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### Incidence of ventilator associated pneumonia and drug-resistant bacterial preponderance: a fact to ponder

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#### ABSTRACT

**Background:** Management of ventilator-associated pneumonia (VAP) in critically ill patients is a challenge to intensivists. This study aimed at identifying microbial factors and infection control practices that influenced incidence of VAP in a tertiary care hospital.

**Methods:** Incidence of VAP among patients admitted to the intensive care units (ICU) from January to December 2016 was estimated. A one year period of study was divided into 3 segments of January to April, May to August, and September to December. Isolation rates of Gram Negative Bacteria (GNB) from respiratory samples and their extensively drug resistance (XDR) pattern were also analyzed.

**Results:** A total of 14 patients had developed VAP. Incidence of VAP in the 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> segments of the year was 25.3, 15.2 and 4.1/1000 ventilator days respectively. *Acinetobacter baumannii* was the causative agent in all patients (100%). Among all GNB isolated the rate of *Acinetobacter baumannii* was 83%, 64%, 59% during the 3 segments of the year. XDR strains were 76%, 62% and 55%. Interventional factors like improvement in infection control practices which included hand hygiene, cohorting of MDR/XDR infected patients and environmental surveillance was noted. **Conclusions:** The VAP incidence declined in the later part of the year than the earlier (25.3 Vs 4.1/1000 ventilator days), with a notable decrease in the isolation of *Acinetobacter baumannii* (p value-0.005) and XDR organisms (p value-0.01). Directly proportionate association of VAP incidence with microbial factors were noted. Infection control measures to curtail MDR organisms should be an important component in the management of patients on ventilators.

Keywords: Acinetobacter, Bacteria, Drug resistance, VAP

#### **INTRODUCTION**

Ventilator-associated pneumonia (VAP) is a common cause of nosocomial infection and is related to significant mortality and morbidity in the health-care setting.<sup>1</sup> It affects almost 27% of patients who are on mechanical ventilation in the ICUs.<sup>2</sup> Multidrug resistant bacteria have been implicated in the etiology of VAP. Both Gram positive and Gram negative bacteria have been associated with VAP, however in low- and middle-income countries, it is found that the multidrug-resistant Gramnegative organisms predominate.<sup>3</sup> Gram negative organisms like *Acinetobacter baumanii, Klebsiella pneumoniae, Pseudomonas aeruginosa, Escherichia coli* and Enterobacter species are frequently associated with VAP.<sup>4</sup>

The presence and frequent isolation of these drug resistant organisms from the ICUs have been found to be an important risk factor for already admitted patients to develop VAP.<sup>5</sup> One of the major reservoirs of drug resistant organisms are the medical equipment, patients

themselves and the health care personnel.<sup>5</sup> Medical equipment, especially the ventilator is usually contaminated by organisms like *Acinetobacter baumanii*.<sup>6</sup> Stringent infection control measures play a vital role in the prevention of transmission of these organisms.<sup>7</sup>

There is paucity of data comparing incidence of VAP with frequency of isolation and presence of drug resistant microorganisms (bacterial preponderance) in the ICUs, and the impact of infection control in the incidence of VAP. This study aimed to identify the microbial factors and infection control practices that influence the incidence of VAP.

#### **METHODS**

#### Setting

This prospective study was reviewed and cleared by the Institute Ethics committee. It was conducted in two adult intensive care units (ICU) of a tertiary care center over a period of one year between January to December 2016. The two ICUs combined, had 22 beds. The one-year study period was divided into three segments;  $1^{st}$  segment between January to April,  $2^{nd}$  between May to August, and the  $3^{rd}$  between September to December.

#### Incidence of VAP

All patients who were admitted to the intensive care units requiring mechanical ventilation and had survived beyond 48 hours were included in the study. Patients who had evidence of pneumonia /ARDS prior to intubation were excluded. The clinical pulmonary infection score (CPIS) consisting of clinical, radiological and microbiological factors was used to diagnose VAP as described earlier.<sup>8</sup> A patient was considered to have VAP if the score was equal to or more than six. All patients on ventilator were reviewed daily to evaluate the CPIS score till extubation. The incidence of VAP was calculated and expressed as event/1000 ventilator days.

#### Microbial factors

Gram Negative Bacteria (GNB) isolated from endotracheal aspirate, bronchoalveolar lavage and protected specimen brush among ventilated patients admitted in ICUs during the period of January to December 2016 were analyzed. The resistance patterns of these organisms were documented. Extensive drug resistance (XDR) was defined as resistance to more than or equal to one antimicrobial agent in all classes but less than or equal to 2 categories.<sup>9</sup>

New interventional factors and infection control strategies were introduced in the 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> segments of the year. The interventions especially in the 2<sup>nd</sup> segment of the year was improvement in the infection control practices which included hand hygiene audit, cohorting of MDR/XDR infected patients, restriction of

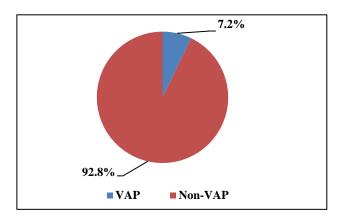
ICU visitors, use of hand rub for visitors, periodic active surveillance of the ICU environment and regular disinfection of ventilator circuits. A fully dedicated respiratory therapist for pulmonary care was introduced in the 3<sup>rd</sup> segment of the year.

#### Statistical analysis

All parameters were descriptively analyzed. Data obtained were expressed as either numbers or percentages (%). A 95% confidence interval was calculated for VAP incidence rates. Categorical variables were compared using chi-square test and a P-value of <0.05 was considered significant.

#### RESULTS

A total of 194 patients were on ventilator support during the study period, 14(7.2%) of whom developed VAP (Figure 1). The mean age of patients who developed VAP was  $45.8 \pm SD 21.30$  years.



## Figure 1: Percentage of patients with ventilator associated pneumonia.

The incidence of VAP during the one-year period was 12.8 episodes per 1000 ventilator days (VDs). *Acinetobacter baumannii* was the single common causative agent of VAP (100%) in all the 14 patients. Six of the 14 patients succumbed to the infection, out of which 3(21%) were attributed to VAP.

Incidence of VAP in the 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> segment of the year was 25.3, 15.2 and 4.1/1000 VDs respectively (Table 1). There was a male preponderance with 9 (64%) of them developing VAP.

Majority of the patients were admitted with a diagnosis of poisoning (33%), rest of them were admitted for trauma (21%), chronic kidney disease (14%), sepsis (14%), snake bite (7%) and COPD (7%). There were 154 Gram negative bacteria (GNB) isolated from different respiratory specimen (Endotracheal aspirate, Bronchoalveolar lavage and protected specimen brush) from the patients who were admitted in the ICUs during the study period.

Variables	1 <sup>st</sup> segment (Jan-April)	2 <sup>nd</sup> segment (May-Aug)	3 <sup>rd</sup> segment (Sep-Dec)	Total Jan-Dec 2016	P -value (1 <sup>st</sup> & 3 <sup>rd</sup> Segment)
No. of patients on ventilator	40	53	101	194	-
Number of ventilator days	276	327	487	1090	-
Number of patients who developed VAP (%)	7 (17.5%)	5 (9.4%)	2 (1.9%)	14 (7.2%)	0.0006
Incidence of VAP/1000 ventilator days (95% CI)	25.3 (11.1-50.1)	15.2 (5.6-33.9)	4.1 (0.6-13.5)	12.8 (7.3-21.0)	0.0006
Mortality among patients with VAP	4	1	1	6	0.85
Isolation of <i>Acinetobacter</i> <i>baumannii</i> from resp. specimen	83%	64%	59%	70%	0.005
Isolation of XDR organisms	76%	62%	55%	64%	0.01

Table 1: Incidence of VAP and outcome in the different segments of the year with isolation rates of Acinetobacter			
baumannii and XDR organisms.			

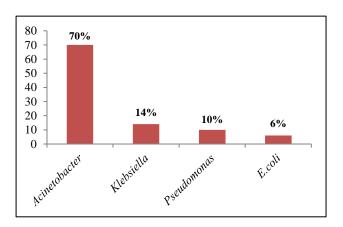
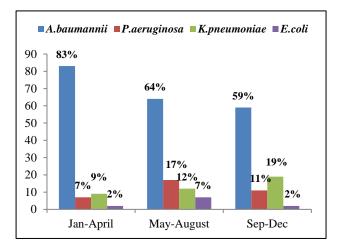


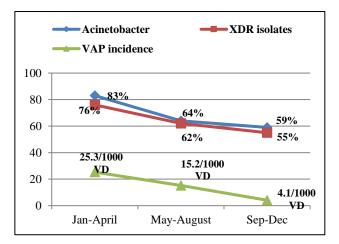
Figure 2: Distribution of Gram negative bacteria isolated from respiratory specimen in ICUs.



## Figure 3: Percentage of isolation of GNB during the 3 different segments of the year.

Among the 154 GNB, isolation rate of *Acinetobacter* baumannii was the highest (70%), followed by *Klebsiella* 

pneumoniae (14%), Pseudomonas aeruginosa (11%) and Escherichia coli (6%) (Figure 2). In all the 3 segments of the year, the isolation rate of Acinetobacter baumannii from respiratory specimen was 83%, 64%, 59% respectively, showing a decreasing trend (Figure 3). There was no statistically significant diminishing or increasing trend noted in the isolation of other organisms like Pseudomonas aeruginosa, Klebsiella pneumoniae and Escherichia coli.



#### Figure 4: Comparison of VAP incidence with Acinetobacter baumannii and XDR isolation in the 3 segments of the year (VD-Ventilator days).

Out of 154 isolates, 98(64%) of the isolates were XDR strains. Distribution of XDR Organisms in the 3 segments of the year was 76%, 62%, 55% respectively (Table 1). The VAP incidence had steadily declined in the third segment of the year (4.1/1000 VDs) as compared to in the first segment (25.3/100 VDs) of the year (P value - 0.0006). Decrease in the incidence of VAP correlated with Isolation rates of *Acinetobacter baumannii* (83% Vs 59%, P value -0.005). This was also reflected in a

decrease in XDR organisms (76% Vs 55%, P value -0.01) - Figure 4 and Table 1. A directly proportionate association of incidence of VAP with that of microbial factors was noted in the study.

There were a few interventional factors introduced in the  $1^{st}$ ,  $2^{nd}$  and  $3^{rd}$  segments of the year. The interventions especially in the  $2^{nd}$  segment of the year, were improvement in the infection control practices like hand hygiene, cohorting of MDR/XDR infected patients, restriction of ICU visitors and usage of hand rub for visitors. Periodic active surveillance of the ICU environment was done, and on two occasions *Acinetobacter baumannii* was isolated from the ventilator circuit/trap fluid following which aggressive disinfection and, thereafter usage of commercially available humidifier fluid was put into use. In addition to the above, a respiratory therapist was appointed during the  $3^{rd}$  segment of the year (Table 2).

# Table 2: Summary of interventions / preventivestrategies instituted during the 3 segments of thestudy period.

Segment of the year	Intervention		
1 <sup>st</sup> Segment (Jan - April)	Hand hygiene before and after contact with respiratory equipment.		
2 <sup>nd</sup> Segment (May - August)	Commercially available humidifier fluid use following <i>Acinetobacter baumannii</i> isolation from ventilator circuit fluid and Ventilator outlet. Cohorting of MDR/XDR infected patients Initiation of hand hygiene audit Handrub for ICU visitors Restriction of ICU visitors Daily infection control team rounds Frequent training of care givers on infection control practices Shoe covers introduced		
3 <sup>rd</sup> Segment (Sep - December)	Recruitment of respiratory therapist (RT) Disinfection of ventilator circuits - regularly done by RT		

#### DISCUSSION

Ventilator associated pneumonia is one of the most common device-associated infections affecting patients in the intensive care units.<sup>10</sup> The incidence of VAP in India and other Asian countries have a wide range between 3.5 -46 /1000 VDs.<sup>11,12</sup> A surveillance conducted over 6 years in 703 ICUs of 36 countries (Latin America, Europe, Eastern Mediterranean, Southeast Asia, and Western Pacific) concluded a VAP incidence of 13.1/1000 VDs.<sup>13</sup> In the present study, 7.2% of patients had developed VAP

with an incidence rate of 12.8/1000 ventilator days (VDs) which is in concordance with previously reported incidence. A male preponderance (64%) in patients with VAP is consistent with earlier reports.<sup>14</sup>

VAP is generally dominated by the Gram-negative bacteria like *Acinetobacter baumannii*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* which are described as "critical" priority organisms by the World Health Organization.<sup>15</sup>

Several studies have also reported *Staphylococcus aureus*, MRSA, Enterobacter species, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae*.<sup>16,17</sup> Studies from India have demonstrated that >50% of VAP is attributed to *Acinetobacter baumannii*.<sup>10,18</sup> In the present study *Acinetobacter baumannii* was the causative agent of VAP in all (100%) the patients. This is probably because *Acinetobacter baumannii* was the predominant (70%) respiratory pathogen isolated from ICU patients on ventilator during the study period.

Mortality among patients with VAP has been reported to be 40% in a large-scale study done among 2960 patients.<sup>19</sup> However, it was 21%, in the present study. Patients who develop VAP with MDR organisms like Pseudomonas aeruginosa and Klebsiella pneumoniae have been noted to have poor prognosis with high mortality in contrast to those with Acinetobacter baumannii Infection.<sup>20</sup> Moreover, "Critical" priority organisms like Pseudomonas aeruginosa and Klebsiella pneumoniae are highly virulent and difficult to eradicate despite effective therapy, especially in the immunocompromised hosts.21

Among the respiratory pathogens isolated from all ventilated patients during the study period, *Acinetobacter baumannii* showed a statistically significant, decreasing trend noted towards the end of the year in comparison to the beginning (83% Vs 59%, P value -0.005). Similar pattern in the isolation of XDR strains were also noted (76% Vs 55%, p -value 0.01). This dip in the drug resistant bacterial isolation from the ICUs very well correlated with a statistically significant steady dip in VAP incidence too (25.3 Vs 4.1/1000 VD, P value -0.0006). Authors attribute this control/ reduction in the drug resistant bacterial isolation to the infection control practices that were introduced during the study period.

Acinetobacter contamination in the ICUs has been found to be one of the recurrent causes of outbreaks of hospital acquired infections like VAP, which is reflected in the present study.<sup>22</sup> Moreover, patients with *Acinetobacter baumannii* infections in the ICUs are a significant risk factor for subsequent patients to develop VAP due to *Acinetobacter baumannii*.<sup>20</sup> Authors too in this study evidenced a high incidence of VAP due to *Acinetobacter baumannii* in the 1<sup>st</sup> segment of the year where *Acinetobacter baumannii* isolation was maximum. A directly proportional association of VAP incidence with Acinetobacter baumannii and XDR microbial isolation has been noted in this study.

The practices that could have contributed to the dip in Acinetobacter baumannii and MDR organism isolation, thereby reducing the VAP incidence were, the improvement and stringent infection control practices implemented in the second segment (May to August) of the year. Some of the notable interventions /changes in practice were strict adherence to hand hygiene audit, daily infection control team rounds, frequent training of care givers on infection control practices and cohorting of patients with MDR/XDR strains in the ICU. Similar studies in the past have also reflected on decreased incidence following bundle-based preventive interventions, daily audits, continual education, regular feedbacks and training.23-25

In addition to infection control measures, placement of a dedicated respiratory therapist in the ICU with primary responsibility of facilitating tracheal toileting by chest physiotherapy and ensuring disinfection of ventilator circuits may have helped in bringing down the rate.

#### CONCLUSION

In conclusion, with microbial preponderance in the ICUs, there exists an augmented incidence in VAP. However, with microbial subservience we describe a >75% reduction in the VAP incidence. Effective infection control measures to curtail drug resistant organisms should be of prime concern and a vital component in the management of patients on ventilator in high dependency critical care units.

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