ADDIS ABABA UNIVERSITY

HEALTH SCIENCE COLLEGE

SCHOOL OF MEDICINE

DEPARTMENT OF ANESTHESIA

Survival Status and Mortality predictors Among Patients with Ventilator Associated Pneumonia admitted to Intensive Care Unit in Addis Ababa Governmental Hospitals: Retrospective Follow-up Study

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Declaration

I, the undersigned investigator agreed to take responsibility for the scientific, ethical, and technical conduct of the research project and provision of the required progress reports as per terms and conditions of the research and publications office of Addis Ababa university. The author surely declared that there is no competing interest.

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ABBREVIATIONS AND ACRONYMS

ICU	Intensive Care Unit
AICU	Adult Intensive Care Unit
VAP	Ventilator Associated Pneumonia
EOVAP	Early Onset Ventilator Associated Pneumonia
LOVAP	Late Onset Ventilator Associated Pneumonia
MDR	Multi Drug Resistant
XDR	Extensive Drug Resistant
DS	Drug Sensitive
MV	Mechanical Ventilator
HAP	Hospital Acquired Pneumonia
TASH	Tikur Anbessa specialized hospital
BMI	Body mass index
ARDS	Acute Respiratory Distress Syndrome
COPD	Chronic Obstructive Pulmonary Disease
FIO2	Fraction of Inspired Oxygen
HR	Hazard Ratio
AHR	Adjusted Hazard Ratio
CHR	Crude Hazard Ratio

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Abstract

Background: Ventilator associated Pneumonia causes extended hospital stays for severely ill patients as well as an increase in their financial burden. It is also linked to poor outcomes including morbidity and mortality. Depending on different studies mortality related to VAP ranges from 0-50% in some studies it can rise to 74%. However, since Ventilator associated Pneumonia mostly affects critically ill patients it is challenging to assess the mortality related to this condition.

Objective: To assess Survival Status and predictors of Mortality Among Adult Intubated Intensive Care Unit Patients with Ventilator-Associated Pneumonia in Addis Ababa Governmental Hospitals from January 2021 to April 2024.

Methods and materials: Health institution based retrospective cohort study was conducted in purposively selected governmental hospitals among 126 adult intensive care unit patients who developed ventilator associated pneumonia. The data was collected using structured data extraction tool. Mortality probabilities were assessed by Kaplan-Meier analysis method and the log-rank test was used for comparison. The Cox proportional hazard model was used to identify predictors of 90 days mortality among adult VAP patients. For all statistical tests, two-sided P values of less than 0.05 was considered to be statistically significant. Ethical clearance was obtained from ethical clearance board of college of health sciences, Addis Ababa university and ethical clearance committee of each hospitals.

Results: A total of 126 VAP patient records were included. The mortality rate of VAP patients was 48.4% (61; 95% CI: 39.7,57.1). Predictors of mortality among VAP patients were use of Vasopressors and inotropes (AHR=2.27), acute kidney injury (AHR=2.12), length of hospital stay (AHR=0.95), length of ICU stay (AHR=0.86), and total days on mechanical ventilator (AHR=1.12).

Conclusions: In this study the overall mortality of VAP patients was high. Thus, early detection of VAP in critically ill patients and managing the possible causes of mortality will improve patient outcome.

Keywords: Intensive care unit**,** Ventilator associated pneumonia, mortality, survival status, Addis Ababa

1. Introduction

1.1.Background

Ventilator-associated pneumonia (VAP) occurs after 48 hours following endotracheal intubation; this helps VAP to be differentiated from community acquired pneumonia (1-3).VAP is the most common nosocomial infection identified in the ICU (4). VAP results from bacterial colonization of pulmonary parenchyma when a patient stays on support of mechanical ventilation. Typically; aspiration of secretions, invasion of the aero-digestive tract or use of contaminated materials results in inoculation of the previously sterile lower respiratory tract (5).

Common pathogens causing VAP are Gram-negative organisms such as Klebsiella, Acinetobacter, Pseudomonas species and Gram-positive species. VAP developed with in four days of mechanical ventilation is termed as Early-onset VAP (EOVAP), whereas VAP developed from fifth day on mechanical ventilation is termed as Late onset VAP (LOVAP). EOVAP is usually caused by antibiotic sensitive bacteria and LOVAP is mostly caused by Multi Drug Resistant Pathogens (MDR) (6).

There are different risk factors associated with the incidence of VAP. Those risk factors include; Intensive care unit (ICU) length of stay for more than 5 days, tracheostomy, preexisting critical illness (coma, acute lung injury) and reintubation (7-10).

VAP causes extended hospital stays for severely ill patients, increase nosocomial infection transmission, as well as an increase in their financial burden. It is also linked to poor outcomes including morbidity and mortality (11, 12).

Critically ill patients with the diagnosis of VAP are exposed to an increased risk of mortality. Higher mortality rates among VAP patients are reported from low income countries (13). However, in some literatures VAP was not associated with increased mortality (2, 4, 13-15). This led to various ranges of mortality rates of VAP patients. Moreover, studies investigating predictors for mortality in VAP patients, provided a contradictory outcome. For example, despite majority of researches indicated that initial inappropriate antibiotics treatment was associated with an increased mortality (12, 16), there are also a substantial number of studies that failed to confirm this connection (17, 18).

Across the studies, different factors were associated with an increased mortality of patients who developed VAP. Some of the factors are duration of mechanical ventilation, malnutrition, advanced age and multi drug resistant pathogens (19, 20). Furthermore, another important factor related to higher mortality is the challenge in the diagnosis of VAP. The set criteria used to diagnose VAP has a wide variety and some factors such as radiographs or the aspect of tracheal secretions are affected by subjective biases. which makes it difficult to diagnose VAP and causes delayed recognition of VAP. Therefore, critically ill patients will be susceptible to delayed antimicrobial treatment and overuse of antimicrobials (21-24).

1.2. Statement of the problem

In intensive care units (ICUs) around the world mechanical ventilation is frequently used as a lifesaving modality for range of severely ill patients. However, one of the most dangerous nosocomial infections in severely ill patients is ventilator associated pneumonia, which is linked to high morbidity and mortality as well as high economic, psychological and social expenses for patients and their families (25, 26). Despite modern safety precaution, there is still high reports of VAP incidence (27). Since VAP has not gone away it is politically acceptable to report it even in high income countries (28).

VAP increases length of ICU stay, the cost of care for the patients and the consumption of antibiotics (29, 30).When compared to Non VAP group, ICU length of stay was 18 $\pm$ 9 days in VAP groups where as it was 9.5 $\pm$ 6 days in Non VAP groups. Which shows ICU length of stay was significantly longer in the VAP patients (31).

Moreover, side effects such as pressure ulcer, muscular weakness, feeding and gastro intestinal disorders, Deep Venous Thrombosis (DVT) and post-traumatic stress disorder (PTSD) were significantly higher in VAP group. In the aspect of total ICU costs ; such as direct cost related to, daily charges ,cost of medications and procedures and indirect costs related to, physiotherapy ,psychotherapy ;there was a two-fold increment in the VAP group when compared to Non VAP group (31).

VAP causes the emergence of antibiotic resistant bacteria. Prolonged mechanical ventilation for more than 7 days is a significant predisposing factor for MDR pathogens (32). VAP also increases the work load and stress for health care workers who care for the patients with VAP as it causes prolonged ICU stays.

Mortality related to Ventilator associated pneumonia is a debating concern. The magnitude of mortality among adult VAP patients varies among different literatures. In some literature mortality related to VAP has a range of 25% -50% (2, 4, 16). In other study, the mortality rate of VAP patients raised to 74% (13). Opposing this range some studies reported that VAP was not affecting mortality of critically ill patients, which means VAP related mortality was 0 in those studies (14, 15). Additionally, since VAP mostly affects critically ill patients, it is challenging to assess the

mortality related to this condition (33). According to these literatures, there is a lack of consensus on mortality rate of VAP patients.

The incidence of VAP and outcomes related to VAP have shown to decrease to its lowest level, by applying different preventive methods in both developed and developing countries, but in Ethiopia the outcome of VAP in critically ill patients has got less emphasis and factors which affect the outcome are still not clearly addressed.

The aim of this study was, therefore, to assess the survival status and predictors of mortality of VAP patients in order to evaluate the mortality rate of VAP patients and to identify modifiable and nonmodifiable factors which affect mortality. This study emphasizes on identifying critically ill patients who are at high risk in mortality related to VAP so that significant risk variables can be modified, and their care can be stratified.

1.3.Rationale of the study

There has been an improvement in the field of medicine and settings of Intensive Care Unit. However, ventilator associated pneumonia remains to be the most common nosocomial infection causing significant morbidity and mortality in critically ill patients. VAP is a worldwide concern in critically ill patients who needs support of mechanical ventilation.

To our literature search, many studies in Ethiopia as well as in Africa showed that in ICU patient, higher mortality was noted on patients who needed mechanical ventilators but the impact of VAP on those patients was not well studied. This study will contribute by adding knowledge on how VAP influence clinical outcomes of critically ill adult patients and also helps to improve quality of care given for those patients.

The results of this study will serve as a baseline data for the development of tools (such as the VAP mortality risk stratification tools). Understanding the important variables which predict mortality helps to develop tools which helps to stratify high risk patients based on the identified variables and to take proper and timely measurements to change the outcome.

The findings of this study will also help to identify clinical practice concerns. Incidence of VAP and its associated outcomes place another burden on top of low resource ICU set up of developing countries like Ethiopia. This research will contribute in efforts made to reduce the economic impact of VAP by identify high risk patients in order to avoid unnecessary interventions.

Moreover, the results of this study have paramount importance for illuminating additional possible determinants of VAP morbidity and mortality outcomes, necessitating future research and will help as a reference for further studies which will be done on this topic.

1.4.Significance of the study

Identifying predictors of mortality in patients with VAP help physicians to timely manage those risk factors and to take appropriate measurements. It helps physicians and all stake holders involved in the health care system, to give more emphasis for in hospital mortality of patients who developed VAP, to formulate effective methods for the treatment and prevention of mortality in VAP patients, and to focus on diagnosis and prevention of VAP.

The result of this study will be beneficial for Patients. This study will help to improve the outcomes of patients who developed VAP by identifying important factors which increase their risk of mortality.

Researchers also will be benefited from this study in order to dig more on VAP and to assess more on mortality by using different study designs. our study will become a baseline data for another studies.

2. Literature review

2.1. Survival status of adult intubated intensive care unit patients with VAP

The attributable mortality related to VAP varies significantly across studies from 0 to 50% (34). This variability can be due to four main reasons. First , difficulty in diagnosis of VAP (4, 35). The diagnosis of VAP has been a challenge which needs a combination of clinical, radiological and microbiological diagnosis. There is a limitation on universally accepted, uniform and agreed diagnostic tests for VAP; which leads to variation in both incidence and mortality of VAP among different literatures. According to some studies, the use of more sensitive diagnostic techniques like bronchoalveolar lavage (BAL) culture, may increase the detection of VAP cases while also lowering the mortality rate because these techniques may pick up less severe infections that less sensitive techniques such as endotracheal aspirate culture, might otherwise miss (36, 37).

Second, early initiation of antimicrobials before collection of samples for microbial testes(38). Third, variation in patient populations. some studies only included particular groups of patients such as patients with influenza (39), COVID 19 (39), trauma (40) or sepsis (41). This causes a variation in the reported rate of mortality. And finally, effectiveness of the antimicrobial and the timing of appropriate antibiotic medication(34, 42).

A retrospective cohort study conducted from 2005 to 2011 on total of 621 patients diagnosed with VAP reported that an overall 30 days mortality related to VAP to be 44.4% (12). Based on a prospective randomized control trial it was reported that VAP was an important predictor of mortality in ICU patients. This study was performed on 466 patients with severe acute respiratory distress syndrome (ARDS), of those 466 patients 93 (20%) of them developed first episode of VAP. The mortality rate observed in those patients with VAP during their ICU stay was 33.3% (31/93). In this study the Hazard ratio of VAP increased from [hazard ratio (HR) 1.65 (1.05–2.61) ($p = 0.03$)] to [Adjusted Hazard Ratio (AHR= 2.21 (1.39–3.52)] after adjustment for confounding factors (43).

A retrospective cohort study done in Azerbaijan from 2014 to 2019, among 121 patients who developed VAP 42.9% of mortality was reported (44). Based on a retrospective follow up study

done from 2015 to 2019 on VAP patients with prolonged mechanical ventilation, the 30 days mortality rate after the diagnosis of VAP was 30 % while the 90 days mortality was 63.7% (45).

Another retrospective cohort study done in Ethiopia among 164 patients, 40 of them developed VAP. Among 40 patients who developed VAP mortality was reported on 15 patients (37.5%)(10).

2.2. Predictors of mortality in patients who developed VAP

2.2.1. Sociodemographic and clinical characteristics

Advanced age was related to an increased susceptibility to mortality in VAP patients(46, 47).Based on a multicentre prospective cohort study conducted in 27 European ICUs mortality in elderly patients who developed VAP was 51%(adjusted odds ratio for old age, 2.1; 95% CI, 1.2-3.9 and adjusted odds ratio for very old age, 2.3; 95% CI, 1.2-4.4). The increased mortality observed in the old age and very old age patients when compared to middle aged patients might be because the increased comorbidities and prevalence of multidrug resistance pathogens in those patients (19).

Based on 8 years follow up study done in 2014, in united states, on total of 854 trauma patients, 676 males and 178 females more incidence of VAP was noticed on male patients. Even if less females acquire VAP, increased mortality was noted in female patients (48).

A retrospective cohort study done among 121 patients who developed VAP showed that a low body mass index (BMI) was associated with increased mortality. In this study malnutrition was stated as a determinant of poor prognosis in patients who developed VAP (44).

Across the studies outcomes of VAP patients is controversial. According to a literature review and metanalysis study on patient outcome of VAP on Traumatic Brain Injury it was found that VAP was not related to mortality. However it was stated that VAP increased duration of mechanical ventilation and ICU length of stay(15). Similarly a study on patients with Acute Brain Injury also stated that VAP has no impact on patient mortality (14). Whereas a study on twenty eight days mortality on blunt traumatic brain injury and co injuries showed that there was an increased mortality by two times in patients with VAP when compared to patients without VAP (49). This

difference can be due to the neurological status of patients during admission and other coexisting illnesses.

A retrospective cohort study done in Thailand on a total of 621 VAP patients found that septic shock was associated with increased mortality in VAP patients. In this study, patients who developed septic shock had more than two times higher risk of mortality when compared to patients who developed severe sepsis (AHR=2.51) (12).

Based on a prospective study done in patients with Acute Physiology and Chronic Health Evaluation II (APACHE II) >25 score at the time of VAP diagnosis was an important predictor of mortality related to VAP with high sensitivity (84.6) and specificity(78.1)(50). Another study also revealed that APACHE II score was a good predictor of mortality in patients with VAP (51).

In a cohort of 336 Acute respiratory distress syndrome (ARDS) patients, VAP was an independent predictor of 90 days mortality (AHR=3.16, 95% CI 2.04 -4.89, p<0.0001) (52).

2.2.2. Time of Onset of VAP and Pathogen

Late -onset VAP (LOVAP) was significantly related to higher ICU mortality with an estimated attributable mortality of 25% (35). Late onset VAP was associated with increased length of ICU stay, prolonged days on mechanical ventilator (MV) and increased mortality of COPD patients than Early onset VAP(EOVAP) (53).

Patients with episodes of monobacterial VAP due to multi drug resistant A. baumannii (MDRAB) exhibited increased mortality when compared to patients with polymicrobial VAP. This correlation may be described by the fact that the possibility of administering a suitable antibiotic treatment decreased with increasing pathogen resistance (54). Another study on 119 patients with Multi Drug Resistant Acinetobacter baumannii (MDRAB) VAP also found a mortality rate of 42% (50/119) (55).

Based on a literature review and meta-analysis study on 126 literatures across all continents, which focused on the prevalence of HAP and VAP caused by MDR A.baumanni and mortality linked to this, the pooled mortality from 27 literatures was 42.6% and the areas with the highest mortality were western Asia, southern Europe and southern Africa (56).

A retrospective cohort study done at medical ICU in Thailand,337 patients with VAP were categorized based on drug resistant patterns of A.baumannii as follows, DS 33(9.8%) ,MDR 72(21.4%), XDR 220(65.3%) & PDR 12(3.6%). And the 30 day mortality rates were 21.2%, 31.9%, 56.8% & 66.7% respectively and concluded that VAP caused by XDR & PDR A.baumannii had an increased mortality rate (12) . In contrast according to ozgur et al XDR A.baumanni has not been found to affect mortality (57).

2.2.3. Duration of invasive ventilation, length of hospital stay, length of ICU stay and interventions in the ICU

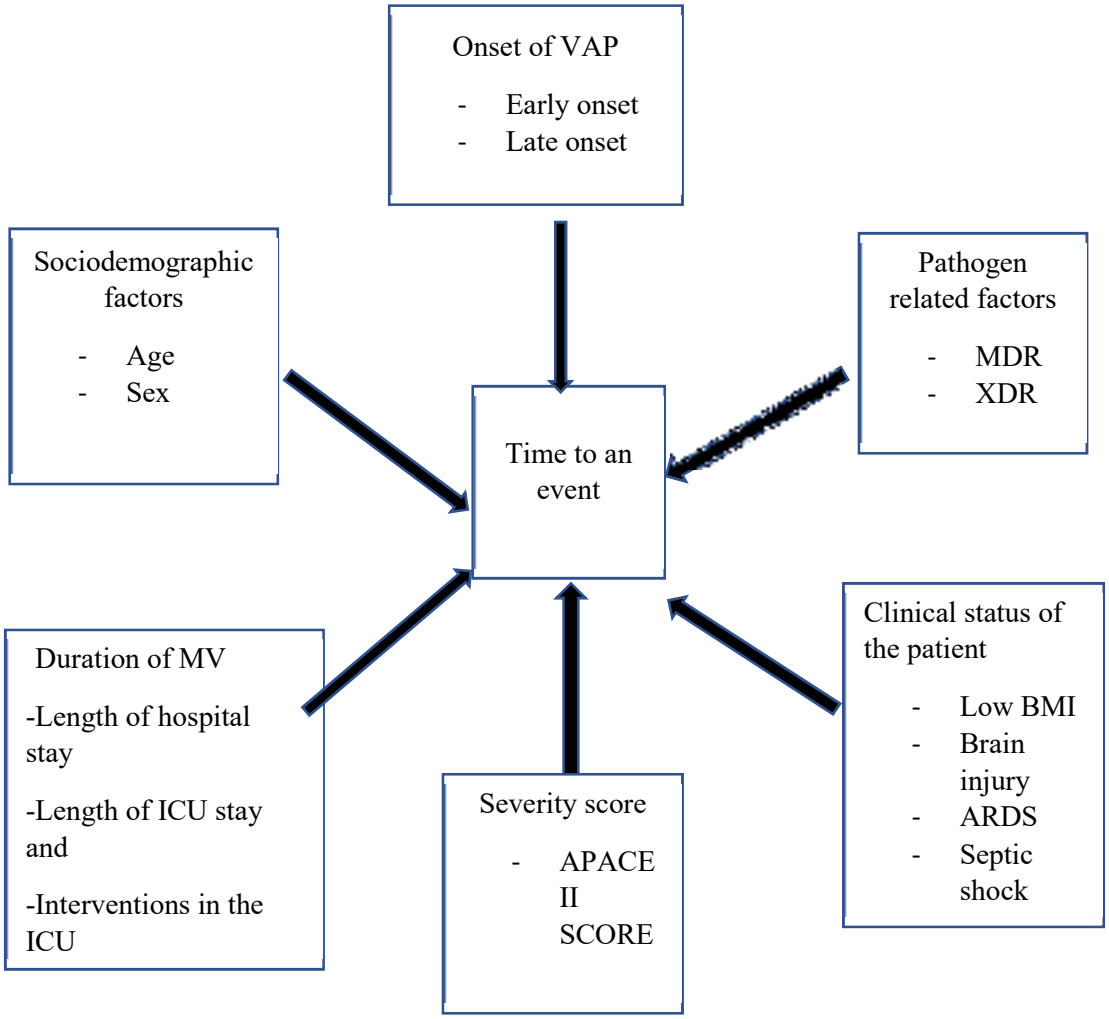
A retrospective cohort study found that hospital length of stay (OR =0.928, 95% CI: 0.915–0.941, P<0.001) and duration of invasive monitoring (OR =1.004, 95% CI: 1.004–1.005, P<0.001) was associated with mortality of VAP (20).

Another systematic review and meta-analysis study on 24 trials of ventilator associated pneumonia prevention, collected 6284 individual patient data by contacting each corresponding authors of the studies. Of the 6284 identified patients from those studies, 1061 patients had developed VAP. And the overall estimated mortality associated to VAP was 13%. In this study the main cause of the attributable mortality related to VAP was prolonged ICU stay. Critically ill Patients who developed VAP had an increased mortality risk per day and decreased probability of ICU discharge after they acquire VAP. Admission of patients in the ICU for longer duration of time causes prolonged exposure to the risk of dying (58). Patients admitted in the ICU for longer durations are more susceptible to stress which weakens their resistance to disease. Associated to this they are prone to high risk of having infections which will be acquired in the ICU.

A retrospective cohort study done in Thailand showed that late and inappropriate antibiotic treatment was an independent predictor of mortality among VAP patients. Administration of antibiotics after 24 hours of VAP diagnosis and antibiotic resistance developed by the pathogen was associated with increased mortality (12).

Based on a retrospective cohort study done on VAP patients from 2015 to 2019, administration of vasoactive agents was associated with both 30 and 90 day mortality (HR=4.01; 95% CI :1.24-12.95,p =0.02) and (HR=4.07; 95% CI :1.93-8.55,p<0.001) respectively (45).

2.3. Conceptual framework



Source: developed by the investigator based on the reviewed literatures

Figure 1: conceptual framework of the study,2024

3. Objectives

3.1.General objective

- To assess Survival status and mortality predictors among adult intubated intensive care unit patients with VAP in Addis Ababa governmental hospitals,2023/2024

3.2.Specific objective

- To assess Survival status of adult intubated intensive care unit patients with VAP in Addis Ababa governmental hospitals
- To identify mortality predictors among adult intubated intensive care unit patients with VAP Addis Ababa governmental hospitals

4. Methodology

4.1.Study area and period

The study was conducted at governmental (public) hospitals in Addis Ababa, Ethiopia. Addis Ababa is a capital city of Ethiopia and the seat of African union. The city has 11 sub cities and 116 districts. the current population of the city is thought to be 4.8 million in the urban area and 2.7 million in the city area. There are 13 public hospitals in the city. Among those public hospitals 6 hospitals are owned by Addis Ababa Health Bureau, 5 hospitals owned by Federal Ministry of Health, 1 Ministry of defense and 1 police force hospital. There are 103 ICU beds in public hospital of Addis Ababa.

Governmental hospitals which had ICU services between January 2021 and April 2024 were considered. Among the total of thirteen public hospitals in Addis Ababa, four hospitals were purposively selected. Those hospitals were selected because of high case flow in those hospitals and they have relatively higher numbers of ICU beds with mechanical ventilators

Accordingly, Tikur Anbessa Specialized Hospital (TASH), St Paul's Hospital Millennium Medical College (SPHMMC), Zewditu Memorial Hospital and St. Peter's Specialized Hospital was included in the study. Tikur Anbessa Specialized Hospital has 12 ICU beds. Of those, 6 beds are medical ICU beds and the remaining 6 beds are surgical ICU beds. And there are 10 functional mechanical ventilators in those ICU's. In St Paul's Hospital Millennium Medical College there are 13 ICU beds with 13 functional mechanical ventilators. At Zewditu Memorial Hospital there are 12 ICU beds with 12 functional mechanical ventilators. St Peter's Specialized Hospital also has 12 beds with 12 functional mechanical ventilators. This study was carried out from March to April 2024.

4.2.Study design

Health institution based retrospective follow-up study was conducted.

4.3.Population

4.3.1. Source Population

All intubated adult intensive care unit patients with the diagnosis of VAP in Addis Ababa governmental hospitals.

4.3.2. Study population

All intubated adult intensive care unit patients with the diagnosis of VAP admitted to ICU from January 2021 to April 2024 in selected public hospitals in Addis Ababa, Ethiopia.

4.4.Sample size determination and sampling procedure

4.4.1. Sample size determination

The sample size for this study was calculated by considering the outcome variable and various significant predictors of the outcome variable. Finally, the maximum sample size was considered. Accordingly, the sample size for the first specific objective was calculated by using single population proportion formula through assumption of 95% confidence internal (CI), 5% margin of error, and estimate of mortality among adult VAP patients was 37.5% from the research done in Tikur Anbessa Specialized Hospital (TASH), Addis Ababa, Ethiopia (10).

Thus, $$n = \frac{Z^2 pq}{d^2}$$

$$n = \frac{z^2 pq}{d^2} = \frac{(1.96)^2(0.375)(0.625)}{(0.05)^2}$$

n= 360

Where; -Z = 1.96 with 95% of confidence interval

p= an estimate level of mortality in patients with VAP=37.5%

q = 1-p

d = margin of sampling error tolerated (0.05)

n = the required sample size

The sample size for the second specific objective of this study was determined by considering various significant predictors of the outcome variable, two-sided confidence level of 95% and power of 80% using Epi info 7 (stat calc) (Table 1).

Table 1: Sample size determination for the study on survival status and mortality predictors among adult intensive care unit patients with ventilator associated pneumonia, 2023/24

Objective 2	Predictor considered	References	Proportion –value (percent of exposed with outcome and percent of unexposed with outcome)	Sample size
predictors of mortality among adult intubated intensive care unit patients with	Initial antibiotic treatment	(12)	% of mortality in early and appropriate treatment = 46.5%	44
			% of mortality in late and inappropriate treatment = 5.9%	
	Sepsis status	(12)	% of mortality in Sever sepsis = 22.5 %	32
			% of mortality in septic shock = 77.5 %	

The calculated sample size for this study was 360 (first objective). However, since the source population was less than 10,000 (N<10,000) correction formula was applied for sample size calculation.

Thus n*final* = $\frac{n}{1+\frac{n}{N}}$

$$n_{final} = \frac{360}{1+\frac{360}{170}} = 115.38 \sim 116$$

Where N = the total number of patients who developed Ventilator Associated Pneumonia=170 within 3 years after situational analysis.

n= the calculated number of sample size

n*final*= the final sample size

Thus, the number of sample size for this study was 116 and with 10 % contingency for incomplete records, the final sample size was 127.6 ~ 128.

4.4.2. Sampling procedure

For the patient records, baseline assessment was conducted at each hospital to determine the average number of VAP patient records between January 2021 to April 2024. Based on that, the estimated total number of VAP cases in the previous three years was 170. Then proportional allocation was done for each hospital by dividing the estimated number of VAP patients from each hospital by the total estimated number of VAP patients multiplied by the sample size. For the VAP cases to be selected, first, patient records with more than two days of mechanical ventilation were identified and collected. Then, all patient records with the diagnosis of VAP were taken, based on eligibility criteria, (Figure 2).

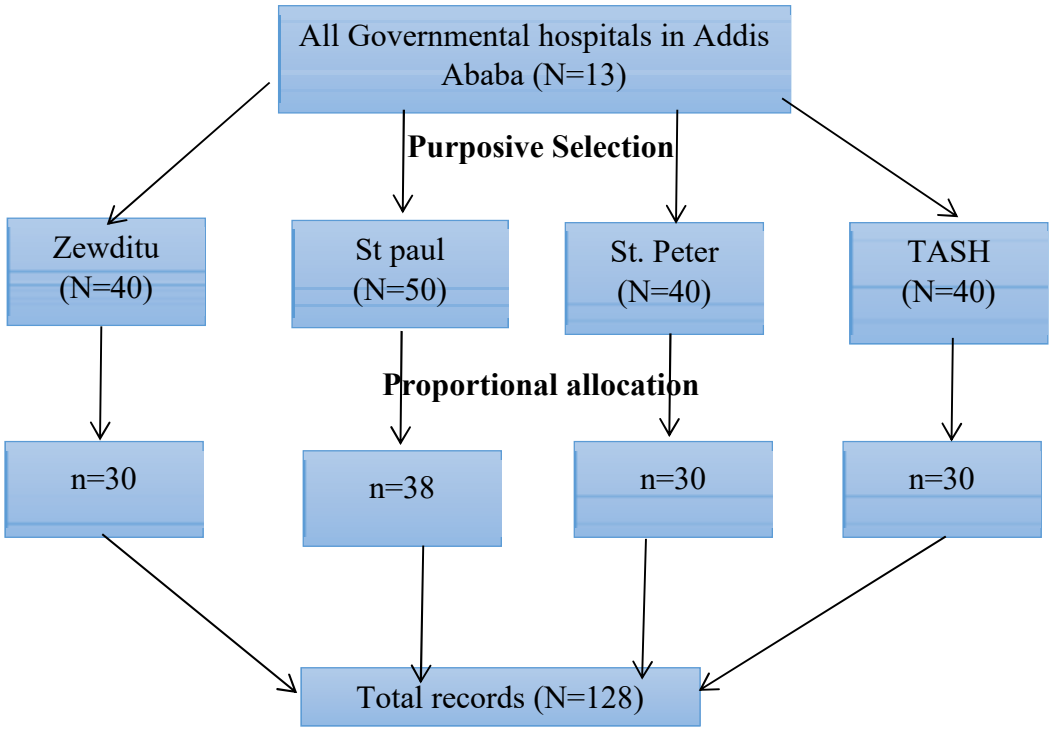


Figure 2: Diagrammatic representation of sampling procedure for the study, 2023/2024.

4.5.Description of Variables

4.5.1. Dependent variable

- Time to an event

4.5.2. Independent Variables

- Sociodemographic and clinical characteristics
    - Age
    - Sex
    - Low BMI
    - Brain injury
    - APACHE II SCORE
    - ARDS
    - Septic shock
- Time of Onset of VAP
    - Early onset
    - Late onset
- Pathogens
    - MDR
    - XDR
- Duration of mechanical ventilation
- length of hospital stay, length of ICU stay and interventions in the ICU

4.6.Eligibility criteria

4.6.1. Inclusion criteria

- Records of adult patients age $\geq$18 years was considered as eligible.
- Patient records which had a clear diagnosis of VAP.
- Records were considered eligible if the data on outcome variable and other important predictor variables were recorded.
- Patient records which had mechanical ventilation for more than 48 hours.

4.6.2. Exclusion criteria

- Patients who developed pneumonia prior to or within 48 hours of mechanical ventilation were excluded

4.7.Data collection methods

4.7.1. Data collection instruments

The data was collected using structured data extraction tool. The tool was developed from a review of previously done studies on the mortality related to ventilator associated pneumonia and predictors of mortality. Data was extracted from patient records which comprises of information on sociodemographic characteristics like age and sex, clinical diagnosis, comorbidities, administered medications and length of ICU, hospital and MV days, the primary indication for mechanical ventilation, interventions in the ICU, onset of VAP, outcome of the patients and date of the outcome.

4.7.2. Data collectors and data collection procedures

The ICU nurse registration books from each hospital were used to obtain the patient registration numbers from January 2021 to April 2024. The books provided information on MV support and the days spent on MV. Afterwards, patient registration numbers for those who required MV support for more than two days were identified. Using those retrieved numbers, patient cards were collected by data clerks. From those collected cards, records with diagnosis of VAP were identified and all VAP records were taken based on the eligibility criteria. The cards were cross checked for the availability of their data and fulfillment of eligibility criteria. Trained data collectors (nurses) other than ICU workers was recruited, one for each hospital, to extract the data from patient cards. The investigator supervised and monitored the overall process of data collection in all sites.

4.8.Data quality control

To ensure data quality, one day training was given for data collectors and data managers on the data extraction tool, method of data collection and the intent of the study. Pretesting of the tool was done on 5% of patient records (6 records), to confirm that the data collectors understood the questions and the response options. Then corrections were made correspondingly, and those

records used for pretesting were excluded from the study. The data collection process was carried out with close monitoring. Then the completed questionnaires were checked on spot and before data entry for any incompleteness, errors and inconsistency.

4.9.Operational definitions and definitions of terms

Ventilator Associated Pneumonia- is a type of ICU acquired pneumonia which occurs after 48 hours following endotracheal intubation (3).

Diagnosis of VAP: VAP was diagnosed based on physicians' decision up on the following criteria:

One or two of the following clinical findings

a. Fever $\geq 38^0$c
b. White blood cell count(leukocytosis) $\geq$ 12000 /mm^3
c. Change in character of sputum (purulent tracheobronchial secretion)
d. Increased mechanical ventilation support

In clinically suspected VAP, positive quantitative culture from tracheobronchial aspirate was used to establish diagnosis of VAP. In some cases, chest x-ray results were also obtained.

Time to an event- event (death) occurred among adult patients within 90 days of diagnosis of VAP.

Survival status of patients - was assessed by following all patients for survival status until 90 days after initial diagnosis of VAP or until death if the patient dies within 90 days.

Length of hospital stay- total days the patient stayed in the hospital including ICU stay.

Incomplete records- records without clear diagnosis of VAP, records missing date of admission and date of intubation.

Administration of vasopressors -use of vasopressors after diagnosis of VAP until a patient develops a certain outcome.

Prolonged mechanical ventilation- requirement for MV support for 21 days or more and at least for 6 hours per day (45).

Development of AKI- AKI developed after the diagnosis of VAP until a patient develops a certain outcome. Included cases are based on the physicians' diagnosis.

Acute Physiology and Chronic Health evaluation II (APACHE II) score- Is used to assess severity of disease. One of several intensive care scoring system. Helps to stratify critically ill patients by using physiologic and laboratory parameters (59).

Early initiation of antibiotics-is if the antibiotics was administered within 24 hours of VAP onset (12).

Late initiation of antibiotics-is if the antibiotics was administered after 24 hours of VAP onset (12).

Appropriate antibiotic treatment- is if the causative pathogen was sensitive to the prescribed antibiotics (12).

Inappropriate antibiotic treatment- is if the causative pathogen was resistant to the prescribed antibiotics (12).

4.10. Data processing and analysis

The data were entered using Epi-Data version 3.1 and cleaning and recoding was done before exporting. Then the data were exported to SPSS version 25 for analysis and were checked for errors and inconsistency and further cleanup was done. Descriptive data were presented using means with standard deviations and/or medians with Inter Quartile Ranges (IQR) and categorical variables were expressed by frequency and percentage. The results were presented in the form of tables, figures and charts. The event of interest in survival analyses was mortality /death among patients diagnosed with VAP. Cumulative mortality probabilities were assessed by Kaplan-Meier analysis method and the log-rank test was used for comparison. The Cox proportional hazards model adjusted on independent variables considered for this study was used to identify predictors of 90 days mortality among adult VAP patients. Variables with P values < 0.25 in bivariate analysis was included as covariates in the final multivariable models. For all statistical tests, two-sided P values of less than 0.05 was considered statistically significant. Crude and adjusted hazard ratios with their 95%CI were estimated to predict the hazard of predictors on the occurrence of mortality related to VAP. Model goodness-of-fit was tested using graphical methods based on Cox-Snell residuals and the hazard follows 45^{o} that full fills the model goodness of fit and proportional hazard assumptions was also assessed statistically by using Schoenfeld residual test. Patients discharged from the hospital, patients who left the Hospital due to referral or other reasons and patients who showed improvement from VAP were taken as censored cases.

4.11. Ethical considerations

Ethical clearance was obtained from ethical clearance board of College of Health Sciences, School Of Medicine Department Of Anesthesia, Addis Ababa university and Ethical clearance committee of each hospital. Official letter was obtained from each hospital ethical clearance committee to each hospital AICU, outpatient department office and record keeping unit officer. All individual working in AICU and patient card store was informed about the study. The data retrieved from each hospital did not include any name. The collected data was kept strictly confidential using password locked computer.

4.12. Dissemination of results

Finding of this study will be submitted to Addis Ababa University, department of Anesthesia. Effort will also be made to publish in peer reviewed journals and present in different national conferences and seminars.

5. Results

5.1.Description of study participants

In this 90 day follow up study, 450 mechanically ventilated patient records were found and reviewed in those selected four hospitals. From those records, one hundred twenty-eight records having VAP diagnosis were screened based on the inclusion criteria. Two records were excluded because of incomplete data making a response rate of 98.4 %. Majority of patient records (30.2%) were taken from St Paul's Millennium Medical College (SPHMMC)**.** Regarding sociodemographic characteristics the mean (standard deviation) age of patients was 46.6 $\pm$ 17.7 and majority 84 (66.7 %) of the study participants were male (Table 2).

5.2.Clinical characteristics of the participants

Among the total of 126 patients, more than half (68.3%) of them had comorbidities. The most common comorbidities were Hypertension 43 (34.1 %) and Type 2 diabetic mellitus 19(15.1%). The most common cause of ICU admission was Neurological disease 84 (66.7%) followed by Trauma 30 (23.8 %), Respiratory disease 36 (28.6%) (Table 2).

Regarding place of intubation and admitting ward, 53 patients were intubated in the ICU. Ninety (71.4%) patients were admitted in the medical ICU while 36(28.6%) patients were admitted in the surgical ICU. Sixty-one (48.4) patients were transferred from Emergency OPD.

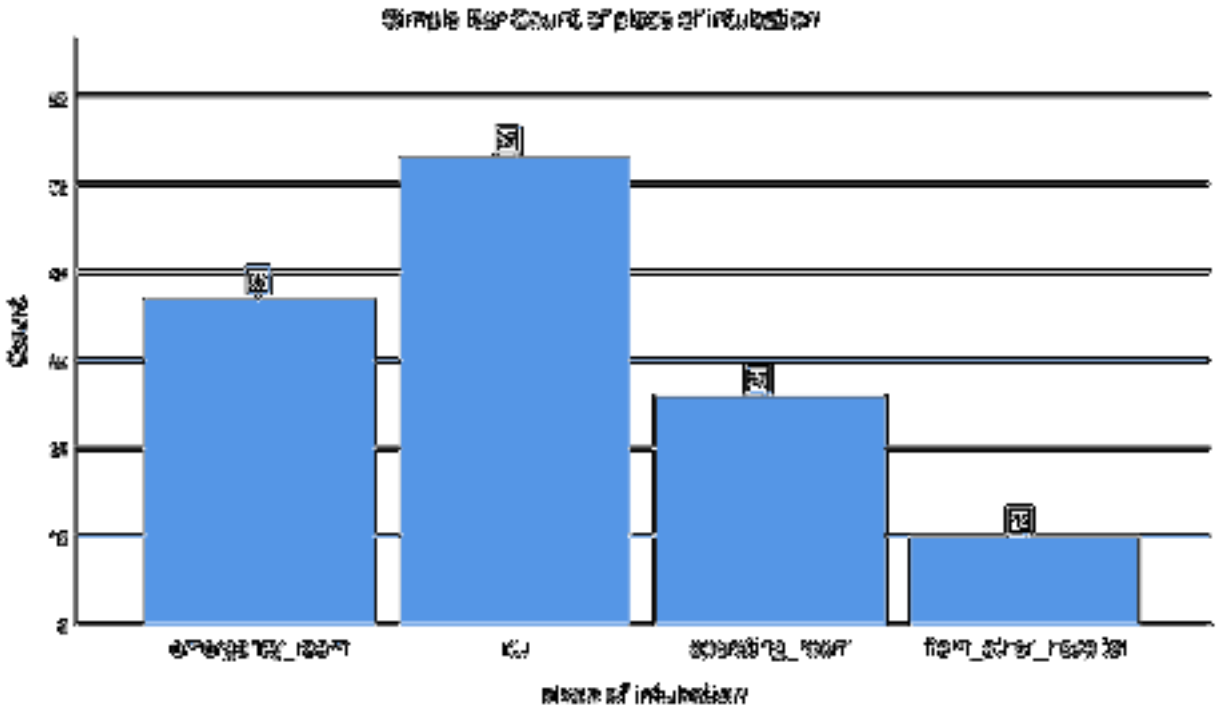


Figure 3: place of intubation of VAP patients in Addis Ababa governmental hospitals, Addis Ababa, Ethiopia.

Table 2: Study characteristics and Sociodemographic characteristics of VAP patients of Addis Ababa governmental Hospitals. Addis Ababa, Ethiopia, 2023/2024 (N=126).

Characteristics	**Category**	**Frequency**	**Percentage (%)**
Name of hospital	St. paul	38	30.2
	Zewditu	30	23.8
	St. peter	30	23.8
	TASH	28	22.2
Sex of the participants	Male	84	66.7
	Female	42	33.3
Age of the participants	< 30	22	17.5
	30-59	68	54.0
	60-74	22	17.5
	≥75	14	11.1
Comorbidity	Hypertension	43	34.1
	Type II DM	19	15.1
	Alcoholic and smoker	10	7.9
	Acute respiratory distress syndrome	9	7.1
Admission diagnosis	Neurological	84	66.7
	Respiratory	36	28.6
	Trauma	30	23.8
	Others *	13	10.3

- Guillain Barre syndrome (GBS), Generalized Tetanus

5.3.Interventions and medications given in the ICU

During their ICU stay, 11 (8.7%) of patients had blood transfusion and 4 (3.2%) had hemodialysis. The most common surgical procedure performed was tracheostomy. It was done for 61 patients and all most in all patients it was done for an indication of prolonged intubation. Other surgical procedures performed were chest tube thoracostomy and feeding gastrotomy in 4 (3.2%) and 5 (4%) patients respectively.

Regarding medications, corticosteroids was given for 46 (36.5%) of the participants and sedation and analgesia was given for 13 (10.3%) patients. Vasopressors and inotropes were also administered in 30 (23.8 %) of the patients. Antibiotics was administered nearly in all patients 122 (96.8%) before the onset of VAP. Almost in all patients 123 (97.6%) patients antibiotics treatment was administered early within 24 hours after the diagnosis of VAP and combined antibiotics was administered in 122 (96.8%) patients.

5.4. Coexisting Complications with VAP after ICU admission

In this study, the most common complication patients encountered in the ICU was sepsis/septicemia 40(31.7 %). Sepsis of chest focus occurred in all septic patients 40 (31.7 %), other focuses were GI focus, sepsis of CNS focus and sepsis of GU focus in combination with chest focus. Additionally, 15 (11.9%) patients had anemia, 53 (42.1%) patients had electrolyte imbalance, acute kidney injury was also prevalent in 45 patients (35.7%).

5.5.VAP characteristics

5.5.1. Causative microorganism and episodes of VAP

Almost in all patients 99 % had only one episode of VAP during their ICU stay except for one patient who had 3 episodes of VAP. In this case only the first episode of VAP was taken. Therefore 126 episodes of VAP was followed. Most of the cases were diagnosed clinically in addition to tracheal aspirate culture. However, in most cases the culture results were not available. From those 126 VAP records only 44 culture results taken from tracheal aspirate were found. Thirty-six VAP incidents were caused by single microbial while 8 of them were caused by poly microbials. The most prevalent microbials were Acinetobacter baumannii 15, Klebsiella species 17, Pseudomonas

species 12 and others were E. coli, Seratua marcescens etc. only a few cases 3 had imaging diagnosis (chest x-ray).

5.5.2. Onset of VAP

The median (IQR) duration of mechanical ventilation before the onset of VAP was 8.5 (5 to 17) days. More than two third 96 (76.2%) of the patients developed late onset VAP.

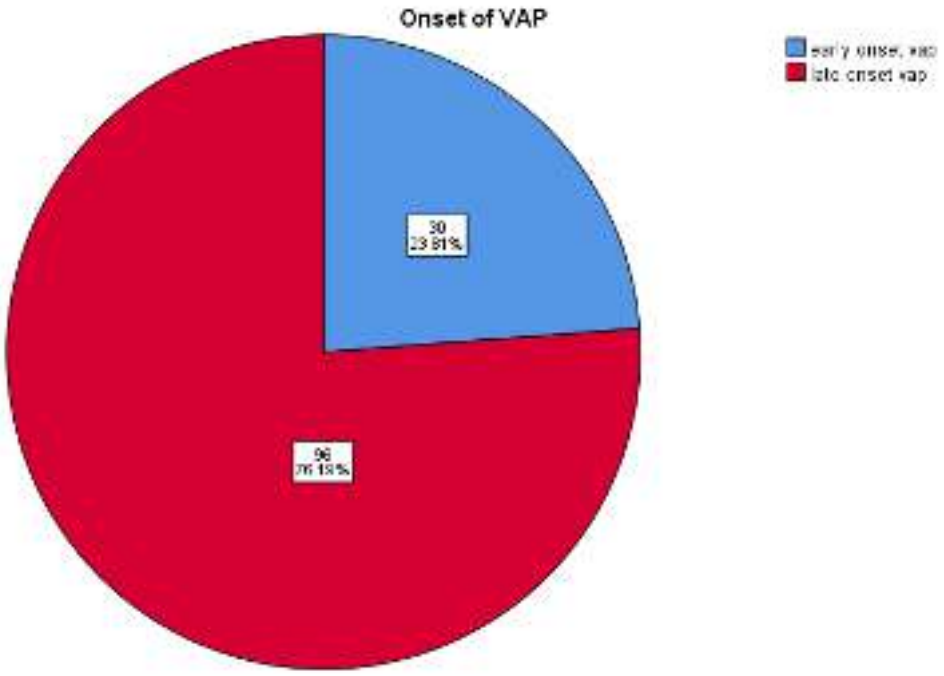


Figure 4: Onset of VAP among AICU patients of Addis Ababa governmental Hospitals. Addis Ababa, Ethiopia, 2023/202

5.6. Length of hospital stay, Length of ICU stay and Total days on mechanical ventilation

The Median (IQR) length of hospital stay of VAP patients was 33.5 (25.8,50) days, and the Median (IQR) length of ICU stay was 29 (22,42) days. The Median (IQR) days spent on mechanical ventilation was 25 (18,34.3) days.

5.7.Survival status of VAP patients

The median (IQR) follow up time was 16.5 (12,26) days with the minimum and maximum days being 1 and 87 days respectively. The total observation was 2552 person-days. In this study, 61 (48.4%) (95%CI: 39.7, 57.1) of patients experienced in hospital mortality and 51 (40.5%) patients were discharged from ICU and 14 (11.1%) patients showed improvement (Figure 5). The incidence of mortality among VAP patients was 23.9 case (95% CI:18.6,30.7) per 1000 person-day observation with the median survival time being 27 days. Life table was used to describe the median survival time.

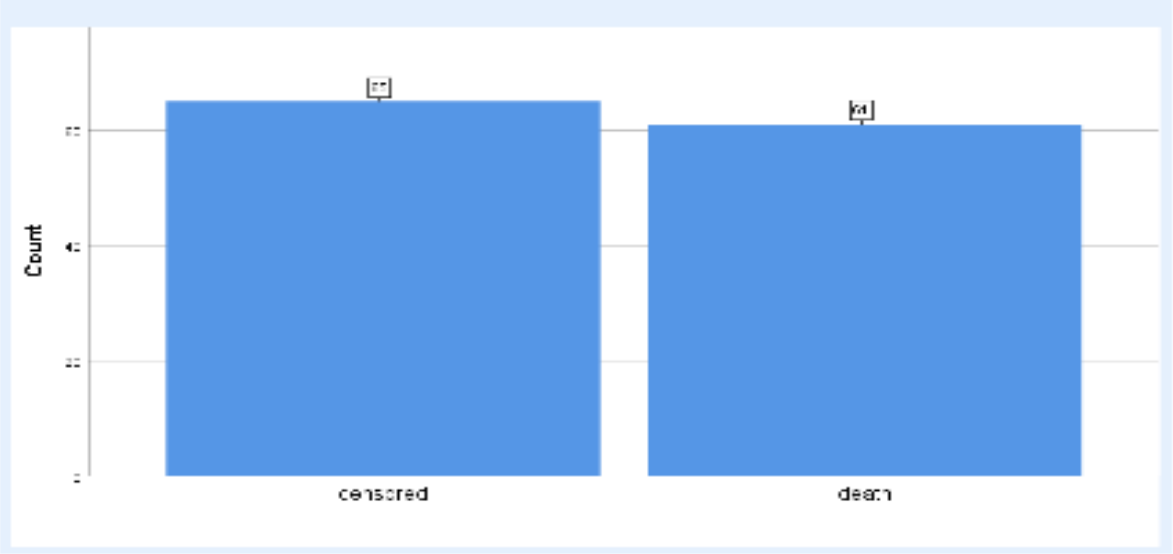


Figure 5: Proportion of survival status among VAP patients admitted in AICUs of Addis Ababa Governmental hospitals, Addis Ababa, Ethiopia, 2023/2024.

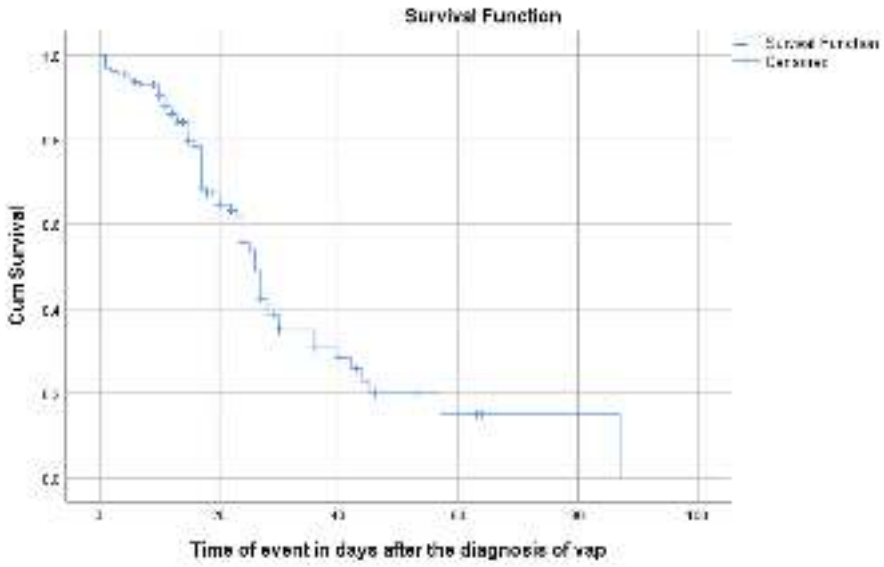


Figure 6: Kaplan-Meier survival and hazard function showing the cumulative probability of survival of VAP patients with time.

Test for equality of failure function

In this study patients who had not taken vasopressors had a better survival curves when compared to the patients who had not taken vasopressors (Log Rank test=0.000) (Figure 7). This study found that patients who had developed Acute Kidney Injury higher probability of mortality when compared to those patients who had not developed AKI. (Log rank test= 0.035) (Figure 8)

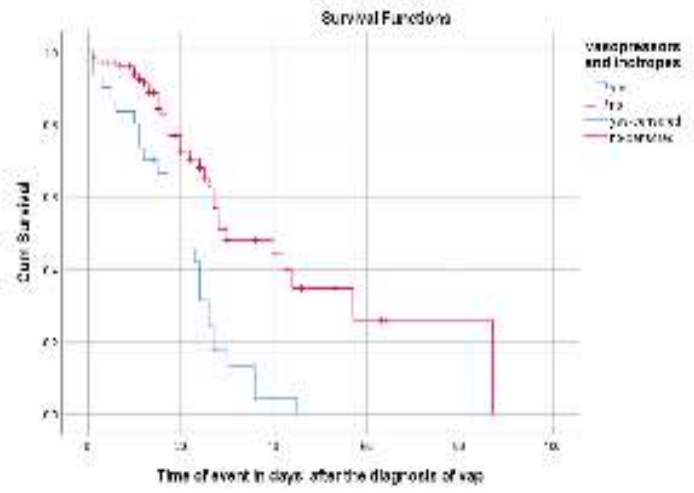


Figure 7: Kaplan-Meier Survival and Hazard function showing the cumulative hazard curves for administration of vasopressors and inotropes

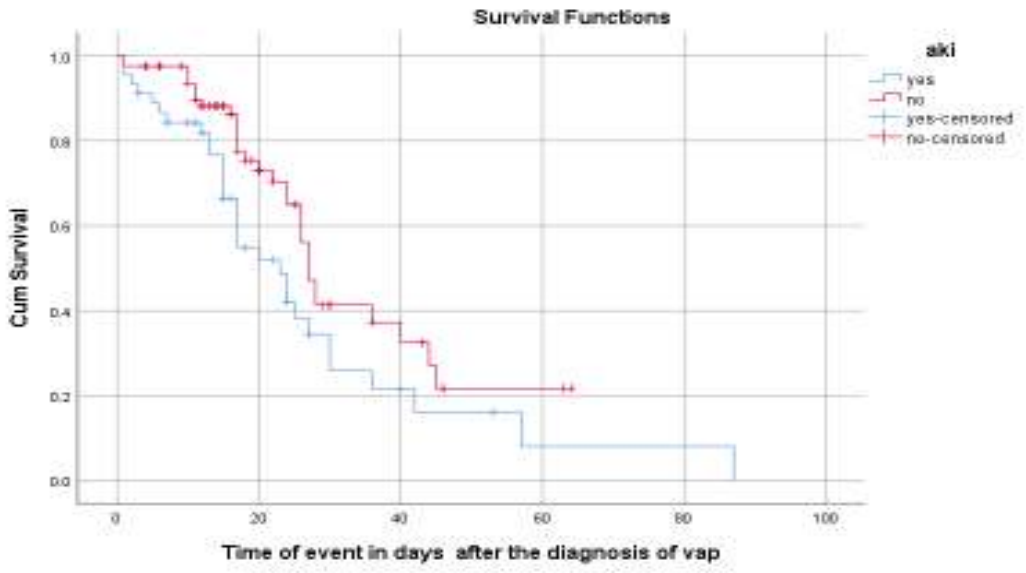


Figure 8: Kaplan-Meier Survival and Hazard function showing the cumulative hazard curves for the development of AKI.

5.8.Predictors of 90-day mortality among VAP patients

In multivariable cox regression model, patients who had taken vasopressors and inotropes had more than two times (AHR = 2.27; 95% CI: 1.27, 4.07) higher risk of mortality compared to those who had not taken vasopressors and inotropes. Patients who developed acute kidney injury during their ICU stay had 2.12 times higher (AHR = 2.12; 95% CI: 1.16,3.87) risk of dying when compared to those who did not develop AKI. In this study, as the days on mechanical ventilation increases the chances of dying also increases by 12% (total days on mechanical ventilation=AHR =1.12; 95%CI: 1.06,1.20). However, as a length of hospital stay increases risk of mortality decreased by 5% (AHR=0.95 ;95%CI: 0.90, 0.99) and as length of ICU stay increases risk of mortality decreased by 14% (AHR=0.86; 0.8,0.92) (Table 3).

Table 3: Multivariable analysis using Cox regression model for predictors of mortality among adult ICU patients with VAP in Addis Ababa governmental hospitals, Addis Ababa, Ethiopia,2023/2024.

Variable	Category	Censored(N)	Death (N)	CHR (95%CI)	AHR (95%CI)
Age	< 30	13	9	1	
	30-59	40	28	1.05 (0.50-2.23)	1.22(0.502.98)
	60-74	10	12	0.96(0.40-2.33)	1.00(0.36,2.83)
	≥75	2	12	1.84 (0.78-4.38)	0.84(0.31,2.25)
Admission diagnosis of Respiratory disease	Yes	15	21	1.94 (1.13-3.33)	1.91(0.98,3.74)
	No	50	40	1	
Sepsis	Yes	11	29	1.57(0.94-2.61)	1.30(0.71,2.37)
	No	54	32	1	
Acute kidney injury	Yes	15	30	1.70 (1.02-2.81)	2.12(1.16,3.87) *
	No	50	31	1	
Electrolyte imbalance	yes	20	33	1.61 (0.97-2.68)	1.24(0.63, 2.45)
	No	45	28	1	
Vasopressor and inotropes	yes	2	28	2.92 (1.74-4.91)	2.27 (1.27-4.07) **
	No	63	33	1	
Tracheostomy	Yes	30	31	0.61(0.36,1.02)	0.87(0.43,1.75)
	No	35	30	1	
Creatinine	≤ 1.3	59	36	1	
	> 1.3	6	25	1.97(1.17-3.30)	1.12(0.61,2.06)
Total days on MV, Median (IQR) days		25(18,34.3)		0.98(0.96,0.99)	1.12(1.06,1.20) ***
Length of ICU stay, Median (IQR) days		29(22,42)		0.94(0.92,0.96)	0.86(0.80,0.92) ***
Length of hospital stay, Median (IQR) days		33.5(25.8,50)		0.94(0.92,0.96)	0.95(0.90,0.99) *

Note: * = p-value <0.05, ** = p-value<0.01, ***= p-value<0.001

6. Discussion

As one of the most prevalent nosocomial infection encountered in the ICU, VAP increases economic and mortality burdens for both patients and attendants. This study collected the data of 126 VAP patients who were admitted in four governmental hospital intensive care units from January 2021 to April 2024.

In this study the mortality rate of VAP patients was 48.4% (95% CI: 39.7, 57.1) which was comparable with the study done in Azerbaijan (42.9%) (44), India (46%) (60) and China (42.8%) (61). However, it was significantly lower than the result from Argentina 63.7% (45), and another study from India 74.17% (62). The possible reason can be that the study conducted in Argentina only included VAP patients with prolonged mechanical ventilation which can increase the risk of mortality. This study included all VAP patients regardless of their days on mechanical ventilator. Another justification can be the smaller sample size of VAP patients in the Indian study with a total of 49 patients when compared to this study and only postoperative patients who underwent neurosurgical procedures were included in the study that might have increased the overall mortality rate reported in the study.

The overall mortality rate in this study was relatively higher when compared to previous study done in Addis Ababa, Ethiopia 37.5% (10). The study was conducted in a single public hospital, and it included all adult patients who were on mechanical ventilation for more than two days and VAP patients identified in the study were 40 (24.3%) patients. This might have caused the difference in the reported mortality rates. The result in this study was also higher than mortality rates reported from developed countries such as Beth Israel Deaconess Medical Center (33.33%) (63) and Thailand (31.1%) (64). The American Thoracic Society (ATS) and the Infectious Disease Society of America (IDSA) reported a mortality rate of 13% in USA and the mortality rate reported in Europe was 29.9% (65, 66). The possible cause for this discrepancy can be the difference in the ICU setup. ICU setup in developed countries had a precise diagnosis of VAP and the appropriate medication for the identified pathogen is also available, which helps in the early intervention and better outcome of VAP patients. However, in our setup, there is a lack of specialized ICU units with adequate equipment, inadequate medical staff with critical care expertise and insufficient access to consulting specialties. There is also shortage of medications, and lack of laboratory capacity (67). This all might have contributed to the compromised care of critically ill VAP

patients. Moreover, the challenge in the diagnosis of VAP may cause misclassification of patients under VAP diagnosis similarly this might cause delay in the appropriate treatment needed for those patients which may lead to mortality. The higher mortality found in this study can also be because more available patients records were those records with death.

In this study patients who received vasopressors had more than two times higher risk of mortality when compared to patients who had not received vasopressors. This result is concordant with the result from the study done in Argentina (45) and Taiwan (68). Vasopressors are cornerstone of care for patients with hypotension, but they are not without side effects. Administration of vasopressors can cause complications such as tachycardia, tachyarrhythmia, hyperglycemia and excessive vasoconstriction leading to organ ischemia or infarction which may increase risk of death in critically ill patients (69). In addition to that, critically ill patients who received vasopressors had a higher risk of developing acute kidney injury when compared with patients who did not receive vasopressors, which also increases risk of mortality (69-71). This study also showed that out of 30 patients who had taken vasopressors 14 (46.7%) patients developed AKI. Moreover, critically ill patients who require vasopressors are those patients with higher hemodynamic instability or patients in which their circulatory system failed to meet the oxygen demand including patients with cardiogenic shock, septic shock, acute heart failure. Those patients are high risk patients to multiorgan failure and death making them in need of Vasopressors and inotropes supplementation (69).

In the present study, patients who developed acute kidney injury during their ICU stay had 2.12 times higher risk of dying when compared to those who did not develop AKI. In this study 35.7% of patients developed AKI. Increased ventilator days, impaired respiratory system mechanics, and increased ICU mortality are all linked to AKI sustained during invasive mechanical ventilation (71). There is inflammatory crosstalk between the kidney and the lung, meaning that damage to one organ causes inflammation and damage to the other (72, 73). AKI imposes difficulties in the applications of lung protective ventilation, as patients with AKI are less likely to compensate the metabolic disturbances that follows the ventilation (74). Patients with AKI may be more prone to ventilator-induced lung injury, a major contributor to multiple organ failure and death in the critically ill patients. Additionally, the likelihood of developing AKI increases three fold in cases of invasive MV (75).

This study found that longer days on mechanical ventilation was related to higher risk of mortality. This result was also in line with the study done by Han, Xiang, et al. (20). The possible justification can be that patients who remain on mechanical ventilation for extended periods of time develop long term complications related to immobilization, such as pressure ulcer, atrophy of the limb and muscles and joint contracture. Furthermore longer days on mechanical ventilation also results in rapid deterioration of diaphragmatic strength termed as Ventilator Induced Diaphragmatic dysfunction (VIDD) which is associated with an increased mortality (76, 77). Studies also have shown that diaphragmatic injury can be developed within 6 to 18 hours after mechanical ventilation, and the level of impairment of diaphragmatic contraction increased with the length of time spent on mechanical ventilation (76, 78). Additionally, prolonged duration of mechanical ventilation may lead to different stress reactions, reducing the function of the body barrier and increasing the risk of infections (20).

The result of this study showed that length of ICU stay was associated to decreased mortality in VAP patients. Similarly, length of hospital stay was also associated with decreasing risk of mortality. This was supported by Xiang Hal et al (20) and Huang, Yi et al (11). However this was not supported by the study done by WG Melsen et al. (58) in which hospital length of stay was associated with an increased mortality of VAP patients. The possible reason for this difference can be that longer ICU and Hospital stays for VAP patients with mild ill ness does not increase mortality. This may be due to the better clinical conditions of those patients that enables them to cope with ICU and hospital related complications such as other nosocomial infections and complications resulting from invasive procedures. Additionally, severely ill VAP patients are more like to die in the early days of ICU admission thus they will not have longer hospital stay meaning that both hospital length of stay and ICU length of stay will not affect their mortality.

7. Strength and limitations of the study

Strength

It was multicenter study which enhances the generalizability of the study results. It has also long follow up time which helps to elucidate long term outcome of VAP patients.

Limitations

In the present study, since the data was collected retrospectively, important variables such as BMI, Albumin level, and culture results were missing, this limited the inclusion of those important predictor variables.

In addition, important investigations needed in methods to assess severity scores in those patients were not available. Investigations includes Arterial Blood Gas Analysis and the scores were APACHE score, SOFA score.

8. Conclusions and Recommendations

8.1.Conclusions

In this study the overall mortality among VAP patients was high. Length of hospital stay, length of ICU stay, days on mechanical ventilation, administration of vasopressors and inotropes and AKI were predictors of mortality in VAP patients.

8.2. Recommendations

For health professionals

- Active treatment of the primary disease and the early withdrawal of patients from mechanical ventilation should be facilitated.
- AKI should be prevented in VAP patients. The interaction between kidney and lung as well as ventilator settings in the context of AKI should be of concern.
- Clinicians should balance the risk and benefits of using vasopressors and inotropes in VAP patients and underlying causes leading to requirement of vasopressors should be controlled.

For stake holders (Hospital Administration)-

- Portable chest-x ray is essential in order to diagnose VAP based on the standard.
- Arterial blood gas analyzers are also essential in order to compute severity scores.
- Proper documentation and storing of patient records needs emphasis.
- The adherence of health professionals to the VAP prevention methods should be assessed.

For researchers –

- Prospective follow up study is required which incorporates BMI, APACHE score and SOFA scores.
- Moreover, prospective studies focusing on homogenous group of patients are recommended in order to better elucidate the differential contributions of the underlying disease type to the mortality of VAP patients.

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Annexes

Annex I: Data extraction tool (Questionnaire)

Patient card no: _____ **Questionnaire/ study ID_____**

Part 1. Sociodemographic characteristics and. Investigations during the diagnosis of VAP

S. no	Questions	Response
001	Name of hospital	1. Menilik II 2. Zewditu 3. St. Peter's 4. TASH
002	Age of the patient	_____(years)
003	Sex of the patient	1. Male 2. Female
004	Renal function testes	1. Creatinine (mg-dl) ---------
005	Liver Function Testes	2. Albumin (ALB) (mg-dl) ---------

Part 2. Clinical Characteristics of the patient and ICU related information

201	Comorbidity	1. Yes 2. No		If '2', go to Q 303
202	Type of comorbidity	Hypertension	1. Yes 2. No	
		DM	1. Yes 2. No	
		COPD	1. Yes 2. No	
		Chronic Kidney D/se	1. Yes 2. No	
		Chronic Liver D/se	1. Yes 2. No	
		Congestive Heart Failure	1. Yes 2. No	
		Malignancy	1. Yes 2. No	
		Acute Respiratory Distress Syndrome (ARDS)	1. Yes 2. No	
		Others (specify)		
203	Admission diagnosis (write specifically)	1. Trauma 2. Respiratory diseases 3. Neurological diseases 4. Cardiovascular diseases		

		5. Intraabdominal diseases 6. Others (specify)	
204	Place of intubation	1. Emergency room 2. ICU 3. Operating room 4. From other hospital	
205	Admitting ward	1. Surgical ICU 2. Medical ICU	
206	Admitted to ICU from	1. Medical ward 2. Surgical ward 3. Gynaecology ward 4. Emergency OPD 5. Operative room	

Part 3. Mechanical ventilation characteristics, Pathogen characteristics

302	Duration of mechanical ventilation before VAP	----------(days)	
303	Total days on mechanical ventilation	----------(days)	
304	Length of stay in ICU	----------(days)	
305	Hospital length of stay (total days the patient stayed in the hospital including ICU stay)	----------(days)	
306	Number of microorganisms causing VAP proven by culture	1. Single microbial 2. Poly microbial	
307	Type of Microorganism causing VAP proven by culture	1. Acinetobacter baumannii	1. Yes 2. No
		2. Klebsiella pneumoniae	1. Yes 2. No
		3. Pseudomonas aeruginosa	1. Yes 2. No
		4. Staphylococcus aureus	1. Yes 2. No
		5. Others (specify)	1.Yes 2. No

Part 4. Interventions done for the patient

401	Type Invasive procedures done	Tracheostomy	1. Yes 2. No
		Blood transfusion	1. Yes 2. No
		Central venous catheter	1. Yes 2. No

		Nasogastric tube	1. Yes 2. No
		Haemodialysis	1. Yes 2. No
		Others (specify)	
402	Medications given	Corticosteroids	1. Yes 2. No
		Vasopressors and Inotropes	1. Yes 2. No
		Others(specify)	
403	Complications in the ICU (write specifically)	Sepsis (write specifically)	1. Yes 2. No
		Acute Kidney injury	1. Yes 2. No
		Electrolyte imbalance	1. Yes 2. No
		Anemia	1. Yes 2. No
		Cardiac arrest	1. Yes 2. No
		Others	
404	Antibiotic treatment before the onset of VAP	1. Yes 2. No	
405	Antibiotic treatment after diagnosis of VAP	1. Single antibiotics 2. Combined antibiotics	
406	Starting date of Antibiotic treatment	1. Early (within 24 hours after VAP onset) 2. Late (after 24 hours of VAP onset)	

Part 5. Patient outcome

501	Patient Out-come	In hospital mortality	1. Yes 2. No
		Discharge from ICU -If 'yes' write the Reason for discharge	1. Yes 2. No
		Improved	1. Yes 2. No
		Other(specify)	
502	Date of the outcome after the diagnosis of VAP	In hospital mortality	--------th day after VAP
		Discharge from ICU	--------th day after VAP
		Improved	---------th day after VAP
		Other(specify)	----------th day after VAP

Annex II: proportional Hazard assumption and Goodness of Fit

Table 1: Schoenfeld residuals

Variables	Rho	Chi2	Df	Prob>chi2
Age	0.15365	1.87	1	0.1719
Admission diagnosis of respiratory disease	0.12114	1.19	1	0.2754
Sepsis	0.09852	0.75	1	0.3849
AKI	0.02818	0.05	1	0.8301
Electrolyte imbalance	0.03319	0.08	1	0.7724
Vasopressors	-0.02203	0.04	1	0.8499
Tracheostomy	-0.04187	0.14	1	0.7045
Creatinine	0.08111	0.44	1	0.5059
Total days on MV	-0.00883	0.00	1	0.9540
Length of ICU stay	0.08124	0.24	1	0.6251
Length of hospital stay	0.03102	0.06	1	0.8027
Global test		4.3	11	0.9602

Figure 1: cox-snell residuals on predictors of mortality among adult ICU patients with VAP in Addis Ababa governmental hospitals, Addis Ababa, Ethiopia,2023/2024.