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Pathogenic and Non-Pathogenic Microbial Presence in Ventilator Associated Pneumonia Patients in Intensive Care Unit and Safety Protocols Under Surveillance of Healthcare Provider: A Research Study

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Article History	Abstract
	Ventilator-associated pneumonia (VAP) is a common hospital-acquired infection that is associated with longer stays in intensive care units (ICUs) and under mechanical ventilation for more than 48 hours. This article explores the prevalence and impact of VAP on mortality and morbidity, emphasizing the microbial associations involved in hospital-acquired infections. Various infections, including Lung infections, surgical site infections, sepsis, and urinary tract infections, are discussed, along with their associated microorganisms. Diagnostic criteria for VAP and related infections are outlined, highlighting the importance of microbiological testing for accurate diagnosis. The underlying factors for VAP acquisition in ICU patients are identified, and prompt antibiotic initiation is emphasized as a critical first-line defense against VAP. In this study, we have populated data from 100 ICU patients, among which 45 were suffering from VAP. It was found that female patients (57.40%) were more affected than male patients (30.43%). The decreasing PaO2 level was seen to be the early sign of infection. It was found that the time of ventilation was the major factor influencing the VAP. The most common organism causing infection in our study was found to be Staphylococcus Aureus (45.1%). The prognosis of early-onset VAP was 35.55% while compared to Late-onset VAP 64.44%. When compared to VAP and Non-VAP patients there was not very huge difference with 55% and 45% respectively. The other factor was age and position. Implementation of Prevention strategies, such as protective environments and HEPA filtration systems, is proposed to reduce VAP incidence. Proper diagnosis, treatment, and prevention are crucial to combatting VAP and enhancing patient outcomes in hospital settings.

1. Introduction

Ventilator-associated pneumonia (VAP) is the second most common cause of infection in intensive care units (ICUs). It is an Airway infection in critically ill patients and one of the most common complications in cases of mechanical ventilation (MV). [1] it is a type of lung infection that affects

patients on invasive breathing equipment in hospitals. Ventilator-associated pneumonia is defined as pneumonia that develops at least 48 hours after endotracheal intubation. [2,3] VAP is commonly linked with infections acquired from longer stays in hospitals under intensive care in Noncardiac ICUs.[4] Most micro-organisms associated with hospitals are termed nosocomial infection whenever we must visit or stay at healthcare facilities.

Patients with weakened immune system, such as immunocompromised and elderly patients, may be more susceptible to nosocomial infections. Other risk factors for nosocomial infections include long duration of hospital stay, multiple underlying comorbidities, frequent visits to health care facilities, long term treatment with immunosuppression treatment like Immunosuppressants, chemotherapy, steroids. Patients who are under mechanical ventilation, recent invasive procedures, indwelling devices and frequent visits to health care facilities are also at high risk for acquiring infection. [5,6]. According to the international guidelines, the following markers must be followed to diagnose the VAP: New lung infiltrates on chest imaging, Decline in Respiratory functions (like acute respiratory distress syndrome), Productive cough and Fever. Based on these findings the treatment of patients can be initiated.

Previous long-term use of high-dose corticosteroids increase the chance of infections caused by gram negative organisms like Legionella and Pseudomonas. Chronic suppurative lung diseases like cystic fibrosis and bronchiectasis increases the risk of infection due to gram-negative pathogens, including antibiotic-resistant strains. [2, 3] In a point prevalence survey by CDC conducted in 2015 in US hospitals determined that 427 hospital acquired infections are identified, out of which pneumonia was the most prevalent infection with 32% of those cases being associated with ventilator and mechanical Breathing. [7] Any infection that we acquire from the intensive care unit have an increased rate of mortality compared to other infections. In General, there are not much information are available about the global epidemiology of ICU infection.

Micro-organisms associated with infections

Micro-organisms are ubiquitous and need favorable conditions to grow, some are fastidious and some take their normal time to replicate and grow. The hospital environment is loaded with a huge amount of them, as we broadly classify them as bacteria gram positive and gram negative, viruses (RNA or DNA viruses), fungi, etc. Catheter associated UTI's, Infection on area of surgery, Central line associated bloodstream infections, Pneumonia that is hospital acquired, and Ventilator Associated Pneumonia are examples of common nosocomial infections [8-11]. Staphylococcus aureus (28.4 %) which may be MSSA or MRSA, and Pseudomonas aeruginosa (25.2 %), and other gram negatives (26.6%) are commonly isolated causative organisms [12].

Table 1: Country, causative organism and its prevalence percentage of micro-organisms causing VAP.

Sr. No.	Country	Causative Organism	Prevalence Percentage	References
1	Europe, Canada, South America	Pseudomonas aeruginosa	27%	13-14
		Staphylococcus Aureus	20%	
		Acinetobacter Species	14%	
2	United State of America	Staphylococcus Aureus	32%	14-15
		Pseudomonas aeruginosa	21%	
		Enterobacter	9%	
		Acinetobacter Species	4.4%	
3	Asia	Staphylococcus Aureus	27%	15-16
		Acinetobacter Species	16%	
		Pseudomonas aeruginosa	14%	
		Klebsiella Pneumonia	9%	

Table 2: Organism and Mortality rate of most common organisms causing VAP.

Sr. No.	Organisms	Mortality Rate	Reference
1	Pseudomonas aeruginosa	Mortality is found to be increased as 13.5%. MDR stain Mortality is 35.8%	13-14
2	Staphylococcus Aureus	MRSA rate is 70%, all-cause hospital (55.5%) and infection-related mortality (IRM) (40.0%)	14-15
3	Acinetobacter Species	Mortality rate of patients with Multi Drug Resistant-Acinetobacter baumannii ranged from 52 to 66%	15-16

Following are the different infections acquired from the hospital setting with their corresponding micro-organisms involved:

Respiratory Tract Infection (RTI)

The major contributing microbes of RTI is Pneumonia. Pneumonia is an infection of the airway and lungs that affects the air sacs (alveoli). These alveoli when filled with foreign antigens and other fluids lead to infection of the lungs. Lung infections are further categorized into upper respiratory and lower respiratory depending upon where microbes fulfil their favorable condition. Hospital-acquired pneumonia was found to increase Length of stay (LOS) by 8 days and has elevated rate of mortality 30-70%. This data includes Both VAP and Hospital-acquired Pneumonia which are non-intubated patients [17].

Upper respiratory tract (URT) infections are mostly caused by viruses and a few bacteria such common cold, Sinusitis, Pharyngitis, Epiglottitis, and Laryngotracheitis. URT comprises the anterior nares, nasal cavity, sinuses, nasopharynx, Eustachian tube, middle ear cavity, oral cavity, oropharynx, and larynx [17].

Lower respiratory tract (LRT) infections are mostly caused by pathogenic bacteria and some viruses such as Bronchitis, Bronchiolitis, and Pneumonia. It is broad terminology which includes acute bronchitis, pneumonia, acute exacerbations of chronic obstructive pulmonary disease/ chronic bronchitis (AECB), and acute exacerbation of bronchiectasis.

Hospital-acquired pneumonia (HAP) is mostly caused by micro-organisms such as MRSA (Methicillin-resistant *Staphylococcus aureus*), and like *Pseudomonas aeruginosa,* and other non-pseudomonal bacteria. They show their activity when the patient has increased stay in the hospital by about 8 days in ICU while intubated also known as Late-onset HAP [18]. When infected with such organisms, the mortality rate ranges from 30–70%. Early-onset HAP occurs less than 5 days from the time of admission in the hospital, the organism which is majorly responsible for this is *Streptococcus pneumoniae* [19].

Surgical Site Infections (SSIs)

These are only associated with surgical wounds that are infected with the air and surface - flora that is present around the wound when not maintained proper hygiene postoperative and the wound starts to discharge within 7-10 days of an operation which led to life-threatening complications. The mostly associated microbes are from the Enterobacteriaceae group, including *Escherichia coli, Klebsiella pneumonia, Salmonella, and Shigella* but *S. aureus* contribute more proportion than others present as the normal flora of the skin surface.

Sepsis or Bacteremia It is cascade of disease caused by the self-defense mechanism of one's own immune system and coagulation system activated by the infestation of microbes in the blood stream. It may be leading to complications like multi organ dysfunction (MODS) or end organ damage.

Urinary Tract Infections (UTI) Type of infection caused by the colonization of microorganisms in the urinary tract. The infections can be acute or chronic depending upon the site of infection and severity which can lead to a life-threatening condition of the patient.

Epidemiology

The epidemiology is very limited in ventilator-associated pneumonia due to the absence of systematized criteria for its diagnosis. On Mechanical ventilation (MV) the pathogenic agents are responsible for infection by infecting the Lung parenchyma when staying for more than 48 hours on MV. VAP is mostly caused by bacterial and fungal microbes. The prevalence of VAP covers 8% - 28% for all intubated patients and mortality ranges from 25% to 50% [19].

Experimental study

A case study was performed in ICU of a tertiary care multispecialty hospital for a duration of 1 year from June 2019 to July 2020. we selected 100 random ICU patients to proceed with the study. Patients of more than 25 years, both the sexes and who were kept on ventilator for more than 2 days were taken into consideration. Patients with existing respiratory conditions like pneumonia, chest infection, Lower respiratory tract infection, asthma etc. were excluded from the study. A proper questionary was set and was distributed among patients' attenders. all the information of the patient was noted down like age, sex, date of administration into the ICU, reason for admission, starting date of ventilator etc. were recorded. we have recorded the ventilation settings regularly along with that patient's vitals (oxygen saturation, BP, heart rate and physical examination) were also monitored. then they were divided into 2 groups (early onset and late onset type) and the most common causative organism which is represented in Table 3. VAP has a strong association with increased no of days of hospital stay and exposure which increase health cost burden leading to other complications.

Table 3: Onset of action of VAP, duration of patient on ventilator, its prognosis, complications and Causative organism.

Onset	Mechanical Ventilation Duration	Prognosis	Complication	Causative organisms
Early	<13	Better	No or Mild	Staphylococcus Aureus
Late	≥ 13 days	Worse	Severe	MRSA, Another gram negative Like P. Aeruginosa

Early onset: VAP occurring in <13 days since hospitalization and increased prognosis. **Late onset:** VAP occurring after ≥ 13 days after hospitalization and high morbidity and mortality, MDR stains, Difficult to treat [18].

Diagnosis:

The different diagnostic procedures that were used are:

Clinical & Microbiological Diagnosis

Fever (≤96.8˚F or ≥100.4˚F)

Leukocytosis (≤4000 or ≥12000 cells/ml)

Purulent tracheal secretions

GED (Gas Exchange Dehydration)

Sputum Cultures

Staphylococcal Nasal Swabs (PCR testing for MRSA)

Radiological Diagnosis

Chest X-ray

CT (Computed tomography)

By evaluating the blood cultures and other findings only the presence of some kind of infection in the body can be confirmed. to know the exact cause and type of the infection sputum culture test needs to be performed. In unconscious patients the sputum culture can be taken from there tracheal tube [20-21].

Sputum cultures

Sputum is produced during the infection of the respiratory tract, and there are different types of sputum for different conditions. Pneumonia and cystic fibrosis are bacterial infections of the lower respiratory tract. This infection attracts the neutrophils which have a green color, further leading to dark yellow or green sputum. In Cystic fibrosis the sputum is yellow-green but in the case of pneumonia, it is green in color. During Pneumonia the alveolar sac in one or both lungs is filled with pus and exudate (fluids) which interferes with the gas exchange. For Methicillin Resistant pneumonia, staphylococcal nasal swabs have a very good negative predictive value but a poor positive predictive value [10].

Procalcitonin testing can be used to judge the VAP which is not the right protocol rather it should be used to decide the course of antibiotics during the VAP. Procalcitonin is generally not elevated in 23% during typical bacterial infection. The diagnosis is used to identify HAP or VAP, and to isolate the culprit, based on this isolate tailored antibiotic is used for the treatment. Based on the evaluations proper

antibiotic treated was provided to the patients. Patients were routinely screened by arterial blood gas (ABG) analysis every 12 hourly and appropriate steps were taken to correct any change.

3. Results and Discussion

In this cohort study 100 patients were involved. the mean age of the patients was found to be 53 years in which there were more females when compared to male patients. among these 100 patients 45 patients developed VAP. it was found that the patients who were non-VAP were on ventilation for 13 days and with VAP were on ventilator for 21 days. it was noticed that as the duration of ventilation increase the patients were more tend to develop VAP. the average days were around 16 days. Based on the study it was found that there were more male patients that were getting effected with VAP when compared to female patients. when oxygen saturation of the patients was monitored in VAP patients, Pao_2 was 85% of the patients was <240 mmHg and in 15% patients the ratio was found to be higher that is >240 mmHg. In 15 out of 45 patients there was an early onset (33.33%) and in rest patients there was a late onset time (66.66%). The total mortality rate in the ventilator patient was found to be 47% out of which 36% were suffering with VAP. this showed that VAP causes higher mortality rate. When evaluated we found that the mortality rate depends on the onset time of the infection. Mortality rate on patients with early onset was less than that of the patients with late onset. In our study the most common causative organism causing VAP was found to be Staphylococcus Aureus (45.1%) followed by Klebsiella Pneumonia (20.5%), Acinetobacter Species and Pseudomonas aeruginosa.

Discussion of Results

In our study we have closely monitored the ICU patients who are more tend to develop VAP based on different factors like Age of the patient, Aspiration, Traumatic patients with burns, Multiple organ failure, Head injury (related to oncology), Contaminated medical equipment, Immunocompromised patients etc. There were more female patients when compared to male patients and the incidence of VAP was also more in female patients than in male. the mean age of the patients was found to be 53 years. A proper demonstration on age gender distribution is represented in Table 4.

Table 4: Age gender distribution of ventilator and VAP patients.

AGE	No of total ventilator patients based on Gender		No of VAP cases based on Gender		% of VAP cases based on Gender	
	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE
25-34	10	10	2	3	20%	30%
35-44	13	16	2	7	15.3%	43.75%
45-54	16	18	7	14	43.75%	77.77%
55 and above	7	10	3	7	42.85%	70%
Total	46	54	14	31	30.43%	57.40%
	100		45			

The incidence percentage of VAP in our study was found to be 45% of the total ventilator patients. among which the female patients with 57.40% were found to be more affected than the male patients 30.43%. When we noted the occurrence of VAP based on duration of ventilation it was found that as the time increases there are more chances of VAP. The patient who was on ventilation for 13 days were Non-VAP and mostly patient since 21 days on ventilation were more VAP. 13 days were taken as a mean duration to calculate the VAP and Non-VAP. The representation of the same is done in Table 5.

Table 5: Duration of ventilation and percentage of VAP.

Ventilation days	Total cases	VAP cases	Percentage of VAP cases
≤13	55	29	52.72%
>13	45	16	35.55%
Total	100	45	

Proper treatment needs to be provided for patients suffering with VAP as pe the guidelines. Immediate initiation of antibiotic remedy is the first defence for VAP. Therefore, a short delay in the administration of drugs can increase the mortality rate. The duration of the therapy depends on the organism causing the VAP. Longer treatment duration can reduce the risk of the invigoration of infection after the

discontinuation of antibiotic therapy. So, prior use of antibiotics can also reduce the heavy use of antibiotics and the associated pressure for multidrug-resistant organisms.

Combination therapy is advised instead of monotherapy when VAP caused by MDR strains is expected in order to provide the broadest initial antibiotic coverage until susceptibilities are established [22]. In this case the patient was administered with multiple antibiotics through IV route based on the type of infection and in severely ill patients colistin therapy was used which helped them a lot. We have also recorded the survival and expiry rate of the patients who got effected with VAP and that without VAP along with onset of VAP. It was found that survival rate of male patients with Early onset VAP was higher. On the other hand, survival rate in both male and female patients in Late onset VAP was found to be less. survival rate in Non-VAP patient was very good in both the genders. The same is represented in Table 6.

Table 6: Outcome of VAP and Non-VAP patients.

Outcome	Early onset VAP		Late onset VAP		Total VAP		Non-VAP
	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	
Expired	2	0	9	10	11	10	16
Survived	8	6	4	6	12	12	39
Total	10	6	13	16	23	22	55
	16		29		45		

It was found that expiry of non-VAP patients was 16 while VAP patient was 21. The difference between two was not very much. By this study we came to know that VAP does not make a very big difference in the expiry rate of the ventilator patients. This shows that there should be proper treatment that needs to be provided to the patients on ventilator and proper hygiene needs to be maintained.

Preventive measures to be taken:

The incidence of VAP can be prevented by taking proper care during the hospital stay. The concerned staff should be more accurate and follow proper hygiene in ICU patients specially patients who are on ventilator. level of consciousness also effects a lot in this condition. There should be special care given to the patients who are unconscious. Some of the measures that can be taken for the prevention of VAP are use of high-flow nasal oxygen or non-invasive positive pressure ventilation (NIPPV) to prevent VAP, prone positioning for nonincubated patients, minimal sedation, ventilator liberation strategy, and multimodal agitation management techniques. Raising the bed's head will lower the VAP rates [23].

Protective environment: This is an SPC (specialized patient care) area within hospitals. Here the air flows from the room into the outside adjacent space, providing positive airflow relative to the corridor [25]. The artificial respiratory equipment must be routinely sterilized and the efficiency test of these types of equipment must be checked by microbiological testing before use.

*HEPA filtration system***:** This system is very much a necessity for patients who are at high risk of acquiring the infection such as immunocompromised patients, persons with severe neutropenia for a very long period, patient who had undergone allogeneic hematopoietic stem cell transplant (HSCT), patients receiving most intensive chemotherapy for AML (acute myelogenous leukemia). Here, we see that the combination between higher number's (≥12) of changes in air per hour (ACH) & the minimum leakage of air into the room is achieved through the use of high-efficiency particulate air (HEPA) [24].

Ventilator Acquired Events Surveillance

A specific type of respiratory conditions known as ventilator-associated events (VAEs) may occur in patients on mechanical ventilation. Ventilator Associated Events (VAEs), ventilator-associated pneumonia (VAP), and ventilator-associated tracheobronchitis (VAT) are examples of VAEs [25-26]. The condition known as ventilator Associated Tracheobronchitis (VAT) resides in between VAP and airway colonization. It is diagnosed using clinical and microbiological criteria and is characterized by inflammation of the trachea and bronchi. VAE avoidance is essential for patient safety. This includes measures such as appropriate hand hygiene, regular cleaning of the patient's mouth with chlorhexidine, and elevating the head of bed between 30 to 45 degrees [25-27]. In addition, early risk identification and management of VAEs, including VAP and VAT, are important in reducing morbidity and mortality particularly in critical patients who are under mechanical ventilation [26-28]. A number of objective

criteria, such as respiratory failure following a period of stability or improvement, are used to identify VAEs [29].

Ventilator-associated events (VAEs) are monitored through surveillance programs in healthcare facilities. Ventilator-associated pneumonia (VAP) was replaced as a possible quality measure for ventilated patients by a surveillance criterion for respiratory complications in ventilated patients, including VAEs, which was discovered by the "The Centre for Disease Control and Prevention" (CDC) [30-31]. HICPAC recommendations address a number of issues, including reducing host risk for infection, monitoring and reporting of infections that are diagnosed, preventing the spread of each disease from person to person, and educating and training healthcare professionals about the prevention and control of lower respiratory tract infections and health-associated pneumonia [32].

4. Conclusion

Nosocomial Infections are arising leading to increased rate of morbidity and mortality in hospitals. Immunocompromised people are at greater risk compared to healthy individuals. Proper sterilization techniques and infection control strategy should be implemented in hospitals and clinical setting to reduce deaths due to infections. There are many types of infections which are Hospital acquired and most of them are resistant and cross contaminative making it difficult to treat. These infections are triggered by some underlying condition or natural trauma, immediate admission to the intensive care unit. The patient is put on mechanical ventilation, and from this MV the patient sometimes gets VAP condition. To reduce the mortality in VAP, diagnosis, and prevention are key roles to prevent it, then the treatment to get out of the MV. A decrease in the PaO2 level is an early predictor of VAP. It was also found that when the patient takes inappropriate antibiotics before the admission to the hospital it reduces the chances of early onset VAP but it leads to development of MDR pathogen. Late onset VAP usually occurs due to lack of predication of VAP and may lead to severe consequences including death. Proper Mechanical Ventilation Events (MVE) surveillance and reporting should be done in hospitals to reduce Infection associated to MV. Proper teaching and training should be provided to health care professional and practitioner in controlling infection.

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