COLLEGE OF MEDICINE AND HEALTH SCIENCE

SCHOOL OF MEDICINE AND PHARMACY

DEPARMENT OF ANESTHESIOLOGY, CRITICAL CARE AND EMERGENCY

RISK FACTORS AND OUTCOME IN PATIENTS WITH VENTILATOR ASSOCIATED PNEUMONIA IN ICU AT CHUK

Memoir submitted in partial fulfillment of the requirements for award of Master of Medicine in Anesthesiology, School of Medicine

College of Medicine and Health Sciences, University of Rwanda

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DECLARATION

I, DUSHIMIMANA Vestine, declare that this dissertation the result of my own work and has not submitted for any other degree at the University of Rwanda or any other institution

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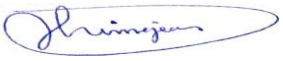
Signature: 

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DEDICATION

I most gratefully dedicate this work to the Almighty God who stayed alongside through my life. I strongly dedicate this to my family for their encouragement and their sacrifice during my studies.

To my research supervisor, all my classmates for the best moments bonded together, finally to all my relatives and friends.

God bless you

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ABSTRACT

Background: Ventilator associated pneumonia is linked to a high mortality rate, increased ICU stay and cost. Identification of risk factors may allow a cost-effective setting of preventive measures.

Aim: To assess incidence; risk factors; outcome for VAP in ICU.

Method: Prospective cohort study, was conducted from January2022 to May 2022 on adult patients who underwent MV beyond 48 hours in ICU/CHUK.VAP was detected using CPIS. Incidence of VAP per 1000 ventilation-days was calculated. Logistic regression was done to pinpoint the predictors of mortality along with predictors of developing VAP. The compliance for triple bundle about VAP prevention was also evaluated for the development of VAP. Elements exhibiting close link with the outcome of interest (P<0.25) took place into multivariable logistic regression to pinpoint independent predictors to the outcome. *P*<0.05 expressed statistical significance.

Result: About 153 participants, 74 arose at the minimum 1 event of Ventilator associated pneumonia in ICU. Incidence about ventilator associated pneumonia noted as 44 per 1,000ventilation-days. Female participants were more apparently more to have VAP (OR=3.1;95%CI 1.38-7.03; P= 0.006) as opposed to male patients. The compliance with the triple bundle was higher among patients who do not acquire VAP than participants with VAP (63+/-16% versus 38+/-12%; p<0.001). Patients who received H2 antagonists are 6.75 times feasible to VAP compared to those who received PPIs. Of 74 patients with VAP, 36 (49%)died in ICU versus27(34%) for those without. In binary logistic regression It coexists statistical significant in the mortality rate among, participants who have diabetes and those who did not have diabetes (OR=3.64; 95%CI: 1.30-10.18; P=0.014).and All the patients who had HIV comorbidity died compared to 39% of those without HIV (p=0.003). The multivariable logistic regression done to pick out independent factors for mortality and revealed that patients with diabetes mellitus were more presumably to die (odd ratio =3.30, 95% confident interval: 1.16-9.35; P=0.024). It coexists a significant difference in ICU stay for cases with VAP than non-ventilator associated pneumonia (P=0.0162 with median(QI-Q3) ICU stay of 8(5-11) days for non VAP and 9(6-14) for VAP.

Conclusion: The incidence of VAP is high. However, an implementation of preventive measures including PPIs' prescription may alleviate their incidence,

Keywords: Incidence, Ventilator associated pneumonia and risk factor

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LIST OF ABBREVIATIONS

CMHS: College of Medicine and Health Sciences

I**CU**: Intensive Care Unity

CHUK: Centre Hospitalier Universitaire de Kigali

HUTH: Kigali university teaching hospital

CPIS: Clinical Pulmonary Infection Score

SPSS: Statistical packages for social sciences

VAP: Ventilator Associated Pneumonia

IRB: Institutional Review Board

UR: University of Rwanda

NPPV: Non-Invasive Positive Pressure Ventilation

MV: Mechanical ventilation

CHG: Chlorhexidine Gluconate

RCTs: Randomized Controlled trials

BAL: Broncho Alveolar Lavage

HAI: Hospital Acquired Infection

HIV: Human Immuno deficiency Virus

OR: Odd Ratio

AOR: Adjusted Odd Ratio

CXR: Chest X Ray

WCC: White Cell Count

ARDS: Acute Respiratory Distress Syndrome

CHAPTER I. INTRODUCTION

1.1. Background

VAP is a health care related infection due to different pathogens (viral, bacterial, fungi) of the respiratory tract occurring thereafter 48 hours on mechanical ventilation. Depending on the time of their onset; It may be those with early onset (within 4days) and late onset (greater than 4 days). (1).Detection of VAP may be made using clinical pulmonary infection score established in 1991, it is composed of clinical features as such as fever ,purulent tracheal secretions ,oxygenation, radiological features such as new infiltrate on CXR or worsening of preexisting infiltrate ,laboratory features such as positive tracheal aspirate, leukocytosis ;each feature has 2 points so the score of 6 or more is diagnostic for VAP.(2).

There are different risk factors predisposing critical patient, mechanically ventilated to VAP such as none bed head elevation at30 to 45^{o}, continuous sedation, reintubation, oral care.(3).A study carried out by A. Haghighi, V.Shafipour, M. Nesami et al showed that when the oral care performed, using chlorhexidine or normal saline reduce occurrence of this illness (4),(5).This disease may lead to prolonged mechanical ventilation and long duration of ICU stay.(6).

There are different preventive measures against ventilator associated pneumonia based on risk factors including head elevation at 30-45^{o}, daily cessation of sedation for spontaneous breathing trial and awakening trial, ulcer prophylaxis , oral care every 4 hours with chlorhexidine and toothbrush.(6)(7).

Outcome measures (mortality rate, length of ICU stay, tracheostomy,). Different studies demonstrated that ventilator associated pneumonia predispose to mortality rate and high incidence. Hina Gadani et al declared that ventilator associated pneumonia mortality with early onset is about 20% while those with late onset is about 66%. In general, ventilator associated pneumonia mortality is estimated 54% compared with non-ventilator associated pneumonia which was about 41%.(3).other study stated that mortality rate of ventilator associated pneumonia is about 50% with incidence of about 40%(8).

In Rwanda only some researchers conducted studies aimed to assess preventive measures, like study done by L. Rumagirwa, B. Bhengu where they were assessing mouth care practice of nurses in ICU /CHUK and found that there is a low level of oral care practice in ICU where about 53.2% don’t use a toothbrush which is best when used twice a day to remove oral plaque; other about 89.4% don’t use chlorhexidine which involve in reduction of ventilator associated pneumonia. Other study conducted at CHUK in all inpatient units by S. Lukas, U. Hogan, V.

Muhirwa et al. showed that hospital acquired infection prevalence were 15.1%. Higher rate observed in intensive care unit (50.0%) (9). But none done to detect determinants and effects of VAP in critical care. Ventilator associated pneumonia patients have long ICU stay, high mortality rate which predispose to the increase use of medical resources and personal resources and lack of bed in ICU for other patients; that why this study involves in assessment of incidence, risk factors and outcome for VAP patients so that guideline and training in regard to VAP should be established.

1.2 Rationale

Assessment of risk factors and outcome in patients with VAP will help at national level, at institutional level or health care providers to set protocols or guideline used in ICU for patient's treatment; to take measures on preventive strategies against ventilator associated pneumonia in ICU.It will involve in reduction of previously used medical resources; it will improve patient's outcome and reduce patient's resources.

1.3 Objective of study

1.3.1General Objective

Assessment of incidence; risk factors and outcome for patients with VAP in ICU.

1.3.2 Specific objectives

i. To assess incidence per 1000 ventilation-days of ventilator associated pneumonia
ii. To assess risk factors for developing VAP
iii. To assess impact of ventilator associated pneumonia on patients 'outcome

1.4 Research question

What is the incidence per1000 ventilator days of VAP?

What are risk factors for VAP in critical care unit at CHUK?

What are impact of VAP on patients 'outcome?

CHAPTERII: LITERATURE REVIEW

2.1 Introduction

VAP is among the HAI diagnosed in critically ill patient who spent more than 48hours on mechanical ventilation. It can cause prolonged weaning time from ventilator, it increases the length of hospital stay resulting into financial issues on patient and huge demand of medical resources.(6). Depend on time onset, Ventilator associated pneumonia is categorized as VAP below four days and VAP beyond four days).(1)

Enduring MV worsened danger to ventilator associated pneumonia 9% - 40%.

VAP rate was 2 per 1000days among 1749 hospital in US, >90% of pneumonia in ICU and 50% appeared in 4 days leading to 20-70% mortality rate increase.(4)

2.2 Diagnosis

VAP diagnosis made by attendant aspect of clinical criteria, radioactive infiltrates and microbial cultures and were combined to CPIS(10).Shannon Fernando et al evaluated diagnostic performance of CPIS contrasting either pulmonary histopathology ,Broncho alveolar cultures as reference standards and revealed that CPIS > 6 had a sensitivity of75.4% and specificity of 68.3% (2).

2.3 Risk factors on ventilator associated pneumonia

In spite of extensive implementation of care process to reduce ventilator associated pneumonia rates, involving bed head elevation, sedation vacations, and daily assessment of readiness to wean; around 10%of patients ventilated more than 48 hours still acquire VAP(11).

This illness is associated with GI contamination to sufferer acquiring MV, oral care plays important role in prevention of VAP. Fernanda, D. Vidal1, A. Karla et al found that tooth brushing plus 0.12%chlorhexidine gel lower incidence of ventilator associated pneumonia (12). other study done by Mullins, S Barsun, showed that prior oral chlorhexidine gluconate intervention, VAP rate was 13.4(6.6-19.5). Later illness was lowered to 0(0-7)($P<0.001$)(7). Excellent mouth care reduces VAP. Other research were comparing two groups; intervention and control group on day three, and five, they found that VAP rate was 10% and 14% as well as 4% and 10% respectively (4).

Aspiration of gastric contents take place more often among patients in supine position rather than semi recumbent(13). Lower grade of VAP was revealed in semi recumbent position,

contrasting to patients kept in supine position (14).VAP detection were lower among patients 45^{o} contrasting to patients at 0^{o} (OR0.47;95%CI,027-0.82;337patients(13).

Failed extubation rate is 2% to 25% of those underwent prepared extubation. unprepared cases are 0.3 to14% ,60% require the ETT again (15).Once intubation is decided, a plan to free the patients is taken (16).

2.4. Outcomes in patient with VAP

This disease is a source fatality in intensive care unit. VAP happens in 25% of cases in ICU beyond forty-eight hours. Its rate about 3 to 51per 1000 ventilator days(17).

Intubation is the risk of VAP occurrence and the risk increases with the increase of mechanical ventilation period. Consequently, avoidance of VAP must be initiated restricting MV time. Various plans have been reported to reach objectives (16).

Tracheostomy is a frequently performed technique for patients need prolonged MV, advantage from tracheostomy include patients comfort and less exposure to sedation. Tracheostomy ameliorate lung recovery and reduce stay(18).

CHAPTERIII: PATIENTS AND METHODS

3.1Study design

Prospective cohort study and covered all participants intubated together with mechanical ventilation for greater 48 hours, admitted in ICU/CHUK from January2022 to May 2022.

3.2Setting

The research conducted at CHUK in Anesthesia and critical care, ICU

3.3 Study population

The population involving in this study were all adults above eighteen years old intubated, on mechanical ventilation over 48 hours, admitted in ICU /CHUK during this study period.

3.3.1 Inclusion criteria

All patients intubated and mechanically ventilated admitted in intensive care unit greater than 48 Hours.

3. 3.2 Exclusion criteria

Pneumonia patients before intubation.

Patients refereed to another hospital already intubated for more than 48 hours.

3.4 Data collection

The data were collected on data predetermined questionnaire; it was developed based on objectives and checked by supervisors. The tool consists of different variables including demographic data; patient diagnosis on admission and comorbidities; points for assessment of risk factors (bed head position, sedation, reintubation and oral care, gastric ulcer prophylaxis), clinical pulmonary infection score for diagnosis of ventilator associated pneumonia and outcome (ICU stay, tracheostomy and mortality rate). The above mentioned variables were monitored and recorded daily on data collection tool.

3.5 Sampling technique

All patients intubated, mechanically ventilated fit for inclusion criteria were enrolled, followed every day; CPIS was applied to identify patients with ventilator associated pneumonia; Its components including (body temperature, Tracheal secretions appearance, Tracheal culture results; CXR, PaO2/FIO2 ratio, and WCC). Total points calculated over 12 points; patient who had ≥ 6 points were recognized as VAP. Its diagnosis was evaluated for first episode.

Table 1:CPIS(19)

variables	0	1	2
T(^{o} c)	≥36.5 and ≤38.4	≥38.5 and ≤38.9	≥39 or ≤36
leukocyte count, per mm^3	≥4000 and ≤11000	<4000 or >11000	<4000 or >11000+ band form ≥ 500
Tracheal secretion	rare	abundant	abundant or purulent
hypoxic index pao2/FIO2,mmHg	>240 or ARDS	--	≤240 and no evidence of ARDS
CXR infiltrate	No infiltrate	Diffuse	Localized
Tracheal culture	negative	--	positive

For each patient; observation was done once day; to see if participant is on continuous sedation or not; bed head elevation at 30^o - 45^{o,} or not; if oral care done or not, till Ventilator associated Pneumonia diagnosis done for first episode during period of mechanical ventilation. Triple bundle compliance scored 3 points, is made by (cessation of sedation, bed head elevation at 30-45^o, oral care); each component scores 1point, average was used to determine trio bundle as variable for every participant who had VAP. During this study period; reintubation and tracheostomy were checked and recorded; length of ICU stays, and if died were documented. 153 participants enrolled were recruited from January 2022 to May2022,

3.6. Data analysis

Data were checked, organized, entered, cleaned and studied using SPPS version 23. Incidence per ventilator days calculated using the formula of (number of participants diagnosed VAP/total number of days on MV) ×1000 ventilator days. Categorical variable was presented in frequencies and percentages in tables. Logistic regression analysis settles a forecast of mortality with predictors of developing ventilator associated pneumonia. Fischer's exact test was applied when cell count >=25%of cells had count <5in group comparison. The independent student t-test applied to link the mean values of continuous variables namely compliance triple bundle (cessation of sedation, bed head elevation at 30 -45 ^{o}, oral care) score across groups of the outcome variables. Factors that showed to be associated with the outcome (either mortality or developing VAP) with p<0.25were taken to the multivariable logistic regression to predict the final model of predictors. Statistical significance for associations was taken at the level $p <$ 0.05.

3.7 Ethical consideration and confidentiality

Ethical clearance No 306/CMHS IRB/2021 was gotten from IRB/CMHS-UR, and Ethic Committee of Kigali University Teaching Hospital; REF: EC/CHUK/001/2022. Consent was provided to the next of kin for every patient or patient him or herself where possible and provided data will only be used for the purpose of this study. The confidentiality was assured as the identity of every participant was assigned to a code number. The list containing every participant information was locked in secured cupboard

3.8 Study limitation

Participants were followed once day; some data may be missed. Among variables such as oral care is done once day in ICU/CHUK and they don't check cuff pressure Other limitation is related to small sample size due to time limitation and there is no standard confirmatory diagnostic test available for VAP.

CHAPTER IV: RESULTS

4.1: Sociodemographic and clinical features of study participants

This study analyzed the data from 153 participants managed in ICU. The median age was 32 years ranging from 19 years to 80 years of age. Male gender was predominant at 75% and 12% of all participants had diabetes, 7% had cardiovascular diseases and 6 patients (4%) had HIV infection (Table 2).

Table2: Sociodemographic and clinical features of study participants

Characteristics	Frequency	%
Age [Median (IQR)]	**32 (27-46)**	
≤35	90	59
36-65	51	33
>65	12	8
sex		
Male	115	75
Female	38	25
Comorbidities		
Diabetes	19	12
Cardiovascular diseases	10	7
HIV coinfection	6	4

IQR: Interquartile range (Q1-Q3)

Considering the frequency of diagnosis of the participants, the most typical diagnosis was Trauma at 31% followed by sepsis at 23%, then intra-abdominal infections at 21% and tumors at 11%(Table 3).

Table 3: Frequency of diagnosis among patients who were at risk of VAP

Diagnosis	n	%
Trauma	47	31

Sepsis	35	23
Intra-abdominal infections	32	21
Brain tumor	16	11
Vascular diseases	7	5
Endocrine disorders	6	4
Hypertensive disorder on pregnancy	5	3
Intoxication	5	3

4.2: The incidence per ventilator days of ventilator associated pneumonia in ICU/CHUK

To have distribution according to CPIS values (those≥6: VAP), 74 out of 153 evolved at the minimum one episode. (table4)

Table 4: Variables to diagnose VAP

Variables		**Frequency**	**%**
		128	84
tracheal secretion	Rare	47	31
	Abundant	48	31
	Abundant purulent	58	38
CXR	No infiltrate	133	87
	Diffuse	10	7
	Localized	10	7
T(^{O}C)	≤36.5or ≥39	104	68
	36.5-38.4	24	16
	38.5-38.9	25	16
Pao2/Fio2	>240 or ARDS	94	61
	≤240 and no evidence of ARDS	59	39
WCC	>400 and <1100	22	14
	≤400 and ≥1100	126	82
	≤400 and ≥ +band form>500	5	3
Tracheal culture	Not done	124	81
	Negative	15	10
	Positive	14	9
VAP diagnosed	Yes	74	48
	No	79	52

74 out of 153evolved at the minimum one episode, incidence per 1000 ventilator days calculated by$\frac{74}{1674}$ ×1000=44per 1000ventilator days.(table 5)

Table 5: Incidence of VAP

No	Day of developing VAP	number of patients acquiring VAP	Ventilator -days for all patients (n=153)
1	Day three	12	
2	Day four	14	
3	Day five	18	
4	Day six	5	
5	Day seven	4	
6	Day eight	21	
Total		74	1674 ventilator -days

4.3: Risk factors for developing VAP

There was a statistical significance difference in the compliance triple bundle according to VAP diagnosis where patients who were not diagnosed with VAP had high mean compliance bundle score of 63% compared to 38% from patients who were diagnosed with VAP (p<0.001). Female patients were 2.6x more apparently to have ventilator associated pneumonia compared to male patients (66% vs 43%), (OR:2.59;95%CI:1.20-5.56; P=0.015). Participants who received H2 antagonists were 5x more apparently to have VAP (76%) contrasting to those who received PPI (39%), (OR=5.01; 95% CI: 2.17-11.5; P<0.001), participants with intra-abdominal infections were 2.9 times more likely to have VAP as those who did not have intra-abdominal infections (OR=2.92; 95%CI: 1.27-6.69; P=0.011) [Table 6].

Table 6: Factors for VAP among study participants

Variables	VAP diagnosis		OR (95% CI)	P value
	VAP	**No VAP**		
Compliance with triple bundle				
Mean ± SD	38+/- 12%	64 +/- 16%		<0.001*
Age				
≤35	41 (46%)	49 (54%)	Ref	
36-65	27 (53%)	24 (47%)	1.34 (0.67-2.67)	0.4
>65	6 (50%)	6 (50%)	1.19 (0.35-3.98)	0.772
Sex				

Male	49 (43%)	66 (57%)	Ref	
Female	25 (66%)	13 (34%)	2.59 (1.20-5.56)	0.015
Gastric ulcer prevention				
PPI	45 (39%)	70 (61%)	Ref	
H2 antagonists	29 (76%)	9 (24%)	5.01 (2.17-11.56)	<0.001
Re-intubation				
Yes	15 (56%)	12 (44%)	1.42 (0.61-3.27)	0.411
No	59 (47%)	67 (53%)	Ref	
Trauma				
Yes	21 (45%)	26 (55%)	0.80 (0.40-1.61)	0.544
No	53 (50%)	53 (50%)	Ref	
Vascular				
Yes	2 (29%)	5 (71%)	0.41 (0.77-2.18)	0.297
No	72 (49%)	74 (50.68%)	Ref	
Intoxication				
Yes	3 (60%)	2 (40%)	1.62 (0.26-10.0)	0.6
No	71 (48%)	77 (52%)	Ref	
Tumors				
Yes	4 (25%)	12 (75%)	0.32 (0.98-1.04)	0.058
No	70 (51%)	67 (49%)	Ref	
Sepsis				
Yes	18 (51%)	17 (49%)	1.17 (0.55-2.49)	0.68
No	56 (48%)	62 (53%)		0.673
Intra-abdominal infection				
Yes	22 (69%)	10 (31%)	2.92 (1.27-6.69)	0.011
No	52 (43%)	69 (57%)		

Receiving gastric ulcer prevention, gender, tumor diagnosis and intra-abdominal infection were considered in the multivariable logistic regression and Receiving H2 antagonists and gender remained in the final model of predictors of being diagnosed with VAP (Table 7).

Table 7: Multivariable analysis of the predictors of VAP

Predictors	OR	95% CI	P value
~~ga~~stric ulcer prevention			
H2 antagonist	6.75	1.91-23.89	0.003
PPI	1.00	Ref	

sex			
Male	1.00	Ref	
Female	3.11	1.38-7.03	0.006
Tumor diagnosis			
Yes	0.49	0.14-1.69	0.261
No	1.00	Ref	
Intra-abdominal infection			
Yes	1.46	0.39-5.33	0.568
No	1.00	Ref	

4.4: Outcome of study participants

The median(days)(QI-Q3) length of stay in ICU was8(5-11) for those without VAP and 9(6-14) for those with it. (p=0.0162). Tracheostomy was performed on 40 patients ;13(33%) with VAP and 27(68%) patients with VAP (OR 0.41; 95%CI ;0.19-0.87 p=0.021). participants with VAP were more apparently to die than those without ventilator associated pneumonia (Table 8).

Table 8: Outcome for patients diagnosed with VAP

Outcome	VAP	No VAP	OR (95% CI)	P value
Length of ICU stay				
median (QI-Q3) in days	9 (6-14)	8 (5-11)	-	0.0162
Tracheostomy				
Yes	13 (33%)	27 (68%)	0.41 (0.19-0.87)	0.021
No	61 (54%)	52 (46%)	Ref	
Final outcome (Mortality)				
Died	36 (49%)	27 (34%)	1.82 (0.95-3.49)	0.07
Survived	38 (51%)	52 (66%)	Ref	

It exists a statistical significant difference in the mortality rate among participants who have diabetes and those who did not have diabetes (OR =3.64; 95%CI: 1.30-10.18; P=0.014). All the patients who had HIV comorbidity died compared to 39% of those without HIV (P =0.003). There does not exist statistical significant association linking mortality and other factors

namely being diagnosed with VAP, age, gender, having cardiovascular disease, and type of admission (Table 9).

Table 9: Factors associated with mortality among participants

Characteristics	Final outcome		OR (95% CI)	P value
	Survival	**Non survival**		
Diagnosed with VAP				
Yes	38 (51%)	36 (49%)	1.82 (0.95-3.49)	0.07
No	52 (66%)	27 (34%)	Ref	
Age				
≤35	59 (66%)	31 (34%)	0.73 (0.21-2.51)	0.624
36-65	24 (47%)	27 (53%)	1.57 (0.44-5.62)	0.484
>65	7 (58%)	5 (42%)	Ref	
Gender				
Male	65 (57%)	50 (44%)	1.47 (0.68-3.17)	0.316
Female	25 (66%)	13 (34%)	Ref	
Comorbidities				
Diabetes				
Yes	6 (32%)	13 (68%)	3.64 (1.30-10.18)	0.014
No	84 (63%)	50 (37%)	Ref	
Cardiovascular diseases				
Yes	5 (50%)	5 (50%)	1.46 (0.56-4.06)	0.56
No	85 (59%)	58 (41%)	Ref	
HIV coinfection				
Yes	0 (0%)	6 (100%)		0.003*
No	90 (61%)	57 (39%)		
Type of admission				
Surgical	25 (56%)	20 (44%)	1.00 (0.33-3.00)	1
Medical	55 (61%)	35 (39%)	0.79 (0.28-2.20)	0.661
Obstetric	10 (56%)	8 (44%)	Ref	

*: Fischer's exact test used

In the multivariate logistic regression analysis of the predictors of mortality being diagnosed with VAP and having diabetes were considered for the multivariable logistic regression and having diabetes mellitus as comorbidity Was independently associated with mortality whereas there was a trend for presence of VAP but without a statistical significance (OR=3.30, 95% CI: 1.16-9.35; p=0.024) (Table 10).

Table 10: Multivariate analysis of the predictors of mortality

Predictors	AOR	95% CI	P value
Diagnosed with VAP			
Yes	1.65	0.84-3.21	0.141
No	1		
Diabetes			
Yes	3.30	1.16-9.35	0.024
No	1		

CHAPTER V: DISCUSSION

In this study, of153 patients followed during the study period 74(48%) patients developed Ventilator associated pneumonia, with incidence of 44 per 1,000 ventilator-days. CPIS of ≥ 6 scores was linked with probability of ventilator associated pneumonia diagnosis at 72% sensitivity and 85% specificity(20). The incidence density revealed in this study is to high when we compare to a narrative review of VAP in adults, patients which showed lower incidence density of 1-2.5 cases per 1000days in North American hospitals and the rate of 18.3 per 1000 ventilator days (10).compare to the other study done in Indian's ICU, of 105 participants were recruited,60(57.14%) of them developed VAP with incidence density of 31.7/1000 ventilator days(21).Another study conducted in India for a duration of 1 year, of 267 patients,74(27.71%)had VAP with high incidence of 39.59per 1000 ventilator days(17).dissimilarity of the incidence can be assigned to difference in number of study population and less duration, use of preventive strategies where there are insufficient staff with limitation of resource to accomplish preventive bundles.

This study showed that VAP is more likely to occur in first two weeks on mechanical ventilation, where at day3, 12 patients had VAP, at day4, 14 patients had VAP and 18patients on day5; it is similar to the another prospective cohort study carried out in ICUs of 4 hospitals in Athens, Greece during period of six months where 175 patients enrolled, 56 (32%) patients developed ventilator associated pneumonia during ICU stay, and their onset of VAP were similar to us. (22).

The results of this research revealed that it exists statistical significant difference in the compliance of triple bundle (oral care, sedation cessation and bed head elevation between 30-45 degree) according to VAP diagnosis where patients who were not diagnosed with VAP had high mean compliance bundle score of 63% compared to 38% from patients who were diagnosed with VAP ($p<0.001$).These are in line with other different studies and guideline which showed that application of ventilator prevention bundle are the most import in prevention ventilator associated pneumonia(23)(24)(25). Data abstracted from 3RCTs analyzing semi recumbent 45^{o} and 4RCTs analyzing the prone position ,ventilator associated pneumonia were lower between 45^{o} contrasting to the patients at 0^{o} (OR0.47,95%CI ,0.27-0.82,337patients) (13).

About reduction of VAP when the bundle is applied is justified by its role in prevention of aspirated secretions nearby the endotracheal cuff which lead into bacteria colonization of lower respiratory tract(26). In addition to the colonization of bacteria some content of gastric juice aspirated involved in pathogenesis as it is a pro-inflammatory ,leading to an increase of histologic lung parenchyma damage.(26). The bundle is the most clinical important to reduce the incidence of VAP; consequently, reduce its complication and the cost. There for a well-organized training and education on VAP prevention bundle among health care provider is requested so that they can understands the impact of applying these bundle.

The present research revealed that patients with intra-abdominal sepsis were 2.9xmore apparently to develop VAP ventilator associated pneumonia than those who did not intra-abdominal infections (OR:2.92; 95%CI: 1.27-6.69; P=0.011) in binary logistic regression but not independent factor for VAP in multivariable logistic regression. Compare to the other study revealed that hospital acquired Peritonitis were independent factor for VAP (OR: 2.873; CI95% 1.299-6.369; P=0.009).(27).HAI are associated with microorganism with antibiotic resistance resulting to prolonged ICU stay and long period on of MV, resulting to VAP. Large number of sample size and study period reflect dissimilarity.

In this study Female patients were 3.1times more likely to have VAP compared to male patients. This is difference to other different studies, a prospective cohort study among 277785 hospital admissions showed that the female gender had a lower incidence of ventilator associated pneumonia(28).Another study also which involved 854 patients showed females develop less VAP but with an increase in mortality rate. (29). This discrepancy may have justified by the fact that in Rwanda there is more old women compared to male. As the advance in age goes with the decrease in immunity, it makes the female susceptible to the VAP.

Patients who received H2 antagonists are 6.75x more apparently to develop VAP compared to those who received PPI. Contrasting with to the large prospective cohort study carried out during 14years of follow up in China among 4940 patients with diabetes showed that the use of protons pump inhibitor was 1.70fold unsafe (30). Another study conducted in China showed that the combination of H_2receptors antagonist and protons pumps inhibitor was the risk of VAP(31).The pneumonia observed in the presented study may be due to aspiration of gastric content which contain gastric acid and cause alveoli inflammation while among the patients who received PPI, there is alkalization of the gastric content and the growth the bacteria which cause the bacteria when aspirated.

The median(days) (IQR) length of stay in ICU 8 (5-11) for patient without VAP while for the patients with VAP was 9 (6-14), (p=0.021). longer stay in ICU; longer duration on mechanical ventilation with increased risk of VAP.

The mortality revealed in this research was not statistically linked to the VAP. It was associated with comorbidity namely diabetes and HIV. This is different to a prospective observation study conducted in clinical university hospital of Valladolid in Spain in the period of May 2008 to May 2015 among 418 patients which showed that VAP is independents factor associated to mortality. The sample size was small to detect statistical significant, this discrepancy may be described by small sample size which not enough to detect this effect. This mortality is not to high when compared to the prospective cohort study conducted in northern Brazil to describe the epidemiology and outcomes of VAP, it showed the higher mortality of 78.l8% among 26.2% cases who were diagnosed with VAP(32). This discrepancy may have justified by the fact that Brazil has the population with more comorbidity when compared to Rwanda. The revealed mortality rate is very closer to the research done in Spain during the period of May 2008 to May 2015 which showed the mortality rate of 47.5% among the patients diagnosed with VAP(33).

VI.CONCLUSION AND RECOMMMENDATIONS

In the present study the higher incidence per ventilator days of ventilator associated pneumonia was patients attending ICU/CHUK predicted by poor compliance to ventilator associated pneumonia prevention bundle, female gender, and used of H2 antagonists as gastric ulcer prophylaxis.

These was a course of high intensive care unit mortality among patients with VAP.

RECOMMENDATIONS:

1. Monitor the occurrence of VAP and compliance with simple but efficient strategies such as triple bundle (sedation cessation, oral care and bed head elevation at 30 -45^{o})
2. Consider female patients at higher risk than male
3. Use PPI for gastric ulcer prevention
4. Conduct a research with a bigger and sufficient sample size to determine the impact of VAP on ICU patient’s outcome

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Appendix 1: QUESTIONNAIRE

TITLE: DATA COLLECTION FORM

SECTION A. SOCIAL DEMOGRAPHIC DATA and clinical characteristics

CODE/ID Number: Date:

Age: …… Gender: M/F

Admission Date: …

Intubation date…. Discharge Date: … diagnosis……. Comorbidities…….. PPI….H2 antagonist…….

SECTION B.VAP DIAGNOSIS (√ will be used to mark the available value every day and used to mark diagnosed VAP)

every day and used to mark diagnosed VAP)

Criteria	**Value**	**points**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**
Tracheal secret-ions	**Rare**	**0**															
	Abundant	**1**															
	Abundant purulent	**2**															
CXR	**No infiltrate**	**0**															
	Diffuse	**1**															
	Localized	**2**															
temperature	**`≥36.5ºc and ≤38.4ºc**	**0**															
	≥38.5ºc and ≤38.9ºc	**1**															
	≥39ºc and ≤36ºc	**2**															
PaO_2/FIO_2	**>240 or ARDS**	**0**															

	≤240 and no evidence of ARDS	**2**															
WCC	**≥4000 and≤11000**	**0**															
	<4000 and >11000	**1**															
	<4000 and >11000+ band forms ≥500	**2**															
Tracheal culture	**Negati-ve**	**0**															
	Positive	**2**															
TOTAL POINTS	**12points/12 points**																
VAP diagnosed if CPIS ≥6 points			**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**

SECTION C. RISK FACTORS (use to mark what is done every day)

SECTION. D: OUTCOME (use to mark what happens)

1.Tracheostomy: **1 2 3 4 5 6 7 8 9 1 0 11 12 13 14 15**

2.Lenght of ICU stay in days

3.Recovery **Y/N**

4.Dischaged **Y/N** **5. Died Y/N**

The number above define the days ,from day1 to day v

Risk factors	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15

sedation	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N
Bed head elevation at 30 to 45^{o}	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N
Oral care	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N
reintubation	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N

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Appendix 2: INFORMED CONSENT FORM

Please read this consent form document before you decide to participate in the study. The researcher will answer all questions you have before signing consent.

Study Title:

RISK FACTORS AND OUTCOME IN PATIENT WITH VENTILATOR ASSOCIATED PNEUMONIA IN ICU AT CHUK

Study Purpose and participant's selection: Assessment of risk factors and outcome in patients with ventilator associated pneumonia will help health care providers to take measures on preventive strategies against ventilator associated pneumonia in ICU. The participants will be the patients admitted in ICU who are intubated and mechanically ventilated above 48 hours and who have the age above 18 years old.

. Procedure: The study will be prospective cross sectional observational study from January 2021 to May 2022, where The participants will involve in allowing identifications data collection including age and gender ID number, the information about time of admission, discharge and length of ICU stay, determination of ventilator associated pneumonia risk factors; with also its diagnosis. Also, the study will include the evaluation of outcome including tracheostomy, duration on mechanical ventilation and mortality rate.

Potential risks of participating: risks of participation in this study are no more than everyday life.

Potential benefit of participating: the benefit maybe directed to the participants themselves or mostly applicable on other patients who may be admitted in ICU for future.

Compensation: The participation in the study in not offered.

Confidentiality: The confidentiality will be assured as the identity of every participant will be assigned to a code number. The list containing every participant information will be locked in secured cupboard. While the study is completed and the data analyzed, the list will be destroyed. Your name will not be used in report of my study.

Voluntary participation: your participation in the study is absolutely voluntary and no penalty for not participating. You are free to ask any question and get the answer regarding the study. You have right to withdraw from the study at any time. All information above was given to the next of kin in case where the participant unable get information depending on disease condition so that may agree that his or her patient may participate in the study.

To whom you may contact about your rights as research participant when you want clarification,

UR/CMHS ethics committee:

Chairperson of the CHMS IRB:0788490522

Deputy Chairperson:0783340040

Chairperson of Ethics Committee at CHUK: 0785466254

Primary Investigator:

DushimimanaVestine

Tel: 0782736118

E-mail: vesdushime91@ gmail.com

I have read the procedure described above. I voluntarily agree to participate in the study and I have received a copy of description.

Participant signature:_____ Date_____

or

Next of Kin of participant:_____ Date_____

Principal investigator signature:_____ Date_____

KWEMERA GUKORERWAHO UBUSHAKASHATSI

Soma iy'inyandikombereyokwemeragukorerwahoubushakashatsi

Umutwew'ubushakashatsi:

IMPAMVU ZITERA KUGIRA UBWOKO BW'UMUSONGA BUFATA ABARWAYI BASHYIZWEMO UDUPIRA TUBAFASHA GUHUMEKA NDETSE NO KUREBA UMUSARURO CG INGARUKA ZIJYANYE NIYO NDWARA MU IZU Y'INDEMBE CHUK

Icyoubushakashatsibugamijen'Uburyoabemerakubukorerwahobatoranwa:

Ububushakashatsibugamijegusuzumaimpamvuziterakugiraubwokobw'umusongabufataabarwayibashyizwemoudupiratubafashaguhumekandetse no kurebaumusaruro cg ingaruka zijyanye niyondwara.Ibyo byose bigamije kuzafasha abaganga mugufata ingamba zo kwirindauwo musonga mu abarwayi barwariye mu inzu zindembe

.Abazakorerwahoubushakashatsibagombakubabarengejeimyakay'ubukure 18;kandi bamaze amasaha arenga 48 ,baba shizemo agapiraka bafasha guhumeka.

Ukobuzakorwa:

Ububushakashatsi buzakorwa dukurikirana abarwayi bari mu inzuy'indembe CHUK kuvaMutarama/2021kugezaGicuransi/2022.tuzafata umwirondoro waburi murwayi uzakorerwaho ubushakashatsi,tuzare baigihe azamara mubitaro,tuzare ba izompamvu zatuma agira uwo musongandetse ningaruka cg umusaruro umurwayi abonamo.

Ingaruka cg ibyagobyabamo: Ntabyagobirimo.

Inyunguzagaragaramo: Inyungu zishobor akuboneka kubazaba baragaragaye mubushakashatsi cg se zikaza garagaraku bandibarwayi bigihe kizaza.

Ibihembo: Ntamafaranga cg ibindibihembo Bihari.

Ibanga: Ibangarizabikwa, amakuruazabikwahifashishijwe code kandihazifashihwaakabati.

Ubushake mu ubushakashatsi: Kugirauruhare mu bushakashatsi ni ubushake, wemerewe kubaza ikibazocyosekandiukakiboneraigisubizo.

Igihe icyo aricyocyose wemerew eguhagarika ubushakashatsi.

Abo wakwifashisha kubijyanye no gusobanukirwa uburenganzirabwawe.

UR/CMHS ethics committee:

Chairperson of the CHMS IRB:0788490522

Deputy Chairperson:0783340040

Chairperson of Ethics Committee at CHUK: 0785466254

Primary Investigator: DushimimanaVestine

Tel: 0782736118

E-mail: vesdushime91@ gmail.com

Nasomyenezaamabwirizaajyanyen”ubushakashatsi ,ndemerakugiticyanjyekubugiramouruhare.

Umukonow;umurwayiitariki _____ _____

cg

umukonow’umurwaza: _____ itariki_____

Ukoraubushakashatsi: _____ itariki _____

Appendix 3.IRB APPROAVAL / ETHICS COMMITTEE CHUK

CMHS INSTITUTIONAL REVIEW BOARD (IRB)

Kigali, 29th /September /2021

Dr Dushimimana Vestine
School of Medicine and Pharmacy, CMHS, UR

Approval Notice: No 306/CMHS IRB/2021

Your Project Title ***"Risk Factors and Outcome in Patients with Ventilator Associated Pneumonia in ICU at CHUK "*** has been evaluated by CMHS Institutional Review Board.

Name of Members	**Institute**	**Involved in the decision**		
		Yes	No (Reason)	
			Absent	**Withdrawn from the proceeding**
Prof Kato J. Njunwa	UR-CMHS	X		
Dr Stefan Jansen	UR-CMHS	X		
Dr Brenda Asiimwe-Kateera	UR-CMHS	X		
Prof Ntaganira Joseph	UR-CMHS	X		
Dr Tumusiime K. David	UR-CMHS	X		
Dr Kayonga N. Egide	UR-CMHS	X		
Mr Kanyoni Maurice	UR-CMHS		X	
Prof Munyanshongore Cyprien	UR-CMHS	X		
Mrs Ruzindana Landrine	Kicukiro district		X	
Dr Gishoma Darius	UR-CMHS	X		
Dr Donatilla Mukamana	UR-CMHS	X		
Prof Kyamanywa Patrick	UR-CMHS		X	
Prof Condo Umutesi Jeannine	UR-CMHS		X	
Dr Nyirazinyoye Laetitia	UR-CMHS	X		
Dr Nkeramihigo Emmanuel	UR-CMHS		X	
Sr Maliboli Marie Josee	CHUK	X		
Dr Mudenge Charles	Centre Psycho-Social	X		

After reviewing your protocol during the IRB meeting of where quorum was met and revisions made on the advice of the CMHS IRB submitted on 29th September 2021, **Approval has been granted to your study.**

Please note that approval of the protocol and consent form is valid for **12 months**.

You are responsible for fulfilling the following requirements:

1. Changes, amendments, and addenda to the protocol or consent form must be submitted to the committee for review and approval, prior to activation of the changes.
2. Only approved consent forms are to be used in the enrolment of participants.
3. All consent forms signed by subjects should be retained on file. The IRB may conduct audits of all study records, and consent documentation may be part of such audits.
4. A continuing review application must be submitted to the IRB in a timely fashion and before expiry of this approval
5. Failure to submit a continuing review application will result in termination of the study
6. Notify the IRB committee once the study is finished

Sincerely,

Date of Approval: The 29th September 2021

Expiration date: The 29th September 2022

Dr Stefan Jansen
Ag. Chairperson Institutional Review Board,
College of Medicine and Health Sciences, UR

Cc:

- Principal College of Medicine and Health Sciences, UR
- University Director of Research and Postgraduate Studies, UR

11th Jan,2022 *Ref.:EC/CHUK/001/2022*

Review Approval Notice

Dear VESTINE DUSHIMIMANA,

Your research project: ***"RISK FACTORS AND OUTCOME IN PATIENTS WITH VENTILATOR ASSOCIATED PNEUMONIA IN ICU AT CHUK "***

During the meeting of the Ethics Committee of University Teaching Hospital of Kigali (CHUK) that was held on 11th Jan,2022 to evaluate your request for ethical approval of the above mentioned research project, we are pleased to inform you that the Ethics Committee/CHUK has approved your research project.

You are required to present the results of your study to CHUK Ethics Committee before publication by using this link:www.chuk.rw/research/fullreport/?appid=492&&chuk.

PS: Please note that the present approval is valid for 12 months.

Yours sincerely,

ETHICS COMMITTEE
CHUK

Dr Emmanuel Rusingiza Kamanzi
The Chairperson, Ethics Committee,
University Teaching Hospital of Kigali

Scan code to verify.

" University teaching hospital of Kigali Ethics committee operates according to standard operating procedures (Sops) which are updated on an annual basis and in compliance with GCP and Ethics guidelines and regulations "