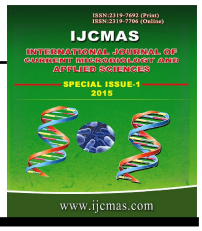
International Journal of Current Microbiology and Applied Sciences
ISSN: 2319-7706 **Special Issue-1 (2015) pp. 163-172**
http://www.ijcmas.com



Original Research Article

Microbiological Profile and Antibiotic Sensitivity Pattern of Bacterial Isolates Causing Urinary Tract Infection in Intensive Care Unit Patients in a Tertiary Care Hospital in Aligarh Region, India

Neha Garg[1]*, Indu Shukla[1], Meher Rizvi[1], Syed Moied Ahmed[2], Abida Khatoon[1] and Fatima Khan[1]

[1]Department of Microbiology, Jawaharlal Nehru Medical College & Hospital, Aligarh Muslim University Aligarh-202002, Uttar Pradesh, India
[2]Department of Anaesthesia, Jawaharlal Nehru Medical College & Hospital, Aligarh Muslim University Aligarh-202002, Uttar Pradesh, India
**Corresponding author*

Keywords

Urinary tract infection, Nosocomial, Intensive care unit, MRSA, ESBL, AmpC, MBL

A B S T R A C T

Urinary tract infection (UTI) is the most common nosocomial infection. More than 80% of nosocomial UTIs are catheter-associated (CAUTI). The aim of the study was to determine the prevalence, microbiological profile and changing pattern of antibiotic sensitivity among the uropathogens causing CAUTI in intensive care unit (ICU) patients. The study was conducted between October 2013 and December 2014 in the Department of Microbiology, Jawaharlal Nehru Medical College & Hospital, AMU, Aligarh, Uttar Pradesh, India. All the patients admitted to ICU with urinary catheter insertion for ≥48 hours were included in the study. Patients with any signs or symptoms of UTI before catheter insertion were excluded. Urine samples were collected in a sterile wide mouthed universal container taking aseptic precautions with a sterile disposable syringe by cleaning and clamping the catheter tube and were processed as per standards. Antimicrobial susceptibility testing was ascertained by Kirby Bauer's Disc diffusion method as per CLSI guidelines. ESBL, AmpC, MBL and MRSA were detected by phenotypic methods. Total of 100 urine samples were collected from ICU patients, out of which 20(20.0%) samples showed significant bacterial growth ($\geq 10^5$ CFU/ml) and 8(8.0%) samples showed growth of *Candida*. Prevalence of UTI was more in female 18(64.2%) than male 10(35.7%) patients. Gram negative bacilli 16(80.0%) were the predominant bacterial isolates followed by Gram positive cocci 4(20.0%). Overall the most common uropathogens isolated were *Escherichia coli* 8(40.0%) followed by *Citrobacter koseri* 4(20.0%), *Staphylococcus aureus* 3(15.0%), *Klebsiella oxytoca* 2(10.0%), *Acinetobacter* species 1(5.0%), *Pseudomonas aeruginosa* 1(5.0%), and *Enterococcus faecalis* 1(5.0%). Most of the Gram negative bacilli were sensitive to amikacin 12(75.0%) and nitrofurantoin 12(75.0%), while all Gram positive cocci were sensitive to vancomycin and cefazolin. Among the combination used, 7(43.7%) isolates were sensitive to cefoperazone-sulbactam and most of the isolates were sensitive to piperacillin-tazobactam 13(81.2%). Among 16 Gram negative isolates, 13(81.2%) were sensitive to imipenem and 3(18.7%) were resistant. MRSA was detected in 2(66.6%) cases. 4(25.0%) were ESBL producers. AmpC was found in 6(37.5%) strains and MBL was detected in 3(18.7%) strains respectively. As most of the ICU patients cannot take oral antibiotic and predominant isolates were from Enterobacteriaecae, so amikacin should be given as an empirical therapy till culture and sensitivity results are awaited.

Introduction

Hospital acquired infections (HAIs) are an important public health problem in developing as well as in developed countries (Celik *et al.*, 2005). The rate of HAIs in ICU is rising, mainly because of increasing use of invasive procedures (Tullu *et al.*, 1998). CAUTI are the most frequent nosocomial infections (Saint and Lipsky, 1999) and are responsible for 20-30% of HAIs in medical or surgical ICUs (Richards *et al.*, 1999). Risk factors associated with CAUTI includes: duration of ICU stay, length of catheterization, female patients, age over 50 years, immunocompromised (diabetes mellitus, cancer, steroid therapy, HIV and organ transplantation) (Wenzel *et al.*, 1976; Garibaldi *et al.*, 1981; Platt *et al.*, 1986; Tasseau *et al.*, 1990). Several microbial agents have been found to be responsible for CAUTI: *Escherichia coli, Pseudomonas aeruginosa, Acinetobacter, Proteus, Klebsiella, Enterobacter, Staphylococcus aureus, Enterococcus faecalis, Candida* and *Enterococcus* (Wagenlehner *et al.*, 2006). CAUTI have been associated with a three-fold increased risk of mortality in hospitals including ICUs because of inappropriate use of antimicrobial agents leading to the spread of antimicrobial resistance and emergence of multidrug resistant uropathogens (Stark and Maki, 1984; Vatopoulos *et al.*, 1999).

The aim of the present study was to determine the prevalence, microbiological profile and changing pattern of antibiotic sensitivity among the uropathogens causing CAUTI in ICU patients in a tertiary care hospital in Aligarh region.

Materials and Methods

Study design

The study was conducted in the Department of Microbiology, Jawaharlal Nehru Medical College & Hospital, AMU, Aligarh, Uttar Pradesh, India, between October 2013 and December 2014. All the patients admitted in ICU with urinary catheter insertion for $\geq$48 hours were included in the study. Patients with any signs or symptoms of UTI before catheter insertion were excluded. The study protocol was approved by the Institutional Ethical Committee of Jawaharlal Nehru Medical College and Hospital, AMU, Aligarh.

Sample collection

Total 100 urine samples were collected in a sterile wide mouthed universal container taking aseptic precautions with a sterile disposable syringe after cleaning and clamping the catheter tube. All the urine samples were sent to the microbiology department for culture and sensitivity testing.

Direct microscopy

Wet mount examination was performed to look for the presence of pus cells, epithelial cells, red blood cells, crystals or microorganisms.

Bacterial identification

Semi-quantitative culture of urine samples was done by calibrated loop method (Leigh and Williams, 1964) on 5% sheep blood agar and MacConkey agar plates and incubated in aerobic conditions at 37°C for 24-48 hours. The urine cultures of colony count $\geq 10^5$ colony forming units (CFU)/mL with no more than two species of microorganisms were considered as positive for UTI and cultures showing growth of more than two types of bacteria were considered contaminated. Positive cultures identified were further subjected to various biochemical reactions (Collee *et al.*, 1996; Forbes *et al.*, 2007).

Antibiotic susceptibility testing

Antibiotic susceptibility testing was performed by Kirby-Bauer's disk diffusion method on Mueller-Hinton agar (Hi Media, Mumbai, India) as per the CLSI guidelines (Clinical Laboratory Standards Institute, 2014) using the commercially available antibiotic discs procured from Hi Media (Mumbai, India).

The antibiotics used for the Gram negative bacilli: amikacin (30µg), gentamicin (10µg), ceftriaxone (30µg), cefepime (30µg), cefixime (15µg), cefoperazone (75µg), cefoperazone-sulbactum (75/75µg), cefoxitin (30µg), levofloxacin (5µg), imipenem (10µg), piperacillin (100µg), piperacillin-tazobactum (100/10µg), ceftazidime (30µg), ceftazidime-clavulanic acid (30/10µg), tobramycin (10µg), and nitrofurantoin (300µg).

Anti-*Pseudomonas* antibiotics used were: amikacin (30µg), cefepime (30µg), ceftazidime (30µg), levofloxacin (5µg), tobramycin (10µg), sparfloxacin (5µg), nitrofurantoin (300µg), imipenem (10µg), piperacillin (100µg) and piperacillin-tazobactum (100/10µg).

The antibiotics used for the Gram positive cocci: Among the Gram positive cocci, the antibiotics tested for *Staphylococcus* species were amikacin (30µg), gentamicin (10µg), cefaclor (30µg), levofloxacin (5µg), moxifloxacin (5µg), cefazolin (30µg), oxacillin (1µg), cefoxitin (30µg), nitrofurantoin (300µg) and vancomycin (30µg).

For *Enterococcus* species, the antibiotics tested were amoxycillin (10µg), azithromycin (15µg), levofloxacin (5µg), cefazolin (30µg), moxifloxacin (5µg), high content gentamicin (120µg), high content streptomycin (300µg), nitrofurantoin (300µg) and vancomycin (30µg).

S. aureus ATCC 25923, *E. coli* ATCC 25922 and *P. aeruginosa* 25873 were used as control strains.

Detection of extended spectrum beta-lactamase (ESBL)

Screening of possible ESBL production was done by using ceftriaxone (30µg) and cefoperazone (75µg). Those isolates with zone diameters $\leq$ 25mm for ceftriaxone and <22mm for cefoperazone were subsequently confirmed for ESBL production. Confirmation was done by noting the potentiation of the activity of cefoperazone in the presence of cefoperazone- sulbactum. An increase in the diameter of $\geq$ 5mm was considered as positive for ESBL detection (Rizvi *et al.,* 2009).

Detection of derepressed AmpC beta lactamase

Isolates resistant to ceftriaxone (30µg), cefixime (15µg), cefoperazone (75µg), cefoperazone-sulbactam (75/75µg), and cefoxitin (30µg) were tested for AmpC production.

Induction of AmpC synthesis was based on the disc approximation assay using imipenem as inducer. Strains were considered stably derepressed when resistance was observed to all cephalosporins and cephalosporin inactivator (Rizvi *et al.,* 2009).

Detection of Metallo-beta-lactamase (MBL)

Detection of MBL was done by Modified Hodge test and Double Disc synergy test using EDTA. The method was as described by Lee *et al.* (2001).

Detection of Methicillin Resistant *Staphylococcus aureus* (MRSA)

All the *Staphylococcus aureus* isolates were tested phenotypically for methicillin resistance by disc diffusion tests using 1µg oxacillin and 30µg cefoxitin.

A zone diameter of ≤ 10 mm was considered resistant for oxacillin and the strains with a zone diameter of ≤19mm were considered resistant to cefoxitin (Bowers *et al.*, 2003).

Results and Discussion

Urinary tract infection (UTI) is one of the most frequent causes of nosocomial infections. Effective treatment of patients with UTIs commonly relies on the identification of the type of organisms and the selection of an effective antibiotic agent to the organism in question.

The pattern of antimicrobial resistance of bacteria producing UTI varies in different regions (Jones, 1996). Monitoring of antimicrobial susceptibility can aid clinicians for prescribing appropriate antibiotics and in prevention of development of drug resistance (Beyene and Tsegaye, 2011).

During the study period, a total of 100 urine samples of ICU patients were collected and processed, out of which 20(20.0%) showed significant bacterial growth (>10^5 CFU/ml) and 8(8.0%) showed growth of *Candida*, but some studies showed higher culture positivity (28.1%) (Al-Jebouri, 2006) and (32.14%) (Pooja Patel and Garala, 2014).

Prevalence of UTI was more in female 18(64.2%) than male 10(35.7%) patients (Table1). Similar prevalence were reported by Manjunath *et al.* (2011) and Jones, 1996. Females are more prone due to their shorter and wider urethra (Jones, 1996).

Table.1 Gender wise distribution of uropathogens (n=28)

Organisms	Male (%) (n=10)	Female (%) (n=18)
Escherichia coli	3(37.5)	5(62.5)
Citrobacter koseri	2(50.0)	2(50.0)
Staphylococcus aureus	1(33.3)	2(66.6)
Klebsiella oxytoca	0(0.00)	2(100)
Acinetobacter spp.	0(0.00)	1(100)
Pseudomonas aeruginosa	1(100)	0(0.00)
Enterococcus faecalis	1(100)	0(0.00)
BYLC (*Candida*)	2(25.0)	6(75.0)

Gram negative bacilli 16(80.0%) were the predominant bacterial isolates followed by Gram positive cocci 4(20.0%) which is consistent with another study (Al-Jebouri, 2006). Overall the most common bacterial isolates were *Escherichia coli* 8(40.0%) followed by *Citrobacter koseri* 4(20.0%), *Staphylococcus aureus* 3(15.0%), *Klebsiella oxytoca* 2(10.0%), *Acinetobacter* species 1(5.0%), *Pseudomonas aeruginosa* 1(5.0%), and *Enterococcus faecalis* 1(5.0%) as shown in Table 2. Our study showed that *E. coli* (40.0%) is still the most common cause of CAUTI in ICU patients. This finding is consistent with the other studies from India and other countries (Mehta *et al.*, 2007; Zaveri *et al.*, 2008; Kang *et al.*, 2011).

Table.2 Distribution of bacterial isolates in the samples (n=20)

Organisms	Number of isolates (n)	Percentage (%)
Escherichia coli	8	40.0
Citrobacter koseri	4	20.0
Staphylococcus aureus	3	15.0
Klebsiella oxytoca	2	10.0
Acinetobacter spp.	1	5.0
Pseudomonas aeruginosa	1	5.0
Enterococcus faecalis	1	5.0

Antibiotic sensititivity pattern of the uropathogens is shown in Table 3 and Table 4. Most of the Gram negative bacilli were sensitive to amikacin 12(75.0%) and nitrofurantoin 12(75.0%), while all Gram positive cocci were sensitive to vancomycin and cefazolin. Among the combination used, 7(43.7%) isolates were sensitive to cefoperazone-sulbactam and most of the isolates were sensitive to piperacillin-tazobactam 13(81.2%). Among 16 Gram negative isolates, 13(81.2%) were sensitive to imipenem and 3(18.7%) were resistant.

Amikacin and nitrofurantoin were found to be the most effective antibiotics against isolated strains especially *E. coli*. Both are cost effective and readily available in developing countries. The consistent and high-level susceptibility of *E. coli* to nitrofurantoin may be influenced by its narrow spectrum of activity, limited indication, narrow tissue distribution, and limited contact with bacteria outside the urinary tract (James *et al.,* 2002). The findings are in agreement with similar surveillance studies (Khameneh and Afshar, 2009; Sasirekha, 2013) and other Indian studies (Akram *et al.,* 2007; Manjunath *et al.,* 2011).

In our study, ESBL production was found in 4 (25.0%) strains (Figure 1). For initial screening of ESBL, cefoperazone/ cefoperazone-sulbactam proved to be more sensitive and specific than the combination (piperacillin/piperacillin-tazobactam) and far more superior to the combination (ceftazidime/ceftazidime-clavulanic acid). The advantage we had was that by administering the combination of cefoperazone/cefoperazone-sulbactam which is recommended for routine use in our hospital, we could accurately arrive at the status of ESBL production in these strains on day one of sensitivity testing. cefoperazone-sulbactam is the preferred drug due to its superior cure rates and lower cost compared to piperacillin-tazobactam in our set-up. In organisms producing both ESBLs and AmpC, clavulanate may induce hyperproduction of AmpC beta-lactamase, leading to hydrolysis of third-generation cephalosporins, thus masking any synergy arising from inhibition of ESBL (Bhattacharjee *et al.,* 2008). Sulbactam is unlikely to cause this problem and appears to be a better alternative to clavulanic acid, not only for detection, but also for treatment of ESBLs.

A total of 6 (37.5%) isolates were stably derepressed for AmpC production (Figure 1). Cefepime sensitivity in conjunction with cefoxitin resistance helped in identification of AmpC producers. Cefepime is more resistant to hydrolysis by AmpC than third generation cephalosporin and can also be used in ESBL detection. In this study, cefepime was placed 20 mm away from cefoperazone-sulbactam; however, it was not useful in detecting ESBLs, perhaps due to hyperproduction of AmpC or the presence of derepressed mutants.

.

MBL are enzymes belonging to Ambler's class B that can hydrolyze a wide variety of beta lactams, including penicillins, cephalosporins, cephamycins, and carbapenems except aztreonam (Hisaaki *et al.,* 2004; Krishna, 2010).

Double disc synergy test is simple to perform and highly sensitive in differentiating MBL-producing isolates (Irene Galani *et al.,* 2008). Thus, implementation of simple method using imipenem EDTA disk for MBL detection is quick, specific, sensitive and reproducible (Uma Chaudhary *et al.,* 2008). 3(18.7%) strains were MBL producers as shown in Figure 1. Production of MBL has tremendous therapeutic consequences since

these organisms also carry multidrug resistance genes and the only viable option remains the potentially toxic polymyxin B and colistin (Veenu gupta *et al.,* 2013).

The identification of the mecA gene is the most reliable method for detecting the MRSA isolates. In our study, the confirmation of the MRSA isolates was done by the oxacillin disc diffusion test which gave a correlative study with cefoxitin. The mecA positive isolates were detected with the cefoxitin disc (30 µg) in predicting oxacillin resistance (Felten *et al.,* 2002; Skov *et al.,* 2003; Cauwelier *et al.,* 2004). The prevalence of MRSA was 66.6%. Other studies in India reported 54.85% (Anupurba *et al.,* 2003) and 31.1% (Rajaduraipandi *et al.,* 2006) MRSA strains in ICU urine samples.

Phenotypic detection of these resistance mechanisms, though not confirmatory, is faster, far more cost effective, less labour intensive, and does not require a high level of technical expertise. It is, therefore, easy to perform on a daily basis, not only in resource-poor countries but also in developed countries. The outcome of phenotypic detection of resistance mechanisms undoubtedly will be better patient care.

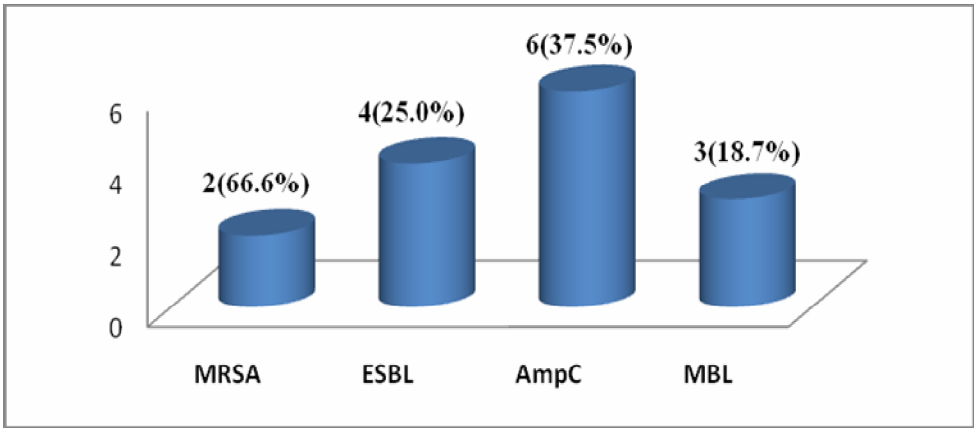
Table.3 Antimicrobial sensitivity pattern of Gram negative bacilli(n=16)

Antibiotics	E.coli n (%)	Citro. koseri n (%)	Kleb. Oxytoca n (%)	Acinetobacter spp. n (%)	P. aeruginosa n (%)
Amikacin	8 (100)	3(75.0)	0(0.00)	1(100)	0(0.00)
Gentamicin	5 (62.5)	4(100)	0(0.00)	----	----
Ceftriaxone	3 (37.5)	0(0.00)	0(0.00)	0(0.00)	----
Cefoperazone	3 (37.5)	0(0.00)	0(0.00)	0(0.00)	----
Cefoperazone-sulbactam	6 (75.0)	1(25.0)	0(0.00)	0(0.00)	----
Cefixime	3 (37.5)	0(0.00)	0(0.00)	0(0.00)	----
Cefipime	4 (50.0)	0(0.00)	0(0.00)	0(0.00)	0(0.00)
Cefoxitin	5 (62.5)	1(25.0)	0(0.00)	0(0.00)	----
Ceftazidime	6 (75.0)	0(0.00)	0(0.00)	0(0.00)	0(0.00)
Ceftazidime-clavulanic acid	7(87.5)	2(50.0)	0(0.00)	1(100)	----
Tobramycin	----	2(50.0)	-----	1(100)	1(100)
Sparfloxacin	----	-----	-----	-----	1(100)
Levofloxacin	5 (62.5)	2(50.0)	0(0.00)	0(0.00)	0(0.00)
Nitrofurantoin	7 (87.5)	3(75.0)	0(00.0)	1(100)	1(100)
Imipenem	8 (100)	3(75.0)	0(0.00)	1(100)	1(100)
Piperacillin	5(62.5)	2(50.0)	0(0.00)	0(0.00)	0(0.00)
Piperacillin-tazobactum	8 (100)	3(75.0)	0(0.00)	1(100)	1(100)

Table.4 Antimicrobial sensitivity pattern of Gram positive bacterial isolates (n=4)

Antibiotics	S.aureus n (%)	E.faecalis n (%)
Amikacin	3(100)	----
Azithromycin	1(33.3)	0(0.0)
Amoxycillin	-----	0(0.0)
Cefazolin	3(100)	1(100)
Cefaclor	1(33.3)	-----
Cefoxitin	1(33.3)	-----
Gentamicin	1(33.3)	-----
High content Gentamicin	-----	1(100)
High content Streptomycin	-----	1(100)
Levofloxacin	1(33.3)	0(0.00)
Moxifloxacin	2(66.6)	1(100)
Nitrofurantoin	2(66.6)	1(100)
Oxacillin	1(33.3)	----
Vancomycin	3(100)	1(100)

Figure.1 Antimicrobial resistance pattern of bacterial isolates



The present study on the bacteriological profiles of the CAUTI showed that the rate of such infections is high, even though it was within the reported range. The insertion of indwelling catheter needs careful prophylactic aseptic standards like stringent adherence to hand washing practices, formulation of antibiotic policy and surveillance activities. The high level of resistance among bacteria causing CAUTI limits the use of antimicrobial agents for therapy. Spread of MDR isolates is a continuous threat in hospitalized patients. Reduction of HAIs and antimicrobial resistance is both a challenge and goal of all ICU's around the world. Continuous surveillance for multidrug resistant strains is necessary to prescribe appropriate empirical treatment and also to assess effectiveness of infection control practices.

It is concluded that in our hospital Gram negative bacteria were more frequently involved in CAUTI than Gram positive bacteria. *E. coli* was the most common cause of CAUTI in our hospital and nitrofurantoin and amikacin were the most effective antibiotics against this infection.

As most of the ICU patients cannot take oral antibiotic and predominant isolates were from Enterobacteriaecae, so for empirical therapy, amikacin should be given till culture and sensitivity results are awaited.

Acknowledgements

The authors would like to thank the personnel of Jawaharlal Nehru Medical College and Hospital, Laboratory and Faculty of Microbiology, Aligarh Muslim University for their cooperation.

References

Akram, M., Shahid, M., Khan, A.U. 2007. Etiology and antibiotic resistance patterns of community acquired urinary tract infections in JNMC Hospital Aligarh, India. *Ann. Clin. Microbiol. Antimicrob.,* 6: 4.

Al-Jebouri, O.A.H. 2006. The relationship between urinary caliculi types and urinary tract infections among patients in Tikrit District. M. Sc. Thesis, College of Medicine, Tikrit University, Tikrit.

Anupurba, S., Sen, M.R., Nath, G., Sharma, B.M., Gulati, A.K., Mohapatra, T.M. 2003. Prevalence of methicillin resistant *Staphylococcus aureus* in a tertiary referral hospital in eastern Uttar Pradesh. *Indian J. Med. Microbiol.,* 21(1): 49–51.

Beyene, G., Tsegaye, W. 2011. Bacterial uropathogens in urinary tract infection and antibiotic susceptibility pattern in jimma university specialized hospital, southwest Ethiopia. *Ethiop. J. Health Sci.,* 21: 141–6. *http://dx.doi.org/10.4314/ejhs.v21i2.69055*.

Bhattacharjee, A., Sen, M.R., Prakash, P., Anupurba, S. 2008. Role of beta-lactamase inhibitors in enterobacterial isolates producing extended-spectrum beta lactamases. *J. Antibact. Chemother.,* 61: 309–314.

Bowers, K.M., Wren, M.W.D., Shetty, N.P. 2003. Screening for methicilin resistance in *Staphylococcus aureus* and coagulase-negative *Staphylococci*: an evaluation of three selective media and Mastlex- MRSA latex agglutination. *Br. J. Biomed. Sci.,* 60: 71–74.

Cauwelier, B., Gordts, B., Descheemaecker, P. 2004. Evaluation of the disc diffusion method with cefoxitin (30 µg) for the detection of methicillin resistant *Staphylococcus aureus*. *Eur. J. Clin. Microbiol. Infect. Dis.,* 23: 389–92.

Celik, I., Inci, N., Denk, A., Sevim, E., Yasar, D., Yasar, M. 2005.Prevalence of Hospital acquired infections in anesthesiology intensive care unit. *Firat. Tip. Dergisi,* 10(3): 132–135.

Clinical Laboratory Standards Institutes, 2014. Performance Standards for antimicrobial susceptibility testing, XXI International Supplement (M100-S21). National Committee for Clinical Laboratory Standards, Wayne, Pennsylvania, USA.

Collee, J.G., Fraser, A.G., Marmian, B.P., Simmons, A. 1996. Mackie and McCartney practical medical microbiology, 14 edn, Standard ed. Churchill Livingstone, London. (Reprinted 1999).

Felten, A., Grandry, B., Lagrange, P.H. 2002. Evaluation of three techniques

for the detection of low level methicillin resistant *S. aureus* (MRSA): a disc diffusion method with cefoxitin and moxalactum, the Vitek-2 system, and the MRSA screen latex agglutination test. *J. Clin. Microbiol.*, 40: 2766–71.

Forbes, B.A., Sahm, D.F., Weissfeld, A.S. 2007. Bailey and Scott's diagnostic microbiology, 12th edn. Mosby Elsevier, St. Louis.

Garibaldi, R.A., Brodine, S., Matsumiya, S.1981. Infections among patients in nursing homes: policies, prevalence, problems. *N. Engl. J. Med.*, 305: 731–5.

Hisaaki Nishio, Masaru Komatsu, Naohiro Shibata. 2004. Metallo-beta-lactamase producing Gram-negative Bacilli: laboratory-based surveillance in cooperation with 13 clinical laboratories in the Kinki region of Japan. *J. Clini. Microbiol.*, 42(11): 5256–5263.

Irene Galani, Panagiota Danai Rekatsina, Despina Hatzaki. 2008. Evaluation of different laboratory tests for the detection of metallo-beta-lactamase production in Enterobacteriaceae. *J. Antimicro. Chemothera.*, 61: 548–553.

James, A.K., Laurie, J., Clyde, T. 2002. Trends in Antimicrobial Resistance among urinary tract infection isolates of *Escherichia coli* from female outpatients in the United States. *Antimicrob. Agents Chemother.*, 46(8): 2540–2545.

Jones, RN. 1996. Impact of changing pathogens and antimicrobial susceptibility pattern in treatment of serious infections in hospitalized patients. *Am. J. Med.*, 100(Suppl.6A): S3–12.

Kang, C.I., Chung, D.R., Son, J.S., Ko, K.S., Peck, K.R., Song, J.H. 2011. Clinical significance of nosocomial acquisition in urinary tract-related bacteremia caused by Gram negative bacilli. *Am. J. Infect. Control*, 39(2): 135–140.

Khameneh, Z.R., Afshar, A.T. 2009. Antimicrobial susceptibility pattern of urinary tract pathogens. *Saudi J. Kidney Dis. Transpl.*, 20: 251–3.

Krishna, B.V.S.2010. New Delhi metallobeta-lactamases: A wake up call for microbiologists. *Indian J. Clini. Microbiol.*, 28(3): 265–66.

Lee, K.Y., Chong, H.B., Shin, Y.A., Yong, K.D., Yum, J.H. 2001. Modified Hodge test and EDTA disc synergy tests to screen metallo beta lactamase producing strains of *Pseudomonas* and *Acinetobacter* species. *Clin. Microbiol. Infect.*, 7: 88–91.

Leigh, D.A., Williams, J.D. 1964. Method for the detection of significant bacteriuria in large groups of patients. *J. Clin. Pathol.*, 17: 498–503.

Manjunath, G.N., Prakash, R., Vamseedhar, A., Shetty, K. 2011. Changing trends in the spectrum of antimicrobial drug resiatance pattern of uropathogens isolated from hospitals and community patients with urinary tract infections in Tumkur and Bangalore. *Int. J. Biol. Med. Res.*, 2: 504–7.

Mehta, A., Rosenthal, B.D., Mehta, Y., Chakravarthy, M., Todi, S.K., Sen, M. 2007. Device associated nosocomial infection rates in intensive care units of seven Indian cities (INICC). *J. Hosp. Infect.*, 67: 168–74.

Platt, R., Polk, B.F., Murdock, B., Rosner, B. 1986. Risk factors for nosocomial urinary tract infection. *Am. J. Epidemiol.*, 124: 977–85.

Pooja Patel, Garala,R.N. 2014. Bacteriological profile and antibiotic susceptibility pattern (antibiogram) of urinary tract infections in paediatric patients. *J. Res. Med. Dent. Sci.*, 2(1).

Rajaduraipandi, K., Mani, K.R., Panneerselvam, K., Mani, M., Bhaskar, M., Manikandan, P. 2006. Prevalence and antimicrobial susceptibility patterns of methicillin resistant *Staphylococcus aureus*: A multicentre study. *Indian J. Med. Microbiol.*, 24(1): 34–38

Richards, M.J., Edwards, J.R., Culver, D.H., Gaynes, R.P. 1999. Nosocomial infections in medical intensive care units in the United States. National Nosocomial Infections Surveillance System. *Crit. Care Med.,* 27: 887–92.

Rizvi, M., Fatima, N., Rashid, M. 2009. Extended spectrum AmpC and metallo-beta-lactamases in *Serratia* and *Citrobacter* spp. in a disc approximation assay. *J. Infect. Dev. Ctries.*, 3(4): 285–94.

Saint, S., Lipsky, B.A. 1999. Preventing catheter-related bacteriuria: should we? Can we? How? *Arch. Intern. Med.*, 159: 800–8.

Sasirekha, B. 2013. Prevalence of ESBL, AMPC B-lactamases and MRSA among uropathogens and its antibiogram. *EXCLI. J.*, 12: 81–8.

Skov, R., Smyth, R., Clausen, M. 2003. Evaluation of a cefoxitin 30 µg disc on isosensitest agar for the detection of methicillin resistant *Staphylococcus aureus*. *J. Antimicrob. Chemother.*, 52: 204–07.

Stark, R.P., Maki, D.G. 1984. Bacteriuria in the catheterized patient. *N. Engl. J. Med.*, 311: 560–4.

Tasseau, F., Chupin, A., Pradier, C., Villers, D., Baron, D., Nicolas, F. 1990. Study of incidence and risk factors of nosocomial urinary tract infection in patients with indwelling urinary catheter in intensive care units. *Agressologie,* 31: 503–4.

Tullu, M.S., Deshmukh, C.T., Baveja, S.M. 1998. Bacterial profile, antimicrobial susceptibility pattern in catheter related nosocomial infections. *J. Postgrad. Med.,* 44: 7–13.

Uma Chaudhary, Hemlata Bhaskar, Madhu Sharma, 2008. ImipenemEDTA disk method for rapid identification of metallo-beta-lactamase producing Gram-negative bacteria. *Indian. J. Med. Res.,* 127: 406–407.

Vatopoulos, A.C., Kalapothaki, V., Legakis, N.J. 1999. Bacterial resistance to ciprofloxacin in Greece: results from the National Electronic Surveillance System. Greek network for the surveillance of antimicrobial resistance. *Emerg. Infect. Dis.,* 5:471—6.

Veenu gupta, Deepinder china, Amarjeet kaur, 2013. Incidence of metallo-beta-lactamase (MBL) producing nonfermenters isolated from urine samples in ICU patients. *Int. J. Pharm. Bio. Sci.,* 4(2): (B)580–585.

Wagenlehner, F.M., Loibl, E., Vogel, H., Naber, K.G. 2006. Incidence of nosocomial urinary tract infections on a surgical intensive care unit and implications for management. *Int. J. Antimicrob. Agents*, 28: 86–90.

Wenzel, R.P., Osterman, C.A., Hunting, K.J., Gwaltney, J.M. 1976. Hospital acquired infections. Part II. Infection rates by site, service and common procedures in a university hospital. *Am. J. Epidemiol.*, 104: 645–51.

Zaveri, J.R., Patel, S.M., Nayak, S.N., Desai, K., Patel, P. 2008. A study on bacteriological profile and drug sensitivity and resistance pattern of isolates of the patients admitted in ICUs of a tertiary care hospital in Ahmadabad. *NJMR*, 2: 330–4.