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RESEARCH ARTICLE

STUDY OF VAP IN A TERTIARY CARE POST GRADUATE TEACHING INSTITUTE IN ROHILKHAND REGION OF NORTH INDIA

^{1*}Verma H, ²Nanda H. S, ³Jauhari M, ⁴Singh S, ⁵Yadav N.

^{1,2,4}Department of Anaesthesia & Critical Care, SRMSIMS, Bareilly
³Department of Pulmonary Medicine & Critical Care, SRMSIMS, Bareilly
⁵Department of General Medicine & Critical Care, SRMSIMS, Bareilly

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ABSTRACT

VAP is defined as development of bacterial pneumonia in patients on mechanical ventilation for > 48hrs. Lack of gold standard diagnostic criteria for VAP leads to either over-diagnosis (leading to overuse of antibiotics) or under-diagnosis (leading to delayed antibiotic use), both of which are potentially harmful situation for the patient. A review of literature shows only few studies have been published on VAP in ICU's of India. With growing incidence of resistance among organisms isolated in VAP, a combined approach of antibiotic restriction along with appropriate de-escalation therapy, effective surveillance and good infection control (isolation and barrier nursing practices) is essential if antibiotic resistance has to be overcome. Our present study was done with an aim to know the incidence of VAP (early and late) in our ICU, to evaluate the impact of VAP on duration of mechanical ventilation, length of ICU stay and mortality (outcome), to find out the organisms isolated and there antibiotic resistance pattern. With this knowledge, we aim to formulate a regional empirical antimicrobial policy which will help us in prompt initiation of appropriate antibiotic regimen and improve patient outcome.

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INTRODUCTION

VAP is considered the most dreaded commonly acquired infection in ICU. VAP is now a days no longer considered an unfortunate occurrence. Rates of occurrence of VAP have become markers of quality of care in ICU. Rates of VAP generally range from 6 -52% and can be as high as 76% depending upon the critical care setting (Davis, 2006 and Kollef, 2000). In general, the surgical ICUs have higher rates of VAP compared to the medical ICU's³ (Leonid *et al.*, 1998). The incidence of nosocomial pneumonia was reported as 21.6% in patients admitted to a cardiothoracic ICU, 14% in surgical ICU and 9.3% in a medical ICU⁴ (Niederman and Craven, 2005). Mortality ranges from 40-80% (Kollef, 1993). Diagnosis of VAP is based on clinical (fever, cough, change in secretions, tachypnea etc), pathological (elevated WBC counts), microbiological (positive cultures like blood/sputum/tracheal aspirate) and radiological (appearance of new infiltrates) parameters. Clinical criteria alone are insufficient in the diagnosis of VAP as a variety of pathologies (pulmonary odema/infarction, ARDS) can mimic pneumonia. Clinical tools such as the Clinical Pulmonary Infection Score (CPIS) has a sensitivity of 72% and specificity of 80% and is not very accurate for diagnosing VAP (Fagon, 2001).

Current practice and opinion is divided on the relative merits of non-invasive and invasive (bronchoscopic) techniques in obtaining specimens for diagnosis. The most common technique of sampling is endotracheal aspirate cultures (non-invasive, cheap, can be done easily, doesn't need expertise and is relatively free of complications). Other invasive methods include PSB (Protected Brush Specimen) and BAL (Broncho-Alveolar Lavage) which are considered better when patient is not responding to initial empirical antibiotic therapy. In terms of impact on outcome, both invasive and non-invasive methods fare similarly. The usefulness of quantitative cultures is in differentiating respiratory tract infection from colonization which is very common in mechanically ventilated patients (Sole Violan *et al.*, 2000 and Fagon *et al.*, 2000). There is growing concern in medical fraternity regarding incidence of multi drug resistance among organisms causing VAP. A Knowledge of local etiological agent causing VAP and their antibiotic resistance pattern is very essential for initiation of appropriate empirical antimicrobial therapy, which inturn will help improve the clinical outcome (Chiranjoy *et al.*, 2003).

MATERIALS AND METHODS

SRMS-IMS is a 950 bedded post-graduate teaching tertiary care institute with 23 bed ICU admitting patients of almost all

*Corresponding author: Verma, H.
Department of Anaesthesia & Critical Care, SRMSIMS, Bareilly

specialities (neurology, neurosurgery, nephrology, cardiology, oncology, gastroenterology, general surgery, respiratory medicine, general medicine). Most of the patients are referred from nursing homes or other primary/secondary care settings. Ours is a resource limited setting, catering primarily to the needs of poor patients of rohilkhand region. 300 patients of either sex in age group of 20-60yrs who were intubated in our ICU & put on mechanical ventilation for > 48hrs were included. Patients admitted with ARDS, pneumonia or developed pneumonia or who died within 48hrs of initiation of mechanical ventilation were excluded. Patients re-intubated in ICU, intubated outside in wards or other hospitals were also excluded. Diagnosis of VAP was made on subjective clinical impression and further substantiated using modified clinical pulmonary infection scoring system & quantitative culture of endotracheal aspirates. A score of > 6 and colony forming units $>10^5$ /ml was used as diagnostic criteria for VAP.

Endotracheal aspirate was collected after 48hrs once VAP was diagnosed by CPISS. A 22 inch 12 Fr suction catheter was inserted into endotracheal tube till resistance is met, then suction catheter is withdrawn for 1 cm and about 1ml of specimen collected and sent to microbiology lab in a sterile mucus extractor. Once the clinical suspicion was established, empirical antibiotic therapy was initiated based on guidelines prescribed by the American Thoracic Society. Patients were routinely screened by arterial blood gas (ABG) analysis every 8-12 hourly and appropriate steps were taken to correct any change. Diagnosis of VAP was made when quantitative cultures of endotracheal aspirates showed $>10^5$ colony forming units/ml. A detailed proforma was made which included name, age, sex, BMI, diagnosis & reason for intubation, day of diagnosis of VAP. Tracheal aspirate reports, organisms isolated & antibiotic sensitivity pattern was also noted. Patient's were followed up till weaned off from ventilatory support, shift out from ICU & final outcome (survival or death).

RESULTS AND DISCUSSION

Ventilator associated pneumonia stands as an important cause of hospital morbidity and mortality. Intubated patients are at risk of developing VAP and the incidence increases with the duration of ventilator support. During prolonged mechanical ventilation, the oropharynx, nasopharynx, sinuses and dentition become colonized with pathogens. These secretions get pooled into the subglottic space. Due to micro-aspiration, these can enter the lower respiratory tract leading to VAP. From Table 1, the incidence of VAP in our ICU is 35%, which is slightly high. In recent studies, the reported incidence of VAP is very low upto 15-30%. The probable reasons for high VAP in our ICU are the nursing ratio of 1:3 for all patients whether on ventilator or not. Heavy patient load and sickness of patients leads to poor implementation of aseptic nursing practices like lack of proper hand hygiene & our nurses regularly use saline/distilled water for suctioning endotracheal tube. Avoidance of early tracheostomy by some of the admitting consultants, probably because of ignorance and backwardness of the patient attendants, leading to delayed consent for tracheostomy. Poor affordability of patients thereby limiting use of subglottic suction, closed suction kits

and new ventilatory circuits for each patient (Gadani *et al.*, 2010). From table 3, it is clear that the predominant ICU patients were males with male: female ratio of 2.1 – 2.3: 1 in almost all groups. The average age groups ranged from 54 to 58 yrs and were comparable among all age groups. The average BMI was 19 to 21 kg/m² and comparable in all age groups. Our medical college is a tertiary care institute set up in a remote village primarily catering to the needs of poor, downtrodden patients of rohilkhand region of Uttar Pradesh. This is reflected by the statistics like low BMI and predominant male patients seeking medical care. The average duration of mechanical ventilation and ICU stay of VAP patients was prolonged by 7-8 days as compared with non VAP patients and the difference was statistically significant (12.63+/- 4.03 day & 14.2+/- 3.95 day vs 5.66+/-1.66 day & 6.67+/- 1.58 day; p value - < 0.001) (Goel *et al.*, 2012).

The average duration of mechanical ventilation and ICU stay of late VAP patients was prolonged by 7-8 days as compared with early VAP patients and the difference was statistically significant (15.4 +/- 2.37 day & 16.97+/-2.14 day vs 8.125 +/- 0.76 day & 9.7 +/- 0.79 day; p value - < 0.001) (Goel *et al.*, 2012). The positive relation between duration of mechanical ventilation and VAP has long been established, but there is controversy as to whether it is the occurrence of VAP that leads to long stay on ventilator or vice versa. However, since most cases of VAP occur early during ventilation, a prolonged stay on ventilator is a result of VAP, rather than being a risk factor of VAP (Kappstein *et al.*, 1992). Non availability of round the clock intensivists leads to unregulated use of sedatives, analgesics and muscle relaxants by resident doctors. This leads to failure of repeated regular spontaneous breath trials, thereby increasing the duration of mechanical ventilation and increasing the chances of VAP. Administration of intravenous sedatives to patients on mechanical ventilation also impairs their cough reflex increasing the risk of aspiration and subsequently predisposing them to development of VAP. Also as our's is a tertiary care hospital and there are large number of patients of neurology, neurosurgery and patients in multiorgan failure who require prolonged duration of mechanical ventilation because of their nature of illness, thereby increasing incidence of late VAP & mortality.

The overall mortality in our ICU is 41.7% (125/300) and mortality among non VAP patients is 35.8% as compared to 52.5% in VAP patients. Mortality rate ranges from 40% to 80% (Aly *et al.*, 2008 and Kollef, 1993). The high incidence of mortality in general in our ICU is because most of the patients are referred from nursing homes after higher antibiotics have already been used. They usually come at an advanced stage of illness, in multi-organ dysfunction & after having exhausted their financial resources. Because of financial constraints of patients, sometimes higher antibiotics have to be compromised, important life support like CRRT cannot be afforded thereby increasing the mortality. The incidence and mortality of late VAP is higher than early VAP (62% vs 38% & 66% vs 30%). Our results are similar to other studies, where early VAP was around 40% and early VAP had better prognosis than late VAP (Wilhelmina *et al.*, 2009). From table 4, we observe that the predominant patients in our ICU, 160 out of 300 were from departments of respiratory

Table 1. Recommended threshold for quantitative cultures in differentiating colonization from infection in ETA (Endotracheal Aspirate), PSB (Protected brush Specimen), BAL (Bronchoalveolar Lavage) (Sole Violan *et al.*, 2000 and Fagon *et al.*, 2000)

	Endotracheal Aspirate	Protected brush Specimen	Bronchoalveolar Lavage
Neutrophils	>25%	>50%	77-82%
Squamous epithelial cells	-	<1%	>1%
Colony count (cfu/ml)	$\geq 10^5$ - 10^6	$\geq 10^3$	$\geq 10^4$
Sensitivity (%)	50-70	33-100	42-93
Specificity (%)	70-85	50-100	45-100

Table 2. Modified clinical pulmonary infection scoring system (Fagon, 2001)

CPIS SCORE	0	1	2
Leukocyte Count	>4,000 and <11,000	<4,000 and >11,000	<4,000 and >11,000 + band forms
Temp	>36.5 and <38.4	>38.5 and <38.9	>39 or <36
Pao ₂ /FiO ₂	>240 or ARDS	-	240 and no ARDS
Chest Radiograph	No Infiltrate	Diffuse Infiltrate	Localized Infiltrate
Culture Of Tracheal Aspirate	Negative	-	Positive

Table 3. Patient Profile

	NON VAP	VAP	EARLY VAP	LATE VAP
INCIDENCE	195 (65%)	105 (35%)	40 (40/105 - 38%)	65 (65/105 - 62%)
MORTALITY	70 (35.9%)	55 (52.5%)	12 (12/40 - 30%)	43 (43/65 - 66%)
MALE	134	72	28	44
FEMALE	61	33	12	21
MECHANICAL VENTILATION (DAYS)	5.66+/-1.66	12.63+/- 4.03	8.125 +/- 0.76	15.4 +/- 2.37
ICU STAY (DAYS)	6.67+/- 1.58	14.2+/- 3.95	9.7 +/- 0.79	16.97+/-2.14
P VALUE	Highly significant		Highly significant	
AGE (mean in yrs)	54.22	57.01	55.78	57.77
BMI(wt in kg/ht in m ²)	19.33	20.48	20.01	20.78

Table 4. Distribution of Patients

	No	%	Early VAP No	Early VAP %	Late VAP No	Late VAP %	Non VAP
1. RESPIRATORY MEDICINE (acute exac COPD/bronchial asthma)	64	21.33%	11	27.5%	11	17%	42
2. CARDIOLOGY (acute MI/LVF, cor pulmonale, CCF)	58	19.33%	10	25%	5	7.7%	43
3. NEUROSURGERY (head injury, hematoma, contusion)	38	12.67%	5	12.5%	15	23.1%	28
4. NEUROLOGY (GBS, encephalitis, meningitis, stroke)	28	9.33%	3	7.5%	12	18.5%	13
5. GENERAL MEDICINE (poisoning, sepsis, MODS, dengue)	24	8%	3	7.5%	7	10.7%	14
6. GENERAL SURGERY (acute pancreatitis, acute abdomen)	23	7.67%	2	5%	7	10.7%	14
7. NEPHROLOGY (UTI-sepsis, AKI, CKD - MODS)	21	7%	2	5%	2	3.1%	17
8. GASTROENTEROLOGY (upper GI bleed, hepatic encephalopathy, CLD)	19	6.33%	1	2.5%	2	3.1%	16
9. RADIATION ONCOLOGY (patients on radiotherapy)	15	5%	2	5%	2	3.1%	11
10. OBSTETRICS - GYNECOLOGY (PIH, APH, PPH, IUD in sepsis/DIC)	11	3.67%	1	2.5%	2	3.1%	8
TOTAL	300	100%	40	100%	65	100%	195

medicine (21.33%), cardiology (19.33%), neurosurgery (12.67%) departments and rest comprised by neurology (9.33%), general medicine (8%), general surgery (7.67%), nephrology (7%), gastroenterology (6.33%), radiation oncology (5%) and obstetrics (3.67%) respectively. Ours is the largest multispeciality hospital in rohilkhand region, equipped with all the super specialities and this is reflected in the variety of patients we receive in our ICU. Incidence of early VAP was highest among patients of respiratory medicine (27.5% - 11/40), followed by patients of department of cardiology (25% - 10/40) and neurosurgery (12.5% - 5/40). We feel that patients

like acute exacerbation of asthma/COPD, acute left ventricular failure, evacuation of EDH/SDH, upper GI bleed, post exploratory laparotomy need ventilatory support for less duration. So chances of late VAP are rare. The incidence of late VAP was highest in patients of neurosurgery (23.1% - 15/65), neurology (18.5% - 12/65), respiratory medicine (17% - 11/65), acute pancreatitis and patients of MODS. Neurology and neurosurgical patients have impaired conscious level, poor cough and swallowing reflexes and abnormal breathing patterns predisposing them to intubation and mechanical ventilation and higher incidence of late VAP as these patients

Table 5. Distribution, Incidence & Mortality among Organisms Causing VAP

ORGANISM	Number	% Incidence (no/105)	Deaths	% Mortality (death/no)	Early VAP No (% - No/40)	Late VAP No (% - No/65)
A. Gram negative	60	57.14%	31	51.7%	20 (50%)	40 (61%)
1. Acenietobacter	20	19.04%	13	65%	5 (12.5%)	15 (23%)
2. Pseudomonas	14	13.33%	7	50%	5 (12.5%)	9 (14%)
3. Klebsiella	10	9.5%	4	40%	3 (7.5%)	7 (11%)
4. Eischerscia	8	7.6%	4	50%	3 (7.5%)	5 (7.7%)
5. Serratia	4	3.8%	1	25%	2 (5%)	2 (3.3%)
6. Enterobacter	2	1.9%	1	50%	1 (2.5%)	1 (1.7%)
7. Citrobacter	2	1.9%	1	50%	1 (2.5%)	1 (1.7%)
B. Gram positive	32	30.5%	14	43.75%	19 (47.5%)	13 (20%)
1. MSSA	14	13.33%	5	30.8%	9 (22.5%)	5 (7.7%)
2. MRSA	18	17.14%	9	50%	9 (22.5%)	9 (14%)
C. Mixed	13	12.4%	10	76.9%	1 (2.5%)	12 (19%)
TOTAL	105	100%	55	52.3%	40 (100%)	65

Table 6. Antibiotic Sensitivity among Gram Positive Organisms

ANTIBIOTIC	MRSA (18)	MRSA (% Sens)	MSSA (14)	MSSA (% Sens)
1. Vancomycin	18	100%	14	100%
2. Linezolid	17	94%	14	100%
3. Teicoplanin	17	94%	14	100%
4. Clindamycin	15	83%	12	86%
5. Ciprofloxacin	11	61%	10	71%
6. Levofloxacin	14	78%	12	86%
7. Tigecycline	18	100%	14	100%
8. Cefoperazone + Sulbactam	14	78%	12	86%
9. Piperacillin + Tazobactam	14	78%	12	86%
10. Amoxicillin + Clavulinic acid	11	61%	11	80%
11. Colistin	18	100%	14	100%
12. Polymyxin B	18	100%	14	100%

Table 7. Antibiotic Sensitivity among Gram Negative Organisms

ANTIBIOTIC	Acenieto bacter(20)	Pseudo monas(14)	Klebsiella (10)	Eischersia (8)	Serratia (4)	Entero bacter(2)	Citro bacter(2)
1. Ceftriaxone	11 (55%)	8 (60%)	6 (60%)	4 (50%)	2 (50%)	2 (100%)	1 (50%)
2. Meropenem	14 (70%)	10 (70%)	8 (80%)	6 (75%)	3 (75%)	2 (100%)	2 (100%)
3. Imepenem	16 (80%)	12 (85%)	9 (90%)	7 (87%)	4 (100%)	2 (100%)	2 (100%)
4. Colistin	19 (95%)	13 (93%)	10(100%)	8(100%)	4(100%)	2 (100%)	2 (100%)
5. Polymyxin B	20(100%)	14(100%)	10(100%)	8(100%)	4 (100%)	2 (100%)	2 (100%)
6. Amikacin	14 (70%)	9 (65%)	7 (70%)	4 (50%)	3 (75%)	2 (100%)	1 (50%)
7. Gentamicin	12 (60%)	7 (50%)	6 (60%)	3 (37%)	2 (50%)	1 (50%)	1 (50%)
8. Levofloxacin	14 (70%)	10 (70%)	8 (80%)	6 (75%)	4 (100%)	2 (100%)	2 (100%)
9. Ciprofloxacin	12 (60%)	7 (50%)	6 (60%)	5 (63%)	2 (50%)	1 (50%)	1 (50%)
10. Cefoperazone + Sulbactam	13 (65%)	10 (70%)	7 (70%)	6 (75%)	4 (100%)	2 (100%)	2 (100%)
11. Piperacillin + Tazobactam	15 (75%)	12 (85%)	8 (80%)	6 (75%)	4 (100%)	1 (50%)	2 (100%)
12. Amoxicillin + Clavulunate.	11 (55%)	8 (60%)	6 (60%)	4 (50%)	2 (50%)	1 (50%)	1 (50%)
13. Ceftazidime	12 (60%)	9 (65%)	7 (70%)	4 (50%)	3 (75%)	1 (50%)	2 (100%)
14. Tigecycline	20(100%)	14(100%)	10(100%)	8 (100%)	4 (100%)	2 (100%)	2 (100%)
15. Doxycycline	15 (75%)	11 (80%)	7 (70%)	6 (75%)	4 (100%)	1 (50%)	2 (100%)
16. Chloramphenicol	20(100%)	12 (85%)	10(100%)	8 (100%)	4 (100%)	2 (100%)	2 (100%)

Table 8. Sensitivity Pattern among Mixed Isolates (>= 3)

ANTIBIOTIC	Acenietobacter (10)	Pseudomonas (8)	Klebsiella (5)	Eischersia (5)	MRSA (7)
1. Ceftriaxone	5 (50%)	4 (50%)	3 (60%)	3 (60%)	-
2. Meropenem	6 (60%)	5 (62.5%)	4 (80%)	5 (100%)	-
3. Imepenem	7 (70%)	6 (75%)	5 (100%)	5 (100%)	-
4. Colistin	8 (80%)	6 (75%)	5 (100%)	5 (100%)	7 (100%)
5. Polymyxin B	10 (100%)	8 (100%)	5 (100%)	5 (100%)	7 (100%)
6. Amikacin	6 (60%)	4 (50%)	3 (60%)	4 (80%)	-
7. Gentamicin	4 (40%)	4 (50%)	3 (60%)	3 (60%)	-
8. Levofloxacin	7 (70%)	5 (62.5%)	4 (80%)	4 (80%)	5 (71%)
9. Ciprofloxacin	5 (50%)	4 (50%)	3 (60%)	4 (80%)	4 (60%)
10. Cefoperazone + Sulbactam	5 (50%)	5 (62.5%)	3 (60%)	3 (60%)	4 (60%)
11. Piperacillin + Tazobactam	7 (70%)	6 (75%)	4 (80%)	4 (80%)	4 (60%)
12. Amoxicillin + Clavulunate.	5 (50%)	5 (62.5%)	3 (60%)	2	4 (60%)
13. Ceftazidime	6 (60%)	5 (62.5%)	4 (80%)	4 (80%)	-
14. Tigecycline	10 (100%)	8 (100%)	4 (80%)	4 (80%)	7 (100%)
15. Doxycycline	7 (70%)	5 (62.5%)	5 (100%)	4 (80%)	5 (71%)
16. Chloramphenicol	10 (100%)	8 (100%)	5 (100%)	5 (100%)	-
17. Clindamycin	-	-	-	-	5 (71%)
18. Vancomycin	-	-	-	-	7 (100%)
19. Teicoplanin	-	-	-	-	7 (100%)
20. Linezolid	-	-	-	-	6 (86%)

require prolonged ventilatory support. Patients who have COPD/ bronchial asthma have a higher predisposition for respiratory infections (VAP), also they receive variety of drugs (steroids) through intravenous & inhalation route (chance of cross infection/contamination by nurses). VAP significantly increases there duration of mechanical ventilation & ICU stay (Wilhelmina *et al.*, 2009 and Gaucouin *et al.*, 2009). From the table 5, it is evident that gram negative organisms are most commonly isolated organism with an incidence of 57.14% (60/105) followed by gram positive 30.4% (32/105) and mixed organism 12.4% (13/105). Acenietobacter (20/105 - 19.33%) is most commonly isolated gram negative organism followed by MRSA (18/105 - 17%), MSSA (14/105 - 13%), pseudomonas (14/105 - 13%), mixed (12/105 - 12.4%), klebsiella (10/105 - 9.4%) and e.coli (8/105 - 7.6%) among VAP. The National Nosocomial Infections Surveillance (NNIS) of CDC of USA reports 60% of nosocomial pneumonias to be caused by aerobic gram negative bacilli (Centers for Disease Control and Prevention, 1986).

In a study done in JIPMER, Pondicherry on VAP in ICU, most cases of VAP were caused by Gram-negative bacteria, *Pseudomonas aeruginosa* (21.3%) and *Acinetobacter baumannii* (21.3%) were the most common Gram-negative bacteria associated with VAP and *Staphylococcus aureus* (14.9%) was the most common Gram-positive bacteria among patients with VAP. MRSA accounted for 42.9% of the VAP due to *Staphylococcus aureus*. VAP was polymicrobial in 27.8% (Joseph *et al.*, 2009). In our study gram positive (*staph aureus* - 32/105) accounted for 30.4% of organisms causing VAP and MSSA accounted for 44% of *staph aureus* (14/32) and MRSA accounted for 56% of *staph aureus* (18/32). The National Nosocomial Infections Surveillance report indicates that *Staphylococcus aureus* causes approximately 20% of the nosocomial lung infections (Navneeth and Sandhya Belwadi, 2002). In a UK study on gram-positive isolates from respiratory tract of ICU patients, 44% of *Staphylococcus aureus* isolates have been reported (Centers for Disease Control and Prevention, 2000 and Johnson *et al.*, 2003). MRSA accounts for 52.3% of *Staphylococcus aureus* nosocomial infections. Our results partially match with the above studies (Navneeth and Sandhya Belwadi, 2002; Centers for Disease Control and Prevention, 2000 and Johnson *et al.*, 2003).

The most commonly isolated organisms in early VAP is MSSA (9) & MRSA (9) followed by Acenietobacter (5) and *Pseudomonas* (5) and in late VAP, it is Acenietobacter (15), mixed organisms (>=3 organisms - 12), pseudomonas (9) and MRSA (9). Mortality is highest among mixed organisms (10/13 - 76.9%) followed by acenietobacter (13/20 - 65%), MRSA (9/18 - 50%) and pseudomonas (7/14 - 50%). From the table 6, it is evident that in our ICU, both MRSA and MSSA are 100% sensitive to Vancomycin, Tigecycline, Colistin and Polymyxin B. Only one MRSA organism isolated showed resistance to both linezolid and teicoplanin. Among MRSA, sensitivity to ciprofloxacin and amoxicillin-clavulunate was lowest (61%) followed by levofloxacin, cefoperazone/sulbactam and piperacillin/tazobactam (78%). Among MSSA, sensitivity to ciprofloxacin was lowest (71%) followed by amoxicillin-clavulunate (80%), levofloxacin,

cefoperazone/sulbactam and piperacillin/tazobactam (86%). From Table 7, we observe that all the gram negative organisms showed 100% sensitivity to newer antibiotics like Colistin, Tigecycline and less commonly used antibiotic like Chloramphenicol. Gram negative organisms like serratia, enterobacter & citrobacter were highly sensitive to almost all antibiotics. Among the more commonly isolated gram negative organisms like acenietobacter, pseudomonas, klebsiella and e.coli, lowest level of sensitivity was observed to ceftriaxone (55-65%), gentamicin (37-60%), ciprofloxacin (50-60%) and amoxicillin-clavulunate (50-60%). The sensitivity among higher antibiotics like doxycycline was 70-80%, levofloxacin was 70-80%, ceftazidime was 50-70%, cefoperazone/sulbactam was 65-75%, piperacillin/tazobactam was 75-85%, meropenem was 70-80%, imipenem was 80-90%. Resistance to colistin was found in one patient each of acenietobacter and pseudomonas.

From Table 8, among mixed isolates most commonly isolated organism was acenietobacter (10) followed by pseudomonas (8) and MRSA (7). All the gram negative organisms were 100% sensitive to polymyxin B and chloramphenicol. All the MRSA were 100% sensitive to vancomycin and teicoplanin followed by linezolid (86%), clindamycin and levofloxacin (71%). The acenietobacter isolated in mixed group showed lowered sensitivity to almost all the higher antibiotics (50% - ciprofloxacin, cefoperazone+sulbactam, 60% - ceftazidime, meropenem, amikacin, 70% - doxycycline, levofloxacin, piperacillin+tazobactam, imipenem, 80% - colistin) (Robert *et al.*, 1980 and Leonid *et al.*, 1998). The pseudomonas isolated in mixed group showed lowered sensitivity to almost all the higher antibiotics (50% - ciprofloxacin, amikacin, 62.5% - ceftazidime, meropenem, cefoperazone+sulbactam, doxycycline, levofloxacin, 75% - piperacillin+tazobactam, imipenem, colistin) (Robert *et al.*, 1980 and Leonid *et al.*, 1998). In the mixed group, incidence of resistance to colistin was seen in 2 cases each of acenietobacter and pseudomonas. Also incidence of resistance to tigecycline was seen in 1 case each of klebsiella and e.coli.

Antimicrobial resistance monitoring helps in optimisation of antimicrobial therapy and is more important in the ICUs as infection and antimicrobial consumption are significantly higher. To maintain a low level of resistant organisms, isolation policies have to be adopted and strictly implemented while handling colonised or infected patients with drug resistant organisms. Barrier-type nursing care and precautions need to be taken while cultures of such patients are awaited. This requires improvement in standards of nursing care. Effective surveillance for presence of resistant organisms in patients referred from local nursing homes should be done. All such patients should be screened for and considered as a source of resistant bacilli, observing special precautions during patient care while the appropriate culture are being processed in the laboratory (Niederman and Craven, 2005). The possibility of reducing resistance by controlling the use of antibiotics is a logical but this is easier said than done. Antibiotic rotation, de-escalation of antibiotic usage upon receiving culture reports and practicing antibiotic holidays can help prevent development of resistance. Educating the doctors in primary and secondary care settings about the rationale use

of antibiotics is also of utmost importance as we have observed a very illogical, irrational and rampant use of higher antibiotics in our region. Measures to regulate the use of higher antibiotics by uncertified medical practitioners and quacks should be implemented (Porzecanski and Bowton, 2006). A combined approach of antibiotic restriction, effective surveillance and good infection control practices is essential if antibiotic resistance is to be overcome.

Limitations of the Study

1. Our diagnosis of VAP was based on clinical impression (Modified CPISS) and quantitative culture analysis of endotracheal aspirate only.
2. Our microbiology does not support us with fungal culture & sensitivity.
3. Our outcome does not include the primary disease & its severity.
4. Other factors which have a co-relation with VAP like supine position, use of sedatives, emergency or planned intubation or re-intubation, use of stress ulcer prophylaxis or steroids and tracheostomy were not studied.

Measures Suggested to Decrease VAP in our ICU

Every member of the critical care unit (ward boys, nurses, resident doctors, treating physicians and critical care specialist) should be made aware of the factors that predispose the patient for development of VAP and the importance of prevention of VAP.

At nursing level

Strict implementation of hand hygiene by all medical, para-medical health professionals. Use of oral chlorhexidine mouth wash twice daily. Avoiding regular use of saline for suctioning.

At level of intensivist

Counseling both the primary consultants and the patients attendants for early tracheostomy. Supervising the work of nursing staff and resident doctors thereby proper implementation of all correct practices. Training the resident doctors and regulating the use of opioid analgesics, sedatives and muscle relaxants. Implementation of sedation and weaning protocols and judicious use of antibiotics and de-escalation therapy whenever possible. Ensuring the use of new ventilatory circuit, closed suction kit and subglottic suction endotracheal tubes for all patients who are put on mechanical ventilation.

At level of hospital administration

1:2 nursing ratio for atleast ventilated patients. Making of cubicles for separate fumigation. Proper disinfection of bed, ecg leads etc before taking the next patient. Regular disinfection of floor twice and whenever soiled in each nursing shift. Providing atleast one intensivist along with a resident doctor in each shift. Providing a supervisor to strictly analyse and point out wrong doing's by doctors and nurses.

Conclusion

Incidence of VAP is high in our ICU and this is leading to significantly prolonged duration of mechanical ventilation and ICU stay. Incidence of late VAP is high in our ICU and it is associated with high mortality. Gram negative organisms account for majority of cases of VAP. Acenietobacter is most commonly isolated gram negative organism in late VAP and Staph aureus is most commonly isolated in early VAP. Patients with mixed (≥ 3) organisms have the highest mortality. The sensitivity to commonly used combination antibiotics like cefoperazone+sulbactam, piperacillin+tazobactam and higher antibiotics like meropenem, levofloxacin, amikacin is on the decline. One case each of resistance to recent antibiotics like colistin, polymyxin b and tigecycline was found among gram negative organism and one case each of resistance to linezolid and teicoplanin was found in MRSA. Surprisingly chloramphenicol which is very rarely used today was found sensitive in all the cases. Every member of the critical care unit (ward boys, nurses, resident doctors, treating physicians and critical care specialist) should be made aware of the factors that predispose the patient for development of VAP and the importance of prevention of VAP. This study conclusively proves the need for corrective measures to be implemented in our ICU. Further studies in future have to be done in order to quantify the impact of the various preventive measures in actually preventing VAP in our ICU.

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