

Original Research Article

Spectrum of microbial infection in an Intensive Care Unit: a single centre tertiary care experience in Southern Indian state of Karnataka

Shruthi S., Balachandra S. Bhat*

Department of Medicine, Yenepoya medical college hospital, Deralakatte, Mangalore, Karnataka, India

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***Correspondence:**

Dr. Balachandra S. Bhat,

E-mail: dr.baluymc@gmail.com

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ABSTRACT

Background: There is an increased incidence of hospital acquired infection, especially in ICU setting, the most common being ICU acquired pneumonia which increases the morbidity, mortality, prolongs hospital stay and consuming more resources. Microbial etiology of intensive care unit (ICU)-acquired pneumonia (ICUAP) determines antibiotic treatment and outcomes which vary from centre to centre. Hence, a study of risk factors, clinical profile of patient, microorganisms and their resistance patterns to antibiotics are important for the diagnosis, prognosis of patient with ICU acquired pneumonia and also in the prevention of the same.

Methods: Patients with ICUAP confirmed microbiologically were prospectively compared according to identification of 1 (monomicrobial) or more (polymicrobial) potentially pathogenic microorganism. Patients without microbiological confirmation were excluded from the study. We assessed clinical characteristics, microbiology and outcome variables.

Results: In the present study 60 patients with ICU Pneumonia were included out of which 50 (83%) had monomicrobial infection. Most common organism isolated in mono microbial infection was *Klebsiella* species (26%), followed by *Acinetobacter* species (25%), out of which 20 percent was multidrug resistant. Multi-drug resistance was similarly frequent in both groups. Outcome variables like initial response to the empiric treatment, length of stay and mortality were similar in both monomicrobial and polymicrobial pneumonia. Mortality rates were higher with higher pneumonia scores (p value <0.002) and with multi organ dysfunction (p <0.008) irrespective of mono microbial or poly microbial infection.

Conclusions: In this study mono microbial infection was more than polymicrobial, the most common organism being *Klebsiella* species followed by *Acinetobacter* species. When empiric treatment is frequently appropriate, mortality rates were higher with higher pneumonia scores and MODS. In our study polymicrobial aetiology did not influence the outcome of ICUAP.

Keywords: Hospital-acquired pneumonia, Intensive care unit acquired pneumonia, Multi Organ Dysfunction, Ventilator-acquired pneumonia

INTRODUCTION

The most common infection in the intensive care unit is hospital acquired pneumonia which encompasses two different entities: pneumonia associated with mechanical

ventilation (ventilator-associated pneumonia or VAP) and severe pneumonia developed during the hospital stay.¹ Intensive care unit (ICU)-acquired pneumonia (ICUAP) is the pneumonia which develops after 48 hours of ICU admission, while ventilator acquired pneumonia refers to

the pneumonia occurring more than 48-72hr after endotracheal intubation.² In the ICU, HAP is associated with an approximate mortality rate of 20 percent. ICUAP is the infection in critically-ill patients which accounts for prolonged mechanical ventilation and length of stay in ICU, and poor outcome.³ The common complication of endotracheal intubation is Ventilator associated pneumonia (VAP) leading to high morbidity and mortality.⁴ Even though the direct impact of this infection on mortality remains debated, it is nonetheless associated with increased morbidity through increased duration of mechanical ventilation (or decrease in ventilator-free days) and increased ICU and hospital length-of-stay.⁵ As a result, HAP is also responsible for an over use of healthcare resources (ventilation, ICU and hospital beds and resources). Finally, it is associated with increased costs related to hospital stay.⁶

Accurate and timely initiation of appropriate antibiotics is necessary to prevent mortality in ICU patients, especially in critically ill patients, with septic shock.^{7,8} Based on observations, since delay in initiating adequate antibiotic therapy for VAP is associated with poor clinical outcomes, initial therapy should be started immediately after diagnostic specimens are obtained. In patients with difficult to treat Bacteria infection, it is often necessary to use broad spectrum empiric antibiotics.^{8,9}

Multi-drug-resistant (MDR) or high-risk pathogens have been isolated in around half of patients with an episode of ventilator-associated pneumonia (VAP) or ICUAP confirmed microbiologically. Risk factors for multidrug resistant, but not severity of illness, should be taken into account in selecting empiric antimicrobial treatment.^{10,11}

ICUAP, can be caused by more than one microbial pathogen. Multiple etiologic organisms are potentially an additional challenge for achieving appropriate antimicrobial treatment in these patients.

A study reported 48% rate of poly microbial infection in VAP, however, the epidemiology and outcomes of patients with mono microbial and poly microbial VAP did not differ significantly.¹² Between 15 % and 73 percent patients with an episode of ICUAP were not previously intubated, namely non-ventilator ICUAP (NV-ICUAP). In this study, a substantial proportion of episodes classified as poly microbial VAP had positive isolation of bacteria usually considered as non-pathogenic microorganism.^{13,14}

Characteristics and outcomes of patients with clinical suspicion of ICUAP with positive and negative microbiologic samples in a real-life ICU population were compared and concluded that Negative microbiologic findings in clinically suspected ICU-acquired pneumonia are associated with less frequent previous intubation, shorter duration of antimicrobial treatment, and better survival.¹⁵

The microbiological data and the resistance pattern varied across various centers. The primary purpose of this study is to analyse the risk factors, clinical profile of patient, microorganisms and their resistance patterns to antibiotics which are important for the diagnosis, prognosis of patient with ICU acquired pneumonia and also prevention of the same.

METHODS

This was a prospective study conducted from January 2018 to September 2019 at Yenepoya medical college hospital a tertiary care centre in southern Indian state of Karnataka. The study was approved by the ethical committee of the university. 60 patients were enrolled as per the following criteria. Sample size calculated assuming that we have 3000 ICU admission with 4% incidence of nosocomial pneumonia, a sample size of 58 was calculated at 95 % confidence interval with 5% confidence limits. Sample size was calculated using open epi version 3.

Inclusion criteria

Patients older than 18 years, admitted to Medical intensive care unit (MICU) for 48 h or more with clinical diagnosis and microbiological confirmation of ICUAP.¹⁶

- Pneumonia was defined as fever or hypothermia with chest x ray showing new infiltrates and also 2 of the 6 criteria listed below.
- Cough with purulent sputum.
- Pleuritic chest pain.
- Hemoptysis
- Dyspnea
- Crepitations on auscultation of chest.

Blood counts showing leucocytosis or band forms

Pneumonia severity score was calculated according to SMARTCOP scoring.¹⁷ The SMART-COP Score for Pneumonia Severity was developed to identify patients at increased risk for intensive respiratory or vasopressor support (IRVS). Total score is 11. 0 to 2 indicates low risk for IRVS. 3 to 4 indicates moderate risk ie (1 in 8), 5 to 6 indicates high risk (1 in 3) and 7 or more indicates severe risk (2 in 3).

Ventilator associated pneumonia occurring 48-72 h of endotracheal intubation or within 48 h of extubation and this being only the first episode, were analyzed and were consecutively enrolled in the study.^{16,18}

Exclusion criteria

Patients with preexisting pneumonia and absence of microbiological confirmation.

All patients underwent detailed history and clinical examination based on a preapproved proforma. Patient's

name was not be mentioned in structured proforma and their names were entered as codes or IP numbers The emphasis was on history of past diabetes, hypertension, chronic kidney disease, history of steroid or immunosuppressant usage, organ transplantation history, pack years of smoking, alcohol use.

The data was collected from medical case files. Complications such as acute kidney injury, requirement of dialysis, MODS, heart failure, hypotension, use of inotropes, length of stay in ICU, ventilator use, number of days of ventilator use, length of stay in hospital was recorded. Records was studied until discharge. Complete blood count including Hb, total count, Chest X ray, Sputum culture and drug sensitivity, Renal function test, Liver function test, Random blood sugar, Arterial blood gas analysis, Serum lactate levels, Blood culture and drug sensitivity were the blood investigations collected.

Course of the patient and outcome

Patients admitted in the ICU were observed for new onset fever, tachypnea, cough with expectoration 48 hours after admission to ICU. Patient on ventilator were observed for fever, tachycardia, drop in saturation, altered sensorium. History of diabetes, hypertension, smoking and other relevant history was taken from medical records. Serial blood investigations were done to look for leukocytosis or leucopenia, Random blood sugar, renal function tests, ABG for metabolic acidosis, liver function tests, ET aspiration fluid was sent for microbiological culture and sensitivity. patients were started on empirical antibiotics with suspected ICUAP as per criteria listed above. Patients were observed for clinical response in the form of decreased respiratory secretions, drop in leucocyte count, improvement in organ dysfunction, shock. patients were followed up till discharge from ICU, or death/ Discharge against medical advice.

Outcome variables

Outcome of patients with mono microbial pneumonia was compared with polymicrobial pneumonia. outcome variables include complications like acute kidney injury, multi organ dysfunction, hypotension and use of inotropes length of stay at ICU, number of days on ventilator, mortality and discharge.

Statistical analysis

The data were entered in excel and all continuous variables were expressed as mean±standard deviation. All categorical variables were expressed as percentages. Outcomes in mono microbial versus poly microbial infection were done using chi square test.

The results for each parameter (numbers and percentages) for discrete data and averaged (mean±standard deviation) for continuous data are presented by student test. The proportion was compared using Chi-square test of

significance. In all above test p value less than 0.05 was taken to be statistically significant. The data was analyzed using Statistical Package for Social Science (SPSS, V 10.5).

Ethical committee clearance was taken for the study bearing protocol number 317/2017.

RESULTS

In this study of 60 patients with ICU Pneumonia, majority of patients were males (45, 75%) with mean age of 54.4 yrs. Of 60 patients 50 patients had Mono microbial and 10 had Poly microbial infection. The baseline characteristics of these patients are shown in Table 1.

Table 1: Baseline characteristics n (%).

Age	54.49±16.07	
	Frequency	Percentage
Gender Males	45(15)	75(25)
Smoking, Yes	33	55
Alcohol, yes	9	15
Diabetes mellitus		
<5 yrs,	10	17.7
5-10 yrs	11	18.3
>15 yrs	3	5
Chronic kidney disease,	6	10.1
Heart failure,	17	28.3
Immuno-compromised state	1	1.7
Steroid overuse	1	1.7
Pre-existing lung diseases	19	31.6

Majority of this study cohort were 55 percentage smokers and 15% of them were alcoholics, 18 percent of patients had history of diabetes mellitus of 5 to10 years duration. Among Hypertensive 25 percent were below 5 years of duration of hypertension. 6 Patients (10%) had chronic kidney disease. 17 patients (28%) had heart failure. 19 patients (31%) had history of chronic lung diseases like Asthma, Chronic obstructive airway disease, interstitial lung disease.

One patient had history of steroid abuse and one patient had immune compromised state due to chemotherapy. Patients with ICUAP were started on empirical antibiotics like piperacillin tazobactam, meropenem, imipenem cilastin.

Microbiological evaluation was done based on sputum cultures and ET aspirate cultures. Out of 60 samples, 50 were Mono microbial infection and 10 were Poly microbial. Most common organism isolated in mono microbial infection was *Klebsiella pneumoniae* (26%), followed by *Acinetobacter baumannii* (25%), multidrug

resistant was 20 percent, Acinetobacter sensitive only to colistin was 5 percent. Other monomicrobial organisms isolated were *Staphylococcus sp* (12.3%), *Pseudomonas sp* (11.7%), *Streptococcus pneumoniae* (1.7%), *Stenotrophomonas sp* (1.7%), *E Coli* (1.7%). Methicillin Resistant *Staphylococcus aureus* detected was 5 percent, staphylococcus sensitive only to Co trimoxazole was 3.3 percent. Coagulase negative *Staphylococcus* was 3.3percent (Figure 1).

In poly microbial infection, *Klebsiella pneumonia* with *Acinetobacter baumannii* coinfection was seen in 3percent, *Klebsiella pneumoniae* with *Pseudomonas* species coinfection seen in 3 percent of patients, other combination are shown in Table 2.

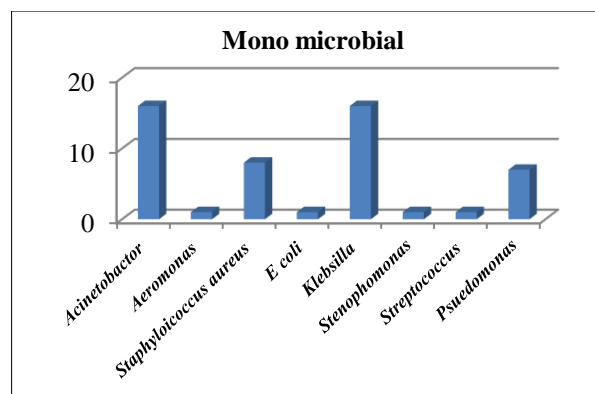


Figure 1: Spectrum of monomicrobial organisms causing ICU pneumonia.

Table 2: Profile of organism causing ICU pneumonia.

Sputum culture and sensitivity Source as compiled	Frequency	Percent	
Mono microbial (50)			
<i>Acinetobacter baumannii</i>	MDR <i>Acinetobacter</i>	12	20
	Colistin sensitive <i>Acinetobacter</i>	3	5
	Citrobacter	1	1.7
<i>Aeromonas</i>	1	1.7	
<i>Staphylococcus species</i>	Coagulase negative staphylococcus	2	3.3
	Staphylococcus sensitive to cotrimoxazole only	2	3.3
	Staphylococcus aureus MRSA	13	0.75
<i>E coli</i>	1	1.7	
<i>Klebsiella</i>	16	26.7	
<i>Stenophomonas</i>	1	1.7	
<i>Streptococcus</i>	1	1.7	
<i>Pseudomonas</i>	7	11.7	
Poly microbial (10)			
<i>E coli, Acineto, Citro MDR</i>	1	1.7	
<i>Klebsiella, Enterococcus</i>	1	1.7	
<i>Klebsiella, MRSA,</i>	1	1.7	
<i>Klebsiella, Pseudomonas</i>	2	3.3	
<i>Klebsiella, Acinetobacter</i>	2	3.3	
MRSA, <i>Pseudomonas</i>	1	1.7	
<i>Pseudomonas, Acinetobacter, Staphylococcal</i>	1	1.7	
<i>Streptococcus, Pneumonococcal</i>	1	1.7	
Total	60	100.0	

Table 3: Outcome variables.

	Death		p value
	No (28)	Yes (32)	
Gender (male, n%)	21 (75)	24 (75)	1
Smoking (yes, n%)	15 (53.5)	18 (56.25)	0.835
Alcohol (yes, n%)	2 (7.14)	7 (21.87)	0.110
Diabetes mellitus (yes, n%)	9 (32.14)	15 (46.88)	0.245
Hypertension (yes, n%)	15 (53.50)	15 (46.88)	0.604
	No (28)	Yes (32)	
COPD (yes, n%)	8 (28.57)	7 (21.87)	0.55
Pneumonia severity score, mean (SD)	6.15 (1.81)	7.75 (2.02)	0.002

	Death		p value
MODS (yes, n%)	8(28.57)	20 (62.5)	0.008
	Monomicrobial	Polymicrobial	Polymicrobial
Gender (male, n%)	37 (74)	8 (80)	0.689
Smoking (yes, n%)	27 (54)	6 (60)	0.727
Alcohol (yes, n%)	7 (14)	2 (20)	0.627
Diabetes mellitus (yes, n%)	21 (42)	3 (30)	0.479
Hypertension (yes, n%)	27 (54)	3 (30)	0.165
CKD (yes, n%)	6 (12)	0 (0)	-
Immunocompromised (yes, n%)	1 (2)	0 (0)	-
Heart failure (yes, n%)	13 (26)	4 (40)	0.262
Pneumonia severity score, mean (SD)	6.94 (2.01)	7.44 (2.46)	0.506
ICU stay- no of days, mean (SD)	12.17 (7.99)	10.56 (5.77)	0.568
Number of days on ventilator, mean (SD)	7.29 (3.62)	7.40 (4.88)	0.941
Death (yes, n%)	29 (58)	3 (30)	0.105
MODS (yes, n%)	25 (50)	3 (30)	0.417

Pneumonia severity score was calculated using SMART COP which predicts the need for intensive respiratory or vasopressor support in patients with pneumonia. Out of 60 patients diagnosed as ICU pneumonia 23 patients were discharged and 32 had mortality. Death frequency was more among diabetic group. No difference in Mortality among hypertensives and non-hypertensives. Mortality were higher in patients with higher pneumonia severity score and with Multi organ dysfunction which is statistically significant as shown in Table 3. Pneumonia severity score, number of days on ventilator and number of days stay in ICU, death did not differ among poly microbial and Mono microbial pneumonia group.

DISCUSSION

The results of our study showed mono microbial infection in majority of the patients as there were only 10 patients with poly microbial infection. Of the monomicrobial infection *Klebsiella pneumonia* outnumbered to *Acinetobacter baumannii* as shown in Table number 2. In a similar European study, the data on 124 patients by Combes et al showed a higher incidence monomicrobial infection compared to polymicrobial.¹²

In our study, *Klebsiella pneumoniae* with *Acinetobacter baumannii* coinfection and *Klebsiella pneumonia* with *Pseudomonas species* coinfection was more frequent. *Acinetobacter baumannii* isolated from the culture was resistant to all group of antibiotics like fluoroquinolones, co trimoxazole and carbapenems, 20 percent of *Acinetobacter baumannii* belong to multidrug resistant group, 5 percent were sensitive only to colistin. The only study published in 2002, that specifically addressed this issue in VAP, found a substantially higher proportion of polymicrobial etiology (48%) which included some bacteria that are considered nonpathogenic for the lung in non-immunosuppressed patients, such as several *Streptococcus species*, *Neisseria spp*, *Enterococcus spp*,

and coagulase-negative Staphylococci.¹² Early administration of appropriate therapy, based on the antibiogram of the VAP pathogens identified by quantitative culture of endotracheal aspirate could lead to an improved outcome of patients with ICU Acquired pneumonia. Appropriate broad-spectrum antibiotics should be used for treatment of multi-drug resistant pathogens to reduce the mortality (Figure 2).

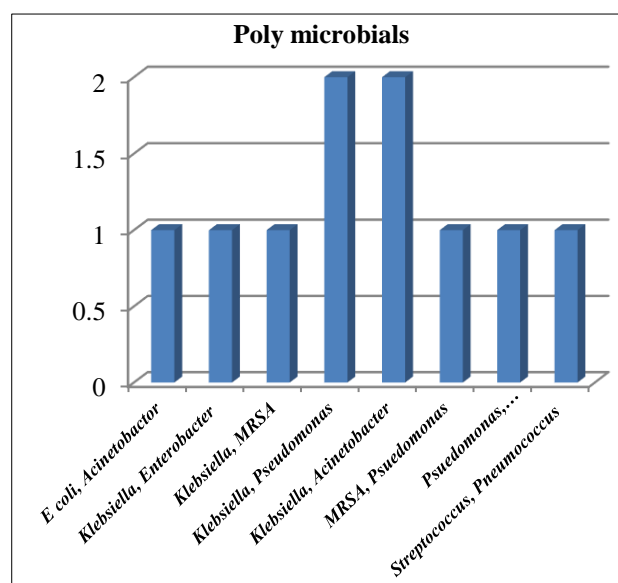


Figure 2: Spectrum of polymicrobial organisms causing ICU pneumonia.

M V Charles et al, studied the aetiological agents in VAP patients and their resistance patterns on 24 patients and concluded that 72 percent of them had monomicrobial infection.¹⁹ In a study by Miquel Ferrer et al data on 256 ICU admitted patients, 84 percent had monomicrobial infection. The most common isolated pathogens were *P. aeruginosa*, Enterobacteriaceae, and MSSA. Methicillin-sensitive *Staphylococcus aureus*, *Haemophilus*

influenzae, and several Enterobacteriaceae were more frequent in polymicrobial pneumonia and there was no association of severity of pneumonia with polymicrobial etiology.²⁰

Some of the organisms like *streptococcus*, *staphylococcus*, *MRSA*, *pneumonococcal*, *stenophomonas*, *aeromonas*, *enterococcus spp.* caused both monomicrobial and polymicrobial infection. Neither there was correlation of polymicrobial etiology with severity of pneumonia nor with mortality. When empiric treatment is frequently appropriate among monomicrobial and polymicrobial group, polymicrobial aetiology does not influence the outcome of ICU Acquired Pneumonia.²⁰

Previous observational studies reported rates of polymicrobial etiology of VAP ranged between 28 % and 50%, Jean-Yves et al studied the descriptive factors of VAP on 567 patients on mechanical ventilator and found 40 percent had polymicrobial infection.²¹⁻²⁴ Patients having VAP were older and had underlying lung disease.²¹ Factors such as age, gender, risk factors like diabetes, hypertension, underlying lung diseases, heart failure, MODS, pneumonia severity score and its correlation with outcome was studied and found that higher the pneumonia score and presence of MODS were associated with poor outcome as shown in Table 3.

Significant attributable mortality for several nosocomial infections exists in a large cohort of critically ill patients, with the highest impact occurring in those with microbiologically diagnosed pneumonia and combined infections was studied by Burgmann et al in 2010. All infections were associated with an increased resource consumption. Effective infection control measures could improve both clinical outcome and proper and effective use of ICU resources.²⁵

Over the last few years, the association between mortality of HAP and inappropriate antibiotic therapy has been intensely investigated. Some studies showed a significantly higher mortality among those patients that received inadequate initial treatment or when there was a delay in initiating treatment. Furthermore, there is a general agreement that inadequate treatment is related to the emergence of resistant pathogens and to a prolonged ICU stay. Inadequacy of the empirical treatment can occur as a result of the presence of an unexpected microorganism or the isolation of a resistant strain of an expected pathogen.²⁶ A study conducted by Marin H stated the most common pathogens associated with the administration of inappropriate antimicrobial treatment among patients with HAP/VAP include potentially antibiotic-resistant Gram-negative bacteria (*Pseudomonas aeruginosa*, *Acinetobacter species*, *Klebsiella pneumoniae*, and *Enterobacter spp.*) and *Staphylococcus aureus*, especially strains with methicillin resistance.²⁷ In this study authors did not correlate the outcome with empirical antibiotic therapy. However, it is important to recognize that the predominant pathogens

associated with hospital-acquired infections as it may vary between hospitals as well as among specialized units within individual hospitals.^{28,29} so updated hospital-specific or unit-specific antibiograms will be helpful in determining the combination of antibiotics most likely to provide initial appropriate treatment of VAP and other hospital-acquired infections.³⁰

Most common cause of ICUAP include aspiration of oropharyngeal secretions, invasive ventilation which prevents physiological and anatomical defenses against aspiration. others include patient position changing, suctioning of secretions, stress ulcer prophylaxis.³¹ Other risk factors to develop pneumonia include age, diabetes mellitus, immunocompromised state, steroid abuse, chronic lung diseases.

Diabetic subjects may have increased risk of aspiration, hyperglycemia, decreased immunity, impaired lung function, pulmonary microangiopathy, and coexisting morbidity. Ability of gram-negative organisms to colonise in respiratory epithelium is more in diabetics and once they are aspirated to lungs they develop pneumonia as there is impaired phagocytosis. Diabetic gastroparesis may itself lead to further aspiration.^{32,33}

Correlation among smokers, alcoholics, IHD heart failure, renal failure, MODS, use of inotropes, severity of pneumonia was studied between mono microbial and polymicrobial group. But we did not find any difference between the two groups. This may not be a significant finding as the sample size of polymicrobial was less compared to mono microbial.

Number of patients enrolled in the study were less and ICUAP was not divided as early and late onset, these were the limitations of the study. However, results of this study may be of clinical relevance to this institution.

CONCLUSION

Based on discussed results it may be concluded that the most frequent infection was monomicrobial with *Klebsiella pneumoniae* followed by MDR *Acinetobacter Baumannii* as common pathogen. Outcome variables like mortality, number of stay in ICU, number of days on ventilator did not differ between monomicrobial and polymicrobial infection. Higher the pneumonia severity score and with multiorgan dysfunction higher was the mortality. Hence this study will be helpful to know the pathogens associated with ICUAP and to prepare unit-specific antibiograms which will be helpful in determining the combination of antibiotics most likely to provide initial appropriate treatment hospital-acquired pneumonia.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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