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Original Research Article

Clinical profile, bacterial profile and outcomes in an intensive care unit of a tertiary care hospital in south India: one year study

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ABSTRACT

Background: Infections still remain as one of the major cause of mortality in low and lower- middle-income countries as reported by Global Burden of Diseases study. Intensive care units (ICU) are a major source of infections in tertiary care hospitals. Widespread multi-drug resistant gram positive and gram negative bacterial isolates are also associated with infections in ICU. A hospital based epidemiological study was to determine the risk factors; bacterial isolates, antibiotic sensitivity and outcomes in ICU patients.
Methods: This prospective study was done at Narayana Medical College and Hospital for 12 months from 1st February 2015 to 31st January 2016. All the risk factors were noted. Patient's outcome noted as death, recovery and transfer to palliative care. Data entry and analysis performed in Microsoft excel, p valve < 0.001 was considered significant.
Results: Three hundred and thirty patients were included in the study (age: 56.16±15 years, 57.6% males). 159 (48.2%) were direct admissions, 103 (31.2%) were transfers from other hospitals. Major cause of admission was neural (29.1%) followed by cardiovascular (21.8%). HTN (52.4%) was major co-morbidity followed by type-2 DM (47.3%). 51.9% culture positivity (n = 539) was observed with sputum 83.6% and blood 24.2%. Gram-negative pathogens were predominant which includes *Acinetobacter baumanii* (13.8%), *Escherichia coli* (20%), *Klebsiella pneumoniae* (14.3%), *Pseudomonas aeruginosa* (9%), *Enterobacter aerogenes* (5.1%). Candida Sp and MRSA, VRE were isolated. In the study 255(77.3%) recovered, 38(11.5%) progressed to death and 37(11.2%) transferred to palliative care. Higher mortality was noticed with *Acinetobacter baumani* (81.6%).
Conclusions: High prevalence of gram-negative bacterial infections and multi-drug resistant isolates was noted in Indian ICUs.

Keywords: *Acinetobacter baumanii*, APACHE-2, Gram-negative infections, Intensive care units, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*

INTRODUCTION

Infections still remain as one of the major cause of mortality in low and lower- middle-income countries as reported by Global Burden of Diseases study.[1] Multiple predisposing factors like poverty, illiteracy, increasing old age, rapid urbanization and emerging viral and bacterial infections are held responsible for the cause of mortality.[2,3] In India infections still remain a major cause of mortality and morbidity.4Intensive care units (ICU) are a major source of infections in tertiary care hospitals.[5-7] Studies in North America and Europe have reported that primary infections (at the time of admission in ICU) and secondary infections (nosocomial, device-related infections) are more common in ICU.[8,9] Prevalence of ICU infections varies between 45% to 58% 10 and incidence rates between 30 to 35%.[11,12] Factors associated with increased risk of infections in ICU are

intrinsic risk factors associated with the patient, invasive medical devices, overcrowding and animate objects which act as reservoirs for bacterial isolates. Higher incidence and prevalence of infections in ICU are associated with higher age, higher APACHE-2 score (Acute physiology and chronic health evaluation) and associated co morbid conditions. Widespread multi-drug resistant gram positive and gram negative bacterial isolates are also associated with infections in ICU. Reports on the emergence of metallo β-lactamase (MBL) and carbapenemase-producing gram negative bacterial isolates, methicillin-resistant *Staphylococcus aureus* (MRSA), Vancomycin-resistant enterococci (VRE) are posing a serious threat in outcomes of patients in ICU.

The present study was sought to determine the prevalence of infections, clinical risk factors, bacterial isolates and antibiotic profile, and outcomes of patients in ICU of a tertiary care hospital. Understanding the prevalence and clinical risk factors would help to develop a strategic mechanism and planning appropriate interventions to curtail the emergence and spread of multi-drug resistant isolates in an ICU further helping in empiric therapy. These interventions and strategies could lead to the successful outcome of the patients from ICU.

METHODS

A prospective epidemiological study was performed in Central Microbiology laboratory of Narayana General and Super specialty hospital, a tertiary care hospital in Andhra Pradesh, India. Institutional ethical committee and research committee of the hospital approved the study. Three hundred and thirty patients who were admitted to the ICU from 1st February 2015 to 31st January 2016 for 12 months were included in the study. Patient's individual consent was not obtained as only the data was taken in the study. A predesigned case report form containing all the demographic data (age, sex, socio-economic status etc) and clinical data (APACHE -2 scores, cause of admission, co-morbidities etc) of the enrolled patients were noted and entered centrally by medical personnel. The admission strategy was clearly cited as per the protocols of ICU. Patients who had surgery 4 weeks prior date of admission were considered as surgical admission.

Traumatic admissions were considered as patients admitting directly or as a result of traumatic complication 30 days prior to admission. All the rest of admissions were considered as a medical cause. Clinically suspected infection was diagnosed at the discretion of attending physician. APACHE-2 score was calculated using all the physiological and laboratory variables. Other associated co-morbidities like HIV, malignancies, anemia, cirrhosis etc. were noted in addition to diabetes, hypertension, chronic renal disease, Heart failure, coronary heart disease and COPD.

For each patient admitted in the ICU blood and urine for culture, sensitivity was done definitely along with other routine investigations. However, specimens like Sputum / Endotracheal secretions, CSF (cerebro spinal fluid), ascitic fluid, pleural fluid were sent for culture sensitivity based on the necessity when required. All the specimens were collected using standard procedures during admission, processed and isolation, identification; antibiotic susceptibility testing was performed using standard clinical laboratory standard institute (CLSI) guidelines.[13]APACHE-2 score was calculated using all the physiological and laboratory variables. The outcome of each patient was recorded as death, palliative care/transfer to other hospitals and recovery.

All the data in the case report form was entered in Microsoft excel worksheet and analyzed. Categorical variables are reported as number and percentages and to test the association between the variables, Chi-square test was used .Continuous variables were presented as mean±SD when variables were normally distributed. To test the mean difference between three groups ANOVA test was used. All the P values having less than 0.05 were considered as statistically significant.

RESULTS

Three hundred and thirty patients were studied during the study period. The mean age of the subjects was 56.16±15 years with 190 (57.6%) males and 140 (42.4%) females. Direct admissions were 159 (48.2%), 103 (31.2%) were transferred from other hospitals and 68 (20.6%) were from wards of the same hospital.

The neural cause was the major reason for admission with 29.1% followed in order by cardiovascular (21.8%), respiratory (20.9%), GIT (10.9%), trauma (10.3%) and last renal with 7%. 47.9% were smokers, 41.5% alcoholics, and 23.9% were both. Most important comorbidities were diabetes (47.3%), hypertension (52.4%), coronary heart disease (42.4%), chronic renal failure (37%) and COPD (37%).9.4% of the subjects were free from comorbidities (Table 1).

Mean APACHE-2 score at the time of admission was 22.12±7.69 (median - 22). 47% of subjects were having the score in the range of 20-29 and 206 (62.4%) were on antibiotics prior to ICU admission.

Of 1039 total specimens sent for isolation of pathogens 539(51.9%) were culture positive with 83.6% from sputum, 64.85% from urine, 23.6% from CSF and 24.2% from blood. A total of 545 bacterial and fungal isolates were isolated from the different type of specimens send from 330 patients.

Gram-negative bacteria were the predominant and included *Acinetobacter baumanii* (13.7%), *Escherichia coli* (20%), *Klebsiella pneumoniae* (14.3%), *Pseudomonas aeruginosa* (9%), *Enterobacter aerogenes*

(5.1%) and gram positive bacteria include Coagulase negative *staphylococci* (13.0%), MRSA (7.1%), *Streptococcus pneumoniae* (2.0%) and *Enterococcus faecalis* (3.1%). Candida sp were 68(12.5%) in number (Table 2).

Table 1: Clinical profile and outcomes of patients admitted into ICU.

Parameters	Patients (n=330) (%)	Parameters	Patients (n=330) (%)
Age (years)		**Source of admission**	
20-30	16 (4.8)	Direct	159 (48.2)
31-40	34 (10.3)	Transfer	103 (31.2)
41-50	65 (19.7)	Ward	68 (20.6)
51-60	80 (24.2)	Reason for ICU admission	
61-70	81 (24.5)	Cardio vascular	72 (21.8)
71-80	39 (11.8)	Digestive/ liver	36 (10.9)
>80	15 (4.5)	Neural	96 (29.1)
Gender		Renal	23 (7.0)
Male	190 (57.6)	Respiratory	69 (20.9)
Female	140 (42.4)	Trauma	34 (10.3)
Smoking/alcohol abuse		APACHE- 2 score	
Smoking	158 (47.9)	<10	23 (7)
Alcohol abuse	137 (41.5)	11-19	85 (25.8)
Co morbidities:		20-29	155 (47)
Hypertension	173 (52.4)	30-39	61 (18.5)
Diabetes	156 (47.3)	>40	6 (1.8)
Chronic renal failure	122 (37)	Duration of stay In ICU	
Chronic obstructive disease	122 (37)	<5 days	126 (38.2)
Coronary heart disease	140 (42.4)	6 -10 days	192 (58.2)
None morbidities	31 (9.4)	>10 days	12 (3.6)
H/O antibiotics prior admission		Outcome	
Administered	206 (62.4)	Death	38 (11.5)
Not administered	124 (37.6)	Ward/recovery	255 (77.3)
		Palliative transfer	37 (11.2)

Table 2: Distribution of isolates from different specimens of ICU.

Isolate	Number of organisms						
	Sputum	**Urine**	**CSF**	**Ascitic fluid**	**Pleural fluid**	**Blood**	Total
MRSA	22	10	1	0	0	6	39
CONS	28	18	7	0	2	16	71
Pneumococci	10	0	0	0	1	0	11
Enterococci	0	15	0	2	0	0	17
Acinetobacterbaumanii	44	18	1	0	0	12	75
Escherichia coli	30	56	8	4	0	11	109
Klebsiellapneumoniae	31	36	2	0	0	9	78
Enterobacteraerogenes	8	15	1	0	0	4	28
Pseudomonas aeruginosa	14	14	6	3	0	12	49
Candida sp	27	32	0	0	0	9	68
Total	**214**	**214**	**26**	**9**	**3**	**79**	**545**

The majority of the isolates were from respiratory and urinary specimens, 214(39.3%) from each followed in order by blood (14.5%), CSF (4.8%), Ascitic fluid (1.65%) and pleural fluid (0.55%) (Table 2). Antibiotic sensitivity pattern of the isolates revealed majority are resistant to commonly used antibiotics. Maximum sensitivity was noted to colistin, polymixin-b and tigecycline among gram-negative bacteria.All the gram-positive bacteria were susceptible to linezolid, vancomycin and resistance were noted among 15% to clindamycin. Maximum resistance was noted to Penicillin among gram-positive bacteria. (Table 3, 4).

Table 3: Antibiogram of gram-negative isolates.

Antibiotic	ACB (n=75) % of sensitivity	E.coli (n=109) % of sensitivity	KPN (n=78) % of sensitivity	PSAE (n = 49) % of sensitivity	EBR (n= 28) % of sensitivity
Imipenem	94.7	89.9	83.4	81.6	89.2
Meropenem	90.7	88	82.05	79.6	89.2
Cefoperazone+sulbactam	82.7	83.5	79.5	75.5	82.1
Piperacillin+tazobactam	88	82.5	89.7	91.8	92.8
Colistin	98.7	100	100	98	100
Polymyxin-b	98.7	100	100	93.8	100
Tigecycline	97.3	99.08	100	100	100

ACB: *Acinetobacterbaumanii*; E.coli: *Escherichia coli*; KPN: *Klebsiellapneumoniae*; PSAE*: Pseudomonas aeruginosa*; EBR: *Enterobacteraerogens*

Table 4: Antibiogram of gram positive isolates.

Antibiotic	CONS (n=71)% of sensitivity	MRSA (n=39) % of sensitivity	Enterococci (n=17) % of sensitivity	Pneumococci (n=11) % of sensitivity
Penicillin	30.9	0	88.2	81.8
Vancomycin	100	97.4	100	100
Linezolid	100	100	100	100
Clindamycin	92.9	87.2	82.3	100

CONS: *Coagulase Negative staphylococcus*; MRSA: *methicillin-resistant staphylococcus aureus.*

Table 5: Associations between outcomes and clinical profiles.

Parameters	Recovery	Palliative	Death	Total	P value
Age (years)± SD	52.49±13.40	69.14±8.82	68.00±17.02	56.15±15.01	P <0.05
Gender					
Males	148	22	20	190.00	P <0.05
	44.85%	6.7%	6.0%	57.6%	
Females	107	15	18	140.00	
	32.4%	4.55%	5.45%	42.4%	
Patten of admission					
Direct	116	21	22	159	P <0.05
	35.15%	6.4%	6.7%	48.2%	
Transfer from another hospital	82	12	9	103	
	24.85%	3.6%	2.7%	31.2%	
Transfer from same hospital ward	57	4	7	68	
	17.3%	1.2%	2.1%	20.6%	
Cause of admission					
CVS	56	9	7	72	P <0.05
	17%	2.7%	2.1%	21.8%	
GIT	31	1	4	36	
	9.4%	0.30%	1.2%	10.9%	
Neuro	62	16	18	96	
	18.8%	4.85%	5.45%	29.1%	
Renal	21	1	1	23	
	6.4%	0.30%	0.30%	7%	
Respiratory	52	10	7	69	
	15.8%	3.0%	2.1%	20.9%	
Trauma	33	0	1	34	
	10.00%	0.00%	0.30%	10.30%	
APACHE-2 score	20.24±6.7	25.81±7.3	31.16±6.85	22.12±7.7	P <0.05
Length of ICU stay (days)	6.00±1.85	6.81±1.7	8.89±2.15	6.19±1.90	P <0.05

Of the 330 subjects in the study 255 (77.3%) recovered, 38 (11.5%) progressed to death and 37 (11.2%) transferred to palliative care. Out of 38 cases progressed to death 20(52.6%) were males and 18(47.4%) were females. The mean±SD duration of stay in the hospital was 6.2±1.9 days. Significant risk factors associated with mortality overall included increased duration of stay in the ICU, more APACHE score, old age, direct admission, neural cause, multiple comorbidities and gram-negative bacterial infections ($p < 0.05$) (Table 5).

Greater mortality was observed in patients from whom *Acinetobacter baumanii* was isolated (81.6%) followed in order by *Escherichia coli* (60.5%), *Pseudomonas aeruginosa* (39.5%), *Klebsiella pneumonia* (23.7%), Candida sp (5/38) and least by *Enterobacter aerogenes*, CONS and MRSA (3/38).

DISCUSSION

Our study clearly demonstrates the overall incidence of infections in an intensive care unit, associated risk factors and outcomes of the patients admitted in ICU. Risk factors for the development of infections in patients of the study were prior antibiotic administration, comorbidities, high APACHE-2 score and old age. Resistance was noted to carbapenems among gram-negative bacteria and MRSA was commonly isolated. The risk factors identified in the study were important because they determine the outcome of the patient admitted to ICU and helps in monitoring for better patient care.

The incidence of infections in ICU is variable globally and more in low-income countries. International Nosocomial Infection Control Consortium (INICC) reported a high rate of mortality in a surveillance study in 422 ICUs of 36 countries in Latin America, Asia, Europe and Africa.[14] MOSAICS study in medical ICUs of Asian countries reported a mortality of 44.5%.[15] A prospective study by INDICAP in Indian medical ICUs also reported a high mortality in different parts of the country.[16] Our study reported a mortality of 11.5% and 11.2% were transferred to palliative care/ transferred to other hospitals. Patients transferred to palliative care were evaluated by the physician and indicated as unlikely to survive. Transfer of terminally ill patients to palliative care is a common practice in low-income countries. However, data regarding outcomes of patients transferred to palliative care are limited in India except one study in Mumbai which is a limitation of our study.[17]

Bacteriological profiles in ICUs are variable from place to place and from region to region. In our study gram-negative pathogens were common which coincides with many of the studies globally. Our findings were consistent with many of the studies indicating in ICUs, *Acinetobacter baumanii, Escherichia coli, Klebsiella pneumoniae, Pseudomonas. aeruginosa, Staphylococcus aureus* are the predominant pathogens.[18,19] All the gram negative isolates of the study displayed a high level of resistance to β-lactam inhibitors indicating production of extended spectrum β-lactamases. Our study identified an increasing trend in resistance towards carbapenems by *Acinetobacter sp, Pseudomonas Sp and Klebsiella sp.* similar pattern of change in resistance is observed in studies of Gladstone P et al, Trivedi TH et al mostly by Acinetobacter sp in ICUs. However detailed gene identification was not done in the study which is a limitation but reporting incidence suggests the presence of NDM-1 gene, this is similar to reports from other ICUs in India by Kumaraswamy et al and Deshpande P et al.[20,21]

In our study, 62.4% of patients were on antibiotics prior to admission in ICU. This explains the irrational and unnecessary prescription of antibiotics in spite of a clear antibiotic policy and control of third and fourth generation cephalosporin antibiotic usage in the hospital. The increase in the prevalence of multidrug resistance among gram-negative isolates of ICU is an important concern. In our study, the major reasons for mortality are increased age, more APACHE-2 score, comorbidities, more length of stay in ICU and gram-negative isolates. These findings are on par with most of the studies in India and abroad. However GARP (Global Antibiotic resistance partnership) guidelines recommend a multipronged strategy to reduce antibiotic resistance in middle and low-income countries.[22]

CONCLUSION

The study clearly demonstrates a significantly high number of infections in ICU. Risk factors for the development of infections are old age, more APACHE-2 score, long duration of stay in ICU, and multiple comorbidities. Multi-drug resistant gram negative bacterial pathogens were isolated. Identification of risk factors in the study helps in the development of empirical antibiotic treatment protocol and management strategies in ICUs. This suggests that appropriate and effective microbiological surveillance practices should be practiced in for prevention of these infections in ICU. Effective formulations of National, International and hospital specific guidelines are required for rational use of 3rd and 4th generation cephalosporins, carbapenems and β-lactam inhibitors.

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