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INCIDENCE OF VENTILATOR-ASSOCIATED PNEUMONIA IN THE CRITICAL CARE UNIT AT KENYATTA NATIONAL HOSPITAL, A PUBLIC TERTIARY CARE HOSPITAL
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INCIDENCE OF VENTILATOR-ASSOCIATED PNEUMONIA IN THE CRITICAL CARE UNIT AT KENYATTA NATIONAL HOSPITAL, A PUBLIC TERTIARY CARE HOSPITAL

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ABSTRACT

Background: **Ventilator-associated pneumonia (VAP), a severe type of hospital-acquired pneumonia develops 48-72 hours after initiation of mechanical ventilation.**
Objectives: **This study aimed to determine incidence of VAP using the Clinical Pulmonary Infection Score (CPIS) which combines clinical, radiographic, physiologic and microbiological data into a numerical result, ranging from 0 to 12, and to identify risk factors associated with its development. A secondary objective was to assess the diagnostic utility of a positive culture of pathogenic bacteria on tracheal aspirate in predicting a positive culture on a mini-Broncho Alveolar Lavage (Mini-BAL).**
Design: **A hospital-based, prospective cross-sectional study carried between 01st January 2015 to 31st March 2015.**
Setting: **Kenyatta National Hospital, a tertiary care hospital**
Subjects: **Ninety-two subjects who met the inclusion criteria were included.**
Results: **Of the 92 patients studied, 50 had a CPIS of ≥6, an incidence of 54.4% (C.I. 44.0-64.7%). Factors that appeared to show an association with VAP included documented aspiration (OR 2.0), a high nurse to patient ratio (OR 4.0), post-surgical patients (OR 2.5) and those who were nasally intubated (OR 4.0) and those with oral candidiasis (OR 3.5). Of the 50 patients that showed a CPIS of ≥6, 46 (92%) patients had a positive culture on tracheal aspirate and 31 (62%) patients demonstrated a positive mini-BAL culture. The sensitivity and specificity of a positive tracheal aspirate in predicting a positive min-BAL culture were 100% (C.I 88.7-100.0%) and 21.1% (C.I 6.2-45.6%) respectively. Negative predictive value of 100.0% (C.I 40.2-100.0%) and a positive predictive value of 67.4% (C.I 52.0-80.5%).**
Conclusion: **Our study, the first documented in East Africa, found a high incidence of VAP. Further studies are needed to compare the diagnostic utility of various invasive and non-invasive tests for diagnosis of VAP.**

INTRODUCTION

Ventilator-associated pneumonia (VAP), a type of hospital-acquired pneumonia that develops 48-72 hours after the initiation of mechanical ventilation is associated with new onset or progressive increase of pulmonary infiltrates, fever, leukocytosis, purulent tracheobronchial secretions, tachypnea, increased minute volume, decreased tidal volume and decreased oxygenation.[1] Ventilator-associated pneumonia is considered one of the most severe type of hospital-acquired pneumonia with a high incidence worldwide. [3-7] These patients have a significantly longer Critical Care Unit (CCU) stay and an overall longer hospital stay, thereby, not only increasing the hospital costs but also an increased mortality rate. Therefore, there is need for hospitals to determine its incidence using a cost effective and sensitive tool to guide adoption of a minimum set of standards for the prevention and early treatment and management of these critically ill patients.

The biggest drawback to the diagnosis of VAP is the absence of a gold standard or clear diagnostic criteria. Clinical features of VAP are nonspecific, therefore, a diagnostic evaluation is required at the time this diagnosis is suspected. [8] A chest radiograph should be performed on all patients with suspected VAP and those with abnormal chest radiograph, secretions from the lower respiratory tract for microscopy, culture and sensitivity are mandatory. [9,10] It can be done either non – bronchoscopically by tracheobronchial aspiration or a mini-Broncho Alveolar Lavage (Mini-BAL), or bronchoscopically by Broncho Alveolar Lavage (BAL) or by using a Protected Specimen Brush (PSB).

As the clinical features of VAP are very non–specific, and lack specificity and sensitivity there have been few studies done comparing the different diagnostic measures. Shakeel et al [11] described a clinical trial for the diagnosis of VAP, that included pulmonary infection (fever, leukocytosis, and purulent secretions), bacteriologic evidence of pulmonary infection and radiologic suggestion of pulmonary infection. Pugin et al [12] created a surrogate clinical marker for VAP called the Clinical Pulmonary Infection Score (CPIS) which combines clinical, radiographic, physiologic and microbiological data into a numerical result with a score of ≥ 6 as a fairly accurate measure of the presence of VAP. Other researchers have found the CPIS has having high sensitivity and specificity in the diagnosis of VAP. [13,14]

There are various risk factors that have been significantly associated with the development of VAP, with impaired consciousness, tracheostomy, re – intubation as well as emergency intubation and presence of a nasogastric tube having significant association. [15-18]

Currently there is no published data about VAP in Kenya, therefore, our study was aimed to determine its incidence in critically ill patients admitted to the CCU at Kenyatta National Hospital (KNH), a tertiary care hospital, with the aim of formulating a policy brief on its incidence with the development of policies for its diagnosis and management.

MATERIALS AND METHODS

This was a hospital–based, prospective cross-sectional study, conducted in the Critical Care Unit (CCU) at the Kenyatta National Hospital (KNH), the largest public hospital in Kenya. Eligible subjects were patients mechanically ventilated ≥ 72 hours, but those with a prior diagnosis of pneumonia were excluded. Ethical approval for the study was obtained from the Kenyatta National Hospital/ University of Nairobi Ethics and Research Committee (*ref*; KNH-ERC/RR/746 18/12/14). The patients were selected using systematic sampling,

such that all patients who were mechanically ventilated for ≥ 72 hours were recruited for the study. Recruitment of patients was done 24 hours a day. The enrolment was continued until the desired sample size was achieved.

The enrolled patients had their temperature recorded at 72 hours using a digital thermometer by the primary investigator. Blood sample for an arterial blood gas analysis was drawn using a heparinized 2cc syringe with a 23-gauge needle from one of the peripheral arteries (radial, brachial or femoral artery) and analyzed using a Siemens® arterial blood gas analyzer and a PaO_2/FiO_2 ratio calculated. A second blood sample using a 2cc syringe was drawn into a heparinized vacutainer for a complete blood count analysis at the hospital's hematology laboratory. A portable chest radiograph requested by the principle investigator was reported at the hospital's radiology department. Endotracheal aspirates were collected into a sterile container using a 16/14 French suction catheter and sent to the hospital's laboratory for microscopy, culture and sensitivity. Results of the temperature, white blood cell count, type of tracheal secretions, calculated PaO_2/FiO_2 ratio, pulmonary radiograph findings, and tracheal aspirate cultures were recorded and the CPIS calculated by the principle investigator (Table 1).

Table 1

Clinical Pulmonary Infection Score (CPIS)

PARAMETER	SCORE	POINTS
Temperature ◦c	≥36.5 and ≤ 38.4	0
	≥38.5 and ≤38.9	1
	≥ 39 or ≤ 36.5	2
Total white blood counts	≥4000 and ≤11000	0
	<4000 or >11000	1
	<4000 or > 11000 and band forms ≥ 50%	Add 1 point
Tracheal secretions	None or scanty	0
	None purulent	1
	Purulent	2
PaO_2/FiO_2 **ratio**	>240 or ARDS or pulmonary contusion	0
	≤ 240 or no ARDS	2
Pulmonary radiograph	No infiltrate	0
	Diffuse (patchy) infiltrate	1
	Localized infiltrate	2
Progression of infiltrate	No radiographic progression	0
	Radiographic progression	2
Culture of pathogenic bacteria on tracheal aspirate	Few quantities or no growth	0
	Moderate or heavy growth	1
	Some pathogenic bacteria seen on Gram stain	Add 1 point

ARDS – acute respiratory distress syndrome

**A score of ≥ 6 was considered suggestive of ventilator-associated pneumonia (17).*

Mini–BAL was performed in all patients who had a CPIS score ≥ 6 using a double catheter technique. A sterile suction catheter of size 16 French was cut 3cm from the distal end to give a final length of approximately 47cm and inserted through the endotracheal tube advanced into the distal airways till resistance was felt. Then a second, 50-cm long, sterile suction catheter of size 8 French was passed through the first catheter and

advanced as far as possible. Twenty milliliters of normal saline was instilled into the distal airways through the inner tube and aspirate was collected in a sterile container and sent to the hospital's microbiology laboratory for bacterial examination and culture and sensitivity.

The possible risk factors for the development of VAP were recorded after 72 hours of CCU admission including method of intubation, type of airway, re–intubation, emergency intubation, duration of mechanical ventilation, oral hygiene, witnessed aspiration, use of prophylaxis for stress ulcers (H_2 blocker or antacid therapy), type of feeding, presence of a nasogastric tube, antibiotic therapy prior to the development of VAP, position of the head, continuous sedation or paralysis, patients who had prior cardiothoracic surgery, patients who are mechanically ventilated for Acute Respiratory Distress Syndrome (ARDS) and patients with an intracranial pressure monitor.

A structured form was used to collect patient's data on age, gender, clinical diagnosis, number of intubations and organisms cultured from the tracheal aspirate and the type of administered antibiotics. Glasgow Coma Scale (GCS), type of intubation, calculated CPIS and some of the associated risk factors associated with the development of VAP were recorded at the time of examination of patient. All data collected was recorded and kept private and confidential to maintain the integrity of the participants involved.

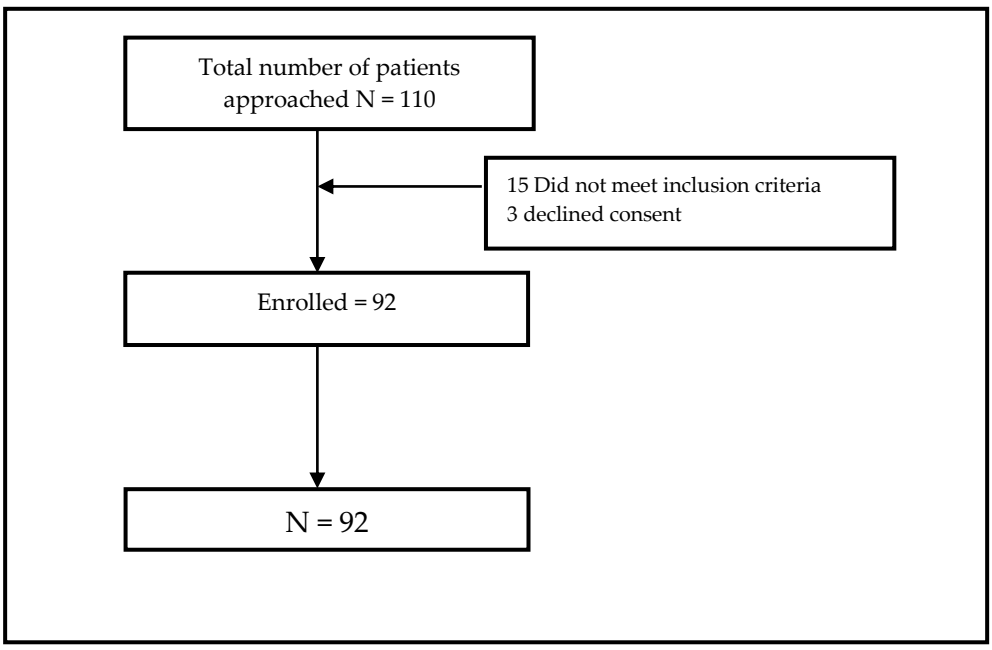
Data was collected from 01st January 2015 to 31st March 2015. And the data obtained was analyzed using Stata data and statistical software (STATA 11.0®).

Categorical data was analyzed using proportions while continuous data was analyzed using mean, medians, standard deviations and interquartile range. Diagnostic utility of positive tracheal aspirate in predicting a positive mini-BAL culture was calculated using a two-by-two contingency table with mini-BAL as "gold-standard". Sensitivity, specificity, positive and negative predictive values and positive and negative likelihood ratios of tracheal aspirate against mini-BAL were also computed. Logistic Regression Analysis, with calculation of odds ratio was done for selected variables to look for any association of the risk factors and the development of VAP. The confidence interval was used to estimate the precision of odds ratio.

RESULTS

One hundred and ten patients were assessed for eligibility with 92 participants fulfilling the inclusion criteria (Figure 1).

Figure 1: Flow chart of Recruitment Process



The mean age of the participants was 28.6 (SD±24.33) years with a median age of 23 years (IQR 7-42.5 years). Majority (63.0%) of the patients were below age of 30 years. There was no gender predominance. Respiratory conditions were the most common diagnosis at admission followed by conditions affecting the central nervous system (Table 2).

Table 2

General characteristics of patients admitted to Critical Care Unit, KNH

Variable n = 92	Frequency (%)
Sex (%)	
Male	46 (50.0)
Female	46 (50.0)
Age (years)	
Children ≤ 18 years	40 (43.4)
Adults 19-65 years	41 (44.6)
Elderly > 65 years	11 (12.0)
Diagnosis on admission	
Respiratory	45 (48.9)
Neurological	15 (16.3)
Obsterical/gynaecological	12 (13.0)
Surgical	7 (7.6)
Haemato-oncological	6 (6.5)
Endrinological	4 (4.4)
Cardiological	2 (2.2)
Genitourinary	1 (1.1)

KNH – Kenyatta National Hospital

Fifty patients showed a Clinical Pulmonary Infection Score (CPIS) of ≥6, giving a calculated incidence of Ventilator Associated Pneumonia (VAP) of 54.4% (C.I. 44.0-64.7%). Although no factors were significantly associated with the development of VAP, factors that appeared to show an association with VAP included documented aspiration, a high nurse to patient ratio, patients who had surgical conditions diagnosed at admission, patients nasally intubated and in those patients, who had oral candidiasis (Table 3).

Table 3

Logistic regression analysis on risk factors for Ventilator Associated Pneumonia

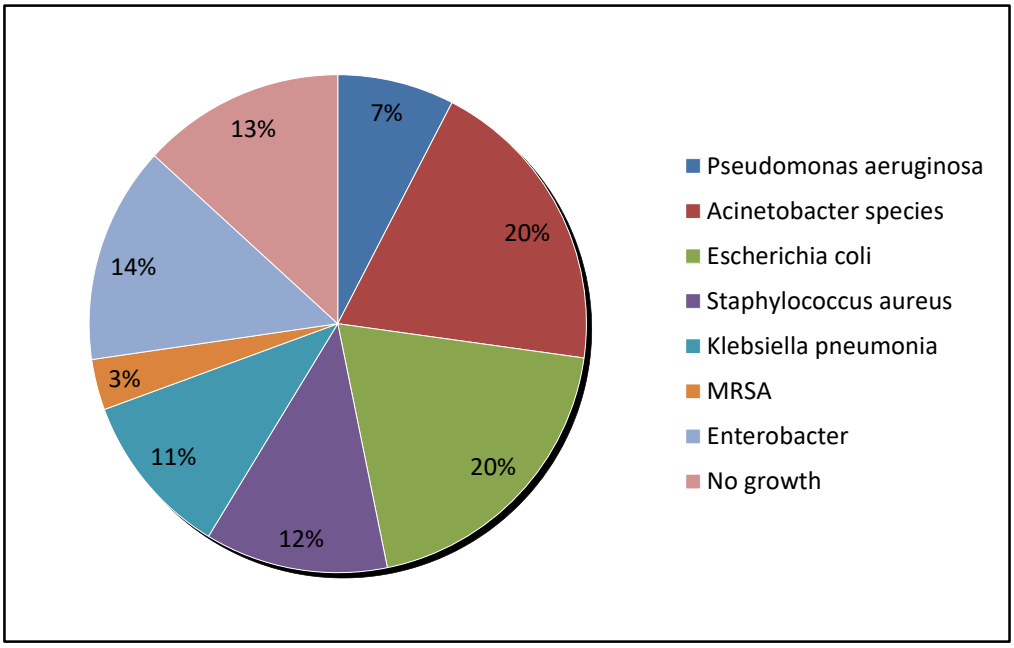
Variable	Total	CPIS ≥6 (%)	Odds (95% C.I)	P value
Gender:				
Male	46	27 (58.7)	1.4 (0.79 - 2.56)	**0.405**
Female	46	23 (50.0)	1.0 (0.56 - 1.78)	
Total	**92**			
System Diagnosis:				
Respiratory	45	26 (57.8)	1.3 (0.76 – 2.5)	
Neurological	15	8 (53.3)	1.1 (0.41 – 3.15)	
Genitourinary	1	1 (100.0)	- (-)	**0.572**
Haemato-oncological	6	3 (50.0)	1.0 (0.20 – 4.95)	
Endrinological	4	1 (25.0)	0.3 (0.03 – 3.20)	
Cardiological	2	0 (0.0)	- (-)	

Surgical	7	5 (71.4)	2.5 (0.49 – 12.89)	
Obsterical/gynaecological	12	6 (50.0)	1.0 (0.32 – 3.10)	
Total	**92**			
Method of Intubation:				
Nasal	5	4 (80.0)	4.0 (0.45 – 35.78)	
Oral	85	40 (47.0)	1.1 (0.73 – 1.72)	**0.498**
Tracheostomy	2	1 (50.0)	1.0 (0.06 – 15.98)	
Total	**92**			
Emergency Intubation:				
Yes	55	27 (49.0)	0.9 (0.57 – 1.63)	**0.219**
No	37	23 (62.2)	1.6 (0.85 – 3.19)	
Total	**92**			
Number of Intubations:				
1	60	33 (55.0)	1.2 (0.73 – 2.03)	**0.864**
≥ 2	32	17 (53.1)	1.1 (0.56 – 2.26)	
Total	**92**			
Semi-recumbent Position:				
Yes	49	25(51.0)	1.0(0.59 – 1.82)	**0.496**
No	43	25(58.1)	1.4(0.76 – 2.55)	
Total	**92**			
Diagnosis of ARDS by primary Physician:				
Yes	4	4 (100.0)	- (-)	**0.062**
No	88	42 (47.7)	1.1 (0.72 – 1.66)	
Total	**92**			
Presence of Intracranial Pressure Monitoring				
Yes	4	2 (50.0)	1.0(0.14 – 7.09)	**0.859**
No	88	40 (45.5)	1.2(0.78 – 1.82)	
Total	**92**			
Presence of Feeding tube:				
Yes	77	43 (55.8)	1.2 (0.80 – 1.98)	**0.516**
No	15	7 (46.7)	0.8 (0.32 – 2.41)	
Total	**92**			
Stress Ulcer Prophylaxis:				
Proton pump inhibitor	28	17 (60.7)	1.5 (0.72 – 3.29)	
H 2 blocker	44	25 (56.8)	1.3 (0.72 – 2.39)	**0.332**
None	20	8 (40.0)	0.7 (0.27 – 1.63)	
Total	**92**			
Oral Hygiene:				
Foul smell	52	24 (46.2)	0.9 (0.49 – 1.48)	
Oral candidiasis	9	7 (77.8)	3.5 (0.72 – 16.84)	**0.205**
Dental caries	1	1 (100.0)	- (-)	
Good	30	18 (60.0)	1.5 (0.72 – 3.11)	
Total	**92**			
Documented Aspiration:				
Yes	6	4 (66.7)	2.0 (0.36 – 10.91)	**0.533**
No	86	46 (53.5)	1.2 (0.75 – 1.75)	
Total	**92**			
Intravenous Sedation:				
Benzodiazepines	68	39 (57.4)	1.3 (0.83 – 2.17)	
Opioids	5	2 (40.0)	0.6 (0.11- 3.99)	**0.599**
None	19	9 (47.4)	0.9 (0.37 – 2.21)	
Total	**92**			
Intravenous Muscle relaxants:				**0.901**
Yes				
No	2	1 (50.0)	1.0 (0.06 – 15.98)	

Total	90	49 (54.4)	1.2 (0.78-1.80)	
	92			
Nurse to Patient Ratio:				
1:1	21	14 (66.7)	2.0 (0.81 – 4.95)	
1:2	61	28 (45.9)	0.8 (0.51 – 1.40)	**0.059**
>1:2	10	8 (80.0)	4.0 (0.85 – 18.83)	
Total	**92**			
Suction Machine to Patient Ratio:				
1:2	24	15 (62.5)	1.6 (0.73 – 3.81)	**0.353**
>1:2	68	35 (51.5)	1.1 (0.66 – 1.71)	
Total	**92**			

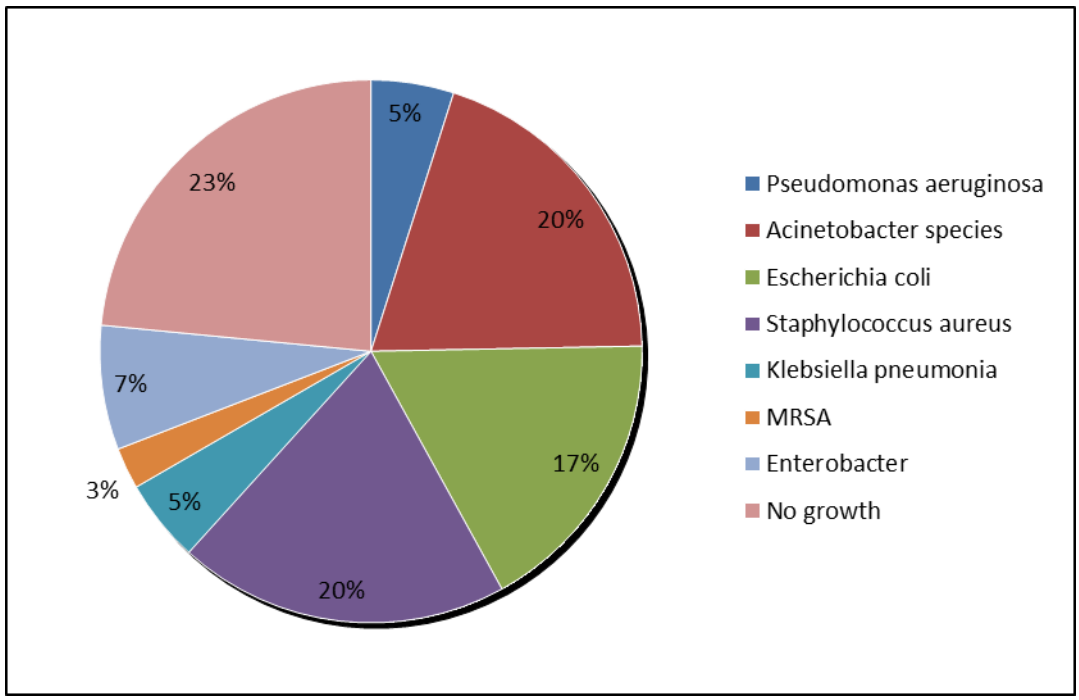
Of the 50 patients that showed a Clinical Pulmonary Infection Score (CPIS) of ≥6, 46 (92%) patients had a positive culture on tracheal aspirate and 31 (62%) patients demonstrated a positive mini-BAL culture. The most common cultured organism in the tracheal aspirate of patients was Acinetobacter species (20%) and Escherichia coli (20%), followed by Enterobacter (14%), Staphylococcus aureus (12%), Klebsiella pneumonia (11%), Pseudmonas aeruginosa (7%) and MRSA (3%) (Figure 2).

Figure 2: Organism cultured on tracheal aspirate in patients admitted to the Critical Care Unit (n=92)



The most common organisms cultured on mini-BAL of patients were Acinetobacter species (20%) and Staphylococcus aureus (20%), followed by Escherichia Coli (17%), Enterobacter (7%), Klebsiella pneumonia (5%), Pseudomonas aeruginosa (5%) and MRSA (3%) (Figure 3).

Figure 3: Organism Cultured on mini-BAL in patients admitted to the Critical Care Unit (N=50)



The sensitivity and specificity of a positive tracheal aspirate in predicting a positive min-BAL culture were 100% (C.I 88.7-100.0%) and 21.1% (C.I 6.2-45.6%) respectively. Negative predictive value (NPV) of 100.0% (C.I 40.2-100.0%) and a positive predictive value (PPV) of 67.4% (C.I 52.0-80.5%). Similarly, positive likelihood ratio (LR+) and negative likelihood ratio (LR-) was 1.27 and 0.0 respectively.

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, [2] its biggest drawback is the absence of a gold standard or clear diagnostic criteria for its diagnosis with limited data on its incidence in the country. To our knowledge, this is the first documented study in Eastern Africa to evaluate the incidence and associated risk factors of VAP which was conducted in Kenyatta National Hospital's (KNH) Critical Care Unit (CCU), the largest public hospital at the apex of the national health care delivery in Kenya.

Our study showed an incidence of VAP as 54.4% (C.I. 44.0-64.7%). Similar results were reported by Vincent et al. [5] who showed an incidence of 47%, however, higher results than that demonstrated by Jordi Rello et al. [4] who showed an incidence of 9.3% in a large US inpatient or by Shanti RD et al. [5] in Malaysia who reported a 16.3% incidence. Studies done within pediatric populations by Brenda MM et al. [6] and Maha et al. [7] demonstrated lower incidence rates of 36.6%

and 10.3% respectively. Our study looked at a much wider age population, from the pediatric patients to adult and the elderly patients, unlike other studies that focused either in the pediatric or the adult groups. However, this was not enough to explain the high incidence of VAP recorded, as there was no statistically significant difference in the incidence among the various age groups and various other patient characteristics may have had an influence.

There are various risk factors associated with the development of VAP. [15-18] Our study looked at the association of several of these risk factors and the development of VAP. Patients admitted to the CCU following surgery had two and half times higher risk of developing VAP. Most of the patients admitted following craniotomy surgeries, due to head trauma, had impaired consciousness and decreased reflexes, predisposing them to higher chances of VAP. Similar results were reported by Joseph NM et al. [17] Witnessed or documented aspiration appeared to show an association with the development of VAP, similar results were reported by Maha et al. [7] This study also appeared to show an association for the development of VAP with inadequate nursing staff in the Critical Care Unit like the study done by Shanti RD et al. [5] Nasal intubation showed a four times higher risk of predisposing to VAP compared to tracheostomy unlike the study done by Joseph NM et al. [17] Patients who had oral candidiasis had three and a half times higher risk of developing VAP, similar to the study done by Kollef et al.[18] which showed a significant association between oral hygiene and VAP.

Other risk factors including emergency intubation, semi-recumbent position, presence of feeding tube, stress ulcer prophylaxis, intravenous sedation did not show an association with the development of VAP in our study, contrary to our expectation.

Although none of the risk factors were significant enough to show and association with the development of VAP, keeping in mind our analysis was not powered to identify all important risk factors in this study population. Further validation of the risk factors identified in this study is necessary, maybe by focusing on particular age and patient characteristics and by increasing the sample size powered enough to study the most common risk factors documented in this study.

Combining knowledge gained from microbiologic examination of bronchoalveolar fluids or tissues in the infected area together with the CPIS and good clinical judgment offer the best for patient treatment. Components of the CPIS can be influenced by other conditions and therefore lead to erroneous or overuse of antibiotics because the causative pathogen is unknown and therefore leading to resistant pathogenic strains. This has led to investigators concluding that a specialized diagnostic procedure is needed which include quantitative culture of the specimens obtained from the lower airways. Various strategies have been studied including the use of tracheal aspirates, bronchoscopic and non-bronchoscopic alveolar lavages to obtain microbiologic samples for quantitative analysis. Although the mini-BAL gives more accurate sampling results compared to sputum or tracheal aspirates, being a more invasive procedure, most clinicians may settle for the less invasive tracheal aspirate cultures in guiding in antibiotic use in the management of VAP.

In our study, of the 50 patients that showed a CPIS of ≥ 6, 46 (92%) patients had a positive culture on tracheal aspirate and 31 (62%) patients demonstrated a positive mini-BAL culture. Tracheal aspirates had a good sensitivity (100.0%) but a poor specificity (21.1%) in predicting a positive mini-BAL culture. The positive and negative predictive

values for tracheal aspirates were 67.4% and 100.0% respectively. The ideal test would be one that has a high sensitivity and specificity and also with high positive and negative predictive values. This study has provided data on possible diagnostic utility of tracheal aspirates in the management of VAP. Tracheal aspirates are also readily available, easily performed with minimum expertise needed with a good turnaround time for results.

CONCLUSION

This study highlighted a relatively high incidence (54.4%) of ventilator-associated pneumonia (VAP) in the Critical Care Unit at the Kenyatta National Hospital, Nairobi, Kenya, as diagnosed using the Clinical Pulmonary Infection Score (CPIS), a simple noninvasive method which is also relatively inexpensive. Currently this data was lacking. Due to its high incidence, there is a need for further revision and reinforcement of the already existing management protocols to prevent the high incidence of VAP.

Factors that appear to show an associated risk with the development of VAP, although not statistically significant, included documented aspiration, a high nurse to patient ratio, a high suction machine to patient ratio, patients who had undergone surgery, patients nasally intubated and in those patients, who had oral candidiasis. Knowledge of important risk factors may reduce morbidity and mortality in patients at risk for the development of VAP with the need for further studies on the same.

This study also highlighted the diagnostic utility of positive tracheal aspirates in predicting a positive mini-BAL culture in the diagnosis of VAP. Further studies are needed to compare the diagnostic utility of various invasive and non-invasive tests used in the management of VAP.

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