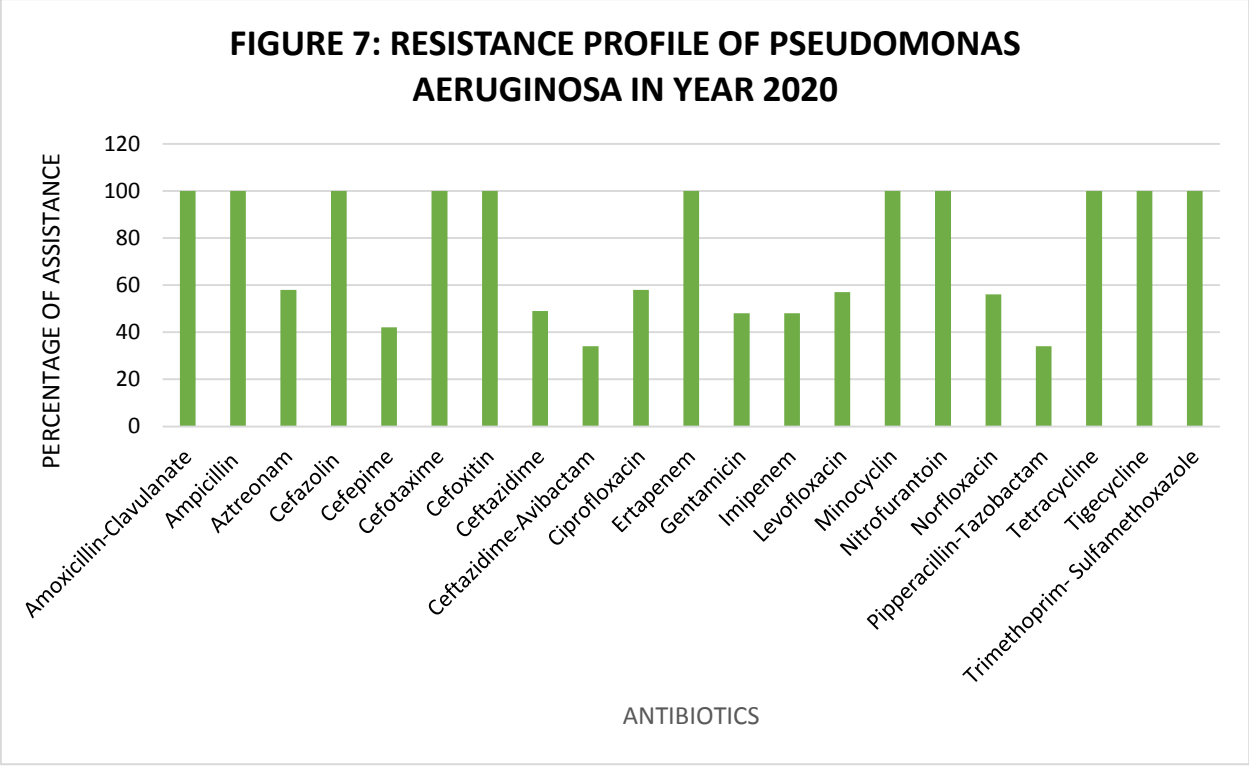


Table 3: Resistance Marker 2020

Isolate		Alert	Carb	Carb A	Carb B	Carb D	Esbl	Esbl alert	Total
E.coli	454	34	5		49	15	529	106	1194
K.pn	184	26	12	2	12	18	65	40	360
P aeru	84	-	3	1	6	-	-	-	94
TOTAL	722	60	20	3	67	33	594	146	1648

Table 4: Comparison between Resistance Profile of Uropathogens in 2019 and 2020

	E.Coli (%)		K. P(%)		P.A(%)	
ANTBIOTICS	**2019**	**2020**	**2019**	**2020**	**2019**	**2020**
Amoxicillin clavulanate	54	47	56	52	100	100
Ampicillin	85	85	100	100	100	100
Azetreonam	72	70	52	47	71	58
Cefazolin	100	100	100	100	100	100
Cefepime	72	72	56	53	43	42
Cefotaxime	82	100	55	67	100	100
Cefoxitin	28	27	47	47	100	100
Ceftazidime	70	70	55	53	41	49
Ceftazidime Avibactam	NIL	17	NT	28	NT	34
Ciprofloxacin	75	73	48	46	63	58
Ertapenem	21	23	37	38	100	100
Gentamicin	32	31	28	26	48	48
Imipenem	16	17	33	31	47	48
levofloxacin	72	72	50	44	63	57
Minocyclin	NIL	28	NT	32	NT	100
Nitrofurantoin	16	15	66	56	100	100
Norfloxacin	75	69	47	44	64	56
Piperacillin Tazobactam	24	22	33	30	31	34
Tetracyclin	66	100	48	100	100	100
Tigecyclin	2	2	18	17	100	100
Trimethoprim sulfamethoxazole	57	55	43	41	100	100
A.B : Acintobacter baumanii, E.COLI: Escherichia Coli, K.P: Klebsiella pneumonia, P.A:Pseudomonas aeruginosa, NT: Not tested, NIL:no resistance						
Note:-Colistin was tested as no break point has been available in BD system, it was not reported.						

Discussion

UTIs is one of the prevalent infection in the entire world and antibiotic susceptibility has fluctuated throughout history. The findings of the present study were also discussed with the study conducted by Dash M, Padhi S, Mohanty I, Panda P, Parida B (2013) to identify the causative uropathogens. E. coli and K. pneumonia were the most common urinary tract pathogens in this investigation.[1][2][7] This is similar to studies from other tertiary care centers. The isolation of pseudomonas aeruginosa was 4.5% (66 of 1469), Other research has shown comparable results.[8]

The antimicrobial susceptibility pattern of uropathogens varies greatly between locations due to drug exposure, antibiotic misuse, and empiric antibiotic use in UTI. In this study, tigecycline, amikacin, piperacillin-tazobactam, and imipenem have shown better activity against most uropathogens with less resistance rate. Similar findings were obtained in investigations undertaken in other locations of India.[5] In other investigations, the most efficient antibiotics against Gram-negative bacteria were imipenem and amikacin.[9][10]

Conclusion

Antibiotic therapy for UTI should be based on sensitivity and resistance patterns because the pattern of resistance of bacteria to specific antibiotics varies over time and in different places. All of the uropathogens examined in this investigation were highly resistant to first-generation cephalosporins. E.coli is still the most prevalent bacteria that cause UTIs.

Nowadays, the overuse of available medicines is expanding the resistance profile. Commonly uropathogen resistance to ampicillin, cefuroxime, ampicillin-sulbactam, and cefuroxime. In this location, these drugs are not suggested as first-line therapy for UTIs. Because only a small percentage of isolates in this study were resistant to tigecycline, amikacin, piperacillin-tazobactam, or imipenem, it's possible that this antibiotic might

be a superior choice for empiric UTI therapy in that region.

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