Antimicrobial Susceptibility Pattern Of Isolates From Cases Of Ventilator Associated Pneumonia (VAP) In Medical And Surgical Intensive Care Units

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Abstract: Background: Healthcare associated pneumonia were reported to be the second most common healthcare associated infection in US intensive care units (ICUs). Aims and Objectives: Present study was aimed to determine the antimicrobial susceptibility pattern of isolates from cases of VAP. Methods: Ventilator associated pneumonia was identified as per the definition of Centre for Disease Control and Prevention. Laboratory confirmation was done by quantitative culture method. Thereafter identification of the organism along with its species and its anti-microbial sensitivity were done by Vitek 2 compact system using various ID and ATB strips. Results: A total of 42 clinical isolates were identified from 31 cases of VAP during the entire study period, Acinetobacter baumannii (n=20, 47.6%) was the predominant isolate. Tetracycline was found to be significantly sensitive (P = 0.008) in SICU isolates of A.baumannii when compared to its counterparts of MICU. Conclusions: Significant colonization is a prerequisite for occurrence of any infection. A thorough review of clinic-pathological as well as radiological findings should be performed while reporting a clinical isolate from tracheal aspirates. [Riddhi P NJIRM 2017; 8(1): 48-53]

Key words: quantitative culture of tracheal aspirats, mechanical ventilation, medical intensive care unit, surgical intensive care unit, Ventilator associated pneumonia.

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Introduction: Ventilator-associated pneumonia (VAP) is defined as pneumonia that occurs 48–72 hours or thereafter following endotracheal intubation, characterized by the presence of a new or progressive infiltrate, signs of systemic infection (fever, altered white blood cell count), changes in sputum characteristics, and detection of a causative agent[1]. It is the second most common nosocomial infection in the intensive care unit(ICU) and the most common in mechanically ventilated patients [2,3].Typically, bacteria causing early-onset VAP include Streptococcus pneumoniae (as well as other streptococcus species), Hemophilus influenzae, methicillin-sensitive Staphylococcus aureus (MSSA), antibiotic-sensitive enteric Gram-negative bacilli, Escherichia coli, Klebsiellapneumonia, Enterobacter species, Proteus species and Serratia marcescens. Culprits of late VAP are typically MDR bacteria, such as methicillin-resistant S. aureus (MRSA), Acinetobacter, Pseudomonas aeruginosa, and extended-spectrum beta-lactamase producing bacteria (ESBL)[2].The exact prevalence of MDR organisms is variable between institutions and also within institutions Approximately 50 % of all antibiotics administered in ICUs are for treatment of VAP[2]. Present study was thus aimed to determine antimicrobial susceptibility pattern of isolates from cases of VAP using quantitative culture method.

Aim and Objective: To characterize and determine antimicrobial susceptibility pattern of isolates from ventilator associated pneumonia.

Methodology: The study included all the patient admitted in the Medical and Surgical Intensive Care Units at Shree Krishna Hospital, Karamsad during the study period (1st May 2012 to 31st May 2013).All patients with endotracheal/tracheostomy tube in situ served as the denominator in the study for calculation of VAP rates.

Criteria For Inclusion: All patients in the MICU or SICU subjected to mechanical ventilation for more than 48 hours, who showed positive culture of tracheal aspirate with a significant colony count (≥ 10^5 CFU/ml) and who showed clinical evidence of pneumonia as described in the definition provided by National Health Safety Network (NHSN), Centre for Disease Control and Prevention (CDC) guidelines were considered a confirmed cases of VAP and were included as a numerator in the study.

Criteria For Exclusion: The study excluded those patients who had evidence of infection being acquired from units other than medical and surgical intensive care unit of Shree Krishna Hospital, Karamsad and/or positive quantitative tracheal aspirate culture within 48 hours of admission to Medical or Surgical Intensive Care Unit. All patients whose quantitative culture had

revealed a colony count of < 10^5 CFU/ml of tracheal aspirate and who did not show clinical evidence of pneumonia were excluded from the study.

Quantitative culture of tracheal aspirate was done and diluted secretions were inoculated on the Nutrient Agar, Sheep Blood Agar and MacConkey Agar and Chocolate agar with a calibrated loop (diameter 4mm, capacity 0.01 ml) and incubated overnight at 37^0c.Optochin disc was placed in inoculated Chocolate agar plate. Sheep Blood Agar and Chocolate agar plates were kept in candle jar. In addition to the above procedure a subculture on Saburaud Dextrose Agar medium was done if fungal growth was suspected and identified as per Standard Operative Procedure. After overnight incubation, culture plates were examined for colony characteristics (color, texture, pigmentation, etc).The cases were included in the study as per the inclusion criteria mentioned above.
Gram staining of the colonies was done to see the morphology and gram reactions. Thereafter identification of the organism along with its species and its anti-microbial sensitivity done by Vitek 2 compact system using various ID and ATB cards depending upon the colony characteristics, morphology, catalase, oxidase and gram reaction of the isolates. If required other biochemical tests and manual antimicrobial sensitivity using Modified Kirby Bauer's disc diffusion technique were done for accurate identification of the microorganisms and their sensitivity pattern respectively. The drug sensitivity was reported as per the Clinical Laboratory Standards Institute (CLSI) guidelines. (Document M 100 January-2012) A positive tracheal aspirates culture was correlated clinically with findings of pneumonia as per the criteria mentioned above.
As it was a prospective study, Ventilator associated pneumonia rates were calculated on monthly basis. Tables and graphs were made to show microbiological profiles of VAP cases. Antimicrobial susceptibility pattern of isolates and comparison of antibiotic profile of A. baumannii isolated from cases of VAP both from MICU and SICU was done. Crude mortality rate was calculated.

Results: During the study period from 1st May 2012 to 31st May 2013, a total of 339samples of tracheal aspirates were submitted to the Microbiology laboratory from hospital of which 203(59.9%) were reported positive for a pathogen whereas 136(40.1%) samples were reported as negative. Out of total tracheal aspirates received during the study period, 141(41.5%) samples were received from MICU whereas 110(32.4 %) samples were received from SICU. While 88 (26%) samples were from other areas of hospital. Among the total samples received from MICU, 86(61%) samples were reported as positive whereas 55 (39%) samples were reported as negative. In the same way, among the total samples received from SICU, 69(62.7%) samples were reported as positive whereas 41(37.3 %) samples were reported as negative. In MICU, a total of 11 positive samples were diagnosed of having ventilator associated pneumonia similarly in SICU, a total of 20 positive samples were reported of having ventilator associated pneumonia.
Demographic profiles of VAP cases from MICU and SICU.

As shown in Figure 01, male 23 (74%) was more common than female 8 (26%) in VAP cases. In SICU male was 90% of total VAP cases

Microbiological profile of VAP cases: As shown in Table 01, a total of 42 clinical isolates were identified from 31 cases of VAP during the entire study period. Out of 42 clinical isolates, Acinetobacter baumannii (n=20, 47.6%) was the predominant isolate while there were only one isolate of C. dulinensis and E. cloacae. As shown in Table 02, A. baumannii was the most common isolate from cases of VAP in MICU and SICU.

As shown in Table 03, 12 (28.5%) of isolates were from cases of early onset VAP whereas 30 (71.5%) of cases were from late onset VAP. With respect to A.baumannii, seven (35%) isolates were from cases of early onset VAP whereas 13 (65%) isolates were from cases of late onset VAP. But this difference was not statistically significant (p value= 0.379) . All five isolates of P.aeruginosa were from late onset VAP. As shown in Figure 02, A.baumannii isolated from VAP cases were 100% susceptible to Colistin, 25% to Tetracycline, 15% to Tobramycin, Meropenem, Imipenem and Levofloxacin. Isolates of P.aeruginosa were 100% sensitive for Colistin and 60% sensitive for Imipenem and Meropenem .As shown in the Figure 03 isolates of E. coli were multidrug resistance (MDR) and sensitive for Amikacin and carbapenems mainly. As shown in Figure 04 in MICU A. baumannii isolated cases were 100% resistant for Tetracycline while only 35% in SICU. Tetracycline was found to be significantly sensitive (P = 0.008) in SICU isolates of A.baumannii

when compared to its counterparts of MICU. A total of 10 cases of VAP expired during the entire study period with a crude mortality rate of 32.25%. As shown in Figure 05, 2(20%) death had occurred in MICU whereas 8 (80%) deaths had occurred in SICU.

Discussion: VAP is frequently difficult to diagnose in ICU patients with an endotracheal tube or a tracheostomy[4].VAP occurs frequently and is associated with significant morbidity in critically ill patients. The primary obstacle in diagnosing VAP is the absence of gold standard criteria and, therefore, VAP continues to be an inconspicuous clinical syndrome.

Isolates in VAP:As shown in Table 2 ,a total of 42 clinical pathogens were isolated from 31 cases of VAP in both ICUs. Except for one isolate of C.dubliniensis all other 41 pathogens were gram negative organisms. In a previous study, gram negative bacilli constitute of 83% of all isolates causingVAP [5]. Acinetobacter baumannii (47.6%) was the predominant isolate followed by E.coli (21.4%), Klebsiella pneumoniae (14.3%) and Pseudomonas aeruginosa (11.9%). Again in MICU and SICU Acinetobacter baumannii was the predominant isolate comprising of 50% and 46.7% respectively. Gram negative bacilli were most common organism isolated in VAP cases, in previous studies[6,7,8]. In contrast to the present study, NHSN update on antimicrobial resistance, 2006 – 07,described S.aureus to be the predominant pathogen accounting for 24.4% of all VAP cases followed by P.aeruginosa accounting for 16.3% of VAP cases. Previous studies described Acinetobacter as a predominant VAP pathogen constituting for 8-50% of all clinical isolates of VAP [9,10,11].

As shown in Figure 4, total of nine (21.4%) of E.coli were isolated from VAP cases where eight isolates were from patients of VAP in SICU. Seven of these isolates from SICU were found to be Extended Spectrum Beta Lactamase (ESBL) producers.

As A.baumannii was the predominant isolate, its antimicrobial profile was also studied. As shown in Figure 2 all A.baumannii isolates were found to be multidrug resistant including Carbapenems except for Colistin which was sensitive in all the isolates. In a previous study resistance to Carbapenems was found to be 36.8% in A.baumannii which was in contrast to the present study[10].As shown in Figure 5, Tetracycline was found to be significantly sensitive (P = 0.008) in SICU isolates of A.baumannii when compared to its counterparts of MICU.

Mortality: A crude mortality rate was calculated for the patients diagnosed of having VAP. Overall mortality rate was found to correlate with previous studies which ranged from 0 – 75% [5,7,9,12-14]. VAP is thought to increase the mortality of the underlying disease by about 30%. [13]. In present study 50%, of the patients who died in the study period belonged to the age group of more than 50 years, this is because advanced age clearly affects the outcome of VAP patients, since older patients do not have significant functional reserves and usually have an unfavourable outcome when they are severely infected.

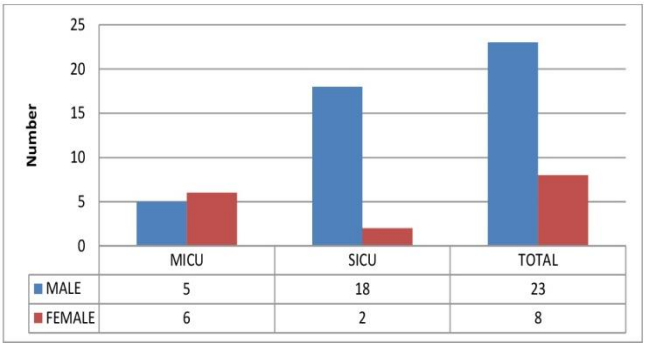

Figure 1: Gender wise distribution of VAP cases

Organism	Number(n =42)	Percent(%)
A.baumannii	20	47.6
E.coli	9	21.4
K.pneumoniae	6	14.3
P. aeruginosa	5	11.9
C. dublinensis	1	2.4
E. cloacae	1	2.4
Total	42	100

Table 1: Clinical isolates of VAP during the entire study period

Organism	MICU n(%)	SICU n (%)
A.baumannii	6(50)	14(46.7)
E. coli	1(8.34)	8(26.7)
K. pneumoniae	3(25)	3(10)
P.aeruginosa	2(16.7)	3(10)
E. cloacae	0(0)	1(3.4)
C.dublinensis	0(0)	1(3.4)
Total	12(100)	30(100)

Table 2: Distribution of clinical isolates n=42 of VAP in MICU and SICU

Time(Days)	A.baumannii n(%)	E.coli n(%)	K.pneumoniae n(%)	P.aeruginosa n(%)	C.dublinensis n(%)	E.cloacae n(%)	Total n(%
<4	7(35)	2(22.2)	1(16.6)	0(0)	1(100)	1(100)	12(28.5%
≥4	13(65)	7(77.8)	5(83.4)	5(100)	0(0)	0(0)	30(71.5%
Total	20(100)	9(100)	6(100)	5(100)	1(100)	1(100)	42(100)

Table 03: Clinical isolates with respect to onset of VAP

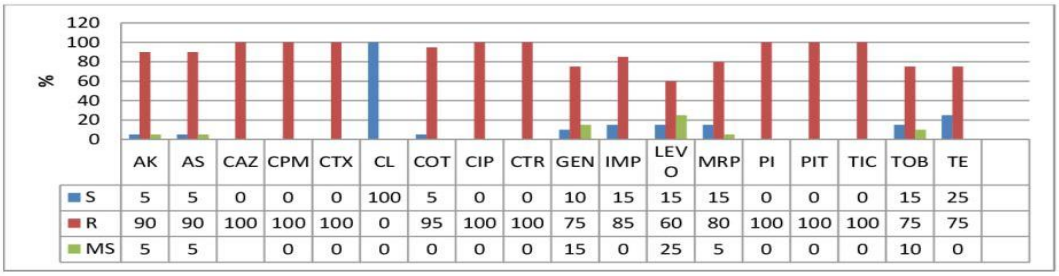

Figure 2: Susceptibility (%) pattern of A.baumannii (n=20) isolated from VAPcases

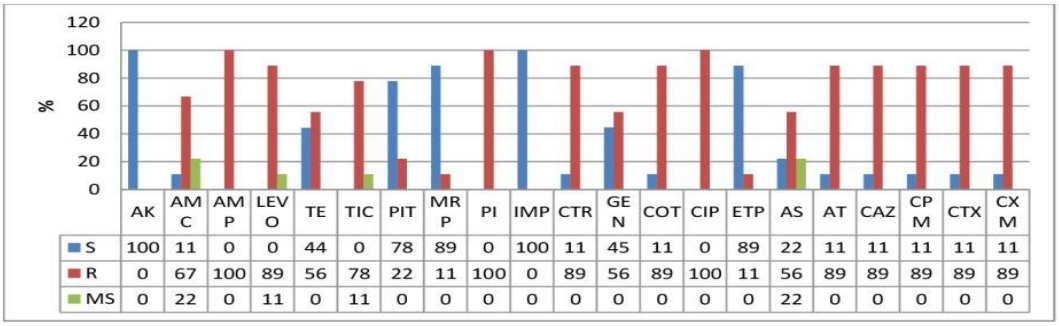

Figure 3: Susceptibility (%) pattern of E.coli (n=9) isolated from VAP cases

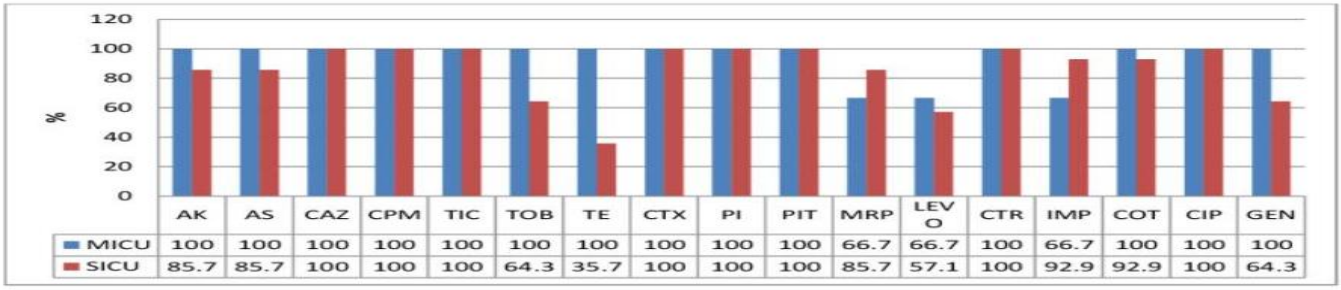

Figure 4: Resistance (%) pattern comparison of A.baumannii (n=20)isolates from cases of VAP in MICU and SICU

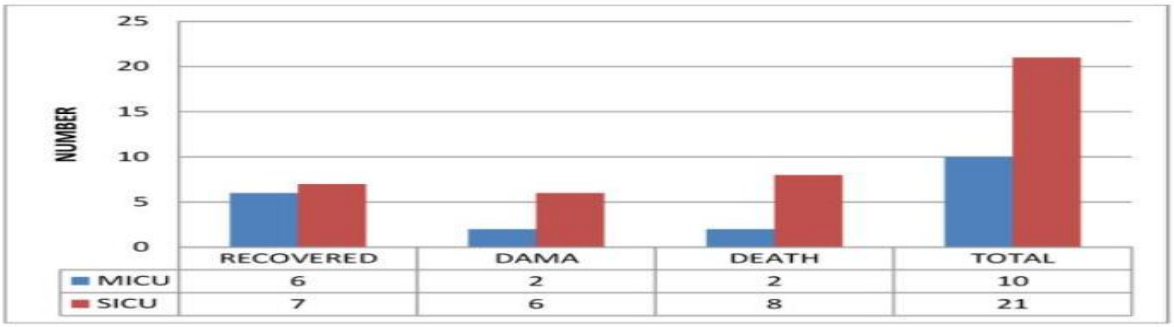

Figure 5: Outcome of cases of VAP in MICU and SICU

Conclusions: The important observations and conclusions of the study were as follows: - Ventilator associated pneumonia was identified as a significant problem causing morbidity and mortality amongst patients of Medical and Surgical Intensive Care Units. A total of 31 cases of VAP were detected from MICU and SICU.

A total of 42 clinical isolates were identified from 31 cases of VAP during the entire study period. Acinetobacter baumannii (n=20, 47.6%) was the predominant isolate in both ICUs as well as in early onset and late onset VAP cases. Multidrug resistant Acinetobacter continues to be the chief causative agent for VAP. It seems that Acinetobacter is an

endemic pathogen in our ICUs and is also responsible for frequent outbreaks. Infections with these drug resistant organisms increase the chances of treatment failure, morbidity and mortality and cost of treatment. Formulation of an antibiotic prescribing policy for ICUs and its strict implementation followed by a regular surveillance and study of their resistant patterns is needed for controlling the spread of antibiotic resistance in such nosocomial pathogens.A thorough review of clinic-pathological as well as radiological findings should be performed while reporting a clinical isolate from tracheal aspirates. Microbiological data should be used for tailoring antibiotic therapy and not be restricted only to diagnosis. The pitfall in using empiric antibiotics for suspicion of VAP is the potential for antibiotic overuse, emergence of resistance, unnecessary adverse effects and potential toxicity. In summary, surveillance data are crucial and should become an important component of hospital infection control program.

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