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DISSERTATION

TITLE: HOSPITAL ACQUIRED INFECTIONS IN THE INTENSIVE CARE UNIT AT KIGALI UNIVERSITY TEACHING HOSPITAL, A RETROSPECTIVE STUDY.

Submitted for partial fulfillment of the requirements for a Master's Degree in anesthesiology and critical care (MMed).

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Done at Kigali, August,2022

DECLARATION

I hereby declare that this dissertation: Hospital acquired infection in the intensive care unit at university teaching hospital, a retrospective study" is my own work.

This study in whole or in party has neither been submitted for publication anywhere nor has been submitted for the award of degree in any other university.

Signed.   Date. 25th August 2022

Dr Jean HABIMANA

I hereby declare that this dissertation has been submitted with my approval as the supervisor.

Signed………………………… Date 31st Augst

Dr Francoise NIZEYIMANA

DEDICATION

To God the Almighty for whom I owe my existence, for his love and blessings.

To beloved my parents and my in low parents

To my beloved wife: Ange IRAKARAMA BANDORA for her love and support.

To my Son: CYOMORO Shimwa Kai Owen Ryan for his blessings brought into my life.

To my siblings especially my Brother Dominique HARINDINTWARI for his great Support.

This work is dedicated.

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ABSTRACT

Background and objectives: According to WHO (World Health Organization), Hospital Acquired Infection (HAI) is an infection that is not typically present at the time of admission, and acquired after hospitalization then manifests after more than 48 hours. Patients in ICU (Intensive Care Unit) are at high risk of getting hospital acquired infections at a rate of 3-5 times compared to general ward. The antimicrobial resistance is high in both low- and middle-income countries. The mortality rate of HAI in ICU exceeds 40% word wide. Data is still low in Rwanda especially ICUs and This is the reason of our study. Our aim is to evaluate the incidence of ICU hospital acquired infection, the common types, the common isolated organisms and related antibiogram.

Methods: We conducted a retrospective observational descriptive study of patients admitted to the adult ICU-HDU (High dependency Unit) at CHUK (Kigali University Teaching Hospital) for a duration of 12 months. Data were collected on patients' characteristics and demographic profile, primary diagnosis of admission, isolated microorganism, the sample source and antimicrobial resistance pattern. All were recorded from ICU logistic book, patients 's medical files and open clinic to data collection sheet. Data were analyzed using Microsoft excel. Pediatric patients and those with active HAI at the time of ICU-HDU admission were excluded.

Results: Total patients found were 309, female 51.9% and male 48.1%, 15% were above 65 years. Most primary admitting diagnosis was trauma at 24%. 98% of patients had urinary catheter, 75% were intubated, 66% were surgical patients, and 36% had a central line placed. The incidence of adult ICU HAI was 21.68% with VAP (Ventilation Associated Pneumonia) as the most common type (63.85%) followed by CAUTI (Catheter Associated Urinary Tract Infection) (15.66%), PBSI (Primary Blood Stream Infection) (13.85%). The incidence density of VAP was 19.0 per 1000 patient-days and that of CAUTI was 2.7 per 1000 patient-days. In general, the most causative organism of HAI was *Klebsiella pneumonia* followed by *Pseudomonas aeruginosa* and Acinetobacter. Other identified organisms were *Escherichia coli*, *Proteus mirabilis*, *Staphylococcus aureus*, *Providencia*, *Citrobacter* and *Enterococcus*. The most common cause of VAP was *K. pneumonia* followed by *P. aeruginosa* then *Acinetobacter*. The most common cause of CAUTI was *K. pneumonia* followed by *Acinetobacter*. The most common cause of PBSI was *K. pneumonia* followed by *S. aureus*

then *E. coli* and *Acinetobacter*. Generally, the antimicrobial resistance rate was more than 50% in all tested antibiotics except carbapenem, nitrofurantoin, amikacin, and chloramphenicol.

Conclusion: The incidence of HAI and antimicrobial resistance in ICU of CHUK is high compared to the population in general wards as well as ICU patients of developed countries. The most common type is VAP. *K. pneumonia* is the most isolated microorganism. We recommend to strengthen the implementation of the existing infection prevention and control (IPC) guidelines in order to reduce the rate of HAI in ICU of CHUK. This implementation can be achieved by regular training of the staff about IPC, increasing the critical care specialized staff and decreasing their workload. Lastly, we suggest further studies with larger sample size and prospective method to be conducted in the future.

Key words: Intensive care unit, hospital acquired infection, incidence, types, microbial organism, antimicrobial resistance., Kigali university teaching hospital.

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LIST OF ABREVIATIONS

BUTH: Butare University Teaching Hospital

CAI: Community Acquired Infection

CAUTI: Catheter Associated Urinary Tract Infection

CDC: Center for Diseases Control

CDI: Clostridium Difficile Infections

CLABSI: Central Line-Associated Bloodstream Infections

GCS: Glasgow Coma Scale

GIT: Gastrointestinal Tract

HAI: Hospital Acquired Infection

HAP: Hospital Acquired Pneumonia

HDU: High Dependent Unit

HIV: Human Immunodeficiency Virus

LCBI: Laboratory Confirmed Bloodstream Infection

LOS: Length of Stay

ENT: Ear, Nose and Throat

CHUK: University Teaching Hospital of Kigali

KFH: King Faisal Hospital

ICU: Intensive Care Unit

IV: Intra Venous

IPC: Infection Prevention and Control

MOH: Ministry of Health

RMH: Rwanda Military Hospital

SBP: Systolic Blood Pressure

PBSI: Primary Blood Stream Infection

UK: United Kingdom

USA: United State of America

UTI: Urinary Tract Infection

VAP: Ventilation Associated Pneumonia

WHO: World Health Organization

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CHAPTER ONE: INTRODUCTION

1. 1. BACKGROUND/PROBLEM

A Hospital Acquired Infection (HAI) is an infection that is not typically present at the time of admission, is acquired after hospitalization, and manifests after more than 48 hours(1) . The most important nosocomial infections in the Intensive Care Unit (ICU) are Central Line Bloodstream Infections(CLBSI), ventilator-associated pneumonia (VAP) and catheter-associated urinary tract infections (CAUTI) (2). Patients in ICU are at high risk of getting hospital acquired infections at a rate of 3-5 times compared to general ward (2) and the prevalence of ICU HAI worldwide exceeds 25%(3). This is due to many reasons including the criticality and resulting immunosuppression of the patient's illness, increased antimicrobial agent use, prolonged hospital stays, and exposure to invasive therapeutic procedures such as endotracheal intubation, peripheral and central line cannulation, and urinary catheterization (2). In addition, poor hand hygiene due to work overload, poor education and training, and low staffing levels enhances the transmission of microorganisms from patient to patient (4). Hospital acquired infections lead to increases in cost of care and hospital period stay, as well as an increased mortality rate especially if the identified microorganism is multi-drug resistant (5).

The ICU incidence of HAI from an international multicenter study was 18.9% for patients admitted for more than 24 hours(6). Although the overall incidence in European and high income countries is low(3.7 patients per 100 admission),the ICU prevalence rate is still estimated at a higher values (19.2%) (7); In India, the incidence of ICU's HAI was estimated at 15.7%. Globally, according to WHO, the incidence of ICU-acquired infection among adult patients in low and middle income countries ranged from 4.4% up to 88.9% and pooled cumulative incidence density was 42.7 episodes per 1000 patient-days; while in developed countries this rate is 17 episodes per 1000 patient-days(8).

The most commonly identified type of infections is ventilation associated pneumonia (VAP) followed by catheter associated urinary tract infection (CAUTI), surgical site infection and then blood stream infections. The most common organism was *Klebsiella* (29%), followed by *Acinetobacter* (24%), *Pseudomonas* (9%), *Candida* (9%),

Staphylococcus (9%). The drug resistance to various antimicrobials was seen to a large extent among the pathogens that were isolated(9).

The morbidity and mortality rate of HAI in Asia ,Australia and the Middle even globally is 30%(10)(8). HAI is the one of the leading causes of death and it has a negative impact on both the health system and patient. These negative impacts include: Increased social economic burden due to direct medical costs and indirect medical costs related to diminished quality of life; prolonged ICU stay; hematological, biochemical, microbiological and radiological tests; medications; extra surgical procedures; increased duration of stay in hospital; additional morbidity and mortality rates; and physical and psychological suffering to the patient(11).

Studies and surveys have been conducted in Rwanda about HAI and were done in other settings than the ICU (pediatric wards, surgical ward or in general the whole hospital). These were not focused on ICU patients and again they have not shown the common sources and antimicrobial resistance demonstrated in the ICU(12) (13) . This is the principal reason for the following study: "Hospital acquired infection in the intensive care unit at CHUK, a retrospective study" and it will provide general information about the incidence of hospital acquired infections and common types and its antimicrobial resistance in Rwanda especially in ICU patients.

1. 2. LITERATURE REVIEW.

1. 2. 1. INTRODUCTION

According to WHO definition, HAI is an infection acquired in hospital by a patient who was admitted for a reason other than that infection, or an infection occurring in a patient in a hospital or other health care facility in whom the infection was not present or incubating at the time of admission (14).

It is a common condition among hospitalized patients and is associated with increased mortality (2). The prevalence of HAI in ICU in a study which has analyzed 88 countries was 22% and the mortality rate was 30% (10). In Rwanda the general mortality rate of in hospital sepsis is 51.4%(15). In some developing countries, the report from WHO of 2010 based on national surveillance showed the following general prevalence for HAI: 17.9% in Tunisia, 14.8% in Tanzania, and 13.9% in Malaysia(8).

The word wide prevalence of HAI by the WHO is estimated at 8.7%, with the most frequently cited locations being the ICU, acute surgical ward, and orthopedic wards (1). The most common source location was documented as surgical wounds, urinary tract

infections, and lower respiratory tract infections(1). Another analysis by the WHO from 1995 to 2010 showed that the incidence of ICU-acquired infections among adult patients in low- and middle-income countries ranged from 4.4% up to 88.9% and pooled cumulative incidence was 42.7 episodes per 1000 patient-days(8). Based on large studies from USA and Europe, HAI incidence density ranged from 13.0 to 20.3 episodes per 1000 patient-days and pooled cumulative incidence was 17.0 episodes per 1000 patient-days in adult high-risk patients in industrialized countries(8). A study conducted in Moroccan University Hospital in 2007 revealed a prevalence of HAI of 17.8% with the highest number in the ICU (50%), the most frequent source being urine(16).

There has not been enough research conducted on the incidence of HAI in middle and low income countries and, in general, the figure below illustrates this(8)(17).
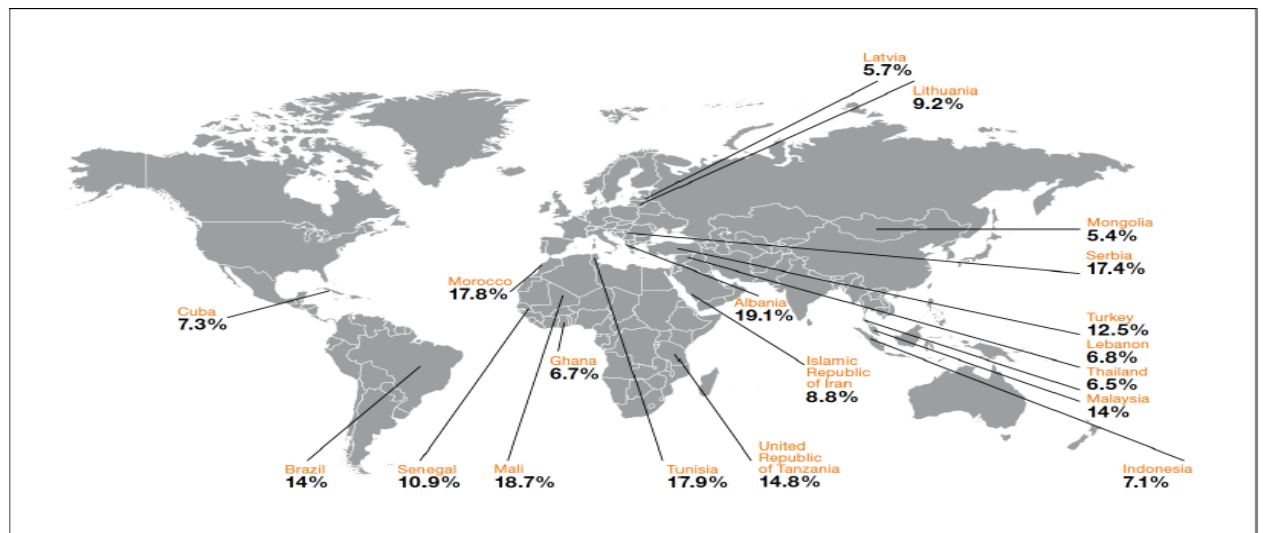
Fig 1.1. **incidence of healthcare-associated infection in low- and middle-income countries**(17)**.**

The prevalence of HAI in CHUK in 2016 was estimated as 15.1% with the highest rate found in ICU at 50% and the lowest in general ward at 12.1% (18).

One study conducted in Rwanda in 2018 at CHUK revealed the most isolated the microbes from blood as *Klebsiella* followed by *Escherichia coli* then *Staphylococcus aureus*; Each of those microbes was resistant to at least one of the 3rd generations cephalosporins; 8% of the *E. coli* present was resistant to imipenem; 82% and 6% of *Staphylococcus aureus* were resistant to oxacillin and vancomycin respectively(19).

1. **2. 2. EXISTING THEORY**

➢ **Hospital Acquired Pneumonia**

Hospital acquired pneumonia is a pneumonia which is developed after 48 hours and did not appear to be incubating at the time of hospital admission(20) and 90% of this is ventilation associated pneumonia (VAP)(17). VAP is a hospital acquired pneumonia which is developed usually 48h-72hours after endotracheal intubation(17). VAP is most commonly seen in ICU patients at an incidence of 9 to 27%(17), and it is associated with a high mortality rate. The cause is often endogenous microorganisms from the digestive system or nose and throat, but also can be exogenous like those from contaminated respiratory equipment(1). The definition of pneumonia is based on radiological changes, purulent septum, new onset of fevers, and more specifically by microbiological analysis with a positive culture(17). VAP is defined by radiologic changes with systemic inflammation (temperature ≥ 38 °C, or leukocyte count > 12,000 or < 4000 cells/ mL), clinical pulmonary signs (i.e. purulent tracheal secretions, bronchial sounds), an increase in ventilation settings from baseline(like PEEP, FiO2) (21), or simply by oxygenation deterioration, clinical signs/symptoms of infection and antibiotic use, and microbiology results(17). The most isolated organisms are *Staphylococcus aureus* (44%), *Acinetobacter baumanii* (30%), *Pseudomonas aeruginosa* (12%), *Stenotrophomonas maltophilia* (7%), *Klebsiella pneumoniae* (6%), and *Serratia marcescens* (2%)(22).

➢ **Catheter Associated Urinary Tract Infection (CAUTI)**

Urinary Tract Infection (UTI) is the most prevalent HAI worldwide and it accounts more than 30%(23).

The cause of CAUTI is due to the use of indwelling urinary catheter and is usually defined by microbiological criteria consisting of a positive, quantitative urine culture (more than 10^5 microorganisms/ml, with a maximum of two isolated microbial species)(20).The bacteria responsible usually arise from the gut flora, either normal (*Escherichia coli*) or acquired in hospital (multi-resistant *Klebsiella*)(1). The incidence is estimated at 3.1% to 6.4% of UTIs are associated urinary catheter(CAUTI) in ICU (24) and the development of an ICU-acquired UTI was more common in women (25).

➢ **Blood Stream Related Infection**

They are two main types of blood stream related infections: Primary bloodstream infection(Laboratory Confirmed Bloodstream Infection (LCBI) that is not secondary to an infection at another body site) and Catheter-associated bloodstream infections(central line catheters, peripheral lines catheter)(26). About 40% of nosocomial infections in ICUs are catheter related (27). It is a small proportion of HAI (approximately 5%) but case fatality rates are high with the most common identified organism being multi drug resistant coagulase-negative *Staphylococcus* and *Candida* species(1). Infection may occur at the skin entry site of the intravascular device, or in the subcutaneous path of the catheter. Colonization of a catheter infection may not exclusively manifest at the catheter insertion site(1). The common risk factors are the duration of catheterization, aseptic technique insertion level, and the frequency of catheter care(1).

➢ **Surgical Site Infection (SSI)**

The incidence of SSI varies from 0.5% to 15% depending on the type of surgery performed and the clinical status of the patient(1). SSI is clinically defined by purulent discharge around a wound or spreading cellulitis from a wound. It is acquired either during the operation from an exogenous source (e.g. from the air, medical equipment, surgeons and other staff) or endogenously from the flora on the skin, operative site, or, rarely, from blood used in surgery(1).The most identified pathogen is *E.coli*(20).

➢ **Clostridium Difficile Infections (CDIs)**

Clostridium difficile infection is a leading cause of nosocomial infection in adult associated diarrhea at a rate of 12.1%(28)(29). This is due to the clostridium difficile which is found in intestinal tract of human and animals, but its spores are also ubiquitous in the environment. It can remain infective on contaminated surfaces for a long period of time, as well as being the most resistant to disinfection(1). It is found in 1 of every 30 healthy adults(1).

1. 2. 3. COMMON SOURCES AND ORGANISMS INVOLVED IN HAI.

Common sources of HAI are from urinary tract infection, respiratory tract infection, blood stream related infection, surgical site infection and others like soft tissue skin, ENT, GIT, and endometritis as it is illustrated on the below diagram from WHO report(1).
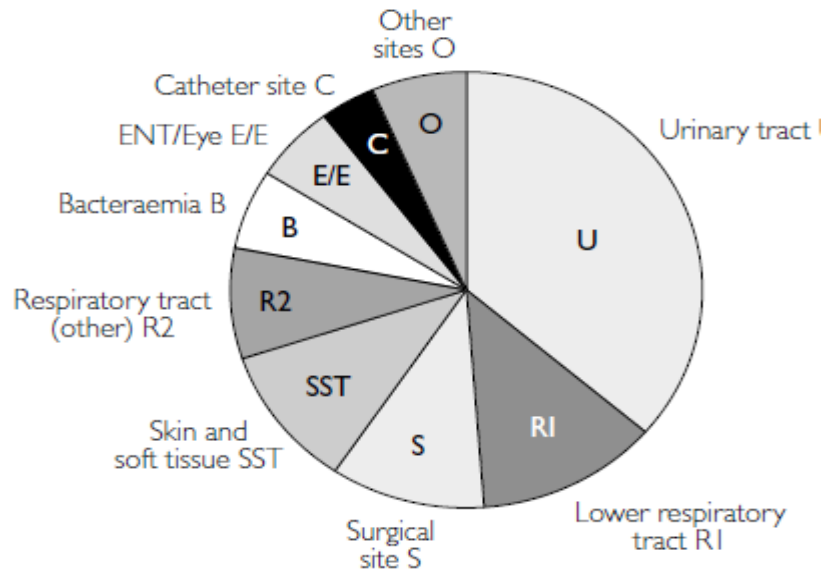
Fig1.2. Sites of the most common nosocomial infections

Microorganisms involved are mainly commensal bacteria (normal flora like cutaneous coagulase negative staphylococci and E coli) and pathogenic bacteria: anaerobic gram-positive rod (clostridium), gram positive bacteria like staphylococcus aureus, gram negative bacteria like Enterobacteriaceae (Escherichia coli, Proteus, Klebsiella, Enterobacter, Serratia marcescens); gram negative bacteria like Pseudomonas spp. Other uncommon microbes are parasites (Giardia lamblia), fungi (Candida albicans, Aspergillus spp., Cryptococcus neoformans, Cryptosporidium) and viruses (hepatitis B and C viruses respiratory syncytial virus (RSV), rotavirus; HIV, Cytomegalovirus, Ebola, influenza viruses, herpes simplex virus, and varicella-zoster virus(1).

Class of micro-organism	Organism	Pathogenicity in hospital patients[a]		
Gram-positive cocci	Staphylococcus aureus	P	(C)	
	Other staphylococci and micrococci		C	
	Streptococci group A	P		
	Streptococci group B		C	
	Streptococci groups C & G	P	(C)	
	Enterococci		C	
	Other nonhaemolytic streptococci		C	
	Anaerobic cocci		C	
Anaerobic bacilli	Histotoxic clostridia		C	
	Clostridium tetani		C	
	Nonsporing Gram-negative bacilli		C	
Gram-negative aerobic bacilli	Enterobacteria: Salmonella, Shigella, enteropathogenic Escherichia coli	P		
	Other Escherichia coli, Proteus, Klebsiella-Serratia-Enterobacter		C	
	Pseudomonas aeruginosa, other pseudomonads		C	
	Flavobacterium meningosepticum		C	
	Acinetobacter		C	
Other bacteria	Corynebacterium diphtherae	P		
	Listeria		C	(O)
	Mycobacterium tuberculosis	P		
	Anonymous mycobacteria			O
	Bordetella pertussis	P		
Viruses	Hepatitis	P		
	Smallpox, vaccinia	P		
	Chickenpox	P		(O)
	Influenza and other respiratory viruses	P		
	Herpes simplex	P	(C)	(O)
	Cytomegalovirus	P	(C)	(O)
	Measles	P		
	Rubella	P		
	Rotaviruses	P		
Fungi	Candida		C	(O)
	Nocardia			O
	Moulds		C	
	Histoplasma, Coccidioides, Cryptococcus	P		(O)
Other	Pneumocystis			O
	Toxoplasma	P		(O)

[a] P = "conventional" pathogen; causes clinical disease in healthy persons.

C = "conditional" pathogen; causes significant disease only in presence of specific predisposing factor.

O = "opportunistic" pathogen; causes generalized disease, but only in patients with profoundly diminished resistance to infection.

(C) = chance or severity of infection greatly increased in predisposed persons.

(O) = gives generalized infection rarely except in patients with profoundly diminished resistance.

Table1.1. Major microbial causes of hospital-acquired infections (30)

1. 2. 4. EMPIRICAL REVIEW

In general, HAI are major challenging infections in high, middle and low income countries especially in intensive care units(31). Sugata Dasgupta et al (2015) finds that in the ICU of a tertiary teaching hospital in Eastern India the overall incidence of HAI was 11.9% with pneumonia as the top cause, followed by UTI and blood stream infections related central venous catheters(32).The time series data from the WHO conducted from 1995 to 2009 and published in 2010 revealed the incidence of ICU acquired infection to range from 4.4% to 88.9%(8).

Similar results were found by İlhami ÇELİK et al in their 2005 prospective study in the ICU of Firat Tip Merkezi (Turkey). It shows an incidence of 72% with VAP (41.2%) most common, followed by UTI (28.2%)(33). In 2019, study done at CHUK by Tori Sutherland et al on antimicrobial resistance among bacterial infection in Rwanda revealed that 43.4% of infection were from wound, 23.2% from urine, 17.9% from blood, and 15.4% from sputum(34).

According to İlhami ÇELİK et al, the microbial organisms prevalence isolated in HAI was Pseudomonas aeruginosa (31.3%) followed by *Staphylococcus aureus* (11.5%).

Referring to the study of Edhem Unver et all done in 2019 in Turkey on microbial organisms causing VAP, the most isolated pathogens in VAP was *Acinetobacter*(62.2%) followed by *Pseudomonas*(17.9%)(35). In the study conducted by Umer Ul Haq et al in Pakistan in 2016 on microbial organism and antimicrobial sensitivity in VAP found that the most isolated microorganism was Pseudomonas aeruginosa (25%) followed by *Methicillin staphylococcus aureus*(MRSA) (18.9%), *Klebsiella* (15.6% , *Actinobacter* (13.3%)(36). Similar study done by Maebed et al in United Kingdom 2019 showed the most prevalent isolated microorganism in VAP as *Klebsiella*(45%) followed by *Acinetobacter*(11.6%)(37). Aarti Sangale et al in 2021 did the similar study and found the most isolated pathogen from VAP as *Acinetobacter baumannii* (38.7%) followed by *Pseudomonas aeruginosa* (17.5%) and *Klebsiella pneumoniae* (16.6%)(38).

According to Mahabubul et al in 2019, Escherichia coli was the commonest isolated pathogen in CAUTI followed by *Proteus, Pseudomonas, Klebsiella*(39);The almost similar results were found by Sunzida Arina et al in their study conducted in 2017 in Bangladesh where they found the most common isolated organism as *Escherichia coli* (38.93%) by *Pseudomonas* (15.98%), *Klebsiella* (8.61%), *Proteus* (7.38%) *Enterobacter*(6.56%) and *Acinitobacter* (1.22%)(40). Mohd Saleem et al in their study conducted in Soud arabia in 2021 and Reham Ramadan et al in their study conducted in Egypt in year 2018 on catheter associated urinary tract infection in ICU showed that the predominant microorganism in CAUTI was Klebsiella pneumoniae (20%)(41)(42).

Referring to Ambroselli et al in their study conducted in Argentina in 2018, the most isolated causative pathogen of blood stream infection was E. coli followed Pseudomonas aeruginosa, Klebsiella and Acinetobacter baumanni(43). Kumar et al in ICU of Indian tertial hospital in 2017 showed that Escherichia coli, Acinetobacter spp., Klebsiella pneumoniae, Pseudomonas aeruginosa, Staphylococcus aureus and Enterococcus spp. were most commonly encountered in blood stream infection(44). Cortes et al in their study

conducted in different hospital of Colombia in 2008 showed that *Staphylococcus aureus*(12.3%), *Klebsiella pneumoniae*(8.2%), *Escherichia coli* (5.7%), *Acinetobacter baumannii*, (4.0%) and *Pseudomonas aeruginosa* (3.8%) were the most isolated microorganisms from bacteremia(45). In Rwanda tertiary hospital precisely CHUK, Habyarimana et al in their study called bacteriological profile and antimicrobial susceptibility patterns of bloodstream infection found that the most prevalent pathogens were *Klebsiella pneumoniae* (31.7%) and *Staphylococcus aureus*(29.3%)(19).

According to the study done by Ambroselli et al in Argentina for surgical patients in 2018, the most isolated microorganism as cause of SSI was Staphylococcus aureus (82.35%)(43). In the study done by Begum et al in Bangradesh surgical wards in 2015 found that the most isolated microorganism was *E.coli*(29.41%) followed by *S. aureus*(27.45%),*P. aeruginosa* (29.85%), and *Acinetobacter*(11.94%)(46). In the study conducted by Negi et al in India 2013 showed the most isolated microorganism from SSI as *Staphylococcus aureus* (50.4%) was the commonest organism followed by *E.coli* (23.02%), *P. aeruginosa* (7.9%) and *Citrobacter species* (7.9%)(47).In 2019 , Mukagendaneza et al conducted the study on SSI in surgical ward patients of CHUK and the most isolated microorganism in this study was Klebsiella (55%), followed by *Escherichia coli* (15%),*Proteus* (12%), *Acinetobacter* (9%) and *Staphylococcus aureus* (6%)(48).

According to İlhami ÇELİK et al, Methicillin resistance was 96% within staphylococci populations(33). Afroz at al in Bangradesh (2017) showed that Colistin has sensitivity to *Klebsiella pneumonia*, *Acinetobacter baumanii* and *Escherichia coli* range from 76 to 100% while almost all other isolates were observed multi drug resistant(49). In 2015, Ntirenganya et al conducted a study on antimicrobial resistance among tertiary hospital of Rwanda from medical wards of CHUK and found that 31.4% were E coli and 58.7% were *Klebsiella* and respectively were resistant to at least one of the third generation cephalosporins, while 8% of E coli were resistance to imipenem, 82% and 6% of Staphylococcus aureus strains were oxacillin and vancomycin resistant respectively(50). In 2019, the study done at CHUK by Tori Sutherland et al showed that Gram-negative bacteria comprised 88.7% of all isolates and 75.9% of them were resistant to ceftriaxone(34).

Another study conducted in Rwanda in 2020 by Muvunyi et al in surgical patients showed that the most common isolated microorganisms were *Escherichia coli* (42%), *Staphylococcus aureus* (18%), and *Klebsiella pneumonia* (15%) and 74% of HAI were resistant to third generation cephalosporins(20).

1. 2. 5. **PROBLEM STATEMENT.**

Many similar studies have been conducted in different countries relating to HAI incidence, sources, and antimicrobial in ICU settings. In Rwanda, we found many studies conducted on antimicrobial agents and incidences, but neither of these studies was focused on ICU patients. This study aims to reveal the incidence, common types of infections, most isolated microbial organisms and antimicrobial resistance specifically present in the ICU at CHUK in Rwanda.

1. 3. AIM AND OBJECTIVES.

1. 3. 1. PRIMARY OBJECTIVE.

To determine the incidence of hospital acquired infection among patients admitted to the intensive care unit (ICU) in CHUK.

1. 3. 2. SPECIFIC OBJECTIVES.

i.   Identify the common types of hospital acquired infections
ii.   Identify the most isolated microbial organisms and related antibiogram.

1. 4. RESEARCH QUESTIONS.

i.   What is the most common type of HAI?
ii.   What is the most isolated microorganism among patients admitted to the ICU at CHUK?

1. 5. HYPOTHESIS.

i.   The most common hospital acquired infection in ICU of CHUK is VAP.
ii.   The most isolated microorganism among patients admitted to the ICU of CHUK with HAI is *Klebsiella pneumonia.*

CHAPTER TWO. METHODOLOGY

2. 1. STUDY DESIGN

This is an observational, descriptive, retrospective study of patients admitted to the ICU and HDU at CHUK for at least 48 hours without any active hospital acquired infection at the time of ICU or HDU admission.

2. 2. STUDY SETTING AND LOCATION

Study was conducted in Rwanda, specifically in the intensive care unit of Kigali University Teaching Hospital for a period of one year (12months), from 1st October 2020 to 30th September 2021.

The ICU of CHUK has 8 beds and 4 beds of HDU and the patient turnover is estimated between 23 to 30 patients per month. The ICU receives patients from the Emergency Department, Obstetrics and Gynecology, Surgery, Trauma, Medical, and sometimes Pediatrics.

2. 3. PATIENT POPULATION

All patients admitted in ICU and HDU /CHUK during the mentioned period of study.

2. 4. INCLUSION CRITERIA

Patient admitted to adult ICU or HDU for at least 48 hours and 72 hours post discharge from ICU or HDU who do not have any HAI during the current hospitalization before ICU or HDU admission.

2. 5. EXCLUSION CRITERIA

✓ All patients admitted in ICU or HDU with suspicion or documented HAI or CAI prior to ICU/HDU admission
✓ All patient below 16 years of age

2. 6. SAMPLE SIZE

All patients admitted in ICU CHUK during the period of the study for at least 48 hours and who are admitted for reasons other than HAI. The duration of the study will be 12 months (from 1st October 2020- 30th September 2021)

2. 7. DATA VARIABLES, SOURCE OF DATA AND DATA COLLECTION

❖ Patient characteristics:
✓ Hospital identification number and initials
✓ Age
✓ Sex
✓ Admitting primary diagnosis
❖ Outcome variables:
✓ Distribution of microbes isolated across clinical specimens:
   • Presence of central line and duration, urinary catheter and duration, being intubated and duration, undergone surgery and type of surgery.
• Documented infection (from culture or clinically documented by treating physician.
• Any culture done.
• Type of sample (urine, sputum or trachea aspirate, blood, tip of central line, others)
• Isolated bacteria/ microbial agents
• Results of antibiogram (antimicrobial resistance or sensitive drug)

Our primary outcome is incidence of HAI. We defined HAI as an infection that is not present at the time of hospital admission and manifest 48 hours after admission to the hospital, confirmed clinically by treating physician or by laboratory investigations(1).

The primary admitting diagnosis was recorded from the file on the admitting sheet as the reason of ICU or HDU written by treating physician. Sepsis and septic shock were defined separately based on sepsis 3 campaign definitions. Shock was defined as one of the following groups: Septic shock, Hemorrhagic shock, Hypovolemic shock, Cardiogenic shock, Neurogenic shock. Trauma was defined as one of the following: blunt abdominal trauma, blunt chest trauma, traumatic brain injury and other related trauma as the reason of ICU admission. Respiratory failure was defined simply as the respiratory fatigue with the need of mechanical ventilation. Obstetrics and gynecology group of diagnosis was defined

as any diagnosis to a peripartum woman other than the one listed, e.g.: preeclampsia, eclampsia, post-partum hemorrhage.

We collected the incidence of specific HAI including HAP, VAP, UTI, CAUTI, PBSI, SSI, Central Line Associated Blood Stream Infection (CLABSI), Clostridium difficile infection. We have defined hospital acquired pneumonia as pneumonia that occurs 48 hours or more after admission to the hospital and did not appear to be incubating at the time of admission(51).

We have defined VAP as a pneumonia that develops more than 48 to 72 hours after endotracheal intubation. Incidence of VAP was the rate of VAP per number of patient-days on a ventilator machine(51).

We have defined hospital acquired UTI as those developed to patient not catheterized or where the urinary catheter remain not more than 2 consecutive days; and we have defined CAUTI as UTI associated with indwelling urinary catheters for more than 2 consecutive days(48hours)(52). Incidence of CAUTI was the rate of UTI per number of patient-days with a catheter.

We have defined Primary BSI (PBSI) as a laboratory confirmed blood stream infection to the patient who doesn't have any central line before 2 consecutive days ago since the time of sampling. CLABSI was defined as a laboratory confirmed bloodstream infection where an organism is identified from blood of patient who had a central line 2 or more consecutive days from the day of sampling(52)(53). Incidence of CLABSI was the rate of BSI per number of patient-days with a central catheter.

We have defined SSI as that reported clinically by a treating physician or microbiologically confirmed with the day of ICU admission up to 30days from the day of surgery to the patient received prophylactic antibiotics before surgery(54). We have classified SSI as superficial, deep or organ-space according to CDC definitions. Incidence of SSI was the number of SSI per patients undergoing surgical operation. HAI incidence was defined as a number of new infection episodes or new patients acquiring an infection per 100 patients followed up for a defined time period Periods and HAI incidence density was defined as a number of infection episodes per 1000 patient-days or device-days. Data collection sheet is attached in the Appendix.

Data collection was done by myself and a trained researcher medical student. I have trained her for a duration of 2 weeks on how our methodology and data collection style. We have worked together for the first 20 patients to ensure that she is comfortable and confident to collect accurate information. Data were recorded from ICU logistic book, patients 's

medical files and open clinic to data collection tool; as you can see it on the appendix; and analyzed using Microsoft excel.

2. 8. ANALYSIS AND STATISTICS

Sources of data have recorded from patients' files and open clinic. Data have recorded on the questionnaire and entered and analyzed by Microsoft excel. The overall incidence was calculated by taking the total number of patients who acquired at least one HAI as numerator and divided by the total number of patients enrolled in the study. The analysis was done using tables.

2. 9. ETHICAL APPROVAL

- **Ethical issues**: Permission to conduct a study has gotten from the IRB of the University of Rwanda. Local ethics approval was given by CHUK ethical committee.

- **Data confidentiality:** Data were entered in a designated format from registers and patient files. Names were used to trace patients from one file to another. Only initials of the patient with the hospital ID number file appeared on the questionnaire. Confidentiality was maintained by keeping questionnaires in a lockable private room, and electronic data were kept in a password protected computer.

- **Specific patient benefit**: The results will help providers and health systems be aware of the incidence of HAIs, know the common sources of infection, once there is a suspicion of HAI. It will also help to know the antimicrobial resistance and sensitivities of the causative microorganism, which will resolve the issue of using unnecessary antibiotics and it will remind the policy makers as well as leaders to strengthen the IPC measures. The results will be the improved patients care and the early prevention and management of patients with a HAI.

- **Community participation and benefit:** The results of this study will shed light on the incidence of HAIs and associated common sources.

- **Feedback and dissemination of results:** The results will be disseminated to health care workers of CHUK-ICU, CHUK Ethical committee and the University of Rwanda research board as the final thesis in completion of a Master's Degree. The results will also be

presented in national and international conferences and submitted in a peer reviewed journal.

2. 10. STUDY LIMITATION

- Missing some important data in files: cultures, poor clinical documentation like; clinical diagnosis of HAI, central line insertion and intubation protocol, loss of files in archive.
- Limited time for research, unfunded study as well as small sample size.
- Retrospective study
- Inability to assess the risks factors, HAI from other microorganisms than bacterial, means Viruses, parasites and fungi.

CHAPTER THREE. RESULTS

The total ICU and HDU admission during the duration of 12 months period was 468 patients. There were 30 patients under 16 years old (pediatrics), 60 files were missed, and 58 files were of patients less than 48hours ,11 patients had an active HAI at admission period and we remained with 309 (66%) patients with complete files for research.

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                        ┌──────────────────────────┐
                        │      468 selected        │
                        └──────────────────────────┘

┌──────────┐   ┌──────────────┐   ┌──────────────┐   ┌──────────────┐
│ 60 files │   │ 30 pediatrics│   │ 11 patients  │   │ 58 patients  │
│ missed in│   │              │   │ had active   │   │ admitted in  │
│ archive  │   │              │   │ HAI          │   │ less than    │
└──────────┘   └──────────────┘   └──────────────┘   │ 48hours      │
                                                      └──────────────┘

           ┌─────────────────────────────────────────┐
           │   Remained 309 patients for research     │
           └─────────────────────────────────────────┘
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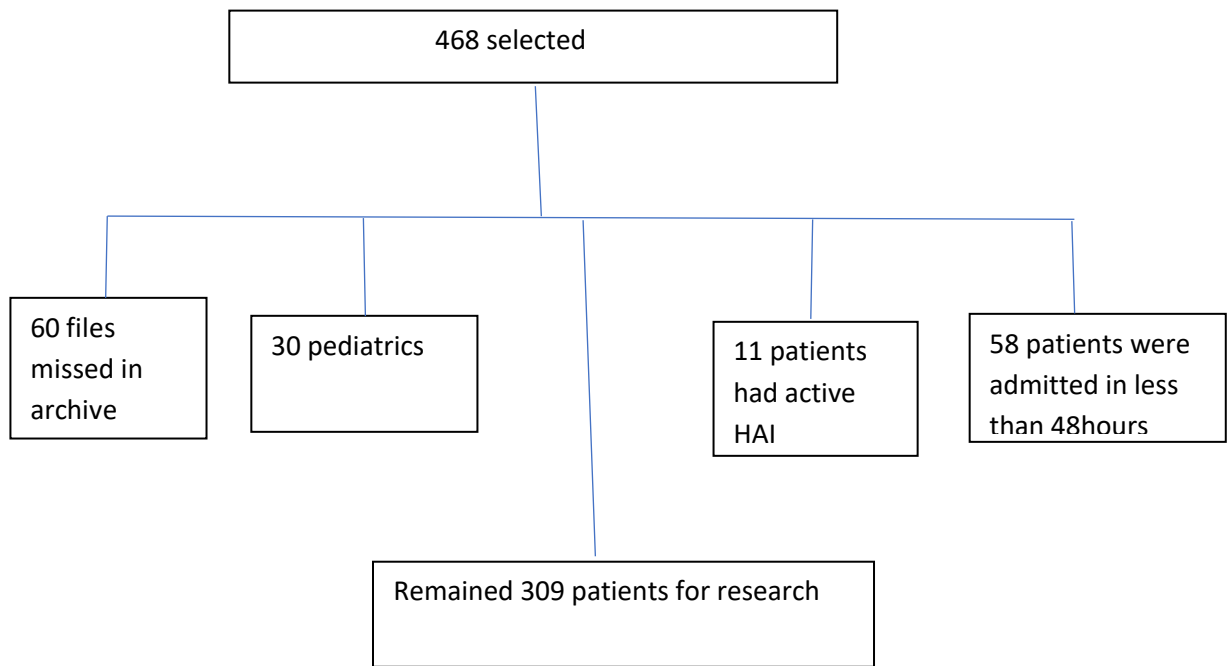
Fig 3. 1. Flow diagram illustrating how patients were selected in the study

Table 3.1. Key demographic and clinical characteristics of patients.

Demographic and clinical characteristics	Total patients admitted in ICU [N-309 (%)]
Age (16-65 Years	262(84.79)
Age > 65 Years	47(15.21)
Males	151(48.87)
Females	158(51.13)
Intubated patients	218(70.55)
Urinary catheterized patients	305(98.70)
Central line placement	36(11.65)
Undergone Surgery	205(66.34)
The mean duration of stays in ICU	3,391/309= 10.9 days
Admitting primary diagnosis	
Shock (Septic, Hemorrhagic, Hypovolemic, Cardiogenic, Neurogenic)	28(9.06)
Sepsis	55(17.79)
Trauma	75(24.27)
Respiratory failure	24(7.76)
Obstetrics/Gynecology	24(7.76)
Stroke	30(9.70)

Data ICU of CHUK from October 2020 to September 2021.

Among the patients with complete files for research, 262 patients (84.78%) were between 16-65 years old and 47 patients (15.22%) were above 65 years. 158 patients (51.13%) were female and 151 patients (48.87%) were male. The most common primary diagnosis of ICU admission was trauma (75 patients=24.27%) followed by sepsis (55 patients= 17.79%) and brain tumor (35 patients=11.32%).

The average ICU/HDU stay was 10.9 days. During the study period ,305 (98.7%) had a urinary catheter. 218 patients (70.55%) were intubated and mechanically ventilated. 205 patients (66.34%) underwent a surgical procedure. 47 patients (15.21%) were old and the central line placement was done on 36 patients (11.65%).

Table 3.2. Incidence and the most common types of infections found in CHUK

Type of HAI	No of HAI N-83	No of patients at risks of a specific HAI	Individual incidence N (%)	Total days durations (ETT, Central line, urinary catheter)	The mean indwelling device duration in days	Rate of HAI per 1,000 patients' days
VAP	53(63.85%)	218	24.3	2780	12.7	19.0
CAUTI	13(15.66%)	305	4.26	4734	15.5	2.7
PBSI	11(13.25%)	309	3.55	--		
SSI	3(3.61%)	205	1.46	--		
HAP	3(3.61%)	309	0.97	--		
CLABSI	0	36	0.00	427	11.8	0.0
UTI	0	309	0.00	--		

Total incidence*(%) = 67/309*100 = 21.68

Overall rate density: 67/3391 patients-days=0.01975 patient-days=19.75 per 1000 patient-days

-- Represent not applicable, no means number, *Percentage (%) represents the total patients with HAI /Total patients in ICU

Table 3.1. Incidence and the most common types of infections found in CHUK

The overall patients who had the ICU hospital acquired infection were 67 patients with the incidence of 21.68% (67/309) and at least each patient had one or more HAI with the total number of HAI in ICU of 83: 57 patients had respiratory HAI (detailed 53 has VAP and 3 had ICU HAP only), 13 patients had.

The overall incidence density was 67/3391 patients-days =19.75 per 1000 patient-days. 53 of 218 (24.3%) mechanically ventilated patients developed VAP at a proportion of 63.8% of all ICU HAI. This is a rate of 19.75 VAP per 1000 ventilated patient-days.13 of 305(4.26%) who had urinary catheter developed UTI at a proportion of 15.66% of all ICU HAI. This is a rate of 2.7 CAUTI per 1000 patient-days. 11 of 309 (3.55%) patients develop PBSI at a proportion of 13.25% of all ICU HAI. 3 of 309 (1.46%) operated patients develop SSI at the proportion of 3.61% of all ICU HAI.

The total duration of urinary catheterization was 4734 days with the mean of 15.5days, thus the incidence density of CAUTI, as defined by the number of patients with CAUTI-days related, is 13 patients over 4734 days=2.7 per 1000 catheter-days.

The total duration of endotracheal tube was 2780days with the mean of 12.7days, thus the incidence density of VAP, as defined by the number of patients with VAP -days related, is 53 patients over 2780 days= 19.0 per 1000 ventilated patient-days.

Table 3.3. Pathogens isolated across culture sources

		Type of HAI			
	Total organisms	VAP	CAUTI	PBSI	SSI*
Pathogens	[(N-100) ;(%-100]	(N-75)	(N-12)	(N-11)	(N-3)
Klebsiella	39(39.00)	30(40.00)	5(41.66)	4(36.36)	0(0.00)
Pseudomonas	23(23.00)	22(29.33)	1(8.33)	0(0.00)	1(33.33)
Acinetobacter	16(16.00)	11(14.66)	2(16.66)	2(18.18)	1(33.33)
E-coli	9(9.00)	5(6.66)	1(8.33)	2(18.18)	1(33.33)
Proteus	6(6.00)	5(6.66)	1(8.33)	0(0.00)	0(0.00)
Staph Aureus	4(4.00)	0(0.00)	1(8.33)	3(27.27)	0(0.00)
Citrobacter	1(1.00)	(0.00)	0(0.00)	0(0.00)	0(0.00)
Providencia	1(1.00)	1(1.33)	0(0.00)	0(0.00)	0(0.00)
Enterococcus	1(1.00)	0(0.00)	1(8.33)	0(0.00)	0(0.00)

Number and proportion of pathogens from a specified sample N (%).

There were 100 organisms isolated with 39 of *Klebsiella*, 23 *Pseudomonas*, 16 *Acinetobacter*, 9 *E. coli*, 6 *Proteus*, 4 *Staphylococcus aureus*, and 1 for *Citrobacter*, *Enterococcus* and *Providencia*.

There were 75 isolates from patients with VAP. The most common organisms isolated from patients with VAP were *Klebsiella* (N=30, 40%) followed by *Pseudomonas* (N=22, 29%).

They were 12 isolates from CAUTI. The most common organisms isolated from patients with CAUTI were *Klebsiella* (N=5, 42%) followed by *Acinetobacter* (N=2, 17%).

They were 11 isolates from PBSI. The most common organisms isolated from patients with PBSI were Klebsiella (n=4, 36%) followed by *Staphylococcus aureus* (n=3, 27%).

They were 3 isolates from SSI which included *Pseudomonas*, *Acinetobacter* and *E coli*.

Table 3.4. Resistance profile of pathogens in relationship to antibiotics tested

				Resistance rate N (%) *			
Pathogens	*Klebsiella*	*Pseudomonas*	*Acineto bacter*	*E. coli*	*Proteus*	*Stath Aureus*	**Overall**
Number of isolated	N-39	N-23	N-16	N-9	N-6	N-4	N-100
Antibiotics	R/Tested (%)	R/Tested (%)	R/Tested (%)	R/Tested (%)	R/Tested (%)	R/Tested (%)	R/Tested (%)
Cephalosporins	38/39(97.43)	18/21(85.71)	15/15(100.0)	8/8(100.0)	4/5(80.00)	-	85/90(94.44)
Fluoroquinolones	18//32(56.25)	19/20(95.00)	11/14(78.57)	5/6(83.33)	4/5(80.00)	1/1(100.0)	60/81(74.07)
Carbapenem	3/34(8.82)	11/20(55.00)	6/16(37.50)	0/7(0.00)	0/5(0.00)	-	30/83(36.14)
Penicillin	33//36(91.66)	10/12(83.33)	8/9(88.88)	8//9(88.88)	4/6(66.66)	4/4(100.0)	69/78(88.46)
Macrolides	1/1(100.0)	-	-	-	-	2/4(50.0	3/6(50.00)
Amikacin	1/37(2.70)	8/20(40.0)	4/16(25.00)	-	1/6(16.66)	-	14/81(17.28)
Gentamycin	30/30(100.0)	8/8(100.0)	11/11(100.0	5/5(100.00)	2/2(100.0)	-	57/57(100.0)
Glycopeptides	2/2(100.0)	1/1(100.0)	-	1/1(100.0)	-	0/2(0.0)	4/7(57.14)
Tetracyclines	1/1(100.0)	-	-	-	-	2/3(66.6	4/5(80.00)
Sulfonamides	16/18(88.88)	3/3(100.0)	2/2(100.0)	5/5(100.0)	3/3(100.0)	-	31/32(96.87)
Polymyxin B	2/8(25.00)	1/7(14.28)	-	-	1/1(100.0)	0/1(0.00)	4/17(52.94)
Chloramphenicol	-	1/5(20.00)	0/1(0.00)	0/2(00.00)	-	-	1/8(12.50)
Nitrofurantoin	-	-	0/3(0.00)	1/1(100.0)	1/2(50.00)	-	2/6(33.33)
Oxacillin	-	-	-	1/1(100.0)	-	0/1(0.00)	1/2(50.00)

*Antibiotics not tested for resistance to pathogens are indicated by (–), * Represent (%) of the number of pathogens resistant to antibiotics /total number of pathogens tested.* **Group of antibiotics tested**: ***Cephalosporin**s (ceftriaxone, cefotaxime, Cephalothin, cefuroxime, Cefoxitin, Ceftazidime/clavulanate, cefotaxime/clavulanate, ceftazidime);* **Fluoroquinolones** (ciprofloxacin, *levofloxacin*); ***Carbapenem** (meropenem, imipenem),* ***Penicillin** (amoxicillin, a*moxicillin-Clavulanic Acid, penicillin, ampicillin, Piperacillin), ***Macrolides** (clindamycin, erythromycin),* ***Glycopeptid**es(vancomycin), ***Tetracyclines** (tetracycline, oxycline), ***Sulfonamid**e (Bactrim, Sulfamethoxazole)*

The resistance rates of >50% were seen in all tested antibiotics except carbapenem (36.14%), nitrofurantoin (33.33%), amikacin (17.28%), and chloramphenicol (12.5%).

Klebsiella had the highest sensitivity to amikacin (97.29%) followed by carbapenem (79.48%) and the highest resistance have seen for gentamycin, macrolides, glycopeptides and tetracyclines at a rate of 100%. *Pseudomonas aeruginosa* had the highest sensitivity to polymyxin B at85.71% followed by amikacin at 60% and the highest resistance have seen for gentamycin, glycopeptides and sulfonamides at a rate of 100%.

Acinetobacter had a highest sensitivity to polymyxin B, chloramphenicol and nitrofurantoin at a rate of 100% where the highest resistance has seen for cephalosporine, gentamycin and sulfonamide at a rate of 100%. *E. coli* had a high sensitivity to carbapenem, amikacin and chloramphenicol at a rate of 100% where the highest resistance was seen for cephalosporine, gentamycin, glycopeptides, sulfonamides, nitrofurantoin and oxacillin at a rate of 100%.

Proteus had the highest sensitivity to carbapenem at a rate of 100% followed by amikacin at a rate of 83.33%, where the highest resistance was seen for gentamycin, sulfonamides and polymyxin B at a rate of 100%.

Staphylococcus aureus had the highest sensitivity for glycopeptides, polymyxin and oxacillin at a rate of 100%, where the highest resistance has seen for fluoroquinolones and penicillin at a rate of 100%.

CHAPTER FOUR. DISCUSSION

In this study conducted in ICU of CHUK, we evaluated 309 patients who were fulfilling the criteria of the study. Backing on our research question and hypothesis, we accept our hypothesis saying that the most common type of HAI in ICU of CHUK is VAP (63.85%) and the common microbial organism isolated is *Klebsiella pneumonia* (39%). We have found again the incidence of HAI as 21.68% and the microbial resistance more than 50% to all tested antibiotics (as they are listed in the results), a part of carbapenem, nitrofurantoin, amikacin and chloramphenicol.

The primary objective of our study was to determine the incidence of HAI in ICU of CHUK which can reflect the recent overall in ICUs of Rwanda as the other similar study done in Rwanda revealed only the prevalence. The rate of HAI in ICU was 21.68%. This rate is higher to the general ward rate in CHUK- Rwanda which was 15.1% (18). There is a big decline in rate of HAI in ICU of CHUK comparing our results to those of 2016 where the rate of HAI was 50%(18). Globally, the rate of ICU HAI exceed 25%(3). This reflect the low rate of this infection in ICU of CHUK as well as low rate to that of Ethiopian ICU which was 25.8%. Our results are in accordance to the one isolated in ICUs of sub-Saharan African countries ranging from 21.2-35.6% (55). The similar results were seen in studies done in middle and low income countries (ranging4 4% up to 88 9%)(8). By looking in ICU's of developed countries it looks higher: European countries 18.9%(6) and Indian's ICUs (15.7%) (9). The LOS in ICU of CHUK was 10.9 days. This results is high compared to the one from high income countries which was 4 days according to Agrawal et al in their study done in India in 2014 (56).The This may be due to an advanced skills of health providers(good number of critical care nurses, intensivists), decreased work load(few hours of work: 8 hours compared to 12 hours in Rwanda) and sufficient resources and means for both patient and hospital (3). The low length of ICU stays seen in developed countries might have a great effect on the decreased rate of HAI compared to our settings.

The overall rate density of HAI in ICU was 19.75 per 1000 patients-days. This rate is low compared to the results found by Robby Markwart et al in their systemic and metanalysis study conducted in 2020; They found this rate at 56.5 per 1000 patients(57). Our result is almost similar to the one reported globally in 2008 which showed the rate between 13 to 20.3 per 1000 patients-days(8). By looking the rate found in middle and low income

countries (42.7 episodes per 1000 patient-days)(8) .This last one reflect the low rate of HAI in ICU-CHUK. The overall rate of HAI is higher compared to the rate of HAI per patient days. This might be explained by the higher average ICU LOS compared to developed countries. The reduction of the length of ICU stay to our patients by fighting against the modifiable risks factors such as; malnutrition, mechanical ventilation, delirium, hypomagnesemia, infection (58), can lead to a reduced rate of HAI.

The most common type of HAI was VAP (63.85%) followed by CAUTI (15.66%) PBSI (13.25%) and lastly HAP and SSI at the same proportion (3.61%). Similar results have found by Santosh Gunasekaran et al in their recent study done in 2020 in India, where they found that the most common HAI was VAP (49%) followed by CAUTI(13%), blood stream infection and SSI were at equal proportion(12%)(9). This means that strategies to reduce the risks factors of VAP, as they are listed in the coming paragraphs, are needed.

The rate of VAP was 19.0 per 1000 ventilated days. This rate is lower compared to that found in Indian's ICUs in the study done by Santosh Gunasekaran et al where it was 39.3 per 1000 ventilated days (9). It is also low compared to low and middle income countries where the rate was 23.9 per 1000 patient-days(8). On the other side, this rate is very high compared to the global VAP rate which is 7.9 per 1000 ventilator-days according to WHO report(8).The mean of ventilated days was 12.7days and this value is higher than the one resulted from developed countries where it was found to range between 2.6 to 7.9 days according to Seneff et al(63). The following strategies can be used in order to reduce the rate of VAP in CHUK as well as in Rwandan ICU's hospitals: Head of the bed elevation at 30 degrees, oral care every 12 hours, daily sedation vacation, use of continuous subglottic suction, deep venous thrombosis prophylaxis, stress ulcer, early extubating and tracheostomy (64).

The rate of CAUTI was 2.74 per 1,000 urinary catheter days. This is results is higher compared to the one reported by CDC National Healthcare Safety Network in 2012. This last one has showed the rate of 1.4 to 1.7 per 1,000 catheter days(53). By contrary this rate is low compared to that of developed Indian's ICUs where it is 16.17 per 1000 catheter days(59). On other hand this rate is lower compared to low and middle income countries where it showed a rate of 8.8 per 1000 patient-days(8). The mean of urinary catheter duration was 15.5 days(60). This mean duration is higher to the one reported by developed countries like ICUs of US where it was 8.7 days according to Kanjet al (61).This rate is

low compared to the studies done by Maha et al in Egypt where the mean was 19.8 days. The following strategies can reduce the rate of CAUTI in Rwanda: Reduction of the utilization of indwelling urinary catheter and unnecessary catheter use, aggressive implementation of the nurse directed catheter removal protocol (indications of physician's catheter insertion order, catheter insertion criteria, biweekly unit-specific feedback on catheter use rates and CAUTI rates),urinary catheter care, prevention of catheter kinking, improvement in sterility of catheterization, removal of urinary catheter as soon as possible it is no longer indicated, education of nurses about CAUTI prevention strategies(62).

Although we have found patients have central line for long time, the CLABSI was not found in any patients. The mean duration for central line was 11.8 days. The explanations can be categorized into two possibilities: Firstly, no sample of central line taken during the period of the study; Secondly there was no clinical suspicion of CAUTI which reflect the absence of this infection in ICU of CHUK. Note that in other ICUs settings and globally, the rate of CLABSI is still significant(65)(8). For these reasons, we recommend the ICU clinical staff to assess clinical signs of central line infection, sampling once there is a suspicion of CLABSI and keep bundles of central line catheter care. These are : hand washing by the operator; putting sterile gloves, gowns, caps and mask by a physician who is doing central line insertion before the procedure; proper skin cleaning using 2% chlorhexidine and 70% isopropyl alcohol, proper draping from head to toe ,choice of insertion site with reduced rate of infection (femoral area to be chosen at the last), daily evaluation of central line need and early removal once it is no longer needed, proper nursing daily hygiene(66).

During our study, they were no hospital-acquired Clostridium difficile infection identified. On the other hand, other settings like adult ICUs of Serbia, were seen at the high rate (18.1%)(67). We recommend to keep hand and food hygiene in order to keep this rate at zero in the ICU of CHUK.

The most common isolated organism in our study was *Klebsiella pneumonia* (39%) followed by *Pseudomonas aeruginosa* (23%) *Acinetobacter baumani* (16%) and *E. coli* (9%). *Klebsiella* was primarily from VAP, CAUTI and PBSI. Almost similar results have found by Santosh Gunasekaran et al in their study conducted Indian ICUs in 2020 in the similar settings. They have showed that *Klebsiella* (29%) was the most common followed by Acinetobacter (24%) then *Pseudomonas* (9%) and *Klebsiella* was primarily isolated in

CAUTI and blood then being secondarily in VAP after *Acinetobacter*(9). *Klebsiella* was again primarily isolated in SSI followed by *Pseudomonas* and *E.coli*(9). Other large studies globally done in similar settings showed the different results as the most isolated organism was *E. coli* (20.1%) and *S. aureus* (17.8%) and were primarily isolated in UTI and SSI (8). Different results were also seen in the other two studies combining both HAI and Community acquired infection (CAI). They were conducted in CHUK adults surgical and medical wards where both found *E. coli* as the most common isolated germ at a rate of 42% in the study of Muvunyi et al(20) and 56.4% from the study of Ntirenganya et al(13).

The antimicrobial resistance rates were more than 50% in all tested antibiotics except carbapenem (36.14%), nitrofurantoin (33.33%), amikacin (17.28%), and chloramphenicol (12.5%). The highest resistance was seen to gentamycin (100%), sulfonamide (96.8%) and cephalosporin (94.4%). This reflects the high rate of polymicrobial resistance. In others previously done studies at CHUK revealed the microbial resistance of HAI of 74% to third generation cephalosporin according to Muvunyi et al (20); and the resistance to penicillin, trimethoprim sulfamethoxazole, and Ampicillin was 91.8%, 83.3%, and 81.8% respectively according to Habyarimana et al(19). This is not too far to the results of our study. The almost similar results to ours were found by Aleksa Despotovic et al in India in year 2020 where the resistance rate to all antibiotics were more than 50% except tigecycline (14%), colistin (9%), and linezolid(0.0%)(67). The CHUK IPC team has developed differently guidelines in order to fight against HAI. These are like: Prevention of health care associated respiratory tract infection guidelines; Prevention of catheter associated urinary tract infection guidelines; Prevention of intravascular associated infection guideline; Prevention of surgical site infection guideline; Cleaning, disinfection and sterilization guideline; Management of healthcare waste guideline; Environmental hygiene guideline; Hand Hygiene guideline; Management of infectious patients' guidelines, clothes changing, visitors management and others. These guidelines have to be revised and implemented in order to reduce the rate of HAI in ICU of CHUK. We can also encourage to do a de-escalation of antibiotics and other strategies such us early controlling source of infection, use of high initial antibiotic dose, doing culture before new antibiotics, previous knowledge about individual, unit or hospital colonizing flora, may help to reduce the rate of antimicrobial resistance in ICU of CHUK. Note that CHUK laboratory is not testing some antibiotics like Colistin, 4th generation cephalosporin and sometimes polymyxin B. For this reason, if the laboratory of CHUK increases its capacity of testing

all antibiotics, we might have the whole picture of antimicrobial resistance as well as widening the antimicrobial treatments options for clinicians.

CHAPTER FIVE. CONCLUSION, LIMITATIONS AND RECOMMENDATIONS

The incidence of HAI and antimicrobial resistance in ICU of CHUK is high. The most common type of HAI is VAP and Klebsiella is the most isolated microorganism. The revision and implementation of the existing IPC measures and guidelines is needed in order to reduce the infection rate. The proper use of antibiotics with its de-escalation and other strategies regarding antibiotics use are needed in order to reduce the resistance as well as reduction of the risks of polymicrobial resistance. The recruitment of a good number of specialized staffing (enough number of critical care nurses and intensivists) as well as reduction of working hours is paramount in reduction of HAI in ICU of CHUK. The augmentation of the CHUK laboratory capacity to test all available antibiotics demonstrate the whole picture of microbial resistance as well as improved clinical outcome to patients with HAI. However, in our study we had some limitations such as assessments of the hospital acquired infection caused by nonbacterial microorganisms like fungi, viruses, parasites; Evaluation of the additional predisposing factors to HAI other than listed in our study such as comorbidities, criticability and others; retrospective study, all due to limited time and unfunded study. For these reasons we recommend further studies with larger sample size and prospective method to be conducted in order to fill these gaps mentioned above.

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APPENDIX.

DATA COLLECTION TOOL

1. Hospital ID, initials

2. Date of hospital admission

3. Date of ICU admission

4. Duration of ICU stay (days

5. Duration of hospital stay (days)

6. Age

7. Sex M/F

8. Admitting Diagnosis

9. Intubated? Y/N

10. Duration of ETT

11. Urinary catheter? Y/N

12. Duration of catheter

13. Central line? Y/N

14. Duration of central line

15. Surgery? Y/N

16. What surgery?

17. Admitted in ICU with HAI? Y/N

18. HAI during the time of ICU stay? Y/N

19. What HAI? (Can be more than one: HAP, VAP, UTI, CAUTI, CLABSI, PBSI, Clostidium difficile infection).

    ❖ HAP? Y/N
      ✓ Was a sample collected?
      ✓ What pathogen?
      ✓ Antibiogram
    ❖ VAP? Y/N:

- ❖
  - ✓ Was a sample collected?
  - ✓ What pathogen?
  - ✓ Antibiogram
- ❖ CAUTI? Y/N
  - ✓ Was a sample collected?
  - ✓ What pathogen?
  - ✓ Antibiogram
- ❖ CLABSI? Y/N
  - ✓ Was a sample collected?
  - ✓ What pathogen?
  - ✓ Antibiogram
- ❖ PBSI? Y/N
  - ✓ Was a sample collected?
  - ✓ What pathogen?
  - ✓ Antibiogram
- ❖ CLOSTRIDIUM DIFFICILE? Y/N
  - ✓ Was a sample collected?
  - ✓ What pathogen?
  - ✓ Antibiogram
- ❖ SSI? Y/N
- ✓ What type of SSI? superficial, deep, organ space

- ✓ Was a sample collected?
- ✓ What pathogen?
- ✓ Antibiogram

Antibiotic	Sensit	Resis	Notes
Cephalothin			
Cefuroxime			
Ceftriaxone			
Cefoxitin			
Cefotaxime			
Ceftazidime/clavulanate			
Cefotaxime/clavulanate			
Clindamycin			
TMP/SMX (Bactrim)			
Amikacin			
Amoxicillin/clavulanate			
Erythromycin			

Gentamicin				Penicillin			
Imipenem				Ampicillin			
Pipercillin				Ciprofloxacin			
Vancomycin				Polymixin B			
Tetracycline				Others			

IRB ETHICS COMMITTEE APPROVAL AND CHUK ETHICS COMMITTEE APPROVAL

CENTRE HOSPITALIER UNIVERSITAIRE
UNIVERSITY TEACHING HOSPITAL

Ethics Committee / Comité d'éthique

30th Dec,2021   Ref.EC/CHUK/143/2021

Review Approval Notice

Dear Jean HABIMANA,

Your research project: "HOSPITAL ACQUIRED INFECTIONS IN THE INTENSIVE CARE UNIT AT UNIVERSITY TEACHING HOSPITAL: INCIDENCE, COMMON TYPES, AND ANTIMICROBIAL RESISTANCE, A RETROSPECTIVE STUDY. "

During the meeting of the Ethics Committee of University Teaching Hospital of Kigali (CHUK) that was held on 30th Dec,2021 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=490&&chuk.

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

Yours sincerely,

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 "

Web Site : www.chuk.rw ; B.P. 655 Kigali- RWANDA Tél.: 00 (250) 252575462. E-Mail: chuk.hospital@chuk.rw

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UNIVERSITY of RWANDA   COLLEGE OF MEDICINE AND HEALTH SCIENCES
DIRECTORATE OF RESEARCH & INNOVATION

CMHS INSTITUTIONAL REVIEW BOARD (IRB)
Kigali, 3rd/November/2021

Dr Jean HABIMANA
School of Medicine and Pharmacy, CMHS, UR

Approval Notice: No 331/CMHS IRB/2021
Your Project Title "Hospital Acquired Infection in Intensive Care Unit at University Teaching Hospital: Incidence, Common Sources and Antimicrobial Resistance, A Retrospective Study" has been evaluated by CMHS Institutional Review Board.

Name of Members	Institute	Yes	Absent	Withdrawn from the proceeding
Prof Kato J. Njunwa	UR-CMHS	X		
Dr Stefan Jansen	UR-CMHS	X		
Dr Brenda Asimwe-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		

Header: Involved in the decision — No (Reason)

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 2nd November 2021, **Approval has been granted to your study.**
Please note that approval of the protocol and consent form is valid for **12 months.**

Email: researchcenter@ur.ac.rw   P.O Box 3286 Kigali, Rwanda   www.ur.ac.rw

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 November 2021
Expiration date: The 29th November 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