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Incidence and Determinants of Ventilator Associated Pneumonia Among Intubated Patients in Bahir Dar Specialized Hospitals Bahir Dar, Ethiopia 2022: A Retrospective Follow up Study

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INCIDENCE AND DETERMINANTS OF VENTILATOR ASSOCIATED PNEUMONIA AMONG INTUBATED PATIENTS IN BAHIR DAR SPECIALIZED HOSPITALS BAHIR DAR, ETHIOPIA 2022: A RETROSPECTIVE FOLLOW UP STUDY

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INCIDENCE AND DETERMINANTS OF VENTILATOR ASSOCIATED PNEUMONIA AMONG INTUBATED PATIENTS IN BAHIR DAR SPECIALIZED HOSPITALS BAHIR DAR, ETHIOPIA 2022.

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Title of thesis	Incidence and determinants of ventilator-associated pneumonia among intubated patients at Felege Hiwot Comprehensive and Tibebe Ghion specialized hospitals, Bahir dar, Ethiopia, 2021
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Approval of Thesis for Defense

I hereby certify that I have supervised, read, and evaluated this thesis titled INCIDENCE AND DETERMINANTS OF VENTILATOR-ASSOCIATED PNEUMONIA AMONG INTUBATED PATIENTS IN BAHIR DAR SPECIALIZED HOSPITALS BAHIR DAR, ETHIOPIA 2022,

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ABSTRACT

Background: Ventilator-associated pneumonia refers to pneumonia that happens at least 48 hours after endotracheal intubation or tracheostomy with no evidence of pneumonia at the time of intubation. It is associated with high economic costs, longer attributable lengths of stay in the hospital, and high mortality, especially when lung infection is caused by high-risk pathogens.

Objective: To determine the incidence and identify determinants of ventilator-associated pneumonia among adult intensive care unit admitted patients at Tibebe Ghion and Felege Hiwot specialized hospitals,Bahirdar Ethiopia,2021.

Methods:A retrospective follow-up study was conducted among 312 randomly selected adult intensive care unit admitted patients since April 2019 to September 2021. A data extraction checklist was used to collect data. The collected data were coded, entered, and cleaned in EpiData version 3.1 and exported to STATA version 14 for analysis.Descriptive analysis was done by using frequency tables, percentages, median and inter-quartile range. Bivariable and multiple variable log binomial analyses were made to identify predictors of ventilator-associated pneumonia.

Results: The study found that 27.9 %(95% CI: 23% -33%) of patients developed ventilator associated pneumonia during their intensive care unit stay. The incidence rate of ventilator associated pneumonia were 45.7 per 1000 ventilator days. length of patients on mechanical ventilator (ARR: 1.24, 95 % CI: 1.17 - 1.31), Blood transfusion (ARR: 2.78, 95 % CI: 1.13 - 6.86), Low GCS (ARR: 2.5, 95% CI: 1.27 - 5.1), corticosteroid/s use (ARR: 2.14, 95% CI: 1.1 – 4.1), and Supine head position (ARR: 8.1, 95% CI: 1.66 - 39.6) were identified as independent risk factors for the development of Ventilator associated pneumonia.

Conclusion and Recommendation: The incidence of Ventilator-associated pneumonia in this study was found to be 27.9 %. The risk factors identified with the development of VAP were ventilation duration,blood transfusion,corticosteroid use, supine head position and low Glasgow coma scale. Further a prospective multicenter study by incorporating additional predictor variables and validation of disease incidence and its risk factors identified in this study is necessary**.**

Keywords: Ventilator-Associated Pneumonia, determinants, Intensive Care Unit

ACRONYMS

AICU…… Adult Intensive Care Unit

ARDS…… Acute Respiratory Distress Syndrome

FHCSH …….. Felege Hiwot Comprehensive Specialized Hospital

ICU ……. Intensive Care Unit

MV …… Mechanical Ventilator

TGSH ……. Tibebe Ghion Specialized Hospital

VAP …… Ventilator-Associated Pneumonia

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1. INTRODUCTION

1.1. Background

Ventilator-associated pneumonia (VAP) refers to pneumonia that happens at least 48 hours after endotracheal intubation or tracheostomy with no evidence of pneumonia at the time of intubation or at the time of admission or at the time of tracheostomy [1-3]. It is a subset of hospital-acquired pneumonia that results from the microbial invasion of the normally sterile lower respiratory tract, which subsequently can overpower the host's defense and establish the infection of the lung[4].

Based on the onset it is classified as early-onset and late-onset. Early-onset VAP occurred in ventilated patients within the first four days (<4 days) of mechanical ventilation which is usually caused by antibiotic-sensitive bacteria. Late-onset VAP refers to VAP that developed in mechanically ventilated patients from the fifth day (≥5days) of mechanical ventilation and it is caused by multidrug-resistant (MDR) pathogens [5].

According to 2016 clinical practice guidelines by the Infectious Diseases Society of America and American Thoracic Society Ventilator-associated pneumonia is diagnosed when there is a new or changing lung infiltrates on chest x-ray and at least two of the following clinical feature: fever (≥ 38^0c), increased white blood cell count (≥ $12*10^9$ WBC/ml), and purulent tracheobronchial secretions[1].

The Presence of VAP was associated with increased risk of hospital morbidity and it remains the most frequent infection among patients hospitalized in the Intensive Care Unit (ICU). It is associated with high economic costs, longer attributable lengths of stay in the hospital, and high mortality, especially when lung infection is caused by high-risk pathogens, such as Methicillin-Resistant Staphylococcus aureus (MRSA), Extended Spectrum ß-lactamase (ESBL)-producing Gram-negative bacteria, and Multiple Drug Resistance (MDR) P. aeruginosa and A. baumannii. The presence of specific host, environmental or pharmacological factors may enhance the propensity of patients to develop VAP [6-8].

Patients at risk of VAP must be managed with a VAP bundle of preventive measures. Compliance with the implementation of ventilator-associated pneumonia prevention bundle significantly reduces the burden and incidence of ventilator-associated pneumonia. The components of ventilator-associated pneumonia prevention bundle were head of bed elevation greater than 30°, daily sedation break and assessment for extubation, peptic ulcer prophylaxis, and deep vein thrombosis prophylaxis[4, 9].

1.2. Statement of the problem

Globally the prevalence of ventilator-associated pneumonia is 15.6% (10), and the cumulative incidence of ventilator-associated pneumonia among different countries ranges from 17.5 % in Canada to 57.5 % in Egypt [11-18].

According to various studies in Asian countries the cumulative incidence of ventilator-associated pneumonia ranges from 18 % in India[19], to 28 % in Turkey[13]. The crude mortality rate of ventilator-associated pneumonia ranged from 16% to 94% compared to 0.2% to 51% in non-VAP patients and 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 ventilator-associated pneumonia. Patients with ventilator-associated pneumonia develop many complications like severe sepsis/septic shock, acute respiratory distress syndrome (ARDS), atelectasis, and infection with MDR organisms which in turn increases cost and morbidity and mortality[12, 20, 21].

In studies assessing economic impact of ventilator associated pneumonia in America found that Patients with VAP had higher mean costs for hospitalization, nursing service, antibiotics, anesthesia, ventilator support, respiratory therapy, and chest x-rays which increases the cost by 40% or higher [22], and the total cost for VAP patients was about 3 fold higher than for non-VAP patients in which this cost was probably associated with prolonged hospitalization of VAP patients[23].

Various studies in developing countries have shown that the implementation of simple, and cost-effective measures like hand washing, proper handling of respiratory tract secretions, oral hygiene with chlorhexidine, and the use of gloves by health workers can result in a significant reduction in the incidence of VAP[20]. Despite major advances in techniques for the management

of ventilator-assisted patients, and the routine use of effective procedures to disinfect respiratory equipment, VAP continues to complicate the course of the patients receiving Mechanical ventilators[13].

Ventilator-associated pneumonia is a major nosocomial infection among intubated ICU patients, which requires purposeful study to reduce its morbidity and mortality. Good knowledge of VAP incidence and its predictors is an important way to decrease its consequences and morbidity[14]. Different studies conducted in Egypt for assessing incidence and risk factors of ventilator associated pneumonia showed the cumulative incidence of ventilator-associated pneumonia varies from 35.4 % to 57.5 %. [11, 12] The prevalence of VAP at the Aga Khan University Hospital, Kenya was 16 %(95% CI: 9.4 %, 24.7 %)[24].

In Ethiopia, there was only one single center cross-sectional study which was conducted at Addis Ababa University to determine the prevalence and associated factors of ventilator-associated pneumonia but the incidence and predictors of ventilator associated pneumonia was still unknown in Ethiopia, particularly in Amhara region. Addis Ababa university study was done with small sample size and did not directly measure the risk ventilator associated pneumonia. Therefore, this study aimed to determine the incidence and predictors of ventilator-associated Pneumonia to implement more effective preventive measures of ventilator associated pneumonia and thereby reduce the morbidity related to ventilator-associated pneumonia.

1.3. Significance of the study

The findings of this study could be used as supplementary data for hospital administration to improve quality of care intensive care unit. The result of this study could provide some information on incidence and determinants of ventilator-associated pneumonia in the Ethiopia, particularly for the Amhara region and it would give benefit for the patient and their families directly or indirectly. The study could be used by health professionals for the prevention and management of ventilator-associated pneumonia. It is also useful not only for the prevention and management of ventilator-associated pneumonia but also used as a source of information for investigators to study the topic further. It would be used by Policymakers in developing guidelines and protocols for the prevention and management of ventilator-associated pneumonia in the Ethiopian context.

2. LITERATURE REVIEW

2.1. Incidence of ventilator-associated pneumonia

Ventilator-associated pneumonia accounts for one-fourth of the infections occurring in critically ill ICU patients and is the reason for half of the antibiotic prescriptions in mechanically ventilated patients[25]. According to an Indian study, the overall incidence of VAP was 27.18% and the incidence density of this study was 19/ 1000 ventilator days[26].

A study conducted at Adama Hospital Medical College for assessing burden and risk factors of health care associated infections showed that incidence rates of ventilator-associated pneumonia was 14.1 cases per 1000 ventilator days[27]. The incidence of VAP was higher either in patients with diseases that prolonged mechanical ventilator (MV) support (e.g., Guillain-Barre syndrome (GBS), tetanus, organophosphorus poisoning, etc.), or in patients with those diseases that predispose to pulmonary infection (such as sepsis, complicated malaria, or immunosuppression). The incidence of ventilator-associated pneumonia increased when there was an increased duration of MV with a mean duration of 23.4 days in patients with ventilator-associated pneumonia than 13.5 days in patients without VAP. The average length of stay in the adult intensive care unit (AICU) for patients who developed VAP was 28 days, whereas the average length of stay for non-VAP patients was appreciably low at 19 days[28]. According to a meta-analysis and systematic review done in mainland China, the pooled cumulative incidence of Ventilator-associated pneumonia was 23.8% [16].

2.2. Determinants of ventilator-associated pneumonia

There are many risk factors for the development of VAP. The factors associated with Patient's characteristics, increased length of mechanical ventilation and prolonged intensive care unit stay, disorders of consciousness, burns, continuous use of intravenous sedatives , prior antibiotic therapy, invasive operations, risks due to intervention, and naso-gastric feeding are the globally recognized factors of ventilator-associated pneumonia[29, 30]

2.2.1. Socio-demographic determinants of ventilator-associated pneumonia

Older patients (≥60 years of age) and male sex were at greater risk for developing VAP [6, 16, 30, 31]. According to a study conducted in Mexico on Incidence and costs of ventilator-associated pneumonia among adults in intensive care unit of a tertiary referral hospital, adult males were the

most risk groups for development of Ventilator-associated pneumonia[32]. The risk of VAP increased by more than 1.15-fold as age increased by 1 year and elderly people were prone to chronic diseases like chronic heart failure, potential respiratory diseases, chronic renal failure, diabetes, hypertension, and more non-metastatic cancers[30]. On the other hand, several studies demonstrated that there was no statistically significant difference between VAP and non-VAP groups regarding the age and sex of patients. [12-14, 19, 33, 34]

2.2.2. Intervention related determinants of ventilator-associated pneumonia

The duration of mechanical ventilation (LOV) or ventilator dependency days, the length of ICU stay, Use of H_2 blockers, the supine head position of patients, reintubated patients, mechanically ventilated patients for more than two weeks, and tracheostomy were independent risk factors for the development of ventilator-associated pneumonia[12-14, 16, 28, 35].

The normal physiology of the respiratory system is to clear the secretions from the larynx and pharynx either by mucociliary action or cough reflex. Mechanically ventilated patients are unconscious and there is no clearance of the secretions in the oropharynx. The duration of patients on mechanical ventilation greater than or equal to 5 days increased the VAP risk 4.81 fold[13]. Prolonged mechanical ventilation can lead to an increased risk of ventilator-associated pneumonia and a variety of complications[30].

Positioning of intubated patients may affect the incidence of ventilator-associated pneumonia. Supine patient positioning is independently associated with the development of ventilator-associated pneumonia, possibly because of an increased risk for gastro-esophageal reflux and aspiration[36]. According to a meta-analysis done in Greece the odds of developing clinically diagnosed VAP were significantly higher among patients positioned supinely compared to patients positioned semi-recumbent 45°. Intubated patients are at higher risk for pulmonary aspiration of gastric pathogens when placed in the fully supine position (0 degrees), as compared with a semi-recumbent position (45°). Thus, intubated patients should be managed in a semi-recumbent position, particularly during enteral feeding [1, 2, 37].

Stress ulcer prophylaxis medications that alter the gastric pH, like H_2 antagonists and antacids, may increase organism counts and increase the risk for ventilator-associated pneumonia

therefore sucralfate should be used instead of H_2 antagonists for stress ulcer prophylaxis in gastro-esophageal bleeding risk patients[36, 38].

Mechanically ventilated patients receiving enteral feedings often have substantial gastric volume, which may increase their risk for gastro-esophageal reflux, aspiration, and ventilator-associated pneumonia. Small-intestinal feeding or the use of motility agents, such as metoclopramide, may therefore protect patients against ventilator-associated pneumonia[36]. Enteral nutrition has been considered a risk factor for the development of VAP, mainly because of the resulting alkalinization of gastric content, gastro-esophageal reflux, and gastro-pulmonary aspiration[2].

Tracheostomy is typically performed in acute respiratory failure, wherein there is a need for prolonged mechanical ventilation, or in those who cannot protect the airway because of facial injuries or an altered level of consciousness[29]. Frequent reintubation is found to be a risk factor for VAP. The main cause for pneumonia associated with frequent reintubation is the aspiration of gastric contents: these patients have their naso-gastric tube in place during reintubation, and their gastric contents are aspirated[29].

2.2.3. Admission diagnosis-related determinants of ventilator-associated pneumonia

The risk of ventilator-associated pneumonia is significantly higher among patients with a primary admitting diagnosis of burn, trauma, central nervous system disease, respiratory disease, and cardiac diseases [15]. On the other hand, there was no statistically significant difference between VAP and non-VAP groups regarding underlying co-morbidities like Diabetes, Chronic Obstructive pulmonary diseases, and Congestive Heart Failure[12]. Because phagocytic functions of alveolar macrophages are impaired in ARDS patients, it was a common risk factor for development of ventilator-associated pneumonia [39].

The level of consciousness has a significant impact on the incidence of VAP. It was found that the incidence of VAP is (50%) in comatose patients. This may be due to the higher chances of aspiration in comatose patients [17]. Patients who had low Glasgow coma scale during admission had higher risk for ventilator associated pneumonia than in patients with higher Glasgow coma scale[40].

3. Conceptual framework

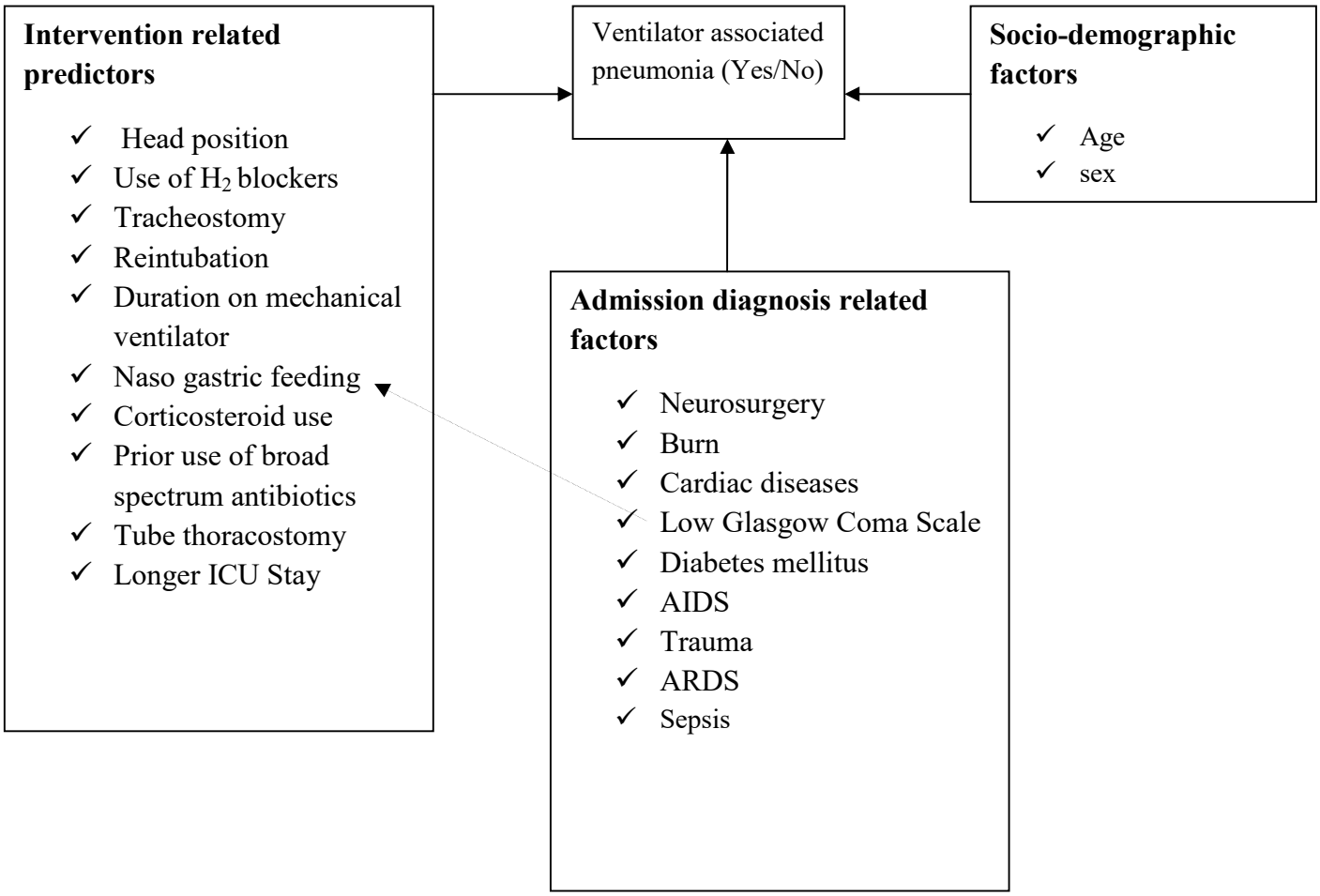

Figure 1: conceptual framework of predictors of ventilator-associated pneumonia at Felege Hiwot comprehensive specialized and Tibebe Ghion specialized hospital, Bahir Dar, Ethiopia, 2021.

4. OBJECTIVES

4.1. General objective

To determine the incidence and identify determinants of ventilator-associated pneumonia among adult intensive care unit admitted patients in Bahir Dar specialized hospitals in 2021.

4.2. Specific objectives

To determine the incidence of ventilator-associated pneumonia among adult intensive care unit admitted patients at Bahir Dar specialized hospitals in 2021.

To identify determinants of ventilator-associated pneumonia among adult intensive care unit admitted patients in Bahir Dar Specialized hospitals in 2021.

5. METHODS AND MATERIALS

5.1. Study design

A retrospective follow-up study was conducted to determine the incidence and determinants of Ventilator-associated pneumonia.

5.2. Study area and period

The study was conducted at Tibebe Ghion Specialized Hospital (TGSH) and Felege Hiwot comprehensive specialized hospital (FHCSH) among patients admitted to adult intensive care units since April 2019 to September 2021. Those hospitals are located in Bahirdar, 575 Kilometer far from Addis Ababa. TGSH starts serving people in 2018, and it provides health care service for more than 5 million people coming from Bahir Dar city, west Gojjam zone, east Gojjam zone, awe zone, north and south Wollo zones, south and north Gondar zones partial part of Benshangul Gumuz and Oromia region. It is one of the teaching hospitals found in Amhara regional state, Bahir dar; which gives a full range of clinical services of specialty and subspecialty care with a total of 450 hospital beds. The hospital has currently a total of 980 permanent staff in different disciplines and other allied staff of college & outsources service areas. The adult intensive care unit is one of the 9wards in Tibebe Ghion specialized hospital, where critical medical and surgical patients are admitted. This facility provides adult and pediatric ICU services with nine beds for adult ICU and 2 beds for pediatric ICU. In the adult intensive care unit there are nine beds, six mechanical ventilators, and nine patient monitors. The hospital serves as a referral Centre for specialized medical and surgical care for various hospitals and clinics within the region. Felege Hiwot comprehensive specialized hospital provides health care service for more than 10 million people coming from different surrounding districts. The hospital has currently a total of 1431 manpower in each discipline and total of 500 hospital beds. Adult Intensive Care unit is one of the 13 wards in FHCSH where critically ill patients were admitted for intubation and critical follow up having twelve beds with 6 mechanical ventilators and 12 monitors.

5.3. Population

5.3.1 Source population

All adult patients who were on a mechanical ventilator for at least 48 hours of duration

5.3.2. Study population

All patients from the age of 15 years and above intubated and on mechanical ventilator for at least 48 hours of duration since April 2019 to September 2021.

5.4. Eligibility criteria

5.4.1. Exclusion criteria

Patients having Pneumonia before Mechanical ventilation or within 48 hours of mechanical ventilation

5.5. Variables

5.5.1. Dependent variable

Ventilator-associated pneumonia (Yes/No)

5.5.2. Independent variables

There were different determinants like 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 mechanical ventilator support, duration on intensive care unit 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 predict the incidence of ventilator-associated pneumonia.

5.6. Operational definitions

- Ventilator-associated pneumonia was diagnosed with:
  - the Presence of a new or progressive chest x-ray infiltrate plus at least two of clinical symptoms:
    - fever > 38^0c with no other recognized causes
    - tachycardia
    - leukocytosis or leucopenia
    - new-onset purulent tracheal secretion
    - increased oxygen requirements in patients on a mechanical ventilator for at least of 48 hours[41].
- Patient use of continuous intravenous sedations: administration of continuous infusions of sedatives 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 including mechanical ventilation

5.7. Sample size Determination and sampling technique

Sample-size of this study was determined by using 24.3 %[42], from a study conducted in Addis Ababa university, and the target sample size was 312 patients, calculated by using a single population proportion formula:

$N = (Z_{\alpha/2})^2 \, p \, (1-p) / d^2$

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

$N = (1.96)^2 \, (0.243 * 0.757) / (0.05)^{2`}$

N = 282.66 ≈ 283

N = 283 + 10% non response rate

N = 312 participants

Sample size this study was also tried to determined by the second objective of study using different predictor variables of ventilator associated-pneumonia as shown on (**Table 1**), but none of them had not give maximum sample size.

Table 1: Sample size determination by using OR/RR of predictor variables for ventilator-associated Pneumonia in TGSH and FHCSH, Bahir Dar, Ethiopia, 2021.

Variables	Confidence level	Power	RR	The ratio of unexposed to exposed	Percent of outcomes in unexposed	Calculated sample size	the p-value in source study
Reintubation(19)	95 %	80 %	RR 3.04	2	16.2	80	<0.0327
NG-tube feeding(19)	95 %	80 %	RR 2.14	2	14.0	225	0.0194
Tracheostomy(18)	95 %	80 %	RR2.59	2	17.9	90	< 0.019

There were a total of 723 patients admitted both at Felege Hiwot comprehensive (372) and Tibebe Ghion specialized hospitals (351), adult intensive care units that were on mechanical ventilator for at least of 48 hours. By writing medical registration number of 723 patients on Microsoft excel program as a sampling frame, the required sample size (312) Study participants were selected randomly by Microsoft excel computer generated simple random sampling technique.

5.8. Data collection methods and techniques

Data were extracted through a semi structured data extraction checklist from the patient's registration book and select medical records of patients who were intubated for at least 48 hours. Then the chart of the selected patients were reviewed in detail. The extraction checklists

contained socio-demographic characteristics, patient admission diagnosis-related conditions, and ICU intervention conditions. The data were extracted by two BSc nurses and supervised by the investigator. The printed checklist, Paper, pencil, rubber, and pen were used to extract data.

5.9. Data management and analysis methods

Data were entered into EpiData version 3.5 and exported to STATA version 14. The descriptive outputs were presented by a median, Inter quartile range, and percent. Bi-variable log-binomial regression analysis was done to have an insight and select candidate predictors for multi-variable log-binomial regression analysis. The variables from bi-variable log-binomial regression with a p-value <0.25 were entered into a multivariable log-binomial regression analysis model to identify independent predictors of ventilator-associated pneumonia. All P values lower than 0.05 were considered statistically significant. The final Regression model fitness was tested by hosmer and lemeshow goodness of fit test and found good fitness with p-value of 0.894.

5.10. Data quality assurance

The data collectors were given training on how to collect data and the collected data was checked for completeness and accuracy on the same day of collection. A pretest was done on five intubated ICU patient cards in Felege Hiwot comprehensive specialized hospital and based on pretest finding there was some rearrangement of data extraction checklists.

5.11. Ethical consideration

This study was approved by the Institutional Review Board of Bahir Dar University, College of Medicine and Health Sciences, and ethical clearance was obtained from the board. Ethical clearance was submitted to Tibebe Ghion specialized hospital chief clinical director and Felege Hiwot Comprehensive specialized Hospital Medical Director. Then the written permissions were obtained from both hospital clinical directors. To ensure confidentiality of the patients' information, the name and address of the patients were not recorded during the data collection. No one other than the investigator was accessing the collected data. Investigator used the collected data only to answer the stated objectives.

6. RESULTS

In this study total of 312 patients were enrolled out of which 183 (58.7%) were male and 129 (41.3%) were female. The median age of patients was 35 years.

6.1. Incidence of ventilator- associated pneumonia

From 312 study participants 87 (27.9 %, 95 % CI: 23% – 33%) patients developed ventilator-associated pneumonia during their intensive care unit stay and the incidence rate of ventilator-associated pneumonia was 45.7 per 1000 ventilator days. The total ventilator days were found to be 1901 days; the median ventilator-days were 5 days with a minimum of 2 days and a maximum of 40 ventilator days. Based on onset of VAP from total patients who develop ventilator associated pneumonia 13 (14.9 %) patients had early onset ventilator-associated pneumonia and the remaining 74 (85.1 %) of patients had late onset VAP.

6.2. Determinants of Ventilator- Associated Pneumonia

6.2.1. Socio-demographic characteristics of patients

Among 312 study participants 183 (58.7 %) were males from these 61(33.3 %) developed Ventilated Associated Pneumonia. While 26 (20.2 %) of females had ventilator associated pneumonia. The participants had a minimum 16 and a maximum 90 years of age with median age of 35 years and inter-quartile range of 25 – 54 years.

6.2.2. Intervention related factors

The median lengths of patients on the mechanical ventilators were 6 days with an inter-quartile range of 3 – 10 days. The median lengths of stay of patients in the intensive care unit were 7 days and inter-quartile range of 4 - 14 days. Around three fourth (76 %) of the participants had naso-gastric tube feeding while only 49(16.2 %) of patients had reintubation (**Table 2).**

Table 2: Intervention-related factors of VAP among patients admitted to adult intensive care unit of Felege Hiwot and Tibebe Ghion hospitals, Bahirdar, 2021.

Intervention related factors		Ventilator-associated pneumonia		
		No (%)	Yes (%)	Total (%)
Reintubation	No	198 (91.2)	55 (64.7)	253 (83.8)
	Yes	19 (8.8)	30 (35.3)	49 (16.2)
Tube thoracostomy	No	202 (90.6)	57 (67.1)	259 (84.1)
	Yes	21 (9.4)	28 (32.9)	49 (15.9)
Tracheostomy	No	215 (95.6)	61 (70.9)	276 (88.7)
	Yes	10 (4.4)	25 (29.1)	35 (11.3)
Corticosteroids use	No	152 (70)	24 (28.2)	176 (58.3)
	Yes	65 (30)	61 (71.8)	126 (41.7)
Naso-gastric feeding	No	72 (32.6)	2 (2.3)	74 (24)
	Yes	149 (67.4)	85 (97.7)	234(76)
Supine head position	No	205 (92.8)	60 (7..6)	265 (86.6)
	Yes	16 (7.2)	25 (29.4)	41(13.4)
Use of histamine blockers	No	120 (53.6)	12 (14)	132 (42.6)
	Yes	104 (46.4)	74 (86)	178 (57.4)
Broad spectrum antibiotic use	No	171 (79.5)	63 (77.8)	234 (79.1)
	Yes	44 (20.5)	18 (22.2)	62 (20.9)
Blood transfusion	No	184 (82.1)	45 (52.9)	229 (74.1)
	Yes	40 (17.9)	40 (47.1)	80 (25.9)
Use continuous IV sedatives	No	196 (87.1)	70 (82.4)	266 (85.8)
	Yes	29 (12.9)	15 (17.6)	44 (14.2)

IV: Intra –Venous

6.2.3. Admission diagnosis-related factors

From the total participants119 (38.5%) had low Glasgow coma scale, from these 47(39.5 %) developed VAP, and only 4 (1.3 %) of the participants had burn as shown below (**Table 3**).

Table 3 Admission diagnosis-related factors of ventilator-associated pneumonia among patients admitted to adult intensive care unit of Felege Hiwot and Tibebe Ghion hospitals, Bahirdar, 2021.

Admission diagnosis-related factors		Ventilator-associated pneumonia		
		No (%)	Yes (%)	Total (%)
Neurosurgery	No	171 (76)	51 (58.6)	222 (71.2)
	Yes	54 (24)	36 (41.4)	90 (28.8)
AIDS	No	195 (94.7)	56 (88.9)	251 (93.3)
	Yes	11(5.3)	7 (11.1)	18 (6.7)
Low Glasgow coma scale	No	150 (67.6)	40 (46)	190 (61.5)
	Yes	72 (32.4)	47 (54)	119 (38.5)
Trauma	No	170 (75.6)	49 (56.3)	219 (70.2)
	Yes	55 (24.4)	38 (43.7)	93 (29.8)
Burn	No	222 (98.7)	86 (98.9)	308 (98.7)
	Yes	3 (1.3)	1 (1.1)	4 (1.3)
Cardiac disease	No	209 (92.9)	82 (94.3)	291 (93.3)
	Yes	16 (7.1)	5 (5.7)	21 (6.7)
Diabetes mellitus	No	214 (95.1)	80 (92)	294 (94.2)
	Yes	11 (4.9)	7 (8)	18 (5.8)
ARDS	No	199 (88.8)	76 (88.4)	275 (88.7)
	Yes	25 (11.2)	10 (11.4)	35 (11.3)
Sepsis out of chest focus	No	180 (80.7)	74 (88.1)	254 (82.7)
	Yes	43 (19.3)	10 (11.9)	53 (17.3)

AIDS: Acquired Immuno Deficiency Syndrome, ARDS: Acute Respiratory Distress Syndrome

6.3. Bi-variable and multi-variable log binomial regression analysis

The bi-variable log-binomial regression analysis identified 11 candidate predictors for the multivariable log-binomial regression model. To be liberal p-value 0.25 as a cut off value was used to enter in to multivariable log binomial regression. In the multivariable analysis variables with p-value of <0.05 were considered as significantly associated with Ventilator Associated pneumonia .Finally five variables including Duration of patients on MV in days, Steroid use, Supine position, Blood transfusion, and Low GCS of patients were identified as predictors of Ventilator Associated Pneumonia(**Table 4)**.

One days increase in mechanical ventilator support is 1.24 (ARR: 1.24, 95 % CI: 1.17 - 1.31) fold increased risk of developing ventilator associated pneumonia. The patients who used corticosteroid drugs had 2.14 (ARR: 2.14, 95% CI: 1.1 – 4.1) times higher risk of developing ventilator associated pneumonia than who were not used corticosteroids.

The risk of developing ventilator associated pneumonia was 8.1(ARR: 8.1, 95 % CI: 1.66 - 39.6) times higher among patients on supine position than semi recumbent position. Patients who were transfused blood were 2.78 (ARR: 2.78, 95 % CI: 1.13 - 6.86) times higher risk for VAP than who were not transfused. Patients with low Glasgow coma scale were 2.5(ARR: 2.5, 95% CI: 1.27 - 5.1) times at risk for ventilator associated pneumonia than patients who had higher GCS.

Table 4: Bi-variable and multivariable analysis of predictors of ventilator Associated pneumonia of patients admitted at FHCSH and TGSH adult intensive care units, Bahir Dar,2021.

Variables	Category	VAP		Bi-variable log binomial analysis			Multi-variable log binomial analysis		
		yes	No	CRR	95 % CI	P-value	ARR	95 % CI	P-value
Duration of patients on MV in days	(IQR)	15	4	1.145	1.17-1.17	0.000	1.24	1.17 - 1.31	<0.001*
Sex	Male Female	61 26	122 103	1.65	1.11 - 2.47	0.014	0.99	0.46 - 2.16	0.753
Tube thoracostomy	Yes No	28 57	21 202	2.5	1.8 - 3.5	0.000	1.16	0.47 - 2.8	0.737
Steroid use	Yes No	61 24	65 152	3.55	2.35 - 5.37	0.000	2.14	1.1 – 4.1	0.023*
Supine position	Yes No	25 60	16 205	2.69	1.93 3.75	0.006	8.1	1.66 - 39.6	0.010*
Blood transfusion	Yes No	40 45	40 184	2.54	1.81 - 3.58	0.000	2.78	1.13 - 6.86	0.027*
AIDS	Yes No	7 56	11 195	1.74	0.93 - 3.25	0.081	0.61	0.3 - 1.26	0.183
Diabetes mellitus	Yes No	7 80	11 214	1.43	0.78 - 2.63	0.250	1.96	0.75 - 5.1	0.169
Low GCS	Yes No	47 40	55 170	1.87	1.32 - 2.67	0.000	2.5	1.27 - 5.1	0.009*
Sepsis	Yes No	10 74	43 180	0.65	0.36 - 1.17	0.150	0.83	0.18 - 3.8	0.811
Tracheostomy	Yes No	25 61	10 215	3.23	2.38 4.39	0.000	0.94	0.37 - 2.3	0.898

ARR: Adjusted relative risk, AIDS: Acquired Immuno Deficiency Syndromes, CI: Confidence Interval, CRR: Crude Relative Risk, GCS: Glasgow Coma Scale, MV: Mechanical Ventilator,: indicates significant association*

7. DISCUSSION

Despite mechanical ventilation being an essential feature of modern intensive care unit service, it is associated with a substantial risk for VAP. It is the most common type of device-associated nosocomial infection among ICU patients. This study found that the cumulative incidence of VAP was 27.9% and the incidence rate of VAP in the study was 45.7 per 1000 ventilator days, which is similar to different studies, a study conducted in Istanbul 28 % [13] and 27.71 % in India[25], but it is different in a study conducted in Egypt with the cumulative incidence of 57.5 % which is much higher than this study finding which may be due to small sample sizes in the Egyptian study [11].In studies conducted in Canada and India, the incidence of VAP was 17.5 %[15] and 18 % [19] respectively, which were lower than our findings. This difference may be due to differences in health facility VAP diagnosis criteria, as in Pondicherry, India used both clinical and microbiological diagnosis criteria whereas; this study only used clinical diagnosing criteria.

Blood transfusion of patients was significantly predisposed for the development of ventilator-associated pneumonia and proved to be an independent risk factor which is different with study conducted in Turkey (95 % CI: 0.4–2.6)[40], this difference may be due to variation of study designs, in Turkey the study design was case-control whereas the study design in this study was a retrospective follow up study design.

In this study low Glasgow Coma Scale was identified as an independent risk factor for the development of ventilator-associated pneumonia which is comparable with studies done in India (95% CI: 1.21 to 4.42), Adiss Ababa University(p-value <0.001) and China (p-value < 0.001)[16, 18, 19, 42], but this finding is different from studies conducted at Mahatma Gandhi Medical College and Research Institute, India (95 % CI: 0.41 to 2.27) [14]. The difference might be due to the sample size was too small in Indian study with a total of 76 study participants as compared with this study.

Patients who had longer stay on Mechanical ventilator support had significantly higher risk of Developing ventilator associated pneumonia, which is in line with different studies conducted in Egypt (95% CI: 4.8–22.9), India (95% CI: 0.25–0.67), Greek (p-value <0.001) and Turkey (p-value <0.001) [12, 43-45], but not in studies conducted at a tertiary care hospital in India[19]. The

reason for difference could be due to the use of both the clinical and microbiological diagnosis criteria in Indian study, where as in our setup only uses clinical diagnostic criteria.

In our setting, supine head position of patients was an independent risk factor for the development of ventilator-associated pneumonia similar with other findings in North Bengal Medical College, India (95% CI: 0.46 – 0.82)[44], while it was not significantly associated with VAP in studies conducted in a tertiary care hospital in India (95% CI: 0.09 to 3.94)[19].

In the current finding, corticosteroids use was significantly associated with the development of ventilator-associated pneumonia similar to findings of a study conducted in Al-Azhar University, Egypt(95% CI: 1.1-9.2)[11] and India(p-value: 0.013) [26] but it was not in studies conducted in India (95% CI: 0.41-2.78)[18, 19], and Turkey(95% CI: 0.75-1.60)[43]. The reason for these differences might be due to differences in method of data analysis; logistic analysis was used in Indian and Turkey studies while log binomial method of analysis was executed in this study.

Tracheostomy was not significantly associated with ventilator associated pneumonia which is the same with, Mahatma Gandhi Medical College and Research Institute, Pondicherry, India[14] however it has significant association in studies conducted at Addis Ababa University [42], a tertiary care hospital in India[19] and in Greek[45].

Sex of patients was not significant factor for VAP, which is similar with studies in Turkey[43] and China[16].

Diabetes mellitus was not independent factor for ventilator associated pneumonia in congruent with reports done in Turkey, India [26, 40, 43] and China [16], on the other hand it was an independent risk factor for VAP in Turkey study, this difference may occur due to small sample size in Turkey.

In this study patients with tube thoracostomy(chest tube) was not identified as risk factor for ventilator associated pneumonia, this finding similar with study reports done in Addis Ababa University (p-value: 0.345)[42], but it is an independent risk factor in a study conducted at Greek[45].

Sepsis out of chest focus is not significant factor for ventilator associated pneumonia which is in line with study reports in France (p-value 0.85) [39], but different from a study finding done in 20 European countries (95 % CI: 9.5-19.9)[46].

8. STRENGTH AND LIMITATION OF THE STUDY

8.1. Strengths

Multiple log-binomial regression analysis of factors was executed to avoid any confounding effect of variables and the study was multi-center to generalize in other settings. Uses of Log binomial regression analysis directly measure the risks.

8.2. Limitations

Since this study was a retrospective study design there were variables that could not be studied retrospectively. The diagnostic criterion used in this study was only clinical and did not use microbiological diagnostic criteria due to unavailability of culture tests in the Hospitals.

9. CONCLUSION

The incidence of Ventilator-associated pneumonia in this study was found to be 27.9 % and it was relatively higher. The independent risk factors identified for the development of VAP were longer duration of patients on a mechanical ventilator, corticosteroid use, Supine position, Blood transfusion, and Low Glasgow Coma Scale. Knowledge of the important risk factors predisposing to VAP may prove to be useful in implementing simple and effective preventive measures including non-invasive ventilation, precaution during emergency intubation, minimizing patients stay on mechanical support and intensive care unit, avoidance of supine position of patients, and minimization use of histamine blockers and corticosteroids.

10. Recommendations

For TGSH and FHCSH, ICU staff physicians and Nurses:

Position patients with low Glasgow coma scale in semi-recumbent position and oral suctioning for patients with oral secretion.

Decrease patient's length of stay on mechanical ventilator support by giving quality care. Position all patients on mechanical ventilator in semi-recumbent position to prevent aspiration of gastric contents.

For researchers:

Carry out further studies on the risks of blood transfusion, corticosteroids use, and impaired consciousness for ventilator-associated pneumonia.

Further a prospective multicenter study by incorporating additional predictor variables and validation of disease incidence and its risk factors identified in this study is necessary.

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12. Annexes

Annex I Data extraction checklists

S.no	Questions		
	Socio-demographic data extraction checklists		
101	Medical record number	……	
102	Age of patient in years	……	
103	Sex of patient	1-male 2-female	
	Intervention related data extraction checklists		
201	Patient intensive care unit admission date	**……**	
202	Patient intubation date	**……**	
203	Did the patient develop ventilator-associated pneumonia	1-yes 2-no	If no skip to 205 or 206
204	Ventilator-associated pneumonia confirmation date	**……**	
205	Patient extubation date	**……**	
206	Duration of mechanical ventilation in days	……(days)	
207	Discharge date of the patient	……	
208	Duration of ICU stay in days	……(days)	
209	Is there reintubation?	1-yes 2-no	If no skip to 209
210	Reason for reintubation	1-deterioration 2-inability to expectorate secretions. 3-other reasons	
211	Tube thoracostomy	1-yes 2-no	
212	Tracheostomy	1-yes 2-no	
213	Corticosteroid/s use	1-yes 2-no	If no skip to 207
214	For how many days does she/he take corticosteroids?	1-for less than 7 days 2-for 7 or more days	
215	Naso-Gastric tube feeding	1-yes 2-no	

216	Was the patient in a supine head position?	1-yes 2-no	
217	Use of H_2 blockers	1-yes 2-no	
218	Prior broad-spectrum antibiotics use	1-Yes 2. no	
219	Blood transfusion	1-yes 2-no	
220	Patient use of continuous intravenous sedatives	1-yes 2-no	
	Admission diagnosis-related data extraction checklists		
301	Patient admission diagnosis	……..	
302	Admission diagnosis of neurosurgery?	1-yes 2-no	
303	Admission diagnosis of AIDS?	1-yes 2-no	
304	Admission diagnosis of trauma?	1-yes 2- no	
305	Low Glasgow Coma scale?	1-yes 2- no	
306	Admission diagnosis of burn	1-yes 2- no	
307	Admission diagnosis of cardiac disease	1-yes 2- no	
308	Does the patient have Diabetes mellitus	1-yes 2-no	
309	Does the patient admitted with the diagnosis of ARDS	1-yes 2-no	
310	Is the patient admitted with the diagnosis of sepsis out of chest focus?	1-yes 2-no	
311	Patient outcome at discharge	1-improved 2-against 3-death 4- refer 5-other	