PREVALENCE AND RISK FACTORS ASSOCIATED WITH THE DEVELOPMENT OF VENTILATOR-ASSOCIATED PNEUMONIA IN PEDIATRIC INTENSIVE CARE UNIT OF TASH, A RETROSPECTIVE CROSS-SECTIONAL STUDY.

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RESEARCH THESIS SUBMITTED TO THE DEPARTMENT OF PEDIATRICS AND CHILD HEALTH, SCHOOL OF MEDICINE, COLLEGE OF HEALTH SCIENCES, ADDIS ABABA UNIVERSITY IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE SPECIA LITY CERTIFICATE OF PEDIATRICS AND CHILD HEALTH

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Approval Sheet

Addis Ababa University College of Health Sciences School of Medicine Department of Pediatrics and Child Health

I, the undersigned Pediatrics and Child Health resident declare that I have submitted my original thesis on the Title: - Prevalence and risk factors associated with the development of ventilator-associated pneumonia in the pediatric intensive care unit of TASH, a retrospective cross-sectional study in partial fulfillment of a specialty program.

Submitted by:

Name of Resident ……..…….. Sign ------- Date….

This research proposal work has been submitted with my approval as an advisor

APPROVED BY:

Advisor Name ……..Signature…….Date…

Acknowledgement

First of all, I would like to thank the almighty GOD and St. Mary, and I would like to say thank you to Addis Ababa University, College of Health Science Department of Pediatrics And Child Health.

My gratitude also extends to my advisors, Dr. Muluwork Tefera for her continuous advice and constructive comments throughout the whole time.

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List of Acronyms and Abbreviations

AAU= Addis Ababa University

CDC =Disease Control and Prevention

TASH= Tikur Anbesa Specialized Hospital

VAP= Ventilator Associated Pneumonia

PICU= pediatric Intensive Care Unit

OR= odds ratio

Sig. = significant

PPI= proton pump inhibitor

HMIS=Health Management Integrated system

CONS= coagulase negative staphaureus

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ABSTRACT

Background: Ventilator-associated pneumonia (VAP), is a severe type of hospital-acquired pneumonia that develops 48 hours after initiation of mechanical ventilation.it is associated with significant morbidity and mortality. According to the recent literature, the incidence of VAP in pediatrics is still very variable, with much higher rates in developing countries compared to developed countries, although there are very few studies from developing countries. The incidence continues to be high despite an improved understanding of the risk factors of VAP. There is no consensus on the preventive strategies akin to adults, in the form of a bundle approach in children.

Objectives: This study aimed to determine the prevalence and risk factors associated with the development of VAP in the PICU of Tikur Anbessa Specialized Hospital (TASH), Addis Ababa, Ethiopia, 2024

Methodology: A retrospective cross-sectional study was conducted by using a consecutive sampling method. All pediatric patients who were ventilated for ≥48 hours within the study period September 2019-september 2023G.C were included. Data was collected from patient charts using a structured information-extracting tool. Both Bivariate and multivariate logistic regression were used to study the association between the risk factors and dependent variables. Continuous and categorical variables were compared using the Chi-square test. Where the P-value of <0.05 was considered significant.

Result: Among the 161 patient, 93(57.7%) were male and the male to female ratio were 1.4:1. The mean±SD age was 5.4±4.5 years. The most common admitting diagnosis was neurologic/neurosurgical condition 44 (27.3%), and cardiovascular diseases 28 (17.4%). The most common indication for ventilation was coma/ impaired consciousness 76(47.2%) followed by respiratory failure 73(45.3%).the prevalence of VAP was 33 (20.5%) with a rate per 1000 ventilator days is 27/1000. On multiple logistic regression analysis, the five identified risk factors were male sex ([AOR]: 34.110, P= 0.043: 95% CI: 1.12-1039.6), Duration of mechanical ventilation in days ([AOR]: 1.501, P= 0.002: 95% CI: [1.155-1.951]), the presence of comorbidities (AOR: 31.445, P=0.025), transportation out of PICU while the patient is intubated ([AOR]: 21.456, P= 0.029: 95% CI: [1.369-336.72]) and compliance to VAP bundle ([AOR]:

31.424, P= 0.026: 95% CI [1.507-655.292]). klebsiella pneumoniae (34%) followed by CONS (27%) and Acinetobacter Species 6(18%) were the most commonly identified organisms from tracheal aspirate

Conclusion: The prevalence of ventilator-associated pneumonia in our hospital (TASH) pediatric intensive care unit is found to be high. The most common causative organisms were Klebsiella pneumoniae and coagulase-negative staph aureus. Knowing the risk factors will help in planning and implementing preventive measures

Keywords: VAP, ventilator-associated pneumonia, PICU, intensive care, pediatrics.

CHAPTER ONE: INTRODUCTION

BACKGROUND OF THE STUDY

Ventilator-associated pneumonia (VAP) refers to a nosocomial pneumonia in patients who are ventilated for more than 48 hours and, second to bloodstream infections, it is the most common hospital-acquired infection (HAI) in children. (1) Studies report that up to 30% of ventilated patients develop a VAP (2).

Ventilator-associated pneumonia (VAP) is one of the major causes of hospital-acquired infections. Despite improvements in aseptic techniques, antibiotic therapy, and supportive care, VAP continues to be a major cause of morbidity and mortality in ICU patients. (1)

The consequences of a VAP may lead to an increase in both mortality and morbidity, which includes longer duration of ventilation and increased duration of pediatric intensive care unit (PICU) as well as overall hospital stay. (2)

In 2015 CDC conducted a point-prevalence survey in a sample of acute care hospitals in U.S. and determined that of the 427 healthcare–associated infections identified, pneumonia was the most common infection with 32% of those being ventilator associated.(8)

To date, there have been some researches about risk factors of VAP in PICU, however, these results indicated that risk factors were varied or contradictory.(4)

To my knowledge in Ethiopia there is no study done on the risk factors associated with the development of VAP.

STATEMENT OF THE PROBLEM

Ventilator-associated pneumonia (VAP) is one of the commonest healthcare-associated Infections in pediatric ICUs. (3) Despite improvements in aseptic techniques, antibiotic therapy, and supportive care, VAP continues to be a major cause of morbidity and mortality of ICU patients. (1)

VAP is diagnosed in >10% of patients on mechanical ventilation, incidence rising with number of ventilator days. In recent decades, the pathophysiology of VAP, VAP risk factors and treatment have been extensively studied. In critically ill pediatric patients, mechanical issues such as insufficient tightness of the ventilator circuit (mainly due to historically based preference of uncuffed tubes) and excessive humidity in the circuit are both significant risk factors of VAP

development. Protocol-based approaches to critically ill patients on mechanical ventilation, closed suctioning, upper body position, enteral feeding and selective gastric acid suppression medication have a beneficial effect on VAP incidence. (9)

The epidemiology, pathogenesis, and outcome of VAP are well described in adults, however, few data exist regarding VAP in pediatric patients. Because of different anatomy, physiology and underlying illnesses from adults, it is important to identify specific prevention for this population in preventing VAP. (4) There are very few studies from developing countries. (1)

So far there is only one study done in Ethiopia, which showed the prevalence of VAP at one of the tertiary hospital, TASH, but in this study, the risk factors associated with the development of VAP were not studied.

The current study will address these variables, and will come up with the possible recommendation and protocols on how to prevent VAP.

SIGNIFICANCE OF THE STUDY

Knowing the outcome and risk factors associated with the development of VAP has significance role in looking at who the problem has devastating effect on the morbidity and mortality of children's admitted to PICU. Above all once the risk factors are identified, it will help in developing strict VAP bundle protocols and guidelines. Different studies have been done in other world on this topic, but in our setup there is no study done at all, although the prevalence in one study at TASH is 18.6%.

This study will fill the gap and put a way forward to develop protocols and guidelines on the prevention and management of Ventilator-associated pneumonia

The results and final recommendations will be used by all members of PICU as the care will be given by the physicians and nursing stuffs.

CHAPTER TWO: LITERATURE REVIEW

The incidence of ventilator associated pneumonia (VAP) in children continues to be high in spite of improved understanding of the risk factors of VAP. There is no consensus on the preventive strategies akin to adults, in form of bundle approach in children. (1)

In a prospective cohort study conducted on patients admitted to the Pediatric Intensive Care Unit (PICU) of a tertiary care institute of North India, from June 2012 through March 2014. (1) All enrolled children were assessed daily for development of ventilator associated pneumonia (VAP) using the case definition given by Centers for Disease Control and Prevention (CDC). Risk factors associated with VAP were calculated by doing bivariate and multivariate analysis.

Results showed among a total of 128 patients were screened and 86 were enrolled. The most common admitting diagnosis was sepsis (16%). (1)

The incidence of VAP according to CDC criteria was 38.4%, while the incidence of microbiologically confirmed VAP was 24.4%. The incidence of ventilator associated tracheobronchitis (VAT) was found to be 11.6 %. (1)

Risk factors for VAP on bivariate analysis were use of proton pump inhibitor (PPI) ($p = 0.027$, OR 5.2, 95% CI 1.1–24.3), enteral feeding ($p < 0.001$, OR 6.5, 95% CI 2.1–19.4) and re-intubation ($p = 0.024$, OR 3.3 and 95%CI 1.1–9.6). On multivariate analysis, use of PPI ($p = 0.03$, OR 8.47, 95% CI 1.19–60.33) and enteral feeding ($p < 0.001$, OR 12.2,95% CI 2.58–57.78) were identified as independent risk factors for VAP.(1)

Acinetobacter was the most frequently isolated organism (47%) followed by Pseudomonas (28%), Klebsiella (15%), E. coli (5%) and Enterobacter (5%). (1)

The conclusion of the study is despite the limited number of study subjects, thereby limiting power of the analysis, the present study conducted upon a robust methodology, reveals a high incidence of VAP in children and simultaneously discloses the commonest etiological organisms and risk factors for VAP. This can possibly lead the way for implementation of improved ways of prevention and treatment of VAP in children in similar settings. (1)

The above research, it has clearly studied the incidence and Risk factors together with causative organisms. In my research, the Risk factors as well as the possible organisms will be studied in a similar fashion. Although my paper will be a retrospective cross-sectional study, there could be a

diagnostic challenge as some charts may not have fully documented diagnostic criteria that fulfill the operational definition to study the prevalence of VAP.

In 2022, a study was done at Red Cross War Memorial Hospital, Cape Town, South Africa by L van Wyk et al. The aim of this study was to evaluate the VAP rate in the pediatric intensive care unit (PICU) over 2 years (2017-2018) and to describe the causative organisms and antibiotic sensitivity/resistance patterns during this period. (2) It was a retrospective, descriptive study using the existing PICU VAP database as well as clinical folders.

Over the 2 years, 31 VAP cases were identified. The VAP rate for 2017 was 4.0/1 000 ventilator days and 5.4/1 000 ventilator days for 2018. Compliance with the VAP bundle was 68% in 2017 and 70% in 2018(2). The most common cultured organism was an extended-spectrum beta-lactamase (ESBL) Klebsiella pneumonia followed by Pseudomonas aeruginosa sensitive to amikacin and carbapenems. (2)

The final conclusion and recommendation of the study is that it is also imperative to improve compliance with the VAP bundle, in order to improve VAP rates. K. pneumoniae and P. aeruginosa were the commonest organisms causing VAPs and empirical use of piptazobactam and amikacin in combination is still appropriate. [(2)]

The study has well analyzed the rate of VAP and the causative organisms in that particular setup, which may have similarities with the TASH PICU setup.

My study will fill the gap in determining the risk factors in addition to the adherence to the VAP bundle, there will be more risk factors will be subjected to analysis.

In 2015, A Multicenter prospective observational cohort study was done in Children's hospitals in the United States. The aim of the study was to assess risk factors and outcomes associated with pediatric ventilator-associated pneumonia.

Prospective evaluation of the prevalence, risk factors, and outcomes of pediatric ventilator-associated pneumonia along with evaluation of diagnostic criterion for pediatric ventilator-associated pneumonia. (3)

The prevalence of pediatric ventilator-associated pneumonia was 5.2% (n = 2,082), for a rate of 7.1/1,000 ventilator days. Patients with ventilator-associated pneumonia had a longer unadjusted ICU length of stay ($p < 0.0001$) and increased length of mechanical ventilation by more than 11 days ($p < 0.0001$). After adjustment for patient factors, ICU length of stay ($p = 0.03$) and

mechanical ventilation days (p = 0.001) remained significant. Patients with ventilator-associated pneumonia were almost three times more likely to die (p = 0.007). Independent risk factors for ventilator-associated pneumonia were reintubation and part-time ventilation. (3)

The final conclusion is these patients have longer length of stay, longer duration of mechanical ventilation, and increased risk for mortality. (3)

From the above study it's clearly seen that the disease burden of VAP is as such significant it affects the developed world.

A Systematic Review done at china in 2013 to identify risk factors of ventilator-associated pneumonia (VAP) in pediatric intensive care unit (PICU). Out of the 205 initially retrieved articles, 9 papers were included. All 4,564 patients were enrolled, including 213 patients with VAP and 4,351 patients without VAP. Among fourteen risk factors, six factors had statistical significances. (4)

Risk factors of VAP and its value of OR were as follows: genetic syndrome (OR =2.04; 95% CI: 1.08-3.86), steroids (OR =1.87; 95% CI: 1.07-3.27), reintubation or self-extubation (OR =3.16; 95% CI: 2.10-4.74), bloodstream infection (OR =4.42; 95% CI: 2.12-9.22), prior antibiotic therapy (OR =2.89; 95% CI: 1.41-5.94), bronchoscopy (OR =4.48; 95% CI: 2.31-8.71).(4)

The final recommendation is Special methods of preventions should be taken in the light of risk factors of VAP in PICU so as to decrease the rate. (4)

The above systematic review has well studied the possible risk factors which are associated with VAP. In similar fashion my study will also include this variables.

A Retrospective, observational, single-center study was done at PICU of a tertiary-care university hospital, France in 2018. The aim of the study was to determine the prevalence of ventilator-associated pneumonia, to describe the risk factors and management of ventilator-associated pneumonia. (5) In the study Consecutive critically ill children mechanically ventilated for greater than or equal to 48 hours between November 2013 and November 2015. (5)

Of 304 patients mechanically ventilated for greater than or equal to 48 hours, 284 were included. Among them, 30 (10.6%) met clinical and radiologic Centers for Disease Control and Prevention criteria for ventilator-associated pneumonia, yielding a prevalence of 7/1,000 mechanical ventilation days. Median time from mechanical ventilation onset to ventilator-associated pneumonia diagnosis was 4 days. (5)

By univariate analysis, risk factors for ventilator-associated pneumonia were younger age, reintubation, acute respiratory distress syndrome, and continuous enteral feeding. (5) Gram-negative bacteria were found in 60% of patients, with a predominance of Haemophilus influenzae and Pseudomonas aeruginosa. (5) Finally the study concluded that Ventilator-associated pneumonia is associated with longer times on mechanical ventilation and in the PICU. (5)

In a prospective observational study done at Spain in 2022, aimed to determine the risk factors for VAP in children and to create a risk score for developing VAP.(6)

Data was collected from database from 2014 to 2019. A total of 3798 patients were included, 97(2.5%) developing VAP. The independent risk factors for VAP were: female (odds ratio [OR]: 1.642, $p = 0.024$), MV > 4 days (OR: 26.79, $p < 0.001$), length in pediatric intensive care unit > 7 days (OR: 11.74, $p < 0.001$), and previous colonisation (OR: 4.18, $p < 0.001$). (6)

In the above study, the risk factors and rate of VAP is partially studied. But the causative micro-organisms were not included in the research. My study will fill the gap and address all the possible risk factors which are included in the previous studies

A cross-sectional study was done from September 2016 to February 2018. The aim was to assess the characteristics and outcomes of mechanically ventilated pediatric Patients in Tikur Anbessa Specialized Referral Hospital, Addis Ababa, Ethiopia. (7)
There were 536 patients admitted to PICU; out of these, 202 (41.2%) were on MV. Sixty three-point six percent of the participants were males and 130 (59.1%) died. The most common indications for the initiation of MV were respiratory problems 46 (20.9%) and 30.59/1000 ventilator days developed complications. Ventilator-associated pneumonia accounted for 18.6% of the complications with 20.9/1000 ventilator days. (7)
Although, the primary target of the study done by tigist B. et al. was not to determine factors associated with VAP and outcomes associated with the diagnosis, it has showed the prevalence of VAP in our setup Looking at how significant is the disease burden, it is very important to identify the risk factors, causative organisms and outcomes.

CHAPTER THREE: OBJECTIVES OF THE STUDY

GENERAL OBJECTIVE

- To know the Prevalence and risk factors associated with the development of ventilator associated pneumonia in pediatric intensive care unit of Tikur Anbessa Specialized Hospital.

SPECIFIC OBJECTIVES

- To know the prevalence of VAP in the pediatric ICU
- To determine factors associated with the development of ventilator-associated pneumonia.
- To identify the causative organisms of ventilator associated pneumonia

CHAPTER FOUR: RESEARCH METHODS & MATERIALS

Study Area and Setting

This research was carried out at Tikur Anbessa Specialized Hospital (TASH) in Addis Ababa, the capital city of Ethiopia. TASH is Ethiopia's largest referral hospital in the country. It has 6 PICU beds, and 13 adult ICU beds, 28 fully functional NICU beds and 13 adult ICU beds as multipurpose for both medical and surgical cases.

Study Design and Study Period

A hospital-based, retrospective cross-sectional study was conducted from 1st September, 2019–30th September, 2023

Source population

All patients who were admitted to PICU

Study population

All pediatric patients who were mechanically ventilated and met the inclusion criteria.

Inclusion Criteria

All pediatric patients who were mechanically ventilated for ≥ 48hrs

Exclusion Criteria

Those who were intubated but received mechanical ventilation for < 48 hrs.

Those who were < 28 days of age and > 14 years.

Prior diagnosis of HAP up on admission to PICU

Sample size determination

The sample size was calculated using the single population proportion formula, and a 5% margin of error at a 95% confidence interval. The prevalence of VAP from previous study done at TASH by Tigist Bach et al. was 18.6%, which is taken as a P- value

$$\frac{(Z\alpha 1/2)^2 * p * q}{w^2}$$

$$\frac{(1.96)^2 * 0.186 * 0.886}{(0.05)^2} = 233$$

With the admission pattern during the study period which is roughly estimated from the HMIS

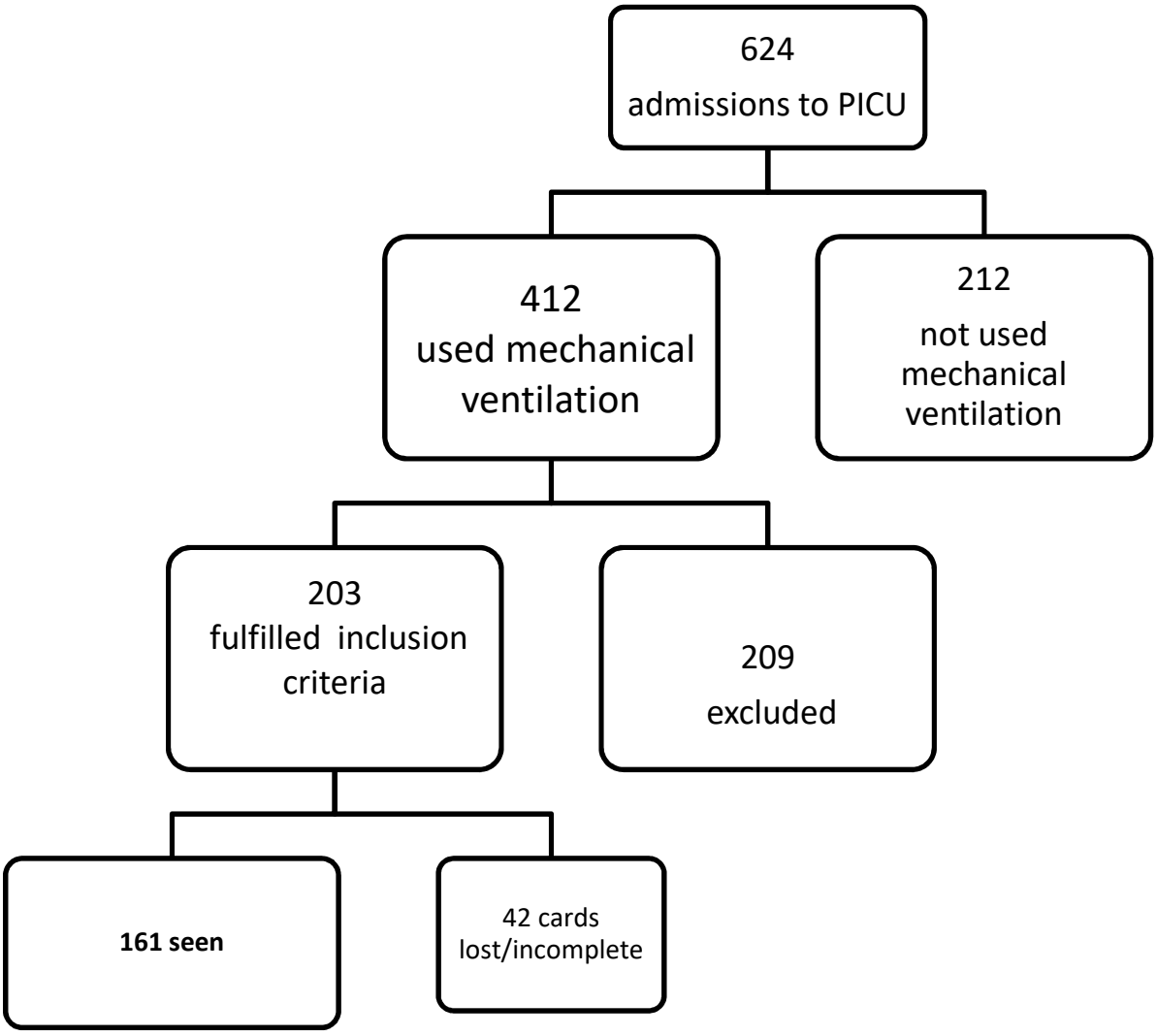
It is required to reduce the sample size using Taro Yemane method

n=N/(N(e)2)=233/(1+233*0.0025)=147.

With 10% missing rate added the final sample size became **161**

Sampling technique

A consecutive non-random sampling technique was used until the required sample size population data is collected



Data collection tool

A structured English version of information extraction format developed from a review of previously done literatures on the identification of risk factors associated with ventilator-associated pneumonia was utilized (1,3,6) . The format contains a closed-ended type of questions i.e. Age, sex, clinical characteristics of the patient like, admission diagnosis, admitting ward, duration of mechanical ventilation before the dx of VAP, the primary indication for mechanical ventilation,

length of mechanical ventilation, onset of VAP and presence of co-morbidity. 2) Possible risk factors.

Data collection procedure and Data Analysis

After proper counting and filtering from pediatric intensive care unit HMIS based on inclusion criteria, Data were collected from the patient record card, laboratory results and daily flow chart. The data was collected by a trained 2 nurses and pediatrics resident. Data entry and analysis was done via SPSS 26.0.

Data quality control

The Data quality was controlled by designing proper data collection materials. Training was also given to data collectors. Then the collected data were checked for completeness on a daily basis by the supervisor and records with incomplete basic information were re-recorded with the missing information by reviewing the patient chart again and records that can't be traced back were discarded. The data were then cleaned, coded, and entered by trained data clerks and principal investigator before analysis.

Study variables

Independent variables:

- Age, sex, admission diagnosis , use of proton pump inhibitor (PPI) , enteral feeding , re-intubation/ self-extubation, Bronchoscopy, duration of MV ,Use of steroids ,Presence of underlying comorbid conditions , compliance with the VAP bundle , culture result of tracheal aspirate

Dependent variables:

- Ventilator associated pneumonia

Operational definitions

Ventilator-associated pneumonia is diagnosed in patients on MV for ≥ 48 hours with a new persistent infiltrate on chest radiograph or new onset crepitation on auscultation and positive tracheal aspirate plus at least 3 of the following(ref. Tgist Bcha et al.)

- Fever (> 38. 0°C or > 100. 4°F) or hypothermia (< 36. 0°C or < 96.8°F)
- Leukopenia (≤ 4000 WBC/mm3) or leukocytosis (≥ 15,000 WBC/mm3)
- New onset of purulent sputum or change in character of sputum, or increased respiratory secretions, or increased suctioning requirements
- New onset or worsening cough, or dyspnea, or apnea, or tachypnea.

Dissemination of the Results

The results of this study will be submitted to Addis Ababa, University College of Health Sciences Department of Pediatrics and Child Health. The copies of this study will also be given Tikur Anbessa specialized hospital critical care unit so that they can use the results for planning and implementation of intervention programs, attempts will be made to publish my work on scientific journals.

Ethical consideration

Ethical clearance was obtained from Addis Ababa University, College of health Sciences, departments of Pediatrics and child Health research and publication Committee. Additionally, the confidentiality of all the data was seriously respected by not mentioning patients' identifiers in the questioner and unauthorized individuals was not allowed to access the data which was collected by using a password-protected computer.

CHAPTER FIVE: RESULT

Socio-demographic and clinical characteristics

During the study period there were 624 admissios to pICU , amog those 412 used mechanical vetilatio , ad of those 203 fulfilled the iclusio criteria , then 161 charts were reviewd with overall response rate of 80%

Among the 161 study patients, 87(54%) where admitted from emergency OPD, 42(26.1%) from operative room and 32(19.9%) where admitted from pediatric ward. Of the 161 study patients, 93 (57.8%) were men and male to female ratio was 1.4: 1 . The mean ± SD age was 5.4 ± 4.50 years (range 2 month-14 years). The most common causes of ICU admission were neurological/neurosurgical diseases 44 (27.3%), and cardiovascular diseases 28 (17.4%). The primary indication for intubation is classified as coma/ impaired consciousness 76(47.2%), respiratory failure 73(45.3%) and neuro-muscular disease 12(7.5%). (Table 1)

The duration of mechanical ventilation were longer among patients who suffered VAP compared to those of Non-VAP 16.8±6.9 and 5.18±4.9 respectively.Most of the patients developed VAP after 7 days of mechanical ventilation

Table 1 socio-demographic and clinical characteristics with their binary logistic regression analysis of patients in PICU at TASH, Addis Ababa, Ethiopia, September 2019 – September 2023 (n=161)

Variables	category	VAP (n=33)	Non VAP(n=128)	P- VALUE
sex	Male female	25 (88.2%) 8(11.8)	68(73.1%) 60(26.9%)	**0.022** Ref.
Age	28 days - 1 yr 1-5 yr > 5 yr-14yrs	6(18.2%) 11(33.3%) 16 (48.5%)	41(32%) 44(34.4%) 43(33.6%)	Ref. 0.576 0.373
duration of mechanical ventilation	mean ± SD days	16.8±6.9	5.18±4.9	**≤0.001**
Admitted to ICU from	Pediatric ward Emergency opd Operative room	7(21.20%) 24(72.70%) 2 (6.10%)	25 (19.5%) 63 (49.20%) 40 (31.30%)	**0.041** **0.008** Ref.
Presence of Comorbidity	Yes No	31 (95.8%) 2(4.2%)	82(72.8%) 46(27.2%)	**0.004** Ref.

Onset of VAP after intubation	No VAP <7days ≥7days	-	128(100%) 13 (39%) 20 (61%)	Ref. 0.998 0.88
Primary indication for mechanical ventilation	Respiratory failure Coma Neuro-muscular disease		12 (16.4%) 16 (21.1%) 5 (41.7%)	61 (83.6%) 60 (78.9%) 7 (58.3%)	0.053 0.129 Ref.
Causes of ICU admission /diagnosis on admission	Trauma respiratory disease Neurologic/NS disease Cardiovascular disease Intraabdominal disease Poisoning Metabolic or renal post-operative follow up sepsis /septic shock		1(3%) 4(12.1%) 10(30.0%) 7(21.2%) 2(6.1%) 0(0.0%) 5(15.2%) 0(0.0%) 4(12.1%)	1(0.8%) 15(11.7%) 34(26.6%) 21(16.4%) 2(1.8%) 3(2.8%) 17(13.3%) 15(11.7%) 20(15.6%)	Ref. 0.945 0.289 0.714 0.556 0.466 0.158 0.999 0.606 0.998

Prevalence of VAP

Among the 161 study patients admitted to pediatric ICU from September 2019 – September 2023G.C. 33 of them developed ventilator associated pneumonia, which is 20.5%.The rate of VAP per 1000 ventilator days is 27/1000.

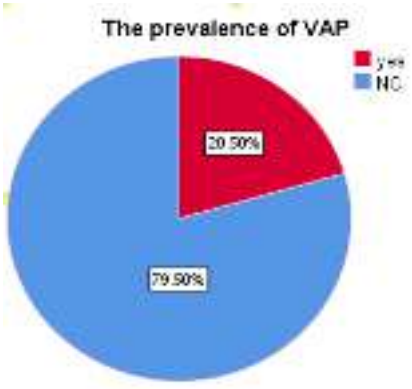


Figure 1: The prevalence of VAP in pediatrics ICU of TASH, from September 2019 – September 2023G.C

Causative micro-organisms

Among the 33(20.5%) of patients who are diagnosed to have VAP, culture of tracheal aspiration was used to identify causative micro-organisms. The most common causative organisms identified where klebsiella pneumoniae (34%) followed by CONS (27%).

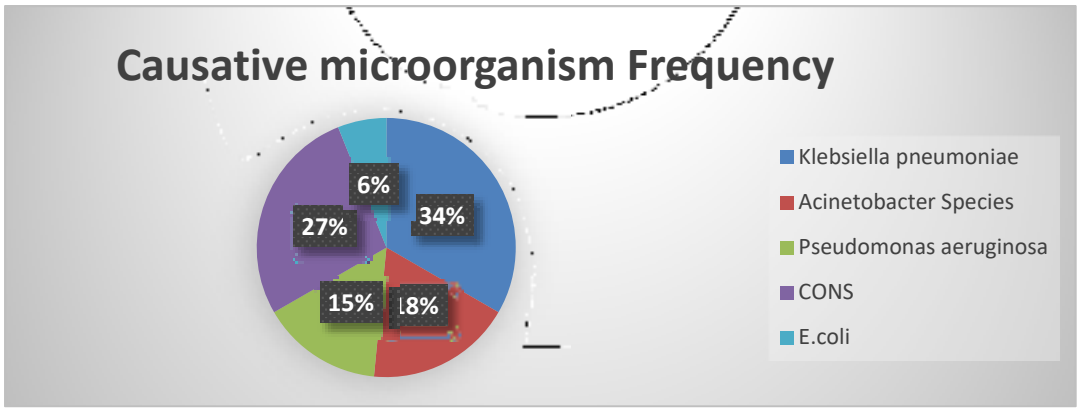


Figure 2 causative organisms identified from tracheal aspirate of patients who developed VAP at TASH pediatric ICU from September 2019 – September 2023G.C.

Onset of VAP

The onset of VAP is one of the factor that determines the outcome. Among 33 patients with VAP most of them developed VAP after/in the 7th day of mechanical ventilation 20(60%). The remains have early onset VAP

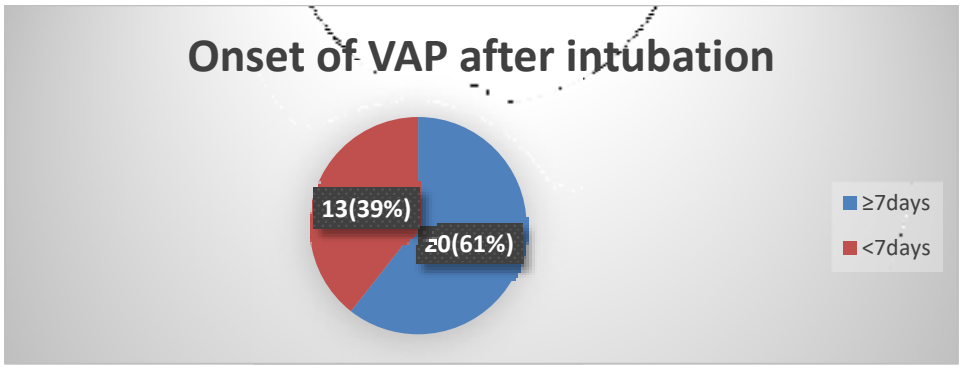


Figure 3 the onset of VAP after intubation in pediatrics ICU of TASH, from September 2019 – September 2023G.C

Possible Risk Factors

As shown below on the table 2, the risk factors for the development of VAP are analyzed as a bivariate logistics regression with the crude odds ratio and p-value calculated.

Among the 33 patients who are diagnosed to have VAP 6(18.1%) had tracheostomy, 9(27.2%) had undergone bronchoscopy, 20(60%) of the patients has at least one time intubation, 14(42.4%) has aspirated gastric content, 33(100%) of them was feed with NG tube, 12(36.3%) had history of transportation out of PICU while intubated, 19(57.5%) of the patients were given steroid at least once while intubated, 24(72.7%) of patients were given PPI either for GI prophylaxis or ulcer treatment, 33(100%) of the patients where on continues IV sedation or paralytic agents, 11(33.3%) of them has undergone surgical procedure either thoracic or thoraco-abdominal, 29(87.8%) of the patients didn't receive care using the VAP bundle protocol.

Table 2 Binary logistic regression analysis of potential risk factor variables among patients in PICU of TASH, Addis Ababa, Ethiopia, September 2019 – September 2023 (n=161)

Potential risk factors	Category	VAP(n=33)	NO-VAP(n=128	COR(odds ratio)	P-Value
Tracheostomy	YES NO	6(18.2%) 27(81.8%)	6(4.7%) 122(95.3%)	4.519 Ref.	**0.014**
Bronchoscopy	YES NO	9(27.3%) 24(72.7%)	23(18%) 105(82%)	1.712 Ref.	0.236
Re-Intubation	YES NO	20(60.6%) 13(39.4%)	15(11.7%) 113(88.3%)	11.590 Ref.	**<0.001**

Aspiration of Gastric Content	YES NO	14(42.4%) 19(57.6%)	46(35.9%) 82(64.1%)	1.314 Ref.	0.493
NGT and enteral feeding	YES NO	33(100%) 0(0.0%)	108(84.4%) 20(15.6%)	49.365 Ref.	0.998
Transportation out of ICU while intubated	YES NO	12(36.4%) 21(63.6%)	10(7.8%) 118(92.2%)	6.743 Ref.	**<0.001**
Use of steroids while intubated	YES NO	19(57.6%) 14(42.4%)	77(60.2%) 51(39.8%)	0.899 Ref.	0.788
Use of proton pump inhibitors	YES NO	24(72.7%) 9(27.3%)	44(34.4%) 84(64.6%)	0.196 Ref.	**<0.001**
Paralytic agent, continuous IV sedation	YES NO	33(100%) 0(0.0%)	81(63.3%) 47(35.7%)	0.000 Ref.	0.997
Surgical drainage mainly thoracic or thoraco-abdominal surgery	YES NO	11(33.3%) 22(66.7%)	26(20.3%) 102(79.8%)	0.510 Ref.	0.117
Compliance with the VAP bundle	YES NO	4(12.1%) 29(87.9%)	71(55.5%) 57(44.5%)	Ref. 9.031	**<0.001**

VAP: ventilator associated pneumonia, **IV**: intravenous, **COR**: crude odds ratio, p-value <0.005
Ref.: reference, **NGT**: naso-gastric tube

Possible Risk factors believed to have an association with the development of VAP were entered in to binary logistic regression analysis and the following variables; sex, duration of mechanical ventilation, admission to PICU from emergency OPD and pediatric ward, presence of co-morbidities, tracheostomy, re-intubation, transportation out of PICU, use of PPI while on MV and compliance with the VAP bundle protocol were found to have significant association as shown in **(Table 3).**

Table 3 Variable associated on binary logistic regression among patients in PICU of TASH, Addis Ababa, Ethiopia, Ethiopia, September 2019 – September 2023 (n=161)

Potential risk factors	Category	VAP(n=33)	NO-VAP(n=128	COR	P-Value
sex	Male female	25 (88.2%) 8(11.8)	68(73.1%) 60(26.9%)	2.757 Ref.	**0.022**
Duration of mechanical ventilation	mean ± SD days	16.8±6.9	5.18±4.9	1.316	**≤0.001**

Admitted to ICU from	Pediatric ward Emergency opd Operative room	7(21.20%) 24(72.70%) 2 (6.10%)	25 (19.5%) 63 (49.20%) 40 (31.30%)	5.600 7.619 Ref.	**0.041** **0.008**
Presence of Comorbidity	Yes No	31 (95.8%) 2(4.2%)	82(72.8%) 46(27.2%)	8.695 Ref.	**0.004**
Tracheostomy	YES NO	6(18.2%) 27(81.8%)	6(4.7%) 122(95.3%)	4.519 Ref.	**0.014**
Re-Intubation	YES NO	20(60.6%) 13(39.4%)	15(11.7%) 113(88.3%)	11.590 Ref.	**<0.001**
Transportation out of ICU while intubated	YES NO	12(36.4%) 21(63.6%)	10(7.8%) 118(92.2%)	6.743 Ref.	**<0.001**
Use of proton pump inhibitors	YES NO	24(72.7%) 9(27.3%)	44(34.4%) 84(64.6%)	0.196 Ref.	**<0.001**
Compliance with the VAP bundle	YES NO	4(12.1%) 29(87.9%)	71(55.5%) 57(44.5%)	Ref. 9.031	**<0.001**

VAP: ventilator associated pneumonia, **COR**: crude odds ratio, p-value <0.005
Ref.: reference, **ICU-** Intensive Care Unit

The above variables seen on (table 3) are those which showed significant association with the dependent variable on bivariate logistic analysis where subjected to multi-variant logistic regression analysis. Below are five (5) variables which has strong association with the development of ventilator-associated pneumonia based on the multi-variant logistic regression analysis result (table 4)

Table 4 Factors associated with the development of VAP on multi-variant logistic regression analysis among patients in PICU of TASH, Addis Ababa, Ethiopia, September 2019 – September 2023 (n=161)

Variables	AOR	95% CI Lower-upper limit	P-value(sig.)
Sex(male)	34.114	[1.121-1038.6]	0.043
Duration of mechanical ventilation in days	1.501	[1.155-1.951]	0.002

Presence of co-morbidities	31.445	[1.542- 641.060]	0.025
Transportation out of ICU while intubated	21.456	[1.369-336.72]	0.029
Compliance with the VAP bundle	31.424	[1.507-655.292]	0.026

AOR-adjusted Odd ratio, ICU- intensive care unit, sig-significance, CI- confidence interval, VAP-ventilator associated Pneumonia

CHAPTER 6: DISCUSSION

Although, Ventilator-associated pneumonia (VAP) is considered one of the most severe forms of hospital-acquired pneumonia with a poor prognosis and an increase use of hospital resources, its biggest drawback is the absence of a gold standard or clear diagnostic criteria for its diagnosis with limited data on its prevalence in the country. To my knowledge, this is the first study in Ethiopia to evaluate the prevalence and associated risk factors of VAP in pediatrics department. Which is conducted at Tikur Anbessa specialized Hospital pediatric Critical Care Unit (PCCU), the largest public hospital in Ethiopia.

In this retrospective study, 161 mechanically ventilated children admitted in a PICU of TASH were analyzed, to determine the prevalence of VAP, to evaluate the associated risk factors, and to document the etiological agents for the same. The prevalence of ventilator associated pneumonia was found to be 20.5%. The rate per 1000 ventilator days is 27/1000.This prevalence is comparable to different studies, in a study done at India by Gnanaguru Vijay et al. the incidence of microbiologically confirmed VAP was 24.4(1), in Malaysia who reported a 16.3% incidence by Brenda MM et al.(11) Iran Ali Amanati et al. (22.9%) (12) .A study from Ethiopia showed the prevalence to be 18.2 % (Tigist Bacha et al.) (7). Incidence and prevalence varies according to geographic regions. USA 5.2% for a rate of 7.1/1,000 ventilator days (3). A Single Center Study from France showed 30(10.6%) met clinical and radiologic CDC criteria for ventilator-associated pneumonia, yielding a prevalence of 7/1,000 mechanical ventilation days. Incidence rate reported from developed countries has been in the range of 5–10% (5, 6, 9), while in developing countries

it is 25–35 %(10). This was reasoned to be because of the difference in the diagnostic criteria, and difference in the patient population (medical, surgical, or both combined) and better ICU setup.

The onset of VAP in this study is dominantly late onset which is after the 7th day of intubation accounting 20(61%) while early onset, occurring at or after 48hrs accounts for the remaining 13(39%).On the opposite a study from Iran by Ali Amanati et al.(12) late VAP was 8.4%.

The most common causative organisms identified from endotracheal aspirate where klebsiella pneumoniae (34%) followed by CONS (27%), Acinetobacter Species 6(18%), Pseudomonas aeruginosa 5(15%), E.coli 2(6%). The findings are comparable to other studies done at India where Gram negative bacilli (Acinetobacter and Pseudomonas) being the important causative agents by Gnanaguru Vijay et al. (1). Van Wyk et al. (2) klebsiella pneumonia (30%) was the most common organism identified from a study done in South Africa which is comparable to this study. In contrary, a study from France show Gram-negative bacteria were found in 60% of patients, with a predominance of Haemophilus influenzae and Pseudomonas aeruginosa. (5) Another study JR Fedžat et al. (13) showed similar micro biologic pattern to this study is Klebsiella pneumoniae 12/42 (28.5%) and Acinetobacter calcoaceticus 7/42 (16.6%) are the dominant causative organisms

As an associated risk factor in this study sex (male sex) is associated with the development of VAP ([OR]: 34.110, P= 0.043: 95% CI: 1.12-1039.6) on multiple logistic regression analysis of risk factors. On other studies (2, 3, 5, 8) sex as a risk factor had no association on bivariate analysis except one study in Spain identified female sex (odds ratio [OR]: 1.642, p = 0.024) (6), as an associated factor for the development of VAP.

The Duration of mechanical ventilation in days is directly associated with the development of VAP on both Bivariate and multivariate logistic regression with (([OR]: 1.501, P= 0.002: 95% CI: [1.155-1.951]). The finding in this study is also supported by other studies: In study from France (5) those with ventilator-associated pneumonia had significantly longer median durations of mechanical ventilation (15 vs 6 d; p < 0.001). Another study from Spain (6) showed MV > 4 days

(OR: 26.79, $p < 0.001$), length in pediatric intensive care unit > 7 days (OR: 11.74, $p < 0.001$) are independent risk factors for the development of VAP.

Prolonged intubation can be a risk factor and at the same time upshot of VAP. On adult it is highly recommended to give trial of extubation on daily basis which is practically difficult on pediatrics population.

In this study the presence of comorbidities had significant association on multivariate logistic regression with (OR: 31.445, P=0.025).this is also supported from other studies like the one from Iran (12), identified being immunodeficiency (p=0.0014) is greater on VAP patients. A systematic review from china (4) showed genetic syndrome (OR =2.04; 95% CI: 1.08-3.86) has significant association with the development of VAP. This study included most of the comorbidities like the presence of chronic illnesses: diabetes mellitus, malignancy, sever acute malnutrition, presence of genetic syndrome…etc. in one as comorbidity.

As a possible risk factor transportation out of PICU while the patient is intubated was subjected to both bivariate and multivariate logistic regression. Result showed significant association on both with ([OR]: 21.456, P= 0.029: 95% CI: [1.369-336.72]).Although few studies analyzed this factor as a possible risk associated with VAP (6). So far there are no studies which supported the finding of this study.

Since implementation of the pediatric VAP bundle, there have been zero incidences of pediatric VAP over the past 18 months. (14). One of the possible risk factor in this study is compliance to VAP bundle. The factor was subjected to both bivariate and multivariate analysis showed strong association with ([OR]: 31.424, P= 0.026: 95% CI [1.507-655.292]). Overall adherence to VAP bundle prevents VAP, this is also supported by other studies (2, 9, 14, and 15). The practice of compliance to VAP bundle is well studied on adult, but in pediatric population the concept is still under studies.

CHAPTER 7: CONCLUSION

This paper focused on reveling the prevalence and risk factors associated with VAP in our setup. In conclusion the prevalence of ventilator-associated pneumonia in our hospital (TASH) pediatric intensive care unit is found to be high. The most common causative organisms are found are klebsiella pneumoniae and coagulase negative staphaureus. This shows both gram-negative and G-positive organisms should be covered during empirical management before tracheal aspirate result is ready.

According to the results of this study five variables/factors male sex, duration of mechanical ventilation prior to the diagnosis of VAP, presence of comorbidities, transportation out of PICU while intubated, and poor compliance to VAP bundle are identified risk factors. Identifying the risk factors will help in implementing preventive majors specially improve compliance with the VAP bundle.

CHAPTER 8. LIMITATION AND STRENGTH OF THE STUDY

Strength: Before this study there is no literature in Ethiopia that studied the risk factors associated with the development of VAP in the pediatric population. It can serve as a baseline for further studies. Risk factors were analyzed both at bivariate and multivariate logistic regression that reduces the effect of confounding variables.

Limitations: During the data collection there were incomplete and lost charts which could have effect on the studied variables. There is no standard tool to diagnose VAP in our setup which limited or narrowed the operational definition to microbiologically confirmed cases. The study was a single centered retrospective chart review so it is difficult to generalize and apply on other setups. Some variables where difficult to study retrospectively.

CHAPTER 9. RECOMMENDATION

For TASH PICU administration and staffs

- It is recommended to strictly follow the standards of VAP bundle and fully incorporate on the follow up chart
- A standardization training should be given on application of VAP bundle care for the nurses and physicians.

For researchers:

- Further research is recommended specially a prospective study on prevalence of VAP in line with validation of the different diagnostic tools.
- Similar wise interventional studies on the identification and possible interventions of risk factors associated with VAP specially the application of VAP bundle of care in pediatrics ICU are areas of further studies.

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ANNEXES

Questionnaire

IC number_____ code_____

I. Characteristics of patients with ventilator-associated pneumonia

1. sex

A. Male B. Female

2. Age _____yrs A. < 1yr B. 1-5yrs c. > 5yrs

3 Presence of VAP A. No B. Yes

.

4. Duration of mechanical ventilation _____(days)

5. Onset of VAP after intubation _____(days)

6. Admitted to ICU from

A. pediatrics ward

B. Emergency OPD

C. Operative room

7. Causative microorganism …….?

8. Primary indication for mechanical ventilation A. Acute respiratory failure

A. Acute respiratory failure

B. Coma or impaired consciousness

C. Neuro-muscular diseases (GBS, myasthenia gravis)

9. Causes of ICU admission were classified as either

A. Trauma

B. respiratory disease,

C. neurologic disorder,

D. cardiovascular disorder,

E. intra-abdominal disorder (GI),

F. Poisoning (usually attempted suicide), or intoxications

G. Metabolic or renal, H. sepsis/septic shok

10. Presence of Co-morbidity ……? A. No B. Yes

Part II - Potential risk factors

No.	Risk factors	Yes	No.
1	Tracheostomy		
2	Bronchoscopy		
3	Re-intubation		
4	Aspiration of gastric content		
5	NGT and enteral feeding		
6	Transportation out of the hospital (ICU) after intubation		
7	Use of steroids		
8	use of proton pump inhibitor (PPI)		
9	Paralytic agents, continuous intravenous sedation		
10	Surgical drainage(mainly thoracic)or thoraco-abdominal surgery		
11.	(1) compliance with the VAP bundle (elevation of bed to 20-30°), daily mouth care using chlorhexidine or tooth brushing)		