



HARAMAYA UNIVERSITY
COLLEGE OF HEALTH AND MEDICAL SCIENCE
SCHOOL OF GRADUATE STUDIES

**PREVALENCE AND ASSOCIATED FACTORS OF VENTILATOR-
ASSOCIATED PNEUMONIA AMONG INTUBATED PATIENTS IN
HIWOT FANA SPECIALIZED COMPREHENSIVE HOSPITAL, HARAR,
ETHIOPIA**

**POST GRADUATE ANESTHESIOLOGY CRITICAL CARE AND PAIN
MEDICINE RESEARCH THESIS**

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**Prevalence and Associated Factors of Ventilator-Associated Pneumonia
Among Intubated Patients in Hiwot Fana Specialized Comprehensive
Hospital, Harar, Ethiopia**

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STATEMENT OF THE AUTHOR

By signing below, I affirm that this thesis is my original work. I have adhered to all ethical and technical standards of scholarship throughout the preparation, data collection, analysis, and compilation of this document. Any scholarly content included has been properly cited.

This thesis is submitted as a fulfil part of the requirements for the Medical Specialty in Anesthesiology Critical Care and Pain Medicine. It will be deposited in the Haramaya University library and made available to borrowers in accordance with library policies. I declare that this Thesis has not been submitted to any other institution for the purpose of obtaining any academic degree or diploma.

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BIOGRAPHICAL SKETCH

My name is Dr. Amanuel Takele. I was born in 1991 in the Oromia Region, Ethiopia. I completed my primary education at Degoye and Chore primary schools, in Ilu Aba Bora Zone and secondary education at Gambella high school in Gambella region. In 2012, I joined at Saint Paul's Millennium Medical College, where I did my doctor of medicine and graduated in 2017. Subsequently, I served as a General Practitioner at Kumi Meles Zenawi Memorial Primary Hospital for two years and General Practitioner at Gambella General Hospital for one and half year. In April, 2022, I joined Haramaya University to pursue a specialization in Anesthesiology Critical Care and Pain Medicine.

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Figure 1: Conceptual framework showing the relationship between potential factors and prevalence of VAP (adapted by principal investigator from different literature)

LIST OF ABBREVIATIONS AND ACRONYMS

ACCPM	Anesthesiology Critical Care and Pain Medicine
AIDS	Acquired Immunodeficiency Syndrome
ARDS	Acute Respiratory Distress Syndrome
CGS	Council of Graduate Studies
CHMS	College of Health and Medical Science
COPD	Chronic Obstructive Pulmonary Disease
HFSCH	Hiwot Fana Specialized Comprehensive Specialized Hospital
HIC	High Income Countries
HIV	Human Immunodeficiency Virus
HRHB	Harari Regional Health Bureau
ICU	Intensive Care Unit
IHRERC	Institutional Health Research Ethics Review Committee
IPC	Infection Prevention and Control
LMICs	Low- and Middle-income Countries
MDR	Multidrug-Resistant
MPH	Masters of Public Health
MV	Mechanical Ventilation
PGY	Post Graduate Year
SGC	School Graduate Committee
SOFA	Sequential Organ Failure Assessment Score
TB	Tuberculosis
VAP	Ventilator Associated Pneumonia

ABSTRACT

Background: Ventilator-associated pneumonia refers to pneumonia that develops in patients receiving mechanical ventilation for at least 48 hours. It is associated with an increased duration of mechanical ventilation, longer stays in the intensive care unit, and higher mortality. The prevalence ranges from 10 to 25% in tertiary care hospitals, but can reach as high as 76% in certain settings and high mortality. This study aims to examine the prevalence and associated factors of ventilator-associated pneumonia to implement more effective preventive measures and reduce morbidity and mortality.

Objective: To assess the prevalence and associated factors of ventilator-associated pneumonia in intubated patients at the Hiwot Fana and Harme Intensive Care Units from December 23, 2024 to January 10, 2025.

Method: Institutional-based cross-sectional study was conducted among 171 intubated patients on invasive mechanical ventilation for more than 48 hours at Hiwot Fana Comprehensive Specialized Hospital (Harme and Hiwot fana intensive care units) from January 1, 2021, to June 30, 2024. Data were collected from patient charts using a structured checklist, which were pretested before use. The data from Kobotool box was then exported to STATA version 17 for cleaning and analysis. Adjusted odds ratios with 95% confidence intervals were calculated and associated factors with a p-value less than 0.05 were considered significant.

Results: Overall 171 study participants were included in this study, 46 developed Ventilator-Associated Pneumonia during their intensive care unit stay, resulting in a prevalence of 26.90% (95% CI: 21.03% -32.77%) The total ventilator days were found to be 1976 days; the median ventilator-days were 7 days with a minimum of 3 days and a maximum of 120 days. Based on onset, 9(19.6%) patients had early onset Ventilator-Associated Pneumonia and the remaining 37 (80.4%) had late onset Ventilator-Associated Pneumonia. Blood transfusion (adjusted odds ratio (AHR): 2.68, 95% CI: 1.03–4.98; P = 0.042), Tracheostomy (AHR: 0.28, 95% CI: 0.08–0.75; P = 0.014), and increased duration of MV (AHR: 4.1, 95% CI: 1.49–10.32; P = 0.005) were significantly associated with the development of Ventilator-Associated Pneumonia.

Conclusions: Nearly one-fourth of the participants developed ventilator-associated pneumonia. Blood transfusion, tracheostomy and duration of mechanical ventilation were significantly associated with ventilator-associated pneumonia.

Keywords: Intubated Patients; Prevalence; Intensive Care Unit; Associated factors; Ventilator-Associated Pneumonia; Mechanical Ventilation

1. INTRODUCTION

1.1 Background

VAP refers to pneumonia that occurs at least 48 hours after endotracheal intubation or tracheostomy, with no evidence of pneumonia at the time of intubation, admission, or tracheostomy (Bassi et al., 2014; Erb et al., 2016). Based on the onset, VAP is classified as early-onset, which occurs within the first four days (≤ 4 days) of MV, usually caused by antibiotic-sensitive bacteria, and late-onset, which occurs from the fifth day (≥ 5 days) of MV and is caused by MDR pathogens. It is associated with an increased duration of MV, longer stays in the ICU, and higher mortality. VAP is the leading cause of death from acquired nosocomial infections, with estimated prevalence ranging from 10% to 65%, and fatality rates of 13-55%. VAP also poses a substantial economic burden (Kollef et al., 2012); the VAP-associated cost in acute-care hospitals in the United States was estimated to be 3 billion USD in 2012 (Zimlichman et al., 2013).

There is a disparity in the epidemiology of VAP across countries. Hospitals in HICs have lower VAP rates than those in LMICs. A combination of surveillance and IPC policies has reduced the incidence of VAP in HICs. Conversely, the VAP incidence in LMICs remains a challenge because these countries often face unique barriers to healthcare delivery and resource availability (Elsheikh et al., 2024). Furthermore, the burden of VAP in LMICs remains unknown due to the lack of standardized infection definitions and the scarcity of IPC organizations and legal infrastructure (Lisboa and Rello, 2008).

Bacteria that colonize the oropharynx and gut, or those acquired mainly by healthcare professionals or other patients are commonly considered the etiologic agents of VAP. Antibiotic-resistant pathogens, such as *Pseudomonas* and *Acinetobacter* species and methicillin-resistant strains of *Staphylococcus aureus*, are more common after prior antibiotic treatment, prolonged hospitalization, or mechanical ventilation, and when other risk factors are present (Park, 2005). Information about the risk factors for VAP is limited. Therapeutic hypothermia is believed to be a major risk factor, especially in contributing to early-onset VAP in adults. Hypoxemia is also considered a risk factor for VAP, as it may lead to complications such as acute lung injury, atelectasis, and reduced bacterial clearance, which could promote VAP (Six et al., 2016).

1.2 Statement of the Problem

VAP is a major nosocomial infection among intubated ICU patients, which requires purposeful study to reduce its morbidity and mortality. Based on the onset, it is classified as early-onset VAP, which occurs within the first four days (≤ 4 days) of MV and is usually caused by antibiotic-sensitive bacteria, and late-onset VAP, which occurs from the fifth day (≥ 5 days) of MV and is caused by MDR pathogens (Kollef et al., 2012).

According to the 2016 clinical practice guidelines by the Infectious Diseases Society of America and American Thoracic Society, VAP is diagnosed when there is a new or changing lung infiltrate on chest x-ray and at least two of the following clinical features: fever ($\geq 38^\circ\text{C}$), increased white blood cell count ($\geq 12 \times 10^9$ WBC/mL), and purulent tracheobronchial secretions (Lisboa and Rello, 2008).

Globally, the prevalence of VAP is 15.6%. The presence of VAP was associated with an increased risk of hospital morbidity, and it remains the most frequent infection among patients hospitalized in the ICU (Bulent and Ertugrul, 2006). The crude mortality rate of VAP ranged from 16% to 94% compared to 0.2% to 51% in non-VAP patients, and the ICU length of stay in VAP patients ranged from 8 to 24 days compared to 2.5 to 13 days in non-VAP patients. VAP was associated with an increased ICU length of stay by 10 days and higher mortality than patients without VAP. Patients with VAP develop many complications, such as severe sepsis, septic shock, ARDS, atelectasis, and infection with MDR organisms, which in turn increase costs, morbidity, and mortality (Cook, 2000).

In a single-center prospective cohort study conducted in Egypt among 315 intubated patients, 19.7% developed VAP (17.1 per 1000 ventilator days) with a mean age of 48 years, and 27.3% were female. The average duration between MV initiation and VAP occurrence was 8 days, with 26 days being the longest, and the mortality among patients with VAP was 62.9% (Elsheikh et al., 2024).

According to a study conducted among adult intubated patients at Bahir Dar University Specialized Hospitals, 27.9% of patients developed VAP during their stay in the ICU, with an incidence rate of 45.7 per 1000 ventilator days. The median ventilator-days were 5, ranging from

2 to 40 days. Based on onset, 14.9% of patients had early-onset VAP, while the remaining 85.1% had late-onset VAP (Belay et al., 2022).

Studies assessing the economic impact of VAP in the United States found that patients with VAP had higher mean costs for hospitalization, nursing services, antibiotics, anesthesia, ventilator support, respiratory therapy, and chest x-rays, increasing the total cost by 40% or more (Kollef et al., 2012). The total cost for VAP patients was approximately three times higher than for non-VAP patients, likely due to prolonged hospitalization (Alp, 2012). The increase in the incidence of VAP can be attributed to various factors, including inadequate suctioning methods, prolonged ICU stays, inappropriate methods for collecting and culturing respiratory secretions, difficulties in eradicating MDR organisms, and inadequate VAP prevention measures (Mastrogianni et al., 2023).

VAP is associated with high economic costs, longer hospital stays, and high mortality, especially when lung infections are caused by MDR pathogens. Various studies in developing countries have shown that simple, cost-effective measures such as hand washing, proper handling of respiratory tract secretions, oral hygiene with chlorhexidine, head-of-bed elevation greater than 30°, daily sedation breaks and extubation assessments, peptic ulcer prophylaxis, deep vein thrombosis prophylaxis, and the use of gloves by healthcare workers can significantly reduce the incidence of VAP (Mehta and Bhagat, 2016). However, no studies have been conducted on the prevalence and associated factors of VAP at Haramaya University or in the Harari region. Therefore, it is crucial to know prevalence of VAP and determine its associated factors to design and implement more effective preventive measures and reduce the associated morbidity and mortality.

1.3 Significance of the Study

The finding of the study will provide more insight and adequate knowledge to hospital administrators and healthcare providers on prevalence and incidence of VAP. By analyzing the prevalence of VAP and its associated factors, this study can inform the development of VAP preventive measures and resource allocation strategies at ICU HARME-Center and HFCSH. Finally, since there is information gap regarding this topic, the finding may serve as baseline for further studies including prospective follow up studies.

1.4 Objective of the Study

1.4.1 General Objective

To assess the prevalence and associated factors of VAP among intubated patients in HFSCCH, Ethiopia from January 1, 2021, to June 30, 2024. Data was collected from December 23, 2024 to January 10, 2025.

1.4.2 Specific Objective

To determine the prevalence of VAP among intubated patients in HFSCCH

To identify the associated factors to VAP among intubated patients in HFSCCH

2. LITERATURE REVIEW

2.1 Prevalence of VAP

Globally, the prevalence of VAP is 15.6%. The presence of VAP was associated with an increased risk of hospital morbidity, and it remains the most frequent infection among patients hospitalized in the ICU (Bulent and Ertugrul, 2006). The crude mortality rate of VAP ranged from 16% to 94% compared to 0.2% to 51% in non-VAP patients, and the ICU length of stay in VAP patients ranged from 8 to 24 days compared to 2.5 to 13 days in non-VAP patients. VAP was associated with increased ICU length of stay (LOS) by 10 days and higher mortality than patients without VAP. Patients with VAP develop many complications like severe sepsis, septic shock, ARDS, atelectasis, and infection with MDR organisms, which in turn increase cost, morbidity, and mortality (Cook D, 2000).

In a single-center prospective cohort study conducted in Egypt among 315 intubated patients, 19.7% developed VAP (17.1 per 1000 ventilator days) with a mean age of 48 years, and 27.3% were female. The average duration between MV initiation and VAP occurrence was 8 days, with the longest being 26 days. The mortality among patients with VAP was 62.9% (Elsheikh et al., 2024). According to a study conducted among adult intubated patients in Bahir Dar University Specialized Hospitals, 27.9% of patients developed VAP during their ICU stay, and the incidence rate of VAP was 45.7 per 1000 ventilator days. The median ventilator-days were 5 days, with a minimum of 2 days and a maximum of 40 days. Based on onset, 14.9% of patients had early-onset VAP, and the remaining 85.1% had late-onset VAP (Belay et al., 2022).

2.2 Associated factors

2.2.1 Socio-Demographic Related Factors

Age does not appear to be particularly associated with the risk of pneumonia in ventilated patients. A secondary analysis of a European cohort study reported 13.7 VAPs per 1000 ventilation days in middle-aged (45–64 years) patients, 16.6 in older patients (65–74 years), and 13.0 in very old patients (≥ 75 years). In contrast, male gender is generally recognized as an independent risk factor for VAP (Blot et al., 2014).

2.2.2 Admission Diagnosis- Related Factors

Incidence rates greatly vary based on the studied population. For example, VAP rates as high as 24.5/1000 ventilator-days have been reported in cancer patients. A high incidence is also reported in trauma patients (17.8% in one series of 511 patients), explained at least in part by the alteration of immune function after major traumatic injury, aspiration resulting from brain injury and lung contusion. The increased incidence observed in COPD patients might be explained by prolonged duration of MV (muscular weakness), high incidence of microaspiration and bacterial colonization (defective mucociliary clearance), and altered local and general host defense mechanisms. Acute respiratory ARDS is also associated with a high risk of VAP (Koulenti et al., 2006).

The most significant clinical complication after burn is pneumonia, with an incidence of 10–65%. A 5-year study of 92 burn children admitted to the pediatric ICU showed that 57% of children had at least one diagnosis and treatment of pneumonia during their clinical course, of which 41% met the diagnostic criteria for VAP. A prospective study of 80 burn patients showed that the incidence of pneumonia in burn patients was 15%, and the incidence of pneumonia in the group with inhalational injury was twice as high as that in the group without inhalational injury (Rogers et al., 2014).

2.2.3 Intervention Related Factors

VAP is reported to affect 5–40% of patients receiving invasive mechanical ventilation for more than 2 days, with large variations depending upon the country, ICU type, and criteria used to identify VAP (Reignier et al., 2013). VAP rates in North American hospitals have been reported to be as low as 1–2.5 cases per 1000 ventilator-days (Bulent and Ertugrul, 2006). European centers, however, report much higher rates. The EU-VAP/CAP study, for example, reported an incidence density of 18.3 VAP episodes per 1000 ventilator-days. LMICs also report higher rates compared to US hospitals and HICs in particular (18.5 vs 9.0 per 1000 ventilator-days; (Koulenti et al., 2006).

These large discrepancies are at least in part explained by differences in definitions, differences in how definitions are applied, diagnostic limitations of all definitions, and differences in microbiological sampling methods (Ego et al., 2015).

Prospective cohort study done Logistic regression analysis demonstrated that tracheostomy (AOR, 6.71; 95% confidence interval [CI], 3.91 to 11.50; $p < 0.001$), multiple central venous line insertions (AOR, 4.20; 95% CI, 2.72 to 6.48; $p < 0.001$), reintubation (AOR, 2.88; 95% CI, 1.78 to 4.66; $p < 0.001$), and the use of antacids (AOR, 2.81; 95% CI, 1.19 to 6.64; $p = 0.019$) were independently associated with the development of VAP. The hospital mortality of patients with VAP was significantly greater than the mortality of patients without VAP (45.5% vs 32.2%, respectively; $p = 0.004$) (Pawar et al., 2003). Indwelling gastric tubes can damage the function of the cardiac sphincter and increase the chance of gastric fluid reflux, resulting in aspiration.

Bacteria colonized in the stomach can be colonized in the pharynx through the stomach's anti-peristaltic action and/or along the gastric tube, and then get into the lower respiratory tract to cause infection. Pulmonary parenchymal injury caused by pneumothorax or hemothorax after thoracic intubation could play an important role in the development of VAP according to a prospective study (Apostolopoulou et al., 2003).

The study included 100 patients with clinically diagnosed VAP, 35 of them were diagnosed with VAP by quantitative culture of endotracheal aspirates. Previous antibiotic therapy and hospitalization for more than 5 days were independent risk factors for drug resistance in VAP pathogens, according to risk factor assessments. In addition, an etiological study of 397 VAP patients also showed that long-term exposure to unnecessary antibiotics was one of the strongest predictors of antibiotic resistance. Multivariate logistic analysis identified prophylactic antibiotic exposure and multiple inadequate antibiotic therapies as independent risk factors for MDR VAP (Čiginskienė et al., 2019).

2.3 Conceptual Framework

This conceptual framework is developed from different literatures (Pawar et al., 2003; Rogers et al., 2014; Blot et al., 2014). This framework showed the relationship between incidence of VAP with Socio-demographic related factors, admission diagnosis related factors and intervention related factors (Figure 1).

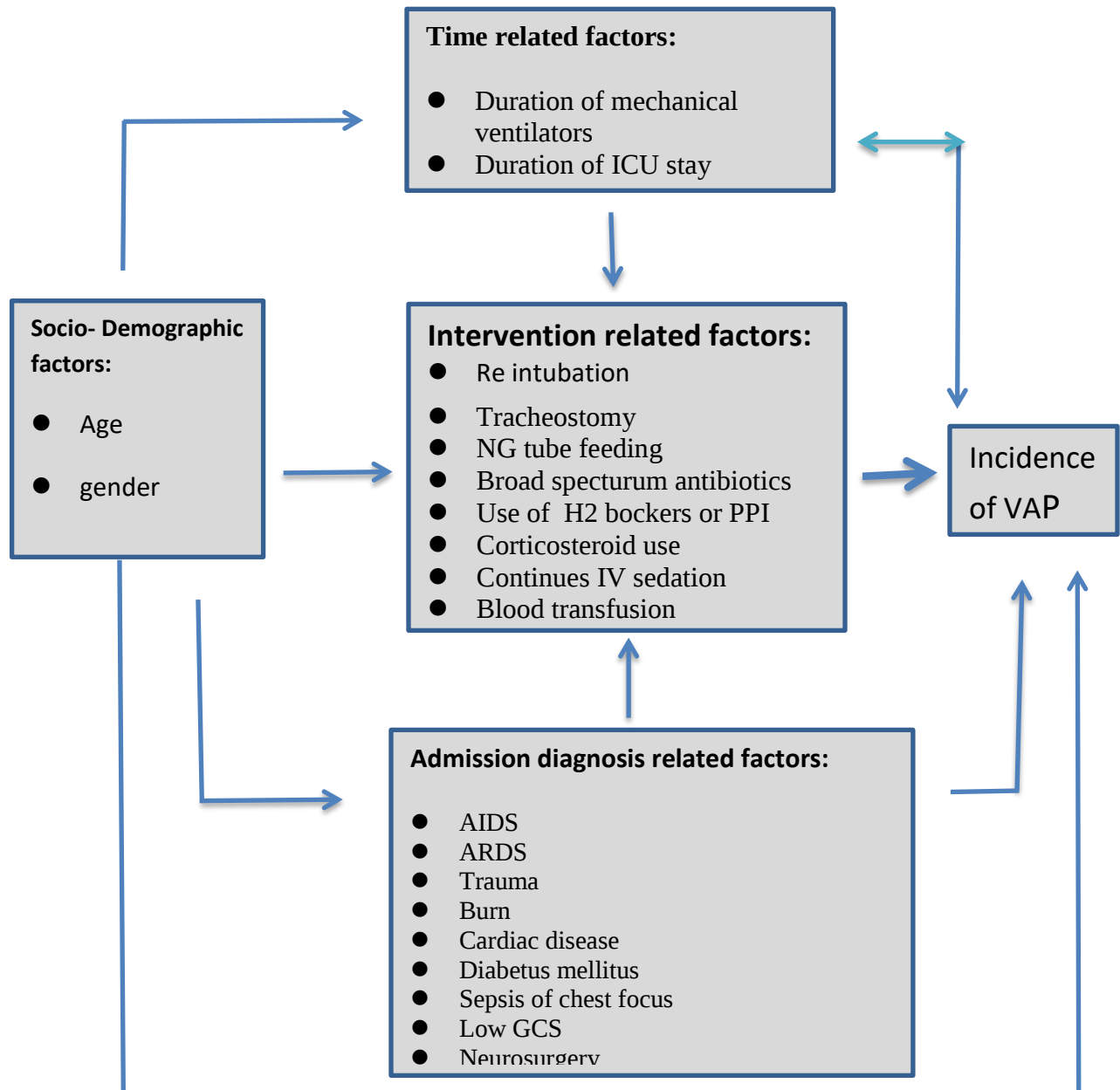


Figure 1: Conceptual framework showing the relationship between potential factors and incidence of VAP (adapted by principal investigator from different literature)

3. METHOD OF THE STUDY

3.1 Study Area and Period

The study was conducted at Haramaya University, HFCSH. It is located in Harar regional government which is located about 533 km from Addis Ababa towards East. HFCSH was established during the Italian invasion of Ethiopia (1928-1933 E.C) to serve Italian soldiers. It was built mainly to provide medical care for the invading army; however, it continued to deliver health service to millions of Ethiopians living below Awash after the expulsion of Italians from Ethiopia.

After downfall of derg, the Hospital was run by HRHB. On July 14, 2010, HRHB handed over the administration and service provision of the hospital to Haramaya University and named HFCSH. HFCSH serves as a teaching referral hospital for the entire Eastern part of Ethiopia, including Eastern Oromia, Dire Dawa City Administration, the Somali Regional State and the Harari Regional State. It serves a total of 20 million populations in the catchment area. Currently, the hospital has about 525 beds with 294 functional rooms to offer different services for the community.

The hospital is currently delivering different health service to the community including: internal medicine, general surgery, Neurosurgery, pediatric surgery, Urology, plastic surgery , Orthopedic surgery, pediatrics, Neurology, pediatric cardiology, Neonatal intensive care, Emergency and critical care, TB/HIV services, intensive medical care, dental care, mental health care, reproductive health services, dermatology and venereal disease services, Maternal and child health (MCH) services, ophthalmic care, ENT, Pathology, Oncology, pharmacy and laboratory, and imaging service. Data was collected from December 23, 2024 to January 10, 2025.

3.2. Study Design

Institutional-based cross-sectional study was conducted.

3.3 Population

3.3.1 Source Population

All patients on invasive mechanical ventilation in HFCSH ICU.

3.3.2 Study Population

All patients on invasive mechanical ventilation for at least 48 hours duration from January 1, 2021, to June 30, 2024.

3.4 Eligibility Criteria

3.4.1 Inclusion Criteria

All patients on invasive mechanical ventilation for at least 48 hours of duration

3.4.2 Exclusion Criteria

Patients having pneumonia before invasive mechanical ventilation or within 48 hours of MV

Patients on invasive mechanical ventilation for more than 48 hours with incomplete records

3.5 Sample Size Determination

3.5.1. Sample size for first objective

The sample-size of this study was determined by using 27.9%, from a study conducted at Bahirdar University Specialized Hospitals (Belay et al., 2022), calculated by using a single population proportion formula:

$$N = \frac{(Z^{\alpha/2})^2 \rho(1-\rho)}{\varepsilon^2} \text{ Where}$$

N = sample size

Z = the standard normal deviate

P = prevalence of the previous study characteristic 95% confidence interval

d = degree of precision or accuracy 5% degree of precision

α = significance level 5% Significance level

$$N = \frac{(1.96)^2 0.279(0.721)}{0.05^2} = 309.108 \approx 310$$

3.5.2 Sample size for the second objective

The sample size for second objective is determined by online openEpi using double population proportion formula using assumptions of 80 % power of the study, 95% confidence interval, and 0.05 margin of error, which makes the maximum sample size of 94.

Table 1: Sample size for the second objective – Institutional-based cross-sectional study on prevalence and associated factors of ventilator-associated pneumonia among intubated patients in HFSC (Hiwotfana and Harme ICU), Ethiopia from January 1, 2021, to June 30, 2024.

Variables	Percent of Outcome in exposed	Percent of Outcome in unexposed	RR	Sample size	Confidence Level	Power	Reference
Reintubation	70	39	1.58	94	95%	80%	(Pawar et al., 2003)
Blood transfusion	81	19	2.23	28	95%	80%	(Elsheikh et al., 2024)
Tracheostomy	62	17.9	2	50	95%	80%	(Patil, 2017)

Therefore, the minimum sample size for this study is the maximum of the two objectives, which is 310. We used this sample size since it is the maximum sample size among the two objectives. Since our total population is less 10000, we use the minimization formula, which is: $n = \frac{n}{1 + \frac{n}{N}} = \frac{310}{1 + \frac{310}{380}} \approx 171$.

3.6 Sampling Procedure and Technique

There are 380 intubated patients admitted to HFCSH (n=200), and HARME (n=180), ICU departments from January 1, 2021, to June 30, 2024. By preparing a sampling frame using the medical registration numbers of patients for both hospitals, 171 (90 from HFCSH and 81 from HARME) participants' cards were drawn by a proportional allocation formula. Study participants were selected randomly by lottery method (simple random sampling technique).

3.7 Data Collection Methods

3.7.1 Data Collection Instrument

The data were collected using a questionnaire adapted from different sources (Koulenti et al., 2006; Belay et al., 2022; Blot et al., 2014). The questionnaire contains four parts: general information, socio-demographic-related factors, admission diagnosis-related factors and intervention-related factors.

3.7.2 Data Collectors

Data were collected by three BSc academic staff at HFCSH who have experience in data collection, and supervised by two general practitioners who were working at HFCSH Harme and Hiwotfana ICU.

3.7.3 Data Collection Procedure

Data were collected at HFCSH Harme and Hiwotfana ICU. Data were collected from previously documented charts on patients who were on a MV for more than 48hrs.

3.8 Study Variables

3.8.1 Dependent Variable

Prevalence of VAP

3.8.2 Independent Variable

Socio-demographic factors (age and sex) and;

Admission diagnosis-related factors (low Glasgow coma scale, ARDS, Neurosurgery, Burn, Cardiac diseases, Diabetes mellitus, AIDS, Trauma, and Sepsis).

In addition, intervention-related factors (duration on MV support, duration on ICU stay, tracheostomy, reintubation, Tube Thoracostomy, Naso gastric feeding, use of corticosteroid, supine head position, use of histamine blockers, blood transfusion, use of continuous intravenous sedatives, and prior use of broad-spectrum antibiotics) that are associated with VAP.

3.9 Operational Definition

VAP was diagnosed with the presence of a new or progressive chest x-ray infiltrate, plus at least two of the following clinical symptoms: fever $>38^{\circ}\text{C}$ with no other recognized causes, tachycardia, leukocytosis or leucopenia, new-onset purulent tracheal secretion, and increased oxygen requirements in patients on a mechanical ventilator for at least 48 hours (Tuche et al., 2008).

Patient use of continuous intravenous sedation: administration of continuous infusions of sedative drugs like diazepam, propofol, and ketamine.

Prior antibiotic administration: intravenous antibiotic administration for longer than 24 hours during any portion of the patient's hospitalization before and during MV.

Low GCS: patients having less than nine GCS during admission to the ICU.

Corticosteroid use: use of corticosteroid drugs like, hydrocortisone, prednisolone, and dexamethasone for greater than 2 days during intubation.

3.10 Data Quality Control

To assure the quality of data, data collectors and supervisors were given a one-day training focusing on the questionnaire, data collection tools, and study's objective. Before actual data collection, a preliminary review was conducted at Jugal General Hospital on 5% (n=10) of sample size. A weeks before actual data collection, a chart were cross-checked to ensure that the instruments are adequate, check list of tools is filled in time, and the data for the charts is complete. Close follow-up and supervision were carried out during the data collection period jointly by the principal investigator and the supervisors. The necessary feed backs were forwarded to the data collectors daily. The collected data were reviewed and checked for its completeness before data entry.

3.11 Data Analysis

Data collected by Kobo toolbox were exported to STATA version 17 for further cleaning and analysis. Descriptive analysis, such as frequencies and cross-tabulation were performed, as well as re-categorization and categorization of categorical and continuous variables were done.

Then, prevalence of VAP was calculated. Logistic regression is used to determine crude and adjusted odds ratio. Bivariate logistic regression analyses carried out to assess the association between the dependent and independent variables and to identify candidates for multivariate analysis. Then, multivariate analysis is performed on the variables which have a P-value < 0.25 to determine factors significantly associated with VAP. Statistical significance was measured by p-values < 0.05 and adjusted odds ratio (AOR) with 95% confidence interval (95% CI).

3.12 Ethical Considerations

Ethical issues within the study were taken into consideration when carrying out the study. Ethical approval and clearance was obtained from IHRERC of CHMS, Haramaya University. A formal letter was submitted to HFCSH from CHMS. Informed voluntary, written and signed consent was obtained from the Chief Clinical Director (Head) of HFCSH. Except the investigators and data collectors, no one had access to patients collected data, name or anything taken from chart. The data were kept coded and locked with no labeling specifying patient name in the research

3.13 Dissemination of Results

The research will be presented and submitted to Haramaya University, HFCSH. The final document copy will be available to those who need it in the university.

4. RESULT

4.1 Prevalence of Ventilator-Associated Pneumonia

Among 171 study participants, 46 developed VAP during their intensive care unit stay, resulting in a prevalence of 26.9% (95% CI: 21.03% -32.77%). The mean age of the participants was 29.7 years (SD $\pm$ 19.4). The total ventilator days were found to be 1976 days; the median ventilator-days were 7 days with a minimum of 3 days and a maximum of 120 days. Based on onset, 9(19.6%) patients had early onset VAP and 37 (80.4%) had late onset VAP. Microbiological diagnosis was made in 33 (71.7%) patients who developed VAP and the commonest pathogens identified were Gram positive diplococci 10 (21.7%) followed by Gram negative bacilli 4(8.7%).

Table 2: Microbiological diagnosis among Patients with VAP ICU of HFCSH (Hiwotfana and Harme ICU) and developed VAP, Ethiopia from January 1, 2021, to June 30, 2024

Pathogen	Frequency	Percent (%)
No growth	13	28.3
Not done	11	24
Gram positive diplococci	10	21.7
Gram negative bacilli	4	8.7
Klebsiella pneumoniae	2	4.3
Streptococcus pneumonia	2	4.3

4.2 Socio-Demographic Characteristics

In this study a total of 171 patients were enrolled out of which 92 (53.8%) were male and 79 (46.2%) were female. The median age of patients was 28 years with inter-quartile range of 15-40 years.

Table 3: Gender distribution among Patients Admitted to ICU of HFCSH (Hiwotfana And Harme ICU), Ethiopia from January 1, 2021, to June 30, 2024

Sex	Freq.	Percent
Male	92	53.8
Female	79	46.2
Total	171	100

4.3 Intervention Related Factors

The median lengths of patients on the mechanical ventilators were 7 days with an inter-quartile range of 4–12 days. The median lengths of stay of patients in the intensive care unit were 10 days and inter-quartile range of 5–15 days.

Table 4: Intervention-Related Factors of VAP Among Patients Admitted to ICU of HFCSH (Hiwotfana And Harme ICU), Ethiopia from January 1, 2021, to June 30, 2024

Variables	Category	VAP		
		Yes (%)	No (%)	Total (%)
Tracheostomy	Yes	15 (48.4)	9 (7.8)	24 (14)
	No	31 (51.6)	116 (92.2)	147 (86)
Reintubation	Yes	12 (26.1)	7 (5.6)	19 (11.1)
	No	34(73.9)	118 (94.4)	152 (88.9)
Blood transfusion	Yes	24 (52.2)	38 (30.4)	62 (36.3)
	No	22 (47.8)	87 (69.6)	109 (63.7)
Gastric feeding	Yes	43 (93.5)	104 (83.2)	147 (86)
	No	3 (6.5)	21 (16.8)	24 (14)
Corticosteroids use	Yes	21 (45.6)	46 (44.2)	67 (39.2)
	No	25(54.4)	79 (55.8)	104 (61.8)
Broad spectrum antibiotics	Yes	38 (82.6)	81 (64.8)	119 (69.6)
	No	8 (17.4)	44 (35.2)	52 (30.4)
Duration on MV(days)	<=7	9 (16.6)	81 (64.8)	90 (52.6)
	>7	37 (83.4)	44 (33.2)	81 (47.4)

4.4 Admission Diagnosis-Related Factors

From the total participants, 73 (42.7%) had low GCS, and only 6 (3.5%) of the participants had burns and 5 (2.9%) had AIDS as shown in Table 5.

Table 5: Admission Diagnostic-Related Factors of VAP Among Patients Admitted to ICU of HFCSH (Hiwotfana and Harme ICU), Ethiopia from January 1, 2021, to June 30, 2024

Variables	Category	VAP		
		Yes (%)	No (%)	Total (%)
Neurosurgery	Yes	9 (19.6)	19 (15.2)	28(16.4)
	No	37 (80.4)	106 (84.8)	143
AIDS	Yes	2 (4.3)	3 (2.5))	5 (2.9)
	No	44 (95.7)	122 (97.5)	166 (97.1)
Burn	Yes	4 (8.6)	2 (1.6)	6 (3.5)
	No	44 (91.4)	121(98.4)	165 (96.5)
Trauma	Yes	12 (26)	31 (33)	43 (25.1)

DM	No	34 (74)	94 (67)	128 (74.9)
	Yes	3 (6.5)	11 (8.8)	14 (8.2)
Cardiac disease	No	43 (93.5)	114 (91.2)	157 (91.8)
	Yes	2 (4.3)	19 (15.2)	21 (12.3)
ARDS	No	44 (95.7)	106 (84.8)	150 (87.7)
	Yes	11 (23.9)	27 (21.6)	38 (22.2)
Sepsis of chest focus	No	35 (76.1)	98 (78.4)	133 (77.8)
	Yes	12 (26.1)	31 (24.8)	33 (19.3)
Low GCS	No	34 (73.9)	94 (75.2)	128 (80.7)
	Yes	21 (45.6)	52 (41.6)	73 (42.7)
	No	25 (54.4)	73 (58.4)	98 (57.3)

Bi-Variable and Multi-Variable Log Binomial Regression Analysis

The bi-variable logistic regression analysis identified 8 candidate factors for the multivariable logistic regression model. To be liberal a p-value of 0.25 as a cut off value was used to enter in to multivariable logistic regression. According to multivariate analysis, blood transfusion (adjusted odds ratio (AOR): 2.68, 95% CI: 1.03–4.98; $P = 0.042$), Tracheostomy (AOR: 0.28, 95% CI: 0.08–0.75; $P = 0.014$), and increased duration of MV (AOR: 4.1, 95% CI: 1.49–10.32; $P = 0.005$) were significantly associated with VAP.

Table 6: Bi-Variable and Multivariable Analysis of Associated factors of VAP Among Patients Admitted to ICU of HFSC (Hiwotfana And Harme ICU), Ethiopia from January 1, 2021, to June 30, 2024

Variables		VAP		Bivariable logistic regression			Multivariable logistic analysis		
		Yes(n=46)	No(n =125)	OR	95% CI	P-value	AHR	95% CI	P-value
Broad Spectrum	Yes	38	81	0.39	0.17-0.90	0.025	0.48	0.16 -1.31	0.147
	No	8	44	1			1		
Tracheostomy	Yes	15	9	6.23	2.49-15.61	0.000	0.28	0.08 – 0.75	0.014*
	No	31	116	1			1		
Reintubation	Yes	12	7	5.95	2.16-16.23	0.000	1.80	0.71-3.48	0.262
	No	34	118	1			1		
Gastric tube Feeding	Yes	43	104	2.89	0.82-10.24	0.086	0.80	0.15-2.75	0.573
	No	3	21	1			1		
Continuous sedation	Yes	25	40	2.53	1.24-4.94	0.008	0.85	0.36-2.18	0.795
	No	21	85	1			1		
Cardiac Disease	Yes	2	19	0.25	0.06-1.12	0.055	2.27	0.55-13.66	0.221
	No	44	106	1			1		
Duration on MV	<=7	9	81	1	0.06-0.26	0.000	4.1	1.49 -10.32	0.005*
	>7	37	44	2			1		
Blood transfusion	Yes	24	38	2.44	1.02-2.55	0.02	2.68	1.03–4.98	0.042*
	No	22	87	1			1		

5. DISCUSSION

The aim of this study is to determine the prevalence and identify associated factors of VAP among patients admitted to intensive care unit and was on MV for more than 48 hours at HFCSH (HIWOTFANA and HARME ICU). Despite MV being an essential element of modern intensive care unit service, it is associated with a substantial risk of VAP. In this study, 26.9% of intubated patients developed VAP. Duration of MV, blood transfusion and tracheostomy were found to be significantly associated with VAP. This study found that the prevalence of 26.9% with which agrees with studies from Bahir Dar University Specialized Hospitals 27.9% (Belay et al., 2022) Istanbul 28%, (Bulent M., 2006), in India 27.71%, (Patil, 2017) but is higher than a study conducted in Egypt, 19.7% (Elsheikh et al., 2024). This may be due to sociodemographic variation, and small sample size in the Egyptian study. In studies conducted in Canada and India, the incidence of VAP was 17.5% (Salama et al., 2014) and 18% (Cook D, 2000) respectively, which were lower than this study's findings. This difference may be due to differences in geographical location of health facilities, VAP diagnosis criteria, as in India they used both clinical and microbiological diagnosis criteria (Ego et al., 2015)., whereas; this study only used clinical diagnosis criteria.

Critically ill patients may be immunocompromised and be at a higher risk of bacterial infections via immunomodulation from medical interventions. For instance, blood transfusion can alter the immune system by inducing immune activation through the induction of human leukocyte antigen alloantibodies and T-cell activation or the promotion of immunosuppression through defective antigen presentation and suppression of lymphocyte blastogenesis. A meta-analysis suggested that a restrictive red blood cell transfusion strategy was associated with a reduced risk of healthcare-associated infections compared with a liberal transfusion strategy (Raghavan M & Marik PE, 2005). Consistent this study patients who received blood transfusions (AHR = 2.28) were significantly predisposed for the development of VAP and it proved to be an independent risk factor, but different from study done in Turkey (95% CI: 0.41–2.78) (Eggimann P & Pittet

D, 2001) this difference may be due to a variation of study designs, in Turkey the study design was case-controlled whereas the study design in this study was an Institutional-based cross-sectional study design.

In this study, patients with a tracheostomy had a 75% lower risk of developing VAP compared to those without a tracheostomy. This suggests that, when performed under proper conditions, tracheostomy may help reduce infection risk and Tracheostomy appears to be protective against VAP, possibly due to reduced need for prolonged intubation in contrast with study done in Addis Ababa University (p-value < 0.001), (Molalign, 2018), which found tracheostomy to be independent risk factor for VAP but this finding is different from studies conducted at Mahatma Gandhi Medical College and Research Institute, India (95% CI: 0.41 to 2.27) (Patil, 2017) which found no significant association between tracheostomy and development of VAP. The difference might be due to the sample size being too small in the Indian study with a total of 76 study participants as compared with this study.

Globally, the prevalence of VAP is 15.6%. The presence of VAP was associated with an increased risk of hospital morbidity, and it remains the most frequent infection among patients hospitalized in the ICU (Bulent & Ertugrul, 2006). Although patients in ICU are a small subgroup of all hospitalised patients they account for approximately 25% of all nosocomial infections. The incidence of nosocomial infections in ICU is high due to underlying disease, severity of illness, type of ICU, length of stay and invasive devices used. Nosocomial pneumonia is the leading cause of death from hospital-acquired infections (Trilla, 1994) (Eggimann P & Pittet D, 2001). Although risk factors for the development of VAP in ICU patients have been assessed in multiple studies, results are frequently controversial mainly due to methodological differences. However, duration of MV, H2 receptor blocker usage, prophylactic antimicrobial therapy, depressed consciousness, massive gastric aspiration(Koulenti et al., 2006) (Čiginskienė et al., 2019), length of stay in ICU, trauma, severity of illness and underlying disease, male gender (Cook et al., 2000), transfer from another hospital ward, a colonized central venous catheter, unplanned extubation, reintubation after weaning (Pawar et al., 2003), supine body position, enteral nutrition, Glasgow coma scale score of less than 9 (Rogers et al., 2014) are reported as independent risk factors for developing VAP in ICU patients.

The presence of an endotracheal tube is a main reason for VAP development: air flowing towards the distal airways moves pathogens, while the trachea has blunted clearance due to reduced ciliary movement and impaired cough. Several measures are considered important in the prevention of VAP, known as the VAP bundle (e.g., avoiding intubation or re-intubation whenever possible, head of bed elevation, hand hygiene, shortening ventilation through sedation interruptions, spontaneous breathing trials, or thromboembolic prophylaxis) (Coppadoro et al., 2019). Subglottic suctioning (Pozuelo-Carrascosa, 2020) and cuff pressure regulation are also commonly monitored components of the ICU care bundles prepared to decrease VAP (Mastrogianni et al., 2023).

This study also found length of ICU stay, and duration of MV as independent predictors but it did not find H2 receptor blockers, male gender, supine body position and enteral nutrition as independent risk factor for VAP. This might be due to almost all the patients received these components of VAP bundle. In this study admission diagnosis like trauma, burn, sepsis of chest focus, DM and neurosurgery were not identified as predictor of VAP which is similar with a studies done in Bahir Dar University Specialized Hospitals (Belay et al., 2022), Turkey (Eggimann P & Pittet D, 2001), India (Patil, 2017) but different from a study finding done in 20 European countries (95% CI: 9.5–19.9) (Tejerina, et al., 2006) which may be due to advanced intensive care services in developed countries.

6. STRENGTHS and LIMITATIONS

6.1 Strengths

This study, conducted as the first of its kind following the establishment of an intensive care unit in the study setting, that will serve as valuable baseline data for future research. The study evaluates multiple potential risk factors of VAP, including patient characteristics, clinical interventions and admission related factors providing a comprehensive assessment of risk factors. The findings have direct implications for ICU practices, particularly regarding interventions like implementing VAP bundle and restrictive blood transfusions, which can guide preventive strategies.

6.2 Limitations

As an institutional-based cross-sectional study, this research may not clearly establish a cause-and-effect relationship. Additionally as this study relied on a retrospective review of medical records, several challenges were encountered. These are poor history documentation and difficulties in interpreting illegible handwriting.

Compared to some referenced studies with larger cohorts and multicenter studies the findings may not be generalizable to other ICUs with different patient populations, resources, or practices since its single centered study with relatively smaller sample size.

The study used clinical diagnostic criteria for VAP, which may lack sensitivity and specificity compared to microbiological confirmation which could lead to misclassification bias.

7. CONCLUSION AND RECOMMENDATIONS

7.1 Conclusion

Nearly one fourth of study participants developed VAP. A longer duration of patients on a MV, blood transfusion, and tracheostomy were significantly associated with VAP. Knowledge of the important risk factors associated with VAP may prove to be useful in implementing simple and effective preventive measures including VAP bundle, non-invasive ventilation, and precaution during emergency intubation, minimizing a patient's stay on mechanical support and in an intensive care unit, and restrictive red blood cell transfusion strategy.

7.2 Recommendations

Overall, VAP remain a significant nosocomial infection and cause of morbidity and mortality in our institution. To effectively reduce mortality and morbidity, I recommend the following.

To health professionals:

Emphasize the importance of early recognition of clinical signs of VAP, diagnosis including microbiological and drug sensitivity testing and appropriate treatment with antibiotics with clear documentation at each level of care.

To hospital:

Enhance critical care by implementing standard VAP bundle and provide ongoing training and education for healthcare professionals on the latest intensive care guidelines and best practices for health professionals.

To researchers:

Use a prospective cohort study design in a multi-center setting to ensure data accuracy, capture unrecorded variables in real-time and to improve generalizability.

Include microbiological confirmation of VAP for more robust diagnostic accuracy and detailed data on intervention timing to better establish temporal relationships.

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9. APPENDICIES

9.1 Information Sheet and Informed Voluntary Consent form for the Head of HFCSH

1. Introduction: Hello, my name is Dr.Amanuel Takele. I'm Post graduate students at Haramaya University Hiwot Fana Specialized Hospital for the partial fulfillment of Assistant Professor in Anesthesiology Critical Care and Pain Medicine.

I would like to review charts on prevalence and associated factors of VAP among intubated patients in HFSCCH (HIWOTFANA AND HARME ICU) from January 1, 2021-June 30, 2024.

2. The study title: Institutional-based cross-sectional study on prevalence and associated factors of VAP among intubated Patients in HFSCCH (HIWOTFANA AND HARME ICU) from January 1, 2021, to June 30, 2024.

3. Purpose of the study: The aim of this research is to determine prevalence of VAP and identify its associated factors which may permit the timely implementation of measures to decrease prevalence and prevent recurrence of VAP among intubated patients in HFSCCH (HIWOTFANA AND HARME ICU), Eastern Ethiopia, from January 1, 2021, to June 30, 2024.

4. Procedure and duration: Data collectors will collect the data from the HMIS registration book to get the card numbers of patients with VAP who were admitted from January 1, 2021, to June 30, 2024. After getting the card numbers, patient charts will be retrieved from the record and documentation office. The checklist contains 4 parts, has 29 items and it will take a maximum of 40 minutes.

5. Risks and benefits: This study poses minimal risks. The research aims to generate valuable insights for researchers and local healthcare professionals to enhance care for intubated patients in ICU and prevent VAP.

6. Confidentiality: Except the investigators and data collectors, no one will have access to your collected data, name or anything taken from chart. The data will be kept coded and locked with no labeling specifying patient name in the research.

7. Contact address: If there are any questions or enquires any time about the study or procedures, please contact in this address.

Principal investigator:

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8. Declaration of Informed Voluntary Consent:

I have read the participant information sheet. I have clearly understood the purpose of research, the procedures, the risks and benefits, issues of confidentiality, the rights of participating and the contact address for any queries. I have been given the opportunity to ask questions for things that may have been unclear. I was informed that the Hospital administration has the right to stop this study from being conducted if any misdeeds and unethical procedures are observed during the data collection process in the institution.

Therefore, I declare my voluntary consent to allow this study to be conducted in this institution on behalf of HFCSH administration with my signature as indicated below.

Name and signature of Head of HFCSH _____ Date_____

Name and signature of principal investigator_____ Date_____

9.2 Data Extraction Check List

Topic: Institutional-based cross-sectional study on prevalence and associated factors of VAP among intubated patients in HFCSH (HIWOTFANA AND HARME ICU) from January 1, 2021, to June 30, 2024, Harar, Ethiopia.

Instruction: Dear data collector, this is a data abstraction form designed to collect data from patients intubated for more than 48hours in HFCSH (HIWOTFANA AND HARME ICU), Harar, Ethiopia. Please try to fill all the requested fields that are prepared in the section of the data abstraction form.

The form has four sections:**Part I: General information**

1. Date_____
2. Name of the supervisor_____

3. Name of data collector _____

Part II: Socio- demographic data of the patients

S.no	Questions	Response/answer
1	Patient code	...
2	Age of patient in years	...
3	Sex	1. Male 2. Female

Part III: Intervention related data extraction checklists

4	Did the patient develop ventilator-associated pneumonia	1. Yes 2. No
5	If yes, Duration of MV in days before developing VAP	...
6	Pathogen identified	...
7	Was antibiotics administered after diagnosis of VAP	1. Yes 2. No
8	Total duration of mechanical ventilation in days	
9	Duration of ICU stay in days	
10	Previous broad spectrum antibiotics	1. Yes 2. No
11	Continuous sedation	1. Yes 2. No
12	Corticosteroid use	1. Yes 2. No
13	Gastric tube feeding	1. Yes 2. No
14	Reintubation	1. Yes 2. No
15	Tracheostomy	1. Yes 2. No
16	VAP Bundle implemented	1. Yes 2. No
17	Blood transfusion	

Part IV: Admission diagnosis-related data extraction checklists

18	Admission diagnosis of neurosurgery?	1-yes 2-no
19	Admission diagnosis of AIDS?	1-yes 2-no
20	Admission diagnosis of trauma?	1-yes 2-no
21	Admission diagnosis of burn?	1-yes 2-no
22	Admission diagnosis of cardiac disease?	1-yes 2-no
23	Low Glasgow coma scale	1-yes 2-no
25	Does the patient have Diabetes mellitus	1-yes 2-no
25	Does the patient admitted with the diagnosis of ARDS	1-yes 2-no
26	Is the patient admitted with sepsis out of chest focus?	1-yes 2-no

9.3 Curriculum Vitae of Principal Investigator

First name(s) /Surname(s): Dr. Amanuel Takele Denu

Telephone(s): +251905995959

E-mail: gbuaman@gmail.com

Nationality: Ethiopian

Date of birth: 03 November 1991

Birth place: Bure, Illubabor

Gender: Male

Desired employment / Occupational field: Governmental

Education Background

Dagoye Elementary School from grade 1 to 4:- 1998 to 2001 G.C.

Core Elementary School from grade 5 to 8:- 2002 to 2006 G.C.

Gambella High School from grade 9 to 12:- 2007 to 2011 G.C.

Saint Paul's Millennium Medical College (Title of qualification Doctor of Medicine, CGPA=3.29/4(Ethiopian grading system)):- 2012 to 2017 G.C.

Work Experience

Junior Medical Practitioner at Kumi Meles Zenawi Memorial Primary Hospital (October, 2017 to August 2019)...Emergency department director and Outpatient department (OPD) director

General Practitioner at Gambella General Hospital (August, 2019 to March, 2022)

Personal Skills and Competences

Ability to analyze data and write reports

Ability to work independently and in a team

Ability to meet deadlines, deliver quality work and take an action oriented approach

Ability to work in harsh circumstances and computer literate (basic computer skills)

Languages

Native SpeakerAfaan oromoo and Amharic

Fluent SpeakerEnglish

Not fluent enough but can communicate wellAnyua, Nuer, and Majang

Training Delivered

S. No	Type of Training Attended	Organized By	Duration Attended	Level of Certificate/Award Provided
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1	Application Software	R.Y.T.H.M Computer Technology	July 01, 2011, to August 20, 2011	Diploma
2	Fundamentals of Leadership	SPHMMC in collaboration with CALS	Feb 21 to 22, 2017	Basic training
3	Leadership	EvaSUE SPHMMC fellowship	Sep 1, 2013, to August 30, 2016	Participatory
4	National Comprehensive HIV Care & Treatment	GRHB in collaboration with ICAP	May 14 to 26, 2018	Basic training
5	Neonatal ICU	GRHB in collaboration with Jimma Specialized Hospital	June 4 to 8, 2018	Basic training
6	Basic Emergency Obstetric & Newborn Care	FMOH and EMA in collaboration with UNICEF	August 13 to 15, 2018	Basic training
7	Basic Emergency Care	SPHMMC CPD Center	Dec 15 to 21, 2018	TOT training
8	National Comprehensive TB, TB/HIV & Leprosy	FMOH in collaboration with ICAP	Mar 04 to 09, 2019	Basic training
9	HIV Rapid Testing	GRHB in collaboration with ICAP	May 17 to 18, 2019	Basic training
10	Routine Viral Load Monitoring	GRHB in collaboration with ICAP	May 19 to 20, 2019	Basic training
11	VAST	HFSCH	January 1 to 4, 2024	Basic training

References

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