Original Article

Microbiology

Study of Multidrug Resistant (MDR) Isolates in Patients with Ventilator Associated Pneumonia in a Rural Hospital

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ABSTRACT

Background and Objective: The identification of microorganisms which cause ventilator associated pneumonia (VAP) is important for formulating appropriate therapies. In this study, we have reported the incidence of VAP and the prevalence of multidrug resistant (MDR) microorganisms from patients who were diagnosed with VAP in our medical-surgical intensive care unit during the period from August 07 to May 08.

Material and Methods: Patients who were on mechanical ventilation for more than 48hrs and in whom ventilator associated pneumonia was suspected, when a new and persistent pulmonary infiltrate appeared on the chest radiograph and who had at-least two of the following criteriae, were included in the study: 1. Fever ≥38°C or hypothermia ≤36°C 2. WBC count ≥ 10000mm^3 or ≤ 4000 mm^3 and 3. Purulent tracheal secretion.

Results: The incidence of VAP in our hospital setting was found to be 45% and the most frequently isolated pathogens were *Pseudomonas spp, Staphylococcus aureus* and members of the family, Enterobacteriacae. Of the 73 isolates which were studied, 36 were found to be MDR .

Conclusion: In conclusion, the incidence of VAP and the prevalence of multidrug resistant microorganisms were quite high in our ICU setup. A local surveillance program at each centre is essential, as the knowledge of local resistant patterns is vital for selecting the appropriate agents for treating infections.

Key Words: Multidrug resistant, Mechanical ventilation, Pneumonia

INTRODUCTION

Ventilator-associated pneumonia (VAP) is an important form of hospital acquired pneumonia and it refers to the pneumonia which develops in mechanically ventilated patients for more than 48 hrs after tracheal intubation or tracheostomy [1,2].

Ventilator associated pneumonia is the most common nosocomial infection which affects patients in the intensive care units (ICUs)[3].

There is an increasing trend of multiple drug resistant (MDR) isolates in the ICU setup, which considerably increases the morbidity, mortality and the days of mechanical ventilation among the hospitalized patients [4,5,6].

The incidence of multi-resistant strains which cause VAP may vary from hospital to hospital, among the types of ICU patients, with antibiotic use and among different patient populations and comorbid conditions [3,4].

The MDR isolates which are present in the ICU and in the hospital environment pose not only therapeutic problems, but also serious concerns for infection control management [5,6]. A local surveillance program is essential at each centre, as the knowledge of local resistant patterns is vital for selecting appropriate agents for treating infections.

So, the present study was undertaken to assess the incidence of the MDR isolates in the patients who developed VAP in our settings.

MATERIAL AND METHODS

A total of 85 patients who were admitted to the ICU of the Medicine and Surgery departments were evaluated over a period from August 07 to May 08.

Selection of the Patient

The patients who were selected for the study were those who were on mechanical ventilation for more than 48hrs with suspected ventilator associated pneumonia, when a new and persistent pulmonary infiltrate appeared on the chest radiograph and had at least two of the following criteriae [3,4,5]:

1. Fever ≥38°C or hypothermia ≤36°C
2. WBC count ≥ 10000mm^3 or ≤ 4000 mm^3
3. Purulent tracheal secretion.

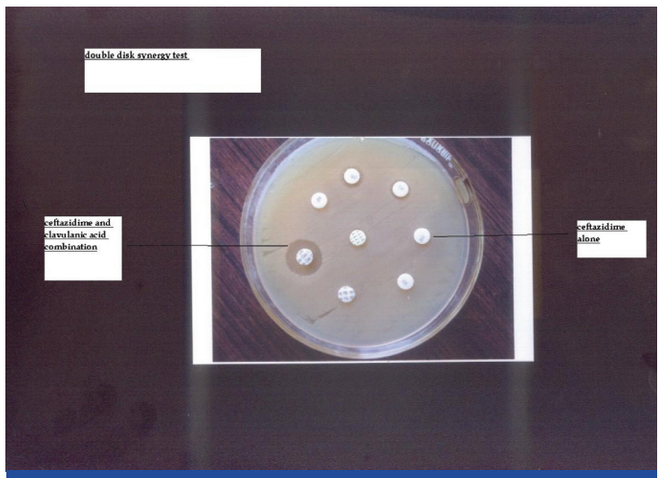
Collection of the Endotracheal Aspirate (ETA)

From patients who fulfilled the above criteriae, ETA was collected by using a Romson's mucus extractor and it was immediately transported to the Department of Microbiology for further processing.

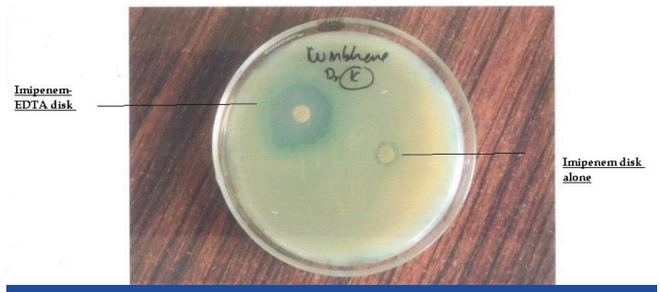
For a definitive diagnosis of VAP, in this study, the quantitative culture threshold was considered as 10^5cfu/ml [7,8,9,10].

Antibiotic sensitivity testing was carried out on Mueller-Hinton agar (MHA) plates by the Kirby Bauer's method.

- MRSA were confirmed by using cefoxitin and oxacillin discs [11].
- Suspected ESBLs were identified by the double disk synergy test, by using ceftazidime and the ceftazidime and clavulanic acid combination [11]. See [Table/Fig-1].
- Suspected AmpC β-lactamases were screened by checking for a decreased sensitivity to the ceftazidime and the cefoxitin discs [12].
- MβL producers were identified by the Imipenem-EDTA disc method [13,14]. See [Table/Fig-2].



[Table/Fig-1]: Culture showing sensitivity



[Table/Fig-2]: Culture showing sensitivity

VAP pathogens such as Pseudomonas spp., Acinetobacter spp., and enteric Gram-negative bacilli who expressed ESBL, AmpC □-lactamases or MBL, MRSA and multidrug-resistant S. pneumoniae (who were resistant to penicillin and at least two other antibiotic classes) were defined as "multi-drug resistant"(MDR) pathogens [6,9].

RESULT

A total 85 patients were evaluated in the period from August 07 to May 08. The quantitative culture results (□10^5 CFU/ml) for pathogenic organisms which caused VAP were significant in 39 (45%) patients. Forty six (55%) patients were not considered to have VAP, as the quantitative cultures of the ETA showed a colony count of <10^5 CFU/ml and they were considered as commensals or colonization.

The infection was polymicrobial in 22(56.41%) cases and mono-microbial in 17(43.58%) cases, while 19(48.71%) were early onset (□ 5days) and 20(51.28%) were late onset (□5days) infections. [Table/Fig-3] shows the characteristics of the VAP patients. The various underlying conditions are shown in [Table/Fig-4 and 5].

The most common organisms which were isolated were *Pseudomonas aeruginosa* [20(27.02%)], followed by *Staphylococcus aureus* [15(20.27%)], *E.coli* [13 (17.56%)], *Klebsiella pneumoniae* [12(16.25%)], *Acinetobacter spp* [5(6.66%)], *Streptococcus pneumoniae* [3 (5.12%)], *H.influenzae* [2 (2.56%)] and *Citrobacter spp* [2(2.56%)] [Table/Fig-6].

Of the 20 *Pseudomonas aeruginosa* strains, 3(1.5%) were M□L and 4(2%) were AmpC □-lactamases producing strains. All the M□L strains were sensitive to azetronem, polymyxin B, colistin and piperacillin-tazobactam and all theAmpC □-lactamases were sensitive to imipenem, meropenem and piperacillin-tazobactam, but they were resistant to azetronam. Of the remaining 13 isolates, 6 (46.13%) were resistant to amikacin, 10 (76.92%) were resistant to ciprofloxacin, 7(53.84%) were resistant to gentamicin, 11(84.61%) were resistant to ceftazidime, 6 (46.13%) showed resistance to azetronam and 3 (23.07%) were resistant to piperacillin-tazobactem.

Characteristic	Patients developing VAP n= 39
Age (years)	75.0 ± 18.0
Sex	
Male	24(61.53%)
Female	15(34.46%)
VAP onset	
Early (< 5days)	19(48.71%)
Late (>5days)	20 (50.28%)
ICU	
Medicine	28(71.79%)
Surgery	11(28.20%)
Infection	
Polymicrobial	22(56.41%)
Monomicrobial	17(43.58%)

[Table/Fig-3]: Characteristics of 39 Patients with VAP

S.N.	Diagnosis	Cases	VAP	%
1	ARDS	13	8	61.53%
2	OPpoisoning	8	4	50%
3	Hypertension& Acute MI	7	4	57.14%
4	CRF	5	3	60%
5	Shock & septicemia	5	2	40%
6	COPD	4	2	50%
7	Malaria	4	1	25%
8	Viral hepatitis	2	-	0%
9	CNS infection	2	1	20%
10	Others	5	3	60%

[Table/Fig-4]: Medicine ICU Cases

ARDS=acute respiratory distress syndrome: OP=Organophosphorus: MI=myocadial infarction: CRF=chronic renal failure: COPD=chronic obstructive pulmonary diseases: CNS=central nervous system: Others=pulmonary embolism , neurological diseases.

S.N.	Diagnosis	Cases	VAP	%
1	RTA	11	5	45.55%
2	Intestinal obstruction	6	2	33.33%
3	Brain tumor	4	1	25%
4	Other	7	3	42.85%

[Table/Fig-5]: Surgical ICU Cases

RTA=road traffic accidents; Others=colon surgery;Upper GI surgery

Organism	No of isolates (%)	MDR (%)
Pseudomonas aeruginosa	20 (27.02)	7 (35.00%)
Staphylococcus aureus	15 (20.27%)	8 (53.33%)
E.coli	13 (17.56%)	10 (76.92%)
Klebsiella pneumoniae	12 (16.21%)	09 (75.00%)
Acinetobacter spp	5 (6.66%)	02 (40.00%)
Streptococcus pneumoniae	3 (4.12%)	–
Hemophilus influenzae	3 (4.56%)	–
Citrobacter spp	2 (3.56%)	–

[Table/Fig-6]: Number of isolates (n = 36)

Of the 15 *Staphylococcus aureus* strains, 8(53.33%) were MRSA and all the MRSA strains were resistant to penicillin and erythromycin, while 100% sensitivity was shown to vancomycin and linezolid. Of the remaining 12 isolates, 10 (83.33%) were resistant to erythromycin, 9 (75%) to ampicillin and 5 (41.66%) to amikacin .

Of the 13 *E.coli* strains, 6(46.13%) were ESBL and 4(30.76%) were AmpC β-lactamase producers.

Of the 12 *Klebsiella pneumoniae* strains, 4 were (33.33%) ESBL and 4(33.33%) were AmpC β-lactamase producers. All the strains of *E.coli* and *K.pneumoniae* were sensitive to imipenem meropenem and piperacillin-tazobactam, while the remaining isolates were sensitive to gentamicin, amikacin, ciprofloxacin and ceftazidime also.

Of the 5 *Acinetobacter spp,* 2(40%) were AmpC β-lactamase producers and they were sensitive to imipenem and meropenem, while no MβL producers were seen . The remaining isolates were sensitive to gentamicin, amikacin, ciprofloxacin and ceftazidime.

Of the total 36 MDR isolates, 24 organisms were from late onset VAP, while 12 MDR isolates were from early onset VAP. *Pseudomonas aeruginosa* was the dominant organism in both the forms of VAP.

DISCUSSION

VAP, a form of hospital acquired pneumonia is a serious infection with a high mortality rate and in the literature, the overall incidence of VAP in ICUs ranges from 10-70% [3,4,6,13,16].

The pathogens which are responsible for VAP vary, depending on the duration of the mechanical ventilation, prior antibiotic exposure and the length of stay in the hospital. *P.aeruginosa, MRSA, Acinetobacter, E.coli* and *Klebsiella pneumoniae* are the most dominant organisms [5,6]. In many studies, it has been shown that the MDR pathogens were mostly associated with late onset VAP than with early onset VAP [15,16].

While considering the epicenters of bacterial resistance, ICUs were found to be the main sources of the upsurges in the numbers of MDR. Among the risk factors, the one that has been emphasized is antimicrobial agent abuse, which exerts a selective pressure on certain groups of microorganisms, thus turning them resistant. In addition, the routine use of invasive techniques as well as ICU overcrowding and the increased susceptibility in this population of patients who usually suffer from severe illnesses, further increase the risk of infection with multidrug resistant microorganisms [3,5,6].

There is high antibiotic resistance in nosocomial, gram negative pathogens which are isolated from ICUs, which are mostly resistant to ceftazidime, ciproflaxcin, gentamicin and amikacin. Though most of the gram negative organisms show susceptibility to carbepenem, the resistance to imipenem is on a rise, all over the world, by means of metallo B-lactamase production [14,15,16]. Our study also showed a gram negative dominance, *Pseudomonas aeruginosa, Staphylococcus aureus, Klebsiella pneumoniae* and *Ecoli* being the commonest pathogens.

In the present study, the incidence of VAP was found to be 45% and the most common organisms which were isolated were *Pseudomonas aeruginosa,* followed by *Staphylococcus aureus,* with (49.31%) the isolates being MDR. The higher incidence of VAP and MDR in our study could be attributed to the presence of co-morbid conditions. Some of the patients were seriously ill with conditions such as organophosphorous(OP) poisoning, road traffic accidents, acute mycocardial infarction, etc. The health seeking behaviour of our patients was different from that which was found in the developed world. Due to limited resources, the patients seek medical help only when it is absolutely inevitable. By the time the patient is referred to the tertiary care centre, his underlying condition becomes well advanced and it may become irreversible. This may necessitate a longer duration of mechanical ventilation which is directly proportional to the development of VAP and subsequently the MDR pathogens.

Potential MDR was a real threat to our ICU and hospital settings and the maximum number of MDR isolates were obtained from patients who had a late onset VAP and who had a history of previous antibiotic exposure, a longer duration of mechanical ventilation and underlying diseases.

So, in conclusion, the potential MDR in ICU and hospital settings emphasizes the judicious use of antimicrobial therapy, so as to decrease the incidence of VAP and the overall morbidity, mortality and the longer stay of patients in the hospital.

Lastly, the combined approaches of rotational antibiotic therapy and educational programs may be beneficial in fighting against such types of pathogens.

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