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"STUDY OF INFECTIONS IN MEDICAL INTENSIVE CARE UNIT IN A TERTIARY CARE HOSPITAL"

Dr. Ratna R Prasad* — Resident, Department of Microbiology, Indira Gandhi Government Medical College, Nagpur *Corresponding Author

Dr. Sharmila S Raut — Professor & Head, Department of Microbiology, Indira Gandhi Government Medical College, Nagpur

ABSTRACT Patients admitted in Intensive Care Units are at great risk for acquiring nosocomial infections; also there is frequent use of invasive devices. We conducted a study to isolate and identify the organisms causing infections in ICU and their antimicrobial resistance pattern. Clinically diagnosed cases of infection after 48 hours of admission in the Medical ICU were included in study. Depending on type of infections various samples were collected and processed as per standard guidelines. VAP was most common infection followed by CAUTI and CLABSI. Their rate (per 1000 device days) being 32.04, 7.62 and 12.25. Among the 185 isolates, Gram negative organisms predominated. *A.baumannii* was the most frequent isolate followed by *K.pneumoniae, P.aeruginosa, S.aureus, E.coli, C.tropicalis, C.albicans etc.* Majority of organisms were highly resistant to common antibiotics used. Problem of multidrug-resistance can be prevented by rational use of antibiotics after standardised antibiotic susceptibility testing.

KEYWORDS : VAP, CAUTI, CLABSI

INTRODUCTION

Patients admitted in Intensive Care Units (ICU) are at great risk for acquiring nosocomial infections. The overall rate of ICU infection is 51.4% and in Asia it is 52.6%.(1) Prevalence of infection in Indian ICU ranges from 4.4% - 33.3%.(2,3,4) While the use of antimicrobial agents has revolutionised our ability to treat infections, it is associated inevitably with the risk of development and spread of antimicrobial resistance. Hospital acquired infections are difficult and more expensive to treat, prolong the hospital stay, and associated with increased patient morbidity and mortality.(4) The prevention, control, and treatment of ICU infections demands thorough knowledge of infection incidence and infection site rates, occurrence rate of organisms, their antimicrobial resistance profile, and potential risk for infection-associated mortality.(5)

Keeping in mind the above factors we conducted a study with the following objectives:

1) To isolate and identify the organisms causing infections in ICU
2) To study their antimicrobial resistance pattern

MATERIAL AND METHODS

The study was carried out in Department of Microbiology at a tertiary care institute, from August 2014 to July 2016. Clinically diagnosed cases of infection after 48 hours of admission in the Medical ICU were included in the study.(6) Depending on type of infections various samples were collected and processed as per the standard guidelines.(7)

SPECIMENS COLLECTED -

- Sputum, endotracheal tube aspirate, tracheostomy tube aspirate in ventilator associated pneumonia (VAP)
- Blood and catheter tip in catheter associated blood stream infection(CLABSI)
- Urine in Catheter associated urinary tract infection (CAUTI)

The isolates were identified on basis of colony morphology, microscopy and biochemical tests.(8) The isolates were subjected to antimicrobial susceptibility testing by Kirby Bauer disc diffusion method(9) as per CLSI guidelines.(10)

STATISTICAL ANALYSIS: Age was presented as mean ± 2SD.

Statistical software EpiInfo™ version 7.2 was used for statistical analysis.

OBSERVATIONS AND RESULTS

Table 1: Age and sex wise distribution (n=427)

Age	Male	Female	Total
10 – 20	12	16	28(6.56)
20 – 30	48	39	87(20.37)
30 – 40	43	60	**103 (24.12)**
40 – 50	53	21	74 (17.33)
50 – 60	45	15	60 (14.05)
60 – 70	48	13	61 (14.29)
70 – 80	13	1	14 (3.28)
TOTAL	**262**	**165**	**427 (100)**

Table 2: Distribution of Infection

Type of infection	Culture positive n=185 (%)	Culture negative n=242	Total n=427
Pneumonia	146(78.92)	166	312
VAP	**121**(65.41)	88	**209**
Other Pneumonia	**25**(13.51)	78	**103**
CAUTI	29(15.67)	43	**72**
CLABSI	10(5.41)	33	**43**

Table 3: Distribution of isolates (n=185)

Isolates	VAP	Other Pneumonia	CAUTI	CLABSI	Total n=185 (%)
Gram negative					
Enterobacteriacea	4	0	5	0	9 (4.87)
E.coli	15	5	3	1	24 (12.98)
K.pneumoniae	3	1	1	0	5 (2.70)
K.oxytoca	2	0	3	0	5 (2.70)
C.koseri	1	0	0	0	1 (0.54)
P.mirabilis					
Non-fermenter					
A.baumannii	56	6	1	0	63 (34.06)
A.lwoffii	2	0	2	0	4 (2.16)
A.nosocomialis	1	0	0	0	1 (0.54)
P.aeruginosa	14	3	1	1	19 (10.27)
B.cepacia	3	0	0	2	5 (2.70)
S.maltophilia	1	1	0	0	2 (1.08)
Gram positive					
S.aureus	18	1	2	1	22 (11.89)
S.epidermidis	0	0	0	4	4 (2.16)
S.pneumoniae	0	2	0	1	3 (1.62)
E.faecalis	0	0	1	0	1 (0.54)
Fungal isolates					
C.albicans	0	3	4	0	7 (3.78)
C.tropicalis	1	2	6	0	9 (4.87)
C.krusei	0	1	0	0	1 (0.54)
Total growth	121 (65.41)	25 (13.51)	29 (15.67)	10 (5.41)	185

Table 4: Antibiotic resistance pattern of Enterobacteriaceae (n=44)							
Antibiotic	*E.coli n=9*	*K.pneumoniae n=24*	*K.oxytoca n=5*	*C.koseri n=3*	*C.frundii n=2*	*P.mirabilis n=1*	Total (n=44)
AMP	9 (100)	24 (100)	5 (100)	3 (100)	2 (100)	1 (100)	44 (100)
AMC	9 (100)	24 (100)	5 (100)	3 (100)	2 (100)	1 (100)	44 (100)
PIT	4 (44.44)	12 (50)	2 (40)	1 (33.33)	1 (50)	1 (100)	21 (47.73)
CZ	8 (88.89)	15 (62.50)	4 (80)	3 (100)	1 (50)	1 (100)	32 (72.73)
CXM	8 (88.89)	16 (66.67)	5 (100)	1 (33.33)	1 (50)	1 (100)	32 (72.73)
CX	5 (55.56)	14 (58.33)	4 (80.00)	3 (100)	1 (50)	1 (100)	28 (63.64)
CTX	8 (88.89)	16 (66.67)	5 (100)	3 (100)	1 (50)	1 (100)	34 (77.27)
CAZ	8 (88.89)	15 (62.50)	4 (80.00)	3 (100)	1 (50)	1 (100)	32 (72.73)
CPM	6 (66.67)	13 (54.17)	3 (60.00)	3 (100)	1 (50)	1 (100)	27 (61.36)
IMP	2 (22.22)	5 (20.83)	2 (40.00)	1 (33.33)	0 (00)	1 (100)	19 (26.38)
GEN	7 (77.78)	12 (50)	2 (40.00)	2 (66.67)	1 (50)	1 (100)	25 (56.82)
AMK	5 (55.56)	7 (29.17)	0 (00.00)	2 (66.67)	1 (50)	1 (100.00)	16 (36.36)
TOB	4 (44.44)	9 (37.50)	2 (40.00)	1 (33.33)	1 (50)	1 (100.00)	18 (40.91)
NET	4 (44.44)	9 (37.50)	2 (40.00)	1 (33.33)	1 (50)	1 (100.00)	18 (40.91)
TET	7 (77.78)	12 (50.00)	2 (40.00)	1 (33.33)	2 (100)	1 (100.00)	25(56.82)
CIP	2 (50)	12 (57.14)	2 (50)	0 (00)	1 (50)	1 (100.00)	18 (56.25)
LEVO	1 (25)	6 (28.57)	0 (00.00)	0 (00.00)	0 (00)	1 (100.00)	8 (25.00)
COT	7 (77.78)	16 (66.67)	5 (100.0)	3 (100.0)	1(50)	1 (100.00)	33 (75.00)
AT	8 (88.89)	15 (62.50)	3 (60.00)	3 (100.0)	1 (50)	1 (100.00)	31 (70.45)

Table 5: Antibiotic resistance pattern of non fermentative bacteria (n=94)						
Antibiotic	***A.baumannii* n=63**	***A.lwoffii* n=4**	***A.nosocomialis* n=1**	***P.aeruginosa* n=19**	***B.cepacia* n=5**	***S.maltophilia* n=2**
PIT	59 (93.65)	1 (25.00)	1 (100.00)	9 (47.37)	--	--
CAZ	62 (98.41)	0 (00)	1 (100.00)	11 (57.89)	3 (60.00)	0 (00.00)
CTX	62 (98.41)	4 (100.00)	1 (100.00)	--	--	--
CPM	61 (96.83)	2 (50.00)	1 (100.00)	10 (52.63)	--	--
AZT	–	–	--	11 (57.89)	--	--
IMP	50 (79.37)	0 (00.00)	1 (100.00)	76 (31.58)	--	--
MERO	--	--	--	--	1 (20.00)	--
GEN	56 (88.89)	1 (25.00)	1 (100.00)	7 (36.84)	--	--
AMK	51 (80.95)	1 (16.67)	1 (33.33)	6 (31.58)	--	--
TOB	50 (79.37)	0 (00.00)	1 (100.00)	6 (31.58)	--	--
CIP	60 (95.24)	1 (25.00)	1 (100.00)	10 (52.63)	--	--
LEVO	45 (71.43)	0 (00.00)	1 (100.00)	2 (10.53)	1 (20.00)	0 (00.00)
COT	54 (85.71)	1 (25.00)	1 (100.00)	--	2 (40.00)	0 (00.00)
CL	0** (00.00)	0** (00.00)	0** (00.00)	0 (00.00)	--	--
PB	0 (00.00)	0 (00.00)	0 (00.00)	0 (00.00)	--	--
CHL*	--	--	--	--	2 (40.00)	0 (00.00)

*Not for urinary isolates as per CLSI 2014 guidelines.
** MIC done by E-strip

Table 6: Antibiotic resistance pattern of Gram positive bacteria (n=30)				
Antibiotic	**S.aureus n=22**	**S.epidermidis n=4**	**S.pneumoniae n=3**	**E.faecalis n=1**
P	22 (100.00)	4 (100.00)	1 (33.33)	1 (100.00)
AMP	--	--	--	1 (100.00)
CXM	--	--	2 (66.67)	--
CX	16 (72.73)	2 (50.00)	--	--
CTX	--	--	2 (66.67)	--
CPM	--	--	1 (33.33)	--
IPM	--	--	0 (00.00)	--
GEN	9 (40.91)	0 (00.00)	--	--
TET	14 (63.64)	0 (00.00)	1 (33.33)	0 (00.00)
CIP	14 (63.64)	0 (00.00)	--	0 (00.00)
LEVO	3 (13.64)	0 (00.00)	0 (00.00)	0 (00.00)
COT	11 (50.00)	0 (00.00)	3 (100.00)	--
E	17 (77.27)	2 (50.00)	2 (66.67)	--
CD	17 (77.27)	2 (50.00)	0 (00.00)	--
LZ	1 (4.55)	0 (00.00)	0 (00.00)	0 (00.00)
VA	0 (00.00)	0 (00.00)	0 (00.00)	0 (00.00)
HLG	--	--	--	0 (00.00)

DISCUSSION:

In our study males predominated 262(61.45%) over females 165(38.55%), the male to female ratio being 1.59:1**(Table1)**. Maximum infected patients (24.07%) were in age group of 30-40 years(24.07%) . **The mean age of the patients was 40.48 ± 15.39** years. Our observation is similar to Shaikh *et.al.* who reported maximum infected patients in younger age group of 16-29 years (38.15%) followed by 30-39 years (26.81%).(3) Sahu MK *et.al.* also reported lower mean age i.e. 20.0 ± 25.43 years; while EPIC II study, and Mythri H *et.al.* reported maximum infected patients in the older age group and the mean age was 60.7, 56 years respectively.(1,11,12)

Out of total 427 cases, majority were of VAP 209 (48.94%) and other pneumonia 103 (24.12%); CAUTI 72(16.86%) was the second most common infection followed by CLABSI 43(10.07%).

The presence of an endotracheal(ET) tube disrupts normal ciliary clearance of bronchial secretions and impairs patient's capacity to cough. Secretions therefore pool above ET tube cuff and intermittently seep around folds in the cuff. Factors that increase the risk of aspiration increase the likelihood of infection. These include (13) -

- Mechanical factors: e.g. emergency intubation, reintubation,

duration of intubation, supine positioning, enteral feeding by using orogastric or nasogastric tubes, use of paralytic agents, and underinflation of endotracheal tube cuff
- Factors that affect mental status such as central nervous system disease, level of consciousness, and level of sedation
- Factors that increase bacterial bioburden in upper respiratory and orogastric tracts, such as duration of hospitalization, nasogastric intubation, prolonged antibiotic exposures, and the use of proton pump inhibitors or other gastric acid suppressants
- Factors that increase handling or breaking of the ventilator circuit, such as inhaled beta-agonist therapy
- Patient factors such as age, pre-existing lung disease, and severity of illness

In the present study a total of 121 laboratory confirmed VAP **(Table 2)** was reported and the rate was found to be 32.04/1000 ventilator-patient days. Our results are in agreement with that of Singh S, Chaturvedi R *et.al*.(14); and Dasgupta S *et.al*.(15) their VAP rate being 32/1000 and 26.6/1000 ventilator days respectively. While a prospective, observational study by Dutta P *et.al*.(16) reported 6.15% VAP. and Mehta *et.al.* reported 10.46 VAP per 1000 ventilator-days.(2)

Catheter associated urinary tract infection (CAUTI) is an important cause of morbidity and mortality in Indian subjects, affecting all age groups.(17) The duration of catheterization is the most important risk factor for the development of CA-bacteriuria. Other risk factor include the lack of systemic antimicrobial therapy, female sex, meatal colonization with uropathogens, microbial colonization of the drainage bag, catheter insertion outside the operating room, catheter care violations, absence of use of a drip chamber, rapidly fatal underlying illness, older age, diabetes mellitus, and elevated serum creatinine at the time of catheterization.(18) The source of microorganisms causing CAUTI can be endogenous, typically via meatal, rectal, or vaginal colonization, or exogenous, such as via contaminated hands of healthcare personnel or equipment. Microbial pathogens can enter the urinary tract either by the extraluminal route, via migration along the outside of the catheter in the periurethral mucous sheath, or by the intraluminal route, via movement along the internal lumen of the catheter from a contaminated collection bag or catheter-drainage tube junction.(19)

In our study there were 29 laboratory confirmed cases of CAUTI**(Table 2)** and the rate was 7.62/1000 catherter-patient days. Our rates matched with Dasgupta S *et.al*., Priya Dutta *et.al* and Singh S, Chaturvedi R et.al., their CAUTI rate being 7.44/1000 9.08/1000 and 9/1000 catheter days.(14,15,16) A prospective surveillance study conducted by Mehta *et.al.*(2) showed that catheter-associated urinary tract infection (CAUTI) rate was low with rate of 1.41 per 1000 catheter-days. Another prospective, site specific surveillance study showed low CAUTI rate of 0.6 per 1000 catheter days.(20)

Intravascular catheters are indispensable in modern-day medical practice, particularly in intensive care units (ICUs). The central venous catheters are often inserted for administration of fluids, blood products, medications, nutritional solutions and hemodynamic monitoring.(21) Although such catheters provide necessary vascular access, their use puts patients at risk for local and systemic infectious complications, including local site infection, CLABSI, septic thrombophlebitis, endocarditis, and other metastatic infections (e.g., lung abscess, brain abscess, osteomyelitis, and endophthalmitis).(22)

In our study there were 10 laboratory confirmed cases of CLABSI**(Table 2)** and rate was 12.25/1000 central line- patient days.Our results are similar to Priya Dutta *et.al.,* and Singh S, Chaturvedi R *et.al*., their CLABSI rate being 13.86/1000 and 16/1000 central venous catheter days(14,16) ; while Dasgupta S *et.al.* Mehta A *et.al.* reported lower rate of 2.46/1000 and 7.92/1000 central line days.(2,15)

The precise pattern of causative organisms, whether bacterial or fungal, varies across countries and between ICUs according to the patient's site of infection, antibiotic protocols, infection control practice, local ecology and resistance patterns.(23) As shown in **table 3**, among the 185 isolates, Gram negative organisms predominated with *A.baumannii* (34.06%) being most common with highest frequency from cases of VAP. Second most common isolate was *K.pneumoniae* (12.98%), followed by *P.aeruginosa* (10.27%) and *E.coli* (4.87%). *S.aureus* (11.89%) was the most common Gram positive isolate, followed by *S.epidermidis* (2.16%), *S.pneumoniae* (1.62%), *E.faecalis* (0.54%). Among the fungal isolates *C.tropicalis* (4.87%) was most common, isolated from cases of CAUTI, followed by *C.albicans* (3.78%), and *C.krusei* (0.54%).

The predominance of *Acinetobacter* in our study matches with that of Pradhan N *et.al.*(24) They reported *Acinetobacter* (34.5%), followed by *Pseudomonas* (32.8%), *Klebsiella* (13.9%), E Coli (12.1%), *Citrobacter* (5%) Candida (1.7%). Study done by Ghanshani R *et.al.* also reported predominance of Gram negative bacteria which included *A.baumannii* (20.9%), *K.pneumoniae* (19.7%), *E.coli* (18.3%), and *P.aeruginosa* (14.0%) while the Gram positive bacteria were *S.aureus* (8.2%) and *Enterococcus* species (5.0%).(25) In a study by Singh AK *et. al.*, most frequent isolates causing RTIs were *Klebsiella* (24.48%), followed by *Proteus* (18.33%) and *E. coli*(12.24%).(26)

Antibiotic resistance pattern of *Enterobacteriaceae* (Table 4)

High resistance was shown to, 2nd and 3rd generation cephalosporins while complete resistance was shown to Ampicillin, Amoxyclav and 1st generation Cephalosporins. Maximum *E. coli* were sensitive to Imipenem (77.78%), and Levofloxacin (75%), while *K. pneumoniae* isolates were sensitive to Imipenem(79.17%), Levofloxacin(71.43%), Amikacin(70.83%).

The extensive use of Cephalosporins in our ICU may have resulted in high rate of resistance to this group of antimicrobials. Singh AK *et.al.* in their study reported that the Gram negative enteric bacilli were uniformly resistant to betalactam antibiotics as well as betalactam-betalactamase inhibitors while resistance to Ciprofloxacin and Ceftriaxone ranged from 50-100% and 25-83.3% respectively.(26) Shalini S *et.al.* in their study reported *K.pneumoniae* had the maximum sensitivity to Imipenem and Amikacin.(27)

Antibiotic resistance pattern of non fermentative bacteria (Table 5)

A.baumannii was highly resistant to Cefotaxime(98.41%), Ceftazidime (98.41%), Cefepime (96.83%), Piperacillin-tazobactum(93.65%), Ciprofloxacin (95.24%), being sensitive only to Colistin and Polymixin B. The major problem encountered by ICU clinicians relates to readily transferable antibiotic resistance expressed by *Acinetobacter* which has a propensity to readily develop resistance to second and third generation antibiotics such as Cefotaxime, Ciprofloxacin, and giving rise to therapeutic problems. As higher generation antibiotics are being developed to overcome problem of resistance against available antibiotics, bacteria are developing mechanisms to resist newer antimicrobials.(28)

P.aeruginosa was mostly resistant to Ceftazidime, Aztreonam (57.89%), followed by, Cefepime, Ciprofloxacin (52.63%), Piperacillin-tazobactum (47.37) while they were 100% sensitive to Colistin, and Tigecycline followed by Levofloxacin(89.47%) and Imipenem (68.42%). The respiratory tract is the most important source of *Pseudomonas* isolates. Nosocomial isolated strains of *Pseudomonas* and *Acinetobacter* spp., are frequently resistant to a broad range of antibiotics. Antimicrobial resistance develops rapidly under selection pressure, and multiple mechanisms are responsible: hyper-production of enzymes, such as beta-lactamases and DNA-gyrases, active efflux pumps, and permeability changes. The National Nosocomial Infection Surveillance (NNIS) study showed 27% fluoroquinolone-resistance in *Pseudomonas* isolates in the ICU and 18% to Imipenem. Furthermore, cross-resistance between fluoroquinolones and other antibiotic agents, such as piperacillin-tazobactam, ceftazidime, and tobramycin is a frequent problem.(29) *Pseudomonas aeruginosa* had the maximum sensitivity to Imipenem and Ceftazidime as reported by Shalini S *et.al*. in their study.(30)

Antibiotic resistance pattern of Gram positive bacteria(Table 6)

S.aureus showed maximum resistance to Penicillin (100%) followed by Tetracyclin, Ciprofloxacin (63.64%), and Cotrimoxazole (50%). All *S.aureus* isolates were sensitive to Linezolid, Vancomycin and Teicoplanin, similar to study done by Pattanayak C *et.al.*(31) In another study *Staphylococci* were 100% resistant to Penicillin and Tetracycline, 80% to Cotrimoxazole, 60% to Erythromycin and Gentamicin and 40% to Amikacin.(26)

Nosocomial infections represent an important cause of morbidity and mortality in this population. Among the 427 cases included in our study, 422 recovered while 6 (1.410%) succumbed to death. ICU-acquired infections increases the hospital mortality. Ylipalosaari P

et.al. in their study showed that the attributable mortality from ICU-acquired infection was 19.6% in the patients without infection on admission and 18.6% in the patients infected on admission.(32) EPIC II also reported higher mortality rates (25.3%) in ICU infected patients.(1)

Intensive care units carry a high risk for nosocomial infections, contributing to an increase in morbidity, mortality, and healthcare costs. Because the pipeline of new antibiotics is running dry, major efforts are needed to slow down the rising problem of multidrug resistance. In order to limit the incidence of ICU nosocomial infections, healthcare providers should adopt aggressive infection control measures. The Centres for Disease Control recommends four strategies for health care settings which includes prevention of infections, proper diagnosis and treatment of infections with rational use of antimicrobials and prevention of transmission.(1,29)

CONCLUSION:

ICU is the epicentre of infections as the patients here are critically ill and there is frequent use of invasive devices. These infections are associated with an increase in morbidity, mortality and healthcare costs. There is an additional problem of multidrug-resistant pathogens and their spread due to new mutations, selection of resistant strains, and suboptimal measures to control the infection. It becomes a challenge for the physicians to treat the infections caused by such resistant organisms.

Infections in ICU are preventable by implementing measures such as hand hygiene, conducting organized surveillance, having a trained infection control team, a system for reporting infection rates to practicing clinicians, and rational use of antibiotics after standardised antibiotic susceptibility testing.

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