Study Of Drug Resistance In Isolates From ICU Infections In A Tertiary Care Hospital

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Abstract: **Background:** Nosocomial Infections are an important cause of morbidity, mortality and economic problems especially in intensive care units (ICUs). **Aim:** This study was conducted to estimate the clinical and bacteriological profile and their antibiotic sensitivity testing in ICU infected patient. **Materials and methods:** 245 patients clinically diagnosed to have infections in ICU were studied prospectively in the Department of Microbiology, Indira Gandhi Govt. Medical College from Sep. 2009- Dec. 2011. Depending on sites of infections various samples were collected and processed as per the standard guidelines. The isolates were subjected to antimicrobial susceptibility testing by Kirby Bauer disc diffusion method as per CLSI 2012 guideline. **Results:** The incidence of pneumonia, blood stream infection and urinary tract infections was 61.6%, 20.1% and 11% respectively. *P. aeruginosa* (16.3%) was the commonest isolate in ICU infection followed by *A. baumannii* (13.5%) and *K. pneumoniae* (11.8%) with maximum sensitivity to imipenem, piperacillin tazobactum and amikacin. All *Staphylococcus* and *Enterococcus* species were sensitive to vancomycin and linezolid. Gram-negative pathogens acquired from ICU patients in our settings show high resistance to antibiotics. **Conclusion:** Regular monitoring of the pattern of resistance of common pathogens in the ICUs is critical in planning the best routines for empirical treatment of infectious patients. [Kombade S NJIRM 2014; 5(2) :60-65]

Key words: ICU infections, multidrug resistance

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Introduction: Infection caused by multidrug-resistant (MDR) bacteria constitutes a serious problem for intensive care unit (ICU) patients throughout the world.[1] Antibiotic resistance in ICU is increasing at an alarming rate, leading to increased morbidity, mortality and treatment costs in ICU setting.[2] The study of infections in the ICU setting has been well-documented in India, both retrospectively and prospectively.[3] Keeping a track of ICU infections is important for outbreak surveillance, to formulate antibiotic policies and to nip any emerging outbreak early before, it leads to serious consequences.[3] This prospective study was carried out to know the pattern of microbial aetiological agents and their antimicrobial resistance in ICU infected patients in a tertiary care hospital.

Material and Methods: The study was carried out in the Department of Microbiology, Indira Gandhi Government Medical College Nagpur. ICU admitted patients clinically diagnosed to have infections were included in the study.[4] Depending on sites of infections, various samples were collected and processed as per the standard guidelines.[5] The isolates were identified and subjected to antimicrobial susceptibility testing by Kirby Bauer disc diffusion method as per CLSI 2011 guideline.[6] All the isolates belonging to enterobacteriaceae group were tested for extended spectrum β–lactamase (ESBL) and Amp C β –lactamase production. ESBL production was tested by CLSI phenotypic confirmatory method.[6] AmpC β - lactamase production, was tested using cefotaxime (30 µg) and cefoxitin (30 µg) placed at a distance of 1.5 cm. Flattening of zone of inhibition produced by cefotaxime on the side nearest the cefoxitin disc were considered as Amp C β - lactamase producer strains.[6] All Enterobacteriaceae, *Pseudomona*s and *Acinetobacter* isolates found resistant to imipenem (I) were tested for metallo-β- lactamase (MBL) production by EDTA disc synergy test.[6,7]

Result: Out of 2,529 ICU admissions during the study period, 245 (9.7%) patients were clinically diagnosed to have infections. Maximum infected patients were in the age group of 51-60 years.
Aetiological agents of different infections are shown in Table 1.

In our study, pneumonia (61.6%) was the commonest ICU infection. Other infections were blood stream infection (BSI), urinary tract Infection (UTI) and surgical site tissue infections (SSTI). *P. aeruginosa* (16.3%) was the commonest isolate in ICU infection followed by *A. baumannii* (13.5%)

Antimicrobial sensitivity of gram negative bacterial isolates is shown in Table 2. β- lactamase profile in gram negative bacilli is shown in Table 3. In our study maximum 21.8% enterobacteriaceae isolates were found to be ESBL producers while only 7.3% were Amp C β- lactamase. In our study maximum 16.7% gram negative bacilli were found to be MBL producers.

Table1. Microbial aetiology of the various infections in ICU

Isolates	Pneumonia (n=151)	BSI (n=49)	UTI (n=27)	SSTI (n=10)	Meningitis (n=2)	Intra-abdominal infection (n=6)	Total n=245 (%)
Gram negative bacilli							**132 (53.9)**
							18 (7.3)
E. coli	8	0	8	1	0	1	29 (11.8)
K. pneumoniae	23	1	1	4	0	0	1 (0.4)
K. oxytoca	1	0	0	0	0	0	5 (2.0)
C. freundii	2	0	0	2	0	1	1 (0.4)
E. cloacae	1	0	0	0	0	0	1 (0.4)
Pr. mirabilis	0	0	0	1	0	0	40 (16.3)
P. aeruginosa	36	3	1	0	0	0	33 (13.5)
A. baumanii	32	1	0	0	0	0	3 (1.2)
A. lwoffi	3	0	0	0	0	0	1 (0.4)
A. hemolyticus	0	1	0	0	0	0	
Gram positive cocci							**15 (6.1)**
S. aureus	9	0	0	0	0	0	9 (3.7)
S. epidermidis	0	0	2	0	0	0	2 (0.8)
S. pneumoniae	2	0	0	0	0	0	2 (0.8)
E. faecalis	0	0	2	0	0	0	2 (0.8)
Fungus							**2 (0.8)**
C. albicans	-	0	2	0	0	0	2 (0.8)

Table 2. Antimicrobial sensitivity of gram negative bacterial isolates

Drugs	*Klebsiella spp* n=30 (%)	*E. coli* n=18 (%)	*C. freundii* n=5 (%)	*E. cloacae* n=1 (%)	*Pr. mirabilis* n=1 (%)	*Acinetobacter spp* n=37 (%)	*P. aeruginosa* n=40 (%)
Ampicillin	0	0	0	0	0	-	-
Amoxyclav	0	1 (5.5)	0	0	0	-	-
Cephazoline	0	1 (5.5)	0	0	0	-	-
Cefuroxime	0	2 (11.1)	0	0	0	-	-
Cefoxitin	2 (6.6)	2 (11.1)	1 (20)	0	0	-	-
Cefotaxime	0	2 (11.1)	3 (60.0)	0	0	3(8.1)	10(25.0)
Ceftazidime	4 (13.8)	4 (22.2)	3 (60.0)	0	0	2(6.1)	17(42.5)
Cefipime	0	2 (11.1)	3 (60.0)	0	0	3(9.1)	14(35.0)
Piperacillin	0	4 (22.2)	3(60.0)	1(100)	0	6(16.2)	17(42.5)
Piperacillin + tazobactum	13 (43.3)	7 (38.8)	5(100)	1(100)	0	21(56.7)	34(85.0)
Imipenem	27 (90.0)	18(100)	5(100)	1(100)	1(100)	22(59.4)	36(90.0)
Aztreonam	1 (3.4)	2 (11.1)	0	0	0	0	0
Gentamicin	10 (33.3)	10 (55.5)	4 (80.0)	1(100	1(100)	7(18.9)	19(47.5)
Amikacin	11 (36.6)	12 (66.6)	4 (80.0)	1(100)	1(100)	15(40.5)	26(65.0)

Tobramycin	2 (6.6)	5 (27.7)	5(100)	0	0	10(27.0)	11(27.5)
Netillin	4 (13.3)	5 (27.7)	3(60)	0	0	7(18.9)	11(27.5)
Ciprofloxacin	9 (30)	2 (11.1)	2 (40.0)	1(100)	1(100)	7(18.9)	14(35.0)
Cotrimoxazole*	0	2/8 (25.0)	-	-	-	1(3.0)	0

Table 3. β- lactamases profile in gram negative bacilli

Gram negative bacilli	ESBL	AMP C	MBL
	Enterobacteriaceae (n=55)		All GNB (n=132)
E. coli (n=18)	4 (22.2%)	2 (11.1%)	0
K. pneumoniae (n=29)	7 (24.1%)	2 (6.9%)	3 (10.3%)
K. oxytoca (n=1)	0	0	0
C. freundii (n=5)	1 (20.0%)	0	0
E. cloacae (n=1)	0	0	0
Pr. Mirabillis (n=1)	0	0	0
P. aeruginosa (n=40)	-	-	4 (10.0%)
A. baumannii (n=33)	-	-	13 (39.4%)
A. lwoffi (n=3)	-	-	2 (66.7%)
A. hemolyticus (n=1)	-	-	0
Total (%)	12 (21.8%)	4 (7.3%)	22 (16.7%)

Table 4 explains the sensitivity pattern of the gram positive isolates. All the isolated staphylococci and enterococci were found to be sensitive to vancomycin, and linezolid.

Drugs	*S. aureus* n=9 (%)	*S.epidermidis* n=2 (%)	*E. faecalis* n=2 (%)	*S.pneumoniae* n=2 (%)	Total- n=15 (%) gram positive cocci
Penicillin G	0	1 (50.0)	0	2 (100.0)	3 (20.0)
Cefoxitin	4(44.4)	1 (50.0)	-	-	5/11 (45.5)
Erythromycin**	0	-	-	1(50.0)	1/11(9.1)
Gentamicin	7(77.7)	2 (100.0)	1 (50.0)	-	10/13 (76.9)
Amikacin	7(77.7)	2 (100.0)	-	-	9/11 (81.8)
Ciprofloxacin	3(33.3)	1 (50.0)	0	2 (100.0)	6 (40.0)
Vancomycin	9(100.0)	2 (100.0)	2(100.0)	2 (100.0)	15 (100.0)
Linezolid	9(100.0)	2 (100.0)	2(100.0)	2 (100.0)	15 (100.0)
Chloramphenicol**	3(33.3)	-	-	0	3/11 (27.3)
Tetracycline	0	0	0	1(50.0)	1 (6.7)
Nitrofurantoin*	-	1/2 (50.0)	2/2(100.0)	-	3/4 (75.00)
Norfloxacin*	-	1/2 (50.0)	1/2(50.00)	-	2/4 (50.00)
Cotrimoxazole*	3(33.3)	0	-	1(50.0)	4/13 (30.8)
Clindamycin**	2(22.2)	-	-	-	2/9 (22.2)

* These urinary antibiotics were tested only in urinary isolates, **Rifampicin, chloramphenicol, clindamycin, erythromycin - these antibiotics were not tested in urinary isolates.

Discussion: Nosocomial infections in ICUs have become increasingly problematic in recent years.[11] An infection in ICU is 4-5 times greater than in general ward.[8] The infection rates in the ICU varied with the admitting services.[3] The rate of ICU infections in our study was found to be 9.7%.The prevalence of ICU infections in other study is estimated to be between 2.3%-49.2%.[9] The rate of infection among ICU patients is within the reported range which might be due to factors such as exposure to invasive procedures, underlying diseases conditions, duration of stay in the ICU, infection sites and multidrug resistant pathogens.

The most frequent infection in the present study was pneumonia (61.6%) followed by BSI (20.0%), UTI (11.0%) and SSTI (4.1%), intraabdominal infection (2.4%) and meningitis (0.8%). Our study reported similar pattern of infection in ICU as pneumonia, followed by BSI, UTI and SSTI as Meric et al,[10] Hughes AJ et al[11]and Yehia et al.[12] However Hassanzadeh et al[2] in 2009 and Shaikh et al[13] in 2008 had reported UTI as the most frequent infection, followed by pneumonia and BSI. The occurrence of pneumonia is high in our study; the reason might be high utilization of invasive procedures like mechanical ventilation in our set up.

In the present study, *P. aeruginosa* (16.3%) was the predominant organism in pneumonia patients followed by *Acinetobacter* spp, (15.1%) *and K. pneumoniae* (12.2%) as shown in Table 1. Jamshidi et al[14] reported *P. aeruginosa* as commonest isolate while other reported *S. aureus* as the commonest aetiological agent.[10] *P. aeruginosa* was the commonest aetiological agent in BSI in our study which is similar to study done by Jamshidi et al.[14] In our study, *E. coli* (29.6%) was the commonest aetiological agent in UTI cases followed by *S. epidermidis* and *E. faecalis* as shown in Table 1. The result is comparable to the studies conducted by Jamshidi et al, [14] Meric et al[10].

Emerging multidrug resistance infection in ICU is a global pandemic and India is no exception to it.[15] Indiscriminate usage of antibiotics and poor infection control practices are the common cause for the rise of multidrug resistant micro-organisms in the ICU.[16] Most of the enterobacteriaceae isolates in our study showed resistance to 1st, 2nd and 3rd generation cephalosporin and tetracycline while maximum sensitivity was found to imipenem (94.5%) and piperacillin-tazobactum (47.3%). In our study 72.7% enterobacteriaceae isolates showed resistance to ciprofloxacin. The resistance of ICU-acquired pathogens against ciprofloxacin might be attributed to its high usage in inpatient and outpatient settings. In the present study (Table 2) among enterobacteriaceae isolates, resistance to amikacin (47.3%) was less frequent than other aminoglycosides (resistance to gentamicin 53%, tobramycin 79% and netillin 91% respectively). Shehabi and Baadran[1] had observed lower resistance to amikacin and gentamicin among *E. coli* (25% and 33% respectively). Hassanzadeh et al[2] had reported 77.8% and 27.3% susceptibility to amikacin in *Klebsiella* spp. and *E. coli.*

In our study 21.8% enterobacteriaceae isolates were ESBL producers while 7.1% were AmpC β-lactamase producers as shown in Table 3. Our observation is similar to the study conducted by Kucukates et al[17] in 2005 and Singhal et al[18] in 2008, who reported 21.1% and 21.8% ESBL production in enterobacteriacae isolates in their studies. Singhal et al[18] had reported 8% AmpC production in his study while Wattal et al[16] in 2010 and Joseph et al[19] in 2010 had reported a high Amp C production (70% and 33.3% respectively).The incidence of ESBL producing strains among clinical isolates has been steadily increasing over the past few years resulting in limitation of therapeutic options. The routine susceptibility tests done by clinical laboratories fail to detect ESBL production so there is a need to do regular screening in laboratory.

In our study, 16.7% GNB isolates were MBL producers (Table 4). Maximum MBL production was seen in *Acinetobacter* spp. (40.5%) followed by *P. aeruginosa* (10.0%) and *K. pneumoniae* (10.3%) isolates. Joseph et al[19] and John et al[20] had obtained 20% and 20.8% MBL producers in nonfermenters in their studies. Wattal et al[16] and Gopalkrishnan et al[21] reported high MBL production (80% and 40% isolates respectively) in their studies. Clinical microbiology laboratories should be extremely vigilant for the imminent detection of MBL in imipenem resistant

Pseudomonas spp. and *Acinetobacter* spp. *A. baumannii* was the second commonest isolate in ICU infection which was drug resistant emerging pathogen in ICU.

MRSA has become a serious problem in ICU because of development of multidrug resistance. We found 66.7% MRSA isolates and 22.2% inducible clindamycin resistant *S. aureus* isolates. Moran et al[22] also reported higher incidence of MRSA in their study. There was an alarming increased incidence of NIs caused by multi drug resistant gram negative bacilli and MRSA in our study. All staphylococci and enterococci were found to be sensitive to vancomycin and linezolid.

Conclusion: ESBL along with MBL are increasing rampantly. It is essential to have an awareness of the prevailing infection in the ICU, the antibiotic likely to work against these infections, a good awareness of any newly emerging pathogen and the early detection of outbreaks. The micro-organisms that cause infections in one part may not be the same in other parts. Thus local data is required to help to formulate antibiotic policies and to nip any emerging outbreak early before, it leads to serious consequences. Antibiotic resistant bacteria are becoming an increasingly difficult problem in ICUs. Hence one of the areas of interest in infections in the ICU is the trend in the antibiotic susceptibility pattern of common pathogens in the ICU.

This study gives an insight into the incidence of pattern of ICU infection and demands to institute various interventional strategies to prevent these infections. There is an urgent need for clinical studies like ours to evaluate strategies for the prevention and management of such infections in critically ill patients. We believe regular monitoring of the pattern of resistance of common pathogens in the ICUs is critical in planning the best routines for empirical treatment of infectious patients.

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