Bacteriology and Antibiotic Sensitivity Pattern of Uropathogens in Patients with Catheter Associated Urinary Tract Infections in a Tertiary Care Hospital, Bhubaneswar, Odisha

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Abstract

Background: Hospital acquired infections (HAI) serves as a significant public health problem in developing as well as in developed country. The incidence of HAIs in ICU is rising, largely because of increasing use of invasive procedures. About 25% of hospitalized patients undergo urinary catheterization hence it enhances the chances of Catheter Associated Urinary Tract Infections (CAUTI) which is difficult to cure.

The present study is designed with the aim to determine the bacterial pathogens causing Urinary tract infections (UTIs) in patients with indwelling urinary catheter and to study their antibiotic susceptibility pattern.

Methodology: This was a Cross-Sectional, hospital-based study carried out from August to September 2018 in a tertiary care hospital in Eastern India. A convenient sample size of 50 Catheterized patients admitted to the hospital from whom urine samples were collected. Fifty urine samples were also collected from non-catheterized patients as control group. Informed written consent was taken from patients before collecting the urine sample. Data was entered and analyzed on Statistical Package of Social Sciences (SPSS) Version 12. Mean and Standard deviation was calculated for quantitative data and proportions were calculated for qualitative data.

Results: The age of the patients ranged from 15 to 90 years with a mean of 50.49 years. Majority (62%) were in 46-75 years age group and were males (68%). The rate of developing UTI was more with increase in duration of catheterization and it was 86% with 8-14 days of catheterization. Among catheterized patients ***Escherichia coli*** was found to be the most frequently isolated pathogen 23(36.5%) followed by ***Klebsiella pneumoniae*** 12 (19%) and ***Enterococcus species*** 8(12.7%). Among the 31 positive samples, 10 samples showed growth of 2 organisms and 6 samples showed growth of 3 organisms.

Conclusion: Reduction of Hospital acquired infections and antibiotic resistance is both a challenge and goal of all health care centers around the globe. To lower our economic burden and improve the healthcare standards of the catheterized patient admitted to the hospital we have to broaden our knowledge regarding safe use of indwelling urinary devices.

Key words: *CAUTI, UTI, Bacteriology, Antibiotic Sensitivity, Escherichia coli, Klebsiella pneumoniae*

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Introduction

Urinary Tract Infection (UTI) is the most common nosocomial infection among hospitalized patients and one of the most important causes of morbidity in the general population. It is caused by the microbial

invasion of the genitourinary tract that extends from the renal cortex of kidney to the urethral meatus. Hospital acquired infections (HAI) serves as a significant public health problem in developing as well as in developed country. The incidence of HAIs in ICU is rising, largely because of increasing use of invasive procedures. About 25% of hospitalized patients undergo urinary catheterization hence it enhances the chances of CAUTIs which is difficult to cure.

Approximately 35% of all Hospital Acquired Infections (HAIs) are contributed by UTIs. Instrumentation of urinary tract, mainly catheterization leads to 66-86% of the infections. The method of insertion, quality of the catheter used, duration of catheterization and host susceptibility also plays a major role in acquiring these infections.

Catheter associated urinary tract infection (CAUTI) is defined by the Center for Disease Control and Prevention (CDC) as "Any urinary tract infection in a patient who had an indwelling catheter in place at the time of or within 48 hours prior to onset of infection". There has not been any minimum period defined for the catheter to be in place for the urinary tract infection to be categorized as CAUTI. CAUTIs may range from asymptomatic bacteremia to symptomatic urinary tract infection. Hospital acquired CAUTIs are mostly due to Multidrug Resistant Strains of the uropathogens, which require higher antibiotics and also these strains may spread to other patients.

Urinary catheters are standard prosthetic medical devices used in managing bladder dysfunction, but unfortunately provides attractive surface for colonization. Majority of uropathogens are faecal contaminants or normal skin flora from the patients periurethral area. For catheter associated infections organisms ascend from urethral meatus along the catheter urethral interface preferably by extra luminal (66%) route. In 34% cases organisms can enter bladder by intraluminal route where they migrate as a result of manipulation of catheter system.

The bacterial pathogens commonly isolated from the catheters are *Escherichia coli, Proteus mirabilis, Pseudomonas aeruginosa, Klebsiella pneumoniae, Staphylococcus epidermidis* and *Enterococcus faecalis*. These bacterial pathogens may originate endogenously or exogenously. Microorganisms which are fully sensitive to antibiotics may become fully resistant in the biofilm mode.

The present study is designed with the aim to determine the bacterial pathogens causing Urinary tract infections (UTIs) in patients with indwelling Urinary Catheter and to study their antibiotic Susceptibility Pattern. This will help and guide the clinicians to make a precise decision regarding treatment and management of such infections.

Materials and Methods

This was a Cross-Sectional, hospital-based study carried out from August to September 2018. A

convenient sample size of 50 Catheterized patients admitted to the hospital from whom urine samples was collected. 50 urine samples were also collected from non-catheterized patients as control group. Informed written Consent was taken from patients before collecting the urine sample.

Selection Criteria were as follows:

Inclusion criteria-

For Cases

1. All ages groups, both sexes, who were on indwelling urinary catheter for at least 2 days.

2. Patients who were suffering from symptoms of UTIs (fever >38ºC, urgency, frequency, dysuria or suprapubic tenderness)

For Controls

1. Urine samples from non-catheterized patients with symptoms of UTIs were included.

Exclusion Criteria

1. Patients with symptoms of UTI prior to catheterization

2. Patients who didn't give consent

Detailed information for each patient was entered in the study proforma.

Sample collection-

After taking approval from the Institutional Research and Ethical Committee and taking written Informed Consent with explaining the detailed procedure and rationale of the study, the samples were collected. Prior to catheter change or removal from each patient, about 10ml of urine was obtained from the distal edge of the catheter tube aseptically using a sterile needle and syringe transferred into sterile universal container. Clean catch mid-stream (CCMS) urine samples from non-catheterized patients were taken in case of control group. Samples were transported to the laboratory with minimum delay. Urine samples were inoculated on Cystine Lactose Electrolyte Deficient (CLED) medium with calibrated loops to determine the Colony Forming Units (CFU) and were incubated aerobically at $37^{o}C$ for 24 hours. A specimen was considered positive, if a single / two potential pathogens were cultured at a concentration of $\geq 10^5$ Colony forming unit (CFU)/ml from CCMS urine or catheterized urine or $\geq 10^3$ CFU/ml of single potential pathogen from catheterized urine specimens.

After 24 hours of incubation, the plates were observed for bacterial growth. Colonies were examined and the identification of the isolated bacteria was made up to Species level on the basis of colony morphology, gram stain, motility & biochemical tests following conventional microbiological techniques. Isolates showing fungal growth were further cultured in Sabouraud's Dextrose Agar and further identification was done by Germ Tube Test.

Bacterial susceptibility to antimicrobial agents was determined by the Kirby Bauer disk diffusion method on Muller-Hinton agar using antibiotic discs procured from Hi Media (Mumbai, India). Isolates were categorized as susceptible, moderately susceptible, and resistant, based upon interpretive criteria developed by the Clinical and Laboratory Standards Institute (CLSI).

The antibiotics used for Gram negative organisms were ampicillin(10µg), amikacin (30 µg), gentamicin (10µg), ceftriaxone (30µg), cefepime (30 µg), cefoperazone (75µg), cefoperazone -sulbactam(75/75 µg), levofloxacin (5µg), imipenem (10 µg), piperacillin - tazobactam(100/10µg), ceftazidime (30 µg), ertapenem(10µg), meropenem(10µg), amoxicillin-clavulanic acid (20/10 µg), and nitrofurantoin(300µg), aztreonam(30 µg), cefuroxime(30µg),ticarcillin-clavulanic acid (75/10µg), ampicillin(10µg), tigecycline(15µg), ciprofloxacin(5µg) &cotrimoxazole(1.25/23.75µg).

The antibiotics used for Gram positive Organisms- levofloxacin 5µg), nitrofurantoin(300µg), vancomycin(30µg), cotrimoxazole (1.25/23.75µg), ciprofloxacin(5µg), erythromycin(15µg), linezolid (30µg), colistin(10µg), teicoplanin(30µg), clindamycin (15µg), ampicillin (10µg) and tigecycline(15µg).

Statistical Analysis

Data was entered and analyzed on Statistical Package of Social Sciences (SPSS) Version 12. Mean and Standard deviation was calculated for quantitative data and proportion was calculated for qualitative data.

Results

In this hospital based observational study carried out in a tertiary level teaching hospital of eastern India, 50 catheterized patients were included. The age of the patients ranged from 15 to 90 years with a mean of 50.49 years. Majority (62%) were in 46-75 years age group. Around one fifth were in younger age group of 15-30 years. (TABLE 1).

Three fourths (75%) of the samples were culture positive in 61-75 years age group followed by 67% in 46-60 years age group. Overall, culture positivity was found in 62% of urine samples. Out of 50 patients, majority were Males -34 (68%) and only 16(32%) were females. Culture positivity was also seen more in males 22(64.7%) as compared to females 9 (56.25%). (TABLE 2).

The rate of developing UTI was more with increase in duration of catheterization and it was 86% with 8-14 days of catheterization. (TABLE 3).

Among catheterized patients *Escherichia coli* was found to be the most frequently isolated pathogen in 23 (36.5%) followed by *Klebsiella pneumonia* in 12 (19%) and *Enterococcus species* in 8(12.7%) samples. Among the 31 positive samples, 10 samples showed growth of 2 organisms and 6 samples showed growth of 3 organisms. However, among the non-catheterized patients, *Escherichia coli* 12(34.3%), *Klebsiella*

pneumoniae 7(20%) and *Staphylococcus species* 5(14.4%) were the commonest isolates. *Candida species* 2(3.2%) and *cryptococcus laurentii* 1(1.5%) were also isolated from the catheterized patients in addition to the bacterial pathogens. (TABLE 4). Maximum number of patients on catheter showing culture positivity where from ICU 26(52%) followed by Medicine Ward 11(22%) and Surgery Ward 8(16%).Among the study population, Hypertension (54%) and Diabetes Mellitus (44%) were the common underlying illnesses followed by cerebrovascular accidents (28%) and Chronic Kidney Disease in 20%.

The in vitro antibiotic susceptibility pattern of the gram-negative pathogens showed high resistance to commonly used antibiotics such as Ampicillin (100%), Cefuroxime (100%) Cefoperazone-Sulbactam (85%),and Piperacillin/Tazobactam (83%).

Klebsiella, Proteus, Pseudomonas and *Serratia* species were found to be the most resistant bacterial pathogens to majority of the antibiotics. Maximum susceptibility of the gram-negative isolates was observed for colistin (69%), cotrimoxazole (55%) and amikacin (50%). *Staphylococcus* species showed 100% susceptibility for Teicoplanin, Vancomycin, Tigecycline, Nitrofurantoin and Cotrimoxazole. Only a single staphylococcal isolate was susceptible for linezolid. All the *staphylococcal* isolates were resistant to Ampicillin, erythromycin, clindamycin and fluoroquinolones. *Enterococcus* species were maximum susceptible to Teicoplanin, Vancomycin and Tigecycline (87.5% each) and highest resistance was seen for Clindamycin and Erythromycin.

TABLE 1: AGE WISE DISTRIBUTION OF PATIENTS INVESTIGATED FOR CAUTI (n=50)

AGE GROUP (in Yrs.)	NUMBER (%)	CULTURE POSITIVITY n (%)
15-30	11(22.0)	6(54.0)
31-45	6(12.0)	2(33.0)
46-60	15(30.0)	10(67.0)
61-75	16(32.0)	12(75.0)
76-90	2(4.0)	1(50.0)
TOTAL	50(100%)	31(62%)

TABLE 2: GENDER WISE DISTRIBUTION OF PATIENTS INVESTIGATED FOR CAUTI (n=50)

GENDER	NUMBER (%)	CULTURE POSITIVITY n (%)
MALE	34(68.0)	22(64.7)
FEMALE	16(32.0)	9(56.25)
TOTAL	50(100%)	31(62%)

TABLE 3: LENGTH OF CATHETERIZATION IN RELATION TO DEVELOPMENT OF SIGNIFICANT BACTERIURIA (n=50)

DURATION (in days)	NUMBER OF SAMPLES n (%)	SIGNIFICANT BACTERIURIA n (%)
2-7	19(38.0)	5(26.0)
8-14	23(46.0)	20(86.0)
>14	8(16.0)	6(75.0)
TOTAL	50(100%)	31(62%)

TABLE 4: DISTRIBUTION OF UROPATHOGENS FROM URINE SAMPLES

ORGANISMS	CATHETERZIED (n=50)	NON-CATHETERIZED (n=50)
	Number (%)	Number (%)
Escherichia coli	23(36.5)	12(34.3)
Klebsiella pneumoniae	13(20.6)	7(20.0)
Enterococcus species	7(11.1)	4(11.5)
Pseudomonas aeruginosa	6(9.5)	1(2.8)
Acinetobacter baumannii	5(8.0)	2(5.7)
Proteus mirabilis	2(3.2)	1(2.8)
Serratia species	2(3.2)	0
Staphylococcus species	2(3.2)	5(14.4)
Enterobacter	0	1(2.8)
Citrobacter species	0	2(5.7)
Candida species	2(3.2)	0
Cryptococcus laurentii	1(1.5)	0
TOTAL	63 (100%)	35(100%)

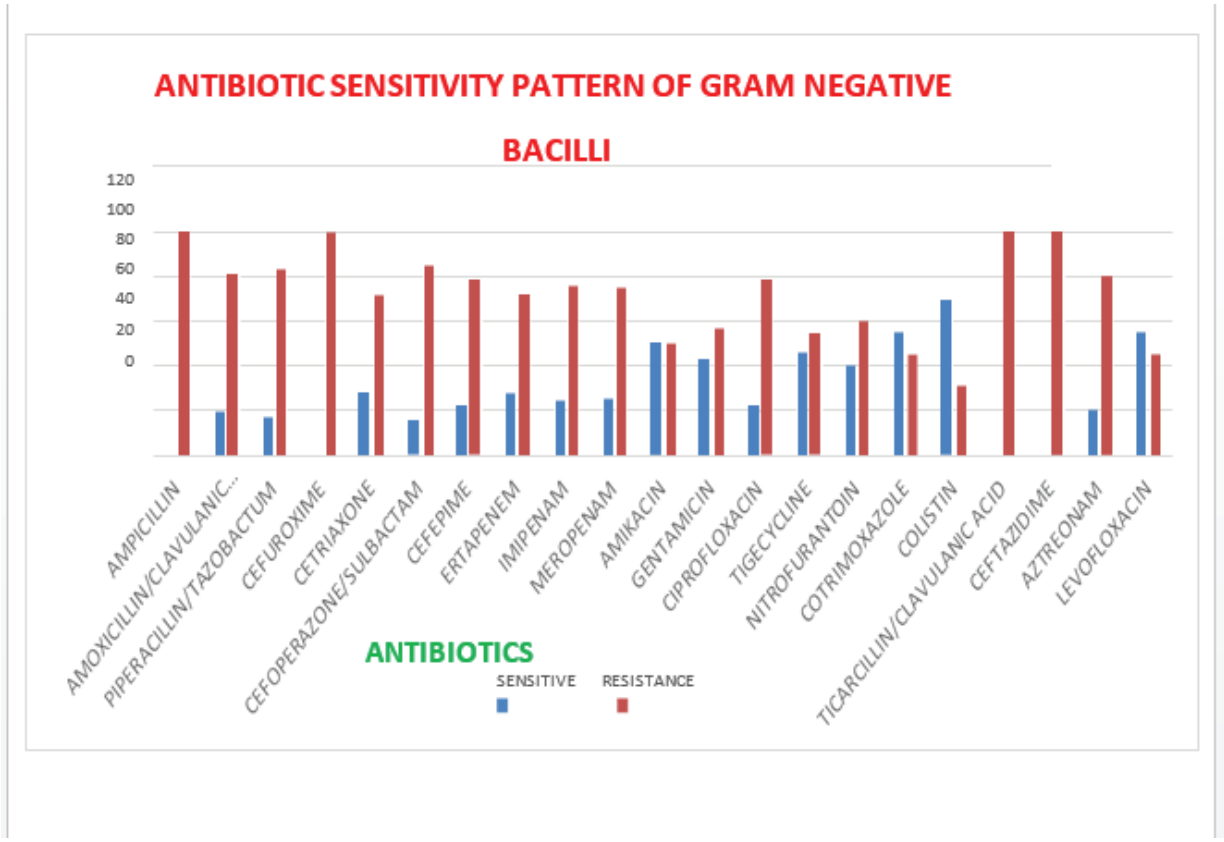

Figure 1: Antibiotic Sensitive and Resistance Pattern of Gram-Negative Bacterial Isolates

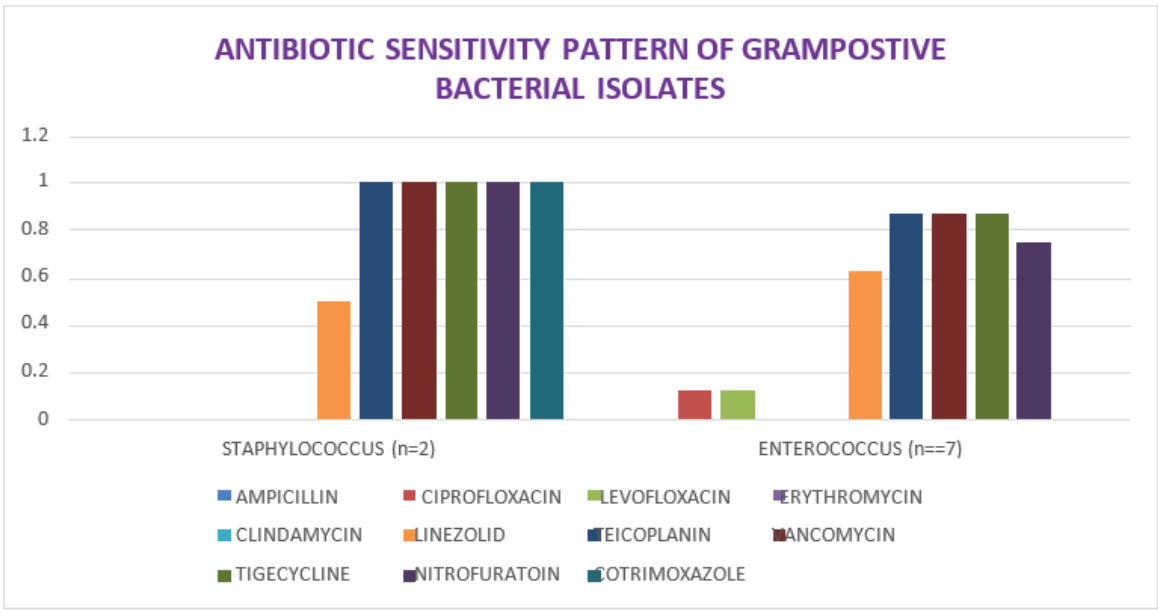

Figure 2: Antibiotic Sensitivity Pattern of Gram-Positive Bacterial Isolates

Discussion

More number of CAUTIs occur due to increased use of urinary catheters which are the second most used foreign body in the patients. Despite good aseptic precautions, more than half of the patients develop bacteriuria during first 10-14 days of catheterization. Monitoring of the Antimicrobial therapy is important as they are becoming resistant to common antibiotics.

The present study was conducted on 50 catheterized patients admitted to our hospital which a tertiary health care center. Out of the 50 patients, who were on indwelling catheters, 31(62%) had significant bacteriuria. This finding is close to the observations of Anthony et al (60.9%), Patil et al (76%) and Tomar et al (74%). But, Tawo S Set al and Majumder et al have seen 88.5% and 90% culture positive cases among their study population.

In our study, the age group 61-75 years predominated and it represented 32% of the total study population, followed by 46-60 years (30%). Culture positivity was also seen maximum in the age group of 61-75 years which can be correlated with the findings of Sayal P et al (46.25%), Niveditha S et al (36%) Leelakrishna P et all (35.2%) who have also seen maximum number of CAUTI cases in the age group more than 60 years.

Occurrence of CAUTI was more in male patients in our study than that of female patients. Out of 34 males, 22 (64%) showed culture positivity whereas 9 (56%) females showed culture positivity out of 16. This finding is comparable with the studies having similar male predominance like Kulkarni et al (68.18%) , N Bhatia et al and Jaggi N et al . However, Setu K S et al have seen female (61.68%) predominance of CAUTI cases in their study as compared to males.(38.2%). Maximum number of samples were collected from males as compared to females in our study & males are more prone to Obstructive Urinary Lesion especially Benign Hypertrophy of Prostate, Carcinoma prostate and stricture associated with advanced age.

In the present study, rate of developing UTI was more with increase in duration of catheterization and it was 86% with 8-14 days of catheterization. Similar findings were also shown by Tomar R et al (87.5%) , Kulkarni SG et al (65%) and Majumdar et al. (71%) . In our study Escherichia coli was the most frequently isolated bacterial pathogen 23(36.5%) followed by Klebsiella species 13(19%), Enterococcus species 7 (12.7%) and Pseudomonas aeruginosa 6 (9.5%) among the catheterized patients. This finding is also consistent with other studies by Tomar R et al , Kulkarni SG et al and Niveditha S et al.

Klebsiella was the 2nd most common organism associated with CAUTI in our study, similar to studies carried out by Kulkarni S G et al and N Bhatia et al .The emergence of Candida species infection (3.2%) in our study is also comparable to other studies such as the study done by Nandini et al (3.84%) , Vinoth et al (4%) and Taiwo et al (3.2%) .

Among the Non-Catheterized patients *Escherichia coli* was also the commonest bacterial pathogen isolated 12(34%). Sayal et al had also similar observations among the Non- catheterized patients (45%). Findings of Abdallah et al also correlates with our study that Escherichia coli was the most common pathogen isolated in both catheterized and non-catheterized patients.

Enterobacteriaceae have several virulence factors responsible for their adherence to the uroepithelium. These gram-negative aerobic bacteria colonize the urogenital mucosa with pili, adhesions, fimbriae (Type 1 fimbriae) and P1 blood group phenotype receptor which makes it the most common cause of UTIs and CAUTIs.

Maximum Culture Positive cases were seen from ICU 26(52%) in our study followed by the samples collected from Medicine ward 11(22%) and Surgery ward 8(16%). As most of the patients in ICU were critically ill and duration of their stay was longer as compared to those staying in the ward, probability of getting culture positivity was maximum among them. Studies carried out by Vinoth M et al have shown maximum number of CAUTI cases among patients from Surgical Ward (58%). Such Area-Specific Monitoring Studies will help to choose the correct empirical treatment by knowing the pathogens responsible for UTIs.

Common underlying illnesses in our study among the catheterized patients were Hypertension (54%) and diabetes mellitus (44%). Hypertension and Diabetes Mellitus both can lead to number of complications leading to hospitalization and subsequently predisposing the patients for acquiring UTI by catheter insertion.

Similar observations were also documented by Niveditha S et al , Sayal P et al and Kulkarni S et al .

The in vitro antibiotic Susceptibility pattern of the Gram-Negative Organisms showed high resistance to commonly used antibiotics like Ampicillin (100%), cefuroxime (100%) Cefoperazone-Sulbactam (85%), and Piperacillin/Tazobactam (83%) and good sensitivity to Colistin (69%), cotrimoxazole (55%) and amikacin (50%). Similar results were documented by Taiwo S et al , Kulkarni SG et al and Garg et al .

Sensitivity pattern of Escherichia coli, which is the commonest bacterial pathogen isolated from catheterized patients was 100% sensitive to colistin and tigecycline followed by nitrofurantoin (78%) Amikacin (73.9%) and Imipenem (52.1%). All the Escherichia coli were resistant to ampicillin and cefuroxime and was less sensitive to ceftriaxone (13%) and Ciprofloxacin. (17.3%). These observations were similar to findings of Ponnusamy P et al & contrary to the study done by Das R N et al which shows high sensitivity to Ampicillin.

Klebsiella was resistant to most of the antibiotics and was only sensitive to few like Colistin (92.3%), tigecycline (53.8%), imipenem (38.4%), Nitrofurantoin (30.7%) & Amikacin (23%). Similar results were seen by Kulkarni SG et al.

Staphylococcus species showed 100% susceptibility for Teicoplanin, Vancomycin, Tigecycline, Nitrofurantoin and Cotrimoxazole. Only a single staphylococcal isolate was susceptible for linezolid. All the staphylococcal isolates were resistant to ampicillin, erythromycin, clindamycin and fluoroquinolones. Enterococcus species were maximum susceptible to Teicoplanin, Vancomycin and Tigecycline (87.5%) and highest resistance was seen for Clindamycin and Erythromycin (0%). Study conducted by Tomar R et al and Garg N et al also showed similar results.

This universal resistance of biofilm cells to antimicrobial agents is very important clinically and has to be considered when initiating antibiotic therapy. Hence there is a need to establish standard guidelines for care of catheter, newer protocols should be developed for maintain long duration of catheters and development of antimicrobial urinary catheters is needed.

Conclusion

The Urinary tract of catheterized patients is highly vulnerable to severe infections. In our study, *Escherichia coli* was the most important pathogen isolated from the UTIs in catheterized patients (34%). Incidence of CAUTIs increases due to longer duration of catheterization.

In this study, Gram Negative Organisms were highly sensitive for colistin (69%), cotrimoxazole (55%) and amikacin (50%) whereas Gram positive organisms were highly sensitive to Teicoplanin (93.75%), Vancomycin (93.75%), Tigecycline (93.75%). Probably microbial biofilms have been integrated with variety of persistent infections which respond dreadfully to the conventional antibiotic therapy and it helps in transfer of antibiotic resistance traits in the nosocomial pathogens by enhancing the mutation rates and by the changing of genes which are responsible for antibiotic resistance.

Reduction of Hospital Acquired and antibiotic resistance is both a challenge and goal of all health care centers around the globe. To lower our economic burden and improve the healthcare standards of the catheterized patient admitted to the hospital we have to broaden our knowledge regarding safe use of indwelling urinary devices.

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Conflict of Interests- None

Source of Funding- ICMR as a Short-Term Studentship (STS) project.

Ethical Considerations-Approval for the study was taken from the Institutional ethical committee.

The informed written consent was taken from the patients prior to the study either in English or local language. The privacy and confidentiality of the patients were maintained.

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