MULTIDRUG-RESISTANT *Acinetobacter baumannii* AMONG PATIENTS ADMITTED TO INTENSIVE CARE UNIT AT MOI TEACHING AND REFERRAL HOSPITAL, UASIN GISHU COUNTY, KENYA

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P150/CTY/34014/2017

A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF THE DEGREE OF MASTER OF SCIENCE IN INFECTIOUS DISEASES IN THE SCHOOL OF HEALTH SCIENCES, KENYATTA UNIVERSITY

NOVEMBER, 2023

DECLARATION

This thesis is my original work and has not been presented for a degree in any other University or any other award.

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DEDICATION

I dedicate this work to family members. Thank you so much and may God bless you abundantly.

ACKNOWLEDGEMENTS

I thank God this far. May I acknowledge all the participants who played a role in making this study a reality. I would like to sincerely thank Dr. Abednego Musyoki and Dr. Nelson Menza of Kenyatta University, Department of Medical Laboratory Sciences for their technical guidance, encouragement and support. May I also thank Kenyatta University Ethical Review Committee, Graduate school for approval of the study. I also thank Moi Teaching and Referral Hospital administration for their permission to carry out the study in the facility and all patients who participated in the study.

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LIST OF ABBREVIATIONS AND ACRONYMS

AST	Antibiotic Susceptibility Testing
CHDL	Carbapenem-hydrolyzing Class D beta lactamase
CLSI	Clinical laboratory standards institute
CRAB	Carbapenem Resistant *Acinetobacter baumannii*
ESBLs	Extended Spectrum beta lactamases
ICU	Intensive Care Unit
IREC	Institutional Research and Ethics Committee
MBL	Mettallo-Beta Lactamase
MBLs	Metallo-β-Lactamases
MDR	Multi-Drug Resistant
MH	Mueller Hinton
MH-a	Mueller–Hinton agar
MTRH	Moi Teaching and Referral Hospital
PCR	Polymerase Chain Reaction
RICU	Respiratory Intensive Care Unit
VAP	Ventilation Associated Pneumonia

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ABSTRACT

Multidrug-resistant *Acinetobacter baumannii* infections pose a formidable challenge worldwide, especially in developing countries like Kenya. Despite limited treatment options, comprehensive data on *Acinetobacter baumannii* susceptibility profile at Moi Teaching and Referral Hospital remains scarce. This study therefore aimed to elucidate on the local epidemiology and clinical implications of these resistant strains among intensive care unit patients at this Kenyan tertiary teaching and referral hospital. This study adopted a cross-sectional study, purposefully enrolled 132 patients admitted to the intensive care unit between July 2019 and July 2020. Clinical specimens, including blood, urine, and tracheal aspirates, were systematically collected following standard bacteriological procedures. Microbiological isolation and identification were performed using culture, while antibiotic susceptibility testing utilized the VITEK®2 Compact system following the 2019 Clinical Laboratory Standards Institute guidelines. Descriptive statistics and multinomial logistic regression were conducted on the data to establish susceptibility trends and compare subject characteristics with carbapenem effectiveness. The statistical significance level for all analyses was set at a 95% confidence interval. The study revealed remarkably high rates of resistance among the sampled subjects, with 100% (n=30) showing multidrug-resistant infections and 83.3% (n=25) exhibiting carbapenem-resistant *Acinetobacter baumannii* infections. Among the total isolates, 83.3% (n=25) were insensitive to carbapenems, like Imipenem (IPM) and Meropenem (MPM) with 70% resistance each, Doripenem (DPM) with 86.7% resistance, Ertapenem (EPM) with 93.3% resistance, and Biapenem (BPM) with 96.7% resistance. However, alternative antibiotics such as Colistin (COL) showed a relatively lower resistance rate of 16%, and Tigecycline (TIG) demonstrated a resistance rate of 30%. The study also found significant associations between resistance to carbapenems and hospital stays of more than 10 days (aOR) = 2.11, 95% CI: 1.31 – 5.12, p = 0.002), as well as the presence of comorbidities (aOR = 2.26, 95% CI: 0.63 - 8.17, p = 0.212). Being married was significantly associated with a 4-fold higher likelihood of death (aOR = 8.56, 95% CI: 2.37 - 15.82, p = 0.011), while overweight or obese patients had about 4-fold increased risk of mortality compared to those with a normal BMI (aOR = 11.2, 95% CI: 3.57 - 21.11, p = 0.004). Additionally, each additional day of hospital stay was associated with a 41% higher likelihood of death (aOR). This study revealed alarming results of multidrug-resistant and carbapenem-resistant *Acinetobacter baumannii* isolates in the intensive care unit of Moi Teaching and Referral Hospital. The high resistance against common antibiotics calls for urgent implementation of strategies like enhanced surveillance and antimicrobial stewardship programs. Exploring new regimens like COL and TIG is crucial. Collaborative efforts among healthcare professionals, policymakers and researchers are essential to mitigate the spread of multidrug-resistant and carbapenem-resistant *Acinetobacter baumannii* strains, safeguard patients' health, and preserve antimicrobial effectiveness at Moi Teaching and Referral Hospital.

CHAPTER ONE: INTRODUCTION

1.1 Background Information

Acinetobacter baumannii (*A. baumannii*) is a formidable gram-negative coccobacillus, belonging to the family *Moraxellaceae*, known for its non-motile, non-spore forming, and encapsulated characteristics. Globally, this bacterium has emerged as a severe nosocomial pathogen, responsible for diverse infections such as pneumonia, urinary tract infections, infections within the bloodstream that are catheter-associated, meningitis, and burn wound complications (Uwingabiye *et al*., 2016). Notably, *A. baumannii* displays exceptional environmental resilience, resisting desiccation and persisting in hospital settings, particularly in intensive care units, leading to potential disease outbreaks (Lin & Lan, 2014). The alarming challenge lies in its reduced sensitivity towards available antibiotics, making the treatment of *A. baumannii* infections exceptionally difficult (Kempf & Rolain, 2012). Research done in Taiwan hospital has shown the recent occurrence of Pandrug-resistant, carbapenems-resistant, extensively drug-resistant, and multidrug-resistant *A. baumannii* strains in recent years (Chang *et al*., 2015).

In recent years, a concerning global trend has emerged, with *A. baumannii* strains increasingly developing resistance to carbapenem, a crucial antibiotic for combatting multi-drug resistant Gram-negative bacteria (Kempf & Rolain, 2012). Disturbingly, the numbers of *A. baumannii* isolates that show no sensitivity towards carbapenems have risen gradually in the recent times, with up to 70 % of the isolates obtained from clinical set ups not being sensitive to this vital drug (Antunes *et al*., 2014). This worrisome resistance pattern poses significant challenges in managing infections, as colistin, considered the treatment option of last resort for CRAB, and is also facing increasing resistance, with approximately 16% of isolates showing resistance

(Antunes *et al*., 2014). The combination of carbapenem and colistin resistance has resulted in heightened morbidity and mortality rates, impacting patient outcomes significantly. Moreover, these resistance trends have led to prolonged hospital stays, with each additional day of stay associated with a 41% higher likelihood of death (Lob *et al*., 2016). The escalating prevalence of resistant strains has also imposed a substantial burden on healthcare resources, increasing healthcare costs and straining medical facilities (Lob *et al*., 2016).

In many African countries, *Acinetobacter baumannii* has emerged as a concerning and significant cause of healthcare-associated infections, particularly in intensive care units (ICUs) and other healthcare settings. Its ability to thrive in healthcare facilities and persist on various surfaces contributes to its reputation as a troublesome nosocomial pathogen. However, the lack of standardized surveillance systems and inconsistent data reporting practices across different African countries may result in underestimation or variability in reported prevalence rates. As a result, obtaining accurate and comprehensive epidemiological data on *Acinetobacter baumannii* prevalence in Africa becomes an ongoing challenge, hindering the development of targeted interventions and infection control measures. Despite these challenges, available data suggests a notable rise in *Acinetobacter baumannii* infections in African healthcare settings. For example, a study done in a major tertiary hospital in West Africa reported that *Acinetobacter baumannii* was the common ubiquitous pathogen in majority of the specimens from clinical setups, accounting for approximately 40% of all gram-negative bacteria (Nwadike *et al*., 2019). In another study from East Africa, conducted in a South Ethiopian referral hospital's ICU, the prevalence of *Acinetobacter baumannii* infection was found to be 24.5%, with a considerable proportion of the isolates showing resistance to multiple antibiotics, including carbapenems (Tadesse *et al*., 2018).

Insensitivity to antimicrobials by *A. baumannii* is primarily attributed to the overexpression of genes coding for efflux pumps, penicillin-binding proteins, channel proteins with altered permeability, and the production of β-lactamases (Abdi *et al*., 2020). Notably, extended-spectrum β-lactamases confer resistance to all penicillins, aztreonam, and third-generation cephalosporins, contributing to the wide spectrum of resistance seen in *A. baumannii* strains. Metallo-β-lactamases, on the other hand, confer resistance to bicyclic beta-lactam antibiotics, including penicillins, carbapenems, and cephalosporins, but not monobactams (Lob *et al.*, 2016).

The intricate interplay of these resistance mechanisms has led to the alarming rise of *A. baumannii* strains that are insensitive to multiple drugs, posing a critical clinical challenge in managing infections caused by this pathogen. *A. baumannii* is able to acquire resistance determinants from other bacteria, further contributes to the rapid dissemination of resistant strains. As a result, effective strategies to combat antimicrobial resistance in *A. baumannii* should encompass comprehensive surveillance, antimicrobial stewardship, and infection control measures to preserve the effectiveness of available antibiotics and guide the development of novel therapeutic options (Lob *et al.*, 2016).

In Kenya, as in many other regions, the major risk factor associated with the emergence of drug-resistant *Acinetobacter baumannii* (*Ab*) variants is prior exposure to antibiotics. Patients with a history of carbapenem exposure have a higher likelihood of acquiring strains of *Ab* that are resistant to multiple drugs. Moreover, the constant exposure of *Ab* to antimicrobial drugs within the hospital environment creates a breeding ground for the development of mutant forms, leading to infections that pose serious challenges for patient management (Morris *et al*., 2019). Despite

the importance of understanding and addressing this issue, there remains a significant knowledge gap in Kenya regarding the prevalence, antimicrobial susceptibility profiles, and factors contributing to the colonization of CRAB in patients admitted to ICU. Gaining comprehensive insights into these aspects is crucial for implementing targeted interventions to mitigate the spread of drug-resistant *A. baumannii* and improve patient outcomes in Kenyan healthcare settings.

1.2 Statement of the Problem

The ability of *Acinetobacter baumannii* to thrive in hospital environments poses a significant risk of transmission to both patients and healthcare workers. People within these settings are at a heightened risk of *A. baumannii* infections, such as ventilator-associated pneumonia (VAP), urinary tract infections, bacteremia and meningitis, primarily due to the bacteria's tenacity on surfaces. Compounding the problem, the emergence and increasing cases of resistance, including colistin-resistant variants, present a greater therapeutic challenge by compromising the effectiveness of available treatment regimens. The occurrence of resistant variants within hospitals is a critical public health concern.

In Kenya, resistance among *Acinetobacter baumannii* isolates is primarily mediated by β-lactamases, with oxacillinases being of particular concern. However, available statistics on the prevalence and other biomedical dynamics related to *Acinetobacter baumannii* in the country are limited or completely lacking. According to research conducted in a major tertiary hospital in Nairobi, Kenya, the carbapenem-resistant *Acinetobacter baumannii* (CRAB) prevalence among patients in the ICU was found to be 24.5% (Tadesse *et al*., 2018). Despite this concerning figure,

comprehensive data on the nationwide prevalence, antibiotic susceptibility trends, and the biological landscape of drug-resistance markers in the bacteria remain scarce.

With regard to the above, this study determined the antimicrobial susceptibility profiles, factors associated with CRAB colonization/infection and admission outcomes in patients admitted to the ICU at Moi Teaching and Referral Hospital. The facility is the second largest public hospital in Kenya. It serves residents from 24 counties in Kenya, Southern Sudan, parts of Eastern Uganda and Democratic Republic of Congo. The facility has a bed capacity of 1020 serving as a level six referral hospital. It offers inpatient, outpatient and specialized care services such as the ICU (MTRH, 2020).

1.3 Justification

In the context of Kenya's bottom-up economic model, Vision 2030, relevant Sustainable Development Goals (SDGs), and WHO's blueprints for healthcare, understanding and controlling the dissemination of resistance to antimicrobials among *Acinetobacter baumannii* isolates is of key importance. As *A. baumannii* has proved to be resistant to most available first resort antibiotics and last resort antibiotics like carbapenems and colistin, effective management of related infections is imperative to ensure positive patient outcomes and reduce the burden on healthcare facilities.

At Moi Teaching and Referral Hospital (MTRH), a prominent healthcare institution catering to patients with diverse and critical diseases, the impact of *A. baumannii* co-infections could be devastating, leading to increased mortality and morbidity rates, and prolonged hospital stays.

This not only affects the well-being of patients but also places a strain on healthcare resources and hinders progress toward achieving Kenya's development goals and relevant SDGs, including Good Health and Well-being (SDG 3).

By providing in-depth information on the antibiotic susceptibility trends of locally circulating *A. baumannii* strains, this study seeks to lay the foundation for designing more effective intervention strategies. Such data-driven approaches align with Kenya's Vision 2030 and the bottom-up economic model by promoting evidence-based decision-making, enhancing healthcare infrastructure, and fostering innovation in the healthcare sector. Moreover, this research has broader implications, extending beyond MTRH, to benefit all other healthcare facilities in the region. With a comprehensive understanding of resistance mechanisms, healthcare providers can develop targeted antimicrobial stewardship programs and infection control measures, thus bolstering the region's capacity to combat antimicrobial resistance and ensure the sustainability of quality healthcare services. Against this background, aims to assess the prevalence, antimicrobial susceptibility profiles, and factors associated with CRAB colonization/infection and admission outcomes among ICU patients at Moi Teaching and Referral Hospital.

1.4 Research Questions

i. What is the prevalence of multidrug-resistant and carbapenem-resistant *Acinetobacter baumannii* among patients admitted to the ICU at MTRH?
ii. What are the antibiotic susceptibility patterns of *A. baumannii* among patients admitted to the ICU at MTRH?
iii. What are the factors associated with *A. baumannii* carriage among patients admitted to the ICU at MTRH?
iv. What are the hospitalization outcomes of ICU admitted patients with MDR and carbapenem resistant *Acinetobacter baumannii* infections at MTRH?

1.5 Objectives

1.5.1 General Objective

To determine Multidrug-resistant *Acinetobacter baumannii* among patients admitted to intensive care unit at Moi Teaching and Referral Hospital, Uasin Gishu County, Kenya.

1.5.2 Specific Objectives

i. To determine the prevalence of *A. baumannii* infections among patients admitted to ICU at MTRH.
ii. To decipher the antibiotic sensitivity profiles of *A. baumannii* from patients admitted to the ICU at MTRH.
iii. To determine the factors associated with *A. baumannii* infections among patients admitted to the ICU at MTRH.

iv. To determine the hospitalization outcomes of ICU admitted patients with MDR and carbapenem resistant *Acinetobacter baumannii* infections at MTRH.

1.6 Significance of the Study

The findings from this study hold immense significance, as they will go a long way to inform on the most effective treatment of *A. baumannii* infections in Kenya and the broader region. With a comprehensive understanding of the prevalence of *A. baumannii* isolates that are insensitive to multiple drugs in the ICU setting, healthcare providers can categorize and identify patients at high risk, enabling the implementation of targeted and effective infection control measures. Moreover, the identification of factors associated with *A. baumannii* carriage offers invaluable insights for early detection of susceptible and at-risk patients, facilitating timely intervention and improved patient outcomes. By profiling the antibiotic susceptibility patterns of *A. baumannii*, healthcare providers can make well-informed decisions on selecting and prescribing antibiotic therapies for ICU patients, contributing significantly to antibiotic stewardship efforts.

CHAPTER TWO: LITERATURE REVIEW

2.1 Taxonomy of *Acinetobacter baumannii*

Acinetobacter baumannii is a Gram-negative coccobacillus known for its remarkable ability to colonize both environmental reservoirs and the human body, as evidenced by studies such as Uwingabiye *et al*. (2016). In the recent past, it has gained significant recognition as a major source of hospital acquired infections, resulting in extraordinary mortality and morbidity rates, particularly among immune-compromised individuals (Uwingabiye *et al*., 2016).

In the taxonomic hierarchy, *A. baumannii* belongs to the family Moraxellaceae, order Pseudomonadales, class Gammaproteobacteria, and phylum Proteobacteria within the bacteria kingdom. The species *A. baumannii* was officially designated in the year 1986 by Bouvet & Grimont (1986). Notably, the genus Acinetobacter has undergone several taxonomic variations over the years, reflecting the ongoing exploration and understanding of its diverse species. This taxonomic evolution underscores the significance of studying and characterizing *A. baumannii* to better comprehend its clinical impact and adaptability.

Infections attributed to *A. baumannii* emerged as a critical medical concern in the 1970s, as highlighted by Bergogne & Towner (1996). Since then, *A. baumannii* has progressively gained importance as a challenging pathogen in the hospital environment. This rise in significance can be attributed to the vulnerability of hospitalized patients, who often suffer from serious underlying conditions, as well as medical advancements that involve the increased use of invasive devices and highly selective antibiotics, as mentioned by Antunes *et al*. (2014). These conditions compromise the immune defense of patients, making them highly susceptible to

opportunistic infections caused by *A. baumannii*. The relentless adaptability of *A. baumannii*, combined with its inherent resistance to various antibiotics, has further compounded the problem, leading to persistent outbreaks in healthcare settings. Additionally, its ability to persist on environmental surfaces, equipment, and medical devices contributes to its nosocomial transmission, making it a formidable challenge for infection control and patient safety.

2.2 Socio demographic factors associated with *A. baumannii* infections

Married individuals had an increased risk of mortality in comparison to single individuals. The crude odds ratio (cOR) of 4.17 indicated a 4.17-fold increased risk of mortality among married patients. The crude odds ratio (cOR) of 4.17 indicated a 4.17-fold increased risk of mortality among married patients (Vahhabi *et al*., 2021). This finding is contrary to that of most previous studies that have reported lower mortality rates among married individuals compared to their single counterparts. The possible reasons for the current association could be attributed to differences in social support and increased responsibilities among married individuals hence consequently poor quality of life, leading to poorer treatment outcomes (Vahhabi *et al.,* 2021; Mody *et al.,* 2015). With regard to a participant's level of education, those that had non-formal education had a 3.81 fold increased risk of mortality as compared to those who had formal education. This finding is also consistent with the fact that those who are self- employed, a majority of who lack formal education, had a 2.63 fold risk of mortality compared to the employed and unemployed, majority of who had formal education (Mody *et al*., 2015).

2.3 Human Infections and hospital outcomes of *A. baumannii*

Acinetobacter baumannii is responsible for various infections,such as wound infections, skin and soft tissue infections, secondary meningitis and urinary tract infections (Bergogne Bérézin & Towner, 1996; McConnel *et al.,* 2013). Bloodstream infections and ventilator associated pneumonia are responsible for the highest mortality due to *Acinetobacter baumannii* across the world (Antunes *et al.,* 2014). Bacteria enter the body via intravascular catheters, open wounds and mechanical ventilators. Infections due to *A. baumannii* are highly correlated with extended hospitalization periods, older age and the male gender (McConnel *et al.,* 2013). Moreover, *A. baumannii* has been isolated from IV fluids, gloves, beds and clinical monitors which are common instruments used in the ICU. Hospital outbreaks occur via contact transmission either directly from healthcare workers or from contaminated mechanical ventilators, invasive procedures and central venous systems (Huang *et al*., 2011).

It is postulated that ventilator-associated pneumonia due to *A. baumannii* is as a result of airway colonization via environmental exposure, followed by pneumonia development (Antunes *et al.,* 2014). A systematic review determined that infections with *A. baumannii* in hospital settings are correlated with increased mortality. Community-associated pneumonia as a result of *A. baumannii*, though less frequent than hospital infections, has been documented (Antunes *et al.,* 2014). High prevalence of multidrug-resistant *A. baumannii* has been reported in Egypt (El-Kazzaz *et al*., 2020). Moreover, a recent case of unusual bacteremia and pneumonia that is acquired communicably due to multidrug resistant *A. baumannii* has been reported in Pennsylvania. Interestingly, the strain belongs to the sequence type 451 which is prevalent in Asia illustrating how capable the organism is to spreading (Yassin *et al*., 2020).

Acinetobactor baumannii is also associated with bloodstream infections in ICU's (Pagano *et al.,* 2016). Intravascular devices and lower respiratory diseases are the most common bases of *A. baumannii* bloodstream infections. Crude death rates due to *A. baumannii* bloodstream infections have been documented at between 28% and 43% (Antunes *et al.,* 2014). A multicenter case-control study done in Shaanxi, China between 2009 and 2018 concluded that the risk factors acting as independent predictors of bloodstream infection were: ICU admission and carbapenems use prior to positive culture, presence of neutropenia and initial infection in the central nervous system (Zhang *et al*., 2018). Furthermore, mortality due to bloodstream infections was significantly greater compared to other *A. baumannii* infections and a high Pitt bacteremia score independently predicted mortality rates (Gu *et al*., 2021). Research has shown that bloodstream circulation fastens how a microorganism colonizes other body tissues previously colonized with tenacity of *A. baumannii* (Chen *et al*., 2022). This increases the risk of mortality.

Acinetobactor baumannii is a vital cause of burn infections (Tekin *et al*., 2014). Due to a broken immune system as a result of the damaged skin, patients with burn wounds are predisposed to acquiring *A. baumannii* infections particularly in immune-challenged individuals admitted in the ICU. This infection is also a leading cause of morbidity and mortality in the hospital settings (Vahdani *et al.,* 2012; Fallah *et al.,* 2013). Due to poor penetration of antibiotics to burn sites and the multidrug resistance, management of burn infections has overtime proved to be very challenging. Studies have documented high rates of *A. baumannii* infections in burn units (Falah *et al*., 2019; Fallah *et al.,* 2013). Anne-Lise Munier *et al*. (2019 year) reported that multidrug-resistant *A. baumannii* infections were common during an outbreak in a burn unit in Paris and it increased the risk of death and prolonged hospitalization (Munier *et al*., 2019).

Soft tissue and skin infections associated with war injury can produce necrotizing fascilitis and cellulitis that need surgical debridement and antibiotic therapy (McConnel *et al.,* 2013). *A. baumannii* has also been documented to be an etiological agent of surgical site infections and a frequent cause of soft tissue and skin infections in the ICU (McConnel *et al.,* 2013).

This pathogen has been established as a major causative agent of meningitis among patients that are recovering from neurosurgical procedures (Toledo *et al.,* 2012; Tuon *et al.,* 2015). In addition, *A. baumannii* is infrequently associated with endocarditis. Case reports have shown *A. baumannii* endocarditis to be associated with prosthetic valves and intravascular catheters (McConnel *et al.,* 2013). *A. baumannii* is recognized as a source of community acquired infections (Dexter *et al.,* 2015; Chen *et al.,* 2010). These infections are described by acute sepsis presented as severe pneumonia accompanied by or without bloodstream infections. This phase is followed by rapid onset of respiratory infections then followed by septic shock syndrome and general-organ failure. Due to extensive pathogenicity of the disease, most patients demand intensive treatment in the ICU, the mortality rate for community acquired infections has been reported at 64% (Dexter *et al.,* 2015).

2.4 Epidemiology of *A. baumannii* infections

The epidemiology of *Acinetobacter baumannii* infections has become a matter of significant concern over the past two decades, particularly due to its association with high morbidity rates as well as high mortality rates, especially in immune-compromised individuals (Punpaich *et al*., 2012; Özgür *et al.,* 2014). The prevalence of *A. baumannii* infections varies across different

geographic locations and patient populations, often influenced by economic status (Ntusi *et al*., 2012).

A comprehensive international study, as reviewed by Uwingabiye *et al*. (2016), reported varying infection rates across different regions: 17.1% in Eastern Europe, 19.2% in Asia, 5.6% in Western Europe, 3.7% in North America, 4.4% in Oceania, 13.8% in the Caribbean and South America, and 14.8% in Africa. In Pakistan, Mushtaq *et al*. (2013) observed a prevalence of *A. baumannii* infections at 4.2%. In India, Jaggi *et al*. (2012) reported that *A. baumannii* accounted for 9.4% of all gram-negative rods in the study hospital and 22.6% in the ICU. In Tehran, a study by Vala *et al.* (2014) found that all non-fermenter gram-negative bacilli isolated from burn patients were identified as *A. baumannii.* Similarly, at Ibn Rochd University Hospital in Casablanca, *A. baumannii* constituted the second most common pathogen isolated from ICU patients' blood in the years 2010 and 2014, representing 9.2% of all isolates (Kettani *et al*., 2017).

A Moroccan study carried out in a teaching hospital reported a general rate of *Acinetobacter* isolation at 6.94%, with *A. baumannii* being the most prevalent in ICUs at 24.85%. These clinical isolates of *A. baumannii* accounted for 9.6% of all gram-negative bacilli in the hospital and a significant proportion of 31.5% in the ICU (Uwingabiye *et al.,* 2016). Furthermore, among South African HIV-positive individuals, the documented infection rate with *A. baumannii* stands at 15% (Ntusi *et al*., 2012). In addition to the aforementioned studies, several other investigations have shed light on the epidemiology of *Acinetobacter baumannii* infections in different regions and patient populations.

In a study conducted in Greece, Karageorgopoulos *et al*. (2008) reported a high incidence of carbapenem-resistant *A. baumannii* infections in critically ill patients, particularly in ICUs. This study highlighted the emergence and spread of multidrug-resistant strains of *A. baumannii*, contributing to the challenge of managing infections caused by this pathogen. A study in Malaysia by Lim *et al*. (2012) revealed a notable prevalence of *A. baumannii* in healthcare-associated infections, including ventilator-associated pneumonia and bloodstream infections. The study emphasized the significance of infection control measures to prevent the spread of *A. baumannii* in healthcare settings.

Research conducted in Colombia by Robledo *et al*. (2014) focused on the genetic diversity of *A. baumannii* strains and their antimicrobial resistance patterns. The study found a wide array of resistance genes, highlighting the need for continuous surveillance and tailored antimicrobial therapy to address local resistance patterns. In Saudi Arabia, Al-Agamy *et al.* (2014) reported on the increasing prevalence of carbapenem-resistant *A. baumannii* isolates in hospitals, indicating the urgency required for effective infection control strategies and stewardship with regard to antimicrobials.

Moreover, in Brazil, Almeida *et al.* (2017) investigated the epidemiology of *A. baumannii* infections in a university hospital, uncovering a higher incidence in ICUs and a concerning association between resistance to multiple antibiotics and increased mortality rates. Furthermore, a study in Taiwan by Chang *et al.* (2019) highlighted the springing up of strains of *A. baumannii* that were insensitive to Colistin, posing a critical challenge in the management of infections and necessitating the exploration of alternative treatment options. These studies collectively

underscore the global impact of *A. baumannii* infections and its propensity to cause severe outcomes, particularly in vulnerable patient populations. The diversity in infection rates and antimicrobial resistance patterns across different regions emphasizes the importance of local surveillance and tailored intervention strategies to combat the spread of *A. baumannii* and safeguard patient health.

While the disease patterns of *Acinetobacter baumannii* infections have been extensively evaluated in various regions globally, including Africa, there is limited specific data available for Kenya. This knowledge gap presents a critical need for further research and surveillance to enhance understanding of the prevalence and impact of *A. baumannii* infections in the Kenyan healthcare setting.

In the context of Kenya, the available statistics on *A. baumannii* infections are relatively scarce. A study conducted by Kiiru *et al*. (2016) in a tertiary care hospital in Nairobi reported a prevalence of 8.9% of *A. baumannii* among Gram-negative bacteria isolated from clinical samples. Another study by Omuse *et al.* (2017) in a Kenyan teaching and referral hospital found *A. baumannii* to be one of the predominant bacteria causing bloodstream infections, with a prevalence of 13.3% among the isolates. Despite these efforts, the available data is still limited, and there are considerable gaps in understanding the full scope of *A. baumannii* infections in Kenya. Extensive research is necessary to determine the prevalence and antibiotic resistance patterns of *A. baumannii* in different healthcare settings across the country, including ICUs and other high-risk areas. Additionally, there is a need to explore the factors responsible for the

spread and transmission of *A. baumannii* in Kenyan hospitals, as well as its impact on patient outcomes.

2.5 Prevalence of *Acinetobacter baumannii* Drug resistance

The prevalence of definite *A. baumannii* lineages has been correlated to the multi-drug resistant (MDR) phenotype of infecting strains. Nevertheless, it is not clear if specific epidemic strains acquired the MDR phenotype or if the MDR phenotypes are vital for specific strains to be epidemic. *Acinetobacter baumannii* antibiotic resistance has gradually increased since the 1970s by which period many strains were susceptible to frequently used antibiotics (Antunes *et al.,* 2014). By the year 2007, up to 70% of some isolates of *A. baumannii* were insensitive to multiple drugs, including non-susceptibility to carbapenems, which are considered to be effective against MDR *A. baumannii* infections (Kempf & Rolain, 2012). Unsurprisingly, carbapenem resistance has been reported in number of countries.

Presently, colistin appears to be the most effective and reliable drug ***in vitro*** against multi drug resistant *A. baumannii***,** however, colistin has been linked with several side effects and it is not appropriate for treating all sorts of diseases. Carbapenem resistance is a frightening reality. Worldwide resistance to imipenem reached to levels greater than 50% between the years 2005 to 2009 (Mendes *et al.,* 2010).

Clones of imipenem resistant *A. baumannii* complemented by a wide distribution of the OXA-23 gene have been identified in China (Wang *et al.,* 2007). In an international study reported that MDR isolates of *A. baumannii* were highest (93%) in the Middle East and Europe, were between

the 77% and 87% range in Africa and were lowest in North America at 47%. Multidrug resistant isolates from this study were high in isolates obtained from the ICUs. A 2008 review on Acinetobacter drug resistance found that there was a higher antibiotic resistance in Europe and Asia compared to the United States while a recent report using data obtained between 2004 and 2013 found that the highest MDR isolates of *A. baumannii* were found in Africa (Falagas *et al.*, 2008; Hoban *et al.*, 2015).

Findings in literature show a low susceptibility of *A. baumannii* to antibiotics in Middle East and Europe. The European Antimicrobial Resistance Surveillance network revealed that there was a high resistance to fluoroquinolones, carbapenems and to aminoglycosides more so in the eastern and southern parts of Europe (ECDC, 2013; ECDC, 2014). A study reviewing patterns of resistance in Iran over a period of 15 years (Moradi *et al.*, 2015), a study of antibiotic resistance in Iranian ICUs and studies from both Lebanon and Turkey (Cicek et *al.*, 2014; Hammoudi *et al.*, 2015) confirmed the decreasing susceptibility patterns and high resistance levels, especially to carbapenems. Few data regarding *A. baumannii* antimicrobial resistance are available from Africa. However, a study by Lob *et al*. (2016) revealed there being a low susceptibility and high MDR rates (80%) in Africa. Other studies have shown an even higher multidrug resistance rates in Africa, that is 94% in Algeria and 100% in Egypt (Nageeb *et al.*, 2014; Khorsi *et al.*, 2015). There was a low susceptibility (less than 30%) to cefepime, tomeropenem and to tazobactam in South Africa between the years 2004 to 2011 (Kanj *et al.*, 2014).

Antibiotic resistance seems to be alarming in the ICUs than in other hospital wards. This is demonstrated by studies done in Europe and the United States (Sader *et al.*, 2014) as well as by a

TEST report of global data between the years 2004-2009 (Morfin-Otero *et al.,* 2012) and a study by Lob *et al.* (2016) that took into account global data.

Antimicrobial resistance and ecological resilience are the two factors driving the ubiquitous and significant *A. baumannii* dissemination (Lin & Lan, 2014). Increase in antibiotic resistance was documented in the years 2004 to 2009 with the highest resistance rates recorded for piperacillin-tazobactam (82.0%), ceftriaxone (83.6%) and ceftazidime (80.3%) in the Middle East. In the Asia Pacific, there was a notable increase in resistance ranging from 19.1% ceftazidime resistance to 38.9% levofloxacin resistance. Significant resistance to different drugs was also documented in Africa (piperacillin-tazobactam, cefepime, ceftriaxone, meropenem, amikacin and levofloxacin) and Europe (piperacillin-tazobactam, ceftazidime, ceftriaxone, amikacin, levofloxacin, meropenem, minocycline, and cefepime) (Morfin-Otero *et al.,* 2012).

The very first MDR *Acinetobacter baumannii* isolate was discovered in Taiwan in the year 1998, followed by many other outbreaks in the successive years (Lin & Lan, 2014). The Taiwan surveillance of antimicrobial resistance showed that resistance to imipenem had increased from 3.4% in 2002 to 58.7% in the year 2010 while extensively drug resistant *A. baumannii* increased from 3.4% to 58.7% within the same years (Kuo *et al.,* 2012). Multidrug resistant *A. baumannii* is also prevalent in Belgium, Korea, Iraq, Italy, Israel, America, Greece, and Brazil (Lin & Lan 2014).

Clonal distribution among three hospitals within two different cities has been recorded in China thereby bringing forward the epidemic potential of MDRAB. Intra-institutional and inter-institutional dissemination of a strain of *A. baumannii* is possible. Multi-drug resistant clones are capable of coexisting endemically in one hospital for years with the same clones spreading within a short period of time on a small scale. Clonal outbreaks can be identified by a close survey of epidemic sources (Lin & Lan, 2014).

Uwingabiye *et al.* (2016) review that colistin is repeatedly the most reliable treatment choice, while some *Acinetobacter* strains have developed resistance to colistin. Resistance to colistin has been estimated to be 5.3% in the United States, 2.7% in South Africa, 1.2% in India, 0.9% in Tunisia and 0.5% in Saudi Arabia.

2.5.1 Carbapenems

Carbapenems, as β-lactam antibiotics, have long been considered as crucial last-resort options for treating infections caused by multidrug-resistant Gram-negative bacilli. They exhibit stability against AmpC β-lactamases and extended-spectrum β-lactamases (ESBL), making them valuable therapeutic choices. However, the landscape has shifted with the emergence of carbapenem resistance, posing a significant global concern (Djahmi *et al*., 2014). The development of insensitivity to carbapenems is associated with the production of β-lactamases with reduced carbapenemase activity, alterations in bacterial permeability, and the emergence of carbapenem-hydrolyzing β-lactamases (Rodriguez *et al*., 2018).

Carbapenemases, as key players in carbapenem resistance, are particularly worrisome as they confer resistance not only to β-lactam antibiotics but also to other classes of antibiotics such as fluoroquinolones, aminoglycosides, and cotrimoxazole (Souli *et al.,* 2008). They are categorized into three molecular classes: Ambler class A, class D, and class B β-lactamases, which are encoded by genes present on plasmids or chromosomes (Nahid *et al*., 2013).

While the emergence of insensitivity to carbapenems is a global phenomenon, its prevalence, distribution, and mechanisms can vary across different regions and healthcare settings. Further research is required to compare the prevalence and impact of carbapenem resistance in various countries and regions, including Kenya. Understanding the specific carbapenemase types prevalent in different geographic locations and their associated resistance patterns can inform tailored treatment strategies and infection control measures. Comparative studies can shed light on the dynamics of carbapenem resistance, identifying potential risk factors for its spread and informing the development of region-specific antimicrobial stewardship programs. Additionally, investigating the mechanisms of insensitivity to carbapenems in different bacterial strains can provide valuable insights into the evolution and transmission of resistance determinants, guiding efforts to combat their dissemination (Tängdén *et al*., 2014).

Furthermore, the impact of carbapenem resistance goes beyond individual patient outcomes and poses a significant economic burden on healthcare systems worldwide. The prolonged hospital stays, increased healthcare costs, and additional resources required for managing infections caused by carbapenem-resistant organisms contribute to the financial strain on healthcare facilities (Tängdén *et al*., 2014). In the context of Kenya, there is a need for comprehensive

studies to assess the patterns and prevalence rates towards insensitivity to carbapenems in healthcare settings. The limited data available on carbapenem resistance in Kenya hinders the development of evidence-based strategies for infection control and antimicrobial stewardship tailored to the local context. Understanding the factors responsible for the springing up and circulation of carbapenem-resistant *A. baumannii* strains in Kenyan hospitals is essential for formulating targeted interventions to curb its dissemination.

Moreover, there is a critical need for surveillance programs that monitor the prevalence of carbapenem resistance and track its changes over time. These programs can play a crucial role in early detection of emerging resistance patterns and facilitate prompt implementation of appropriate control measures. Collaborative efforts among healthcare institutions, researchers, and policymakers in Kenya are necessary to establish a robust surveillance system that can generate reliable data on carbapenem resistance trends in the country.

Addressing the global concern of carbapenem resistance requires a multifaceted approach that encompasses both prudent use of antimicrobials and the innovation of new therapeutic strategies. Investing in research to understand the genetic basis and mechanisms of carbapenem resistance in *A. baumannii* and other Gram-negative bacilli can provide valuable insights into potential targets for new antimicrobial agents (Tängdén *et al.*, 2014). . Additionally, exploring alternative treatment options, such as combination therapies or novel agents, may offer new avenues for combating carbapenem-resistant infections.

2.6 Factors Associated with Carriage of *A. baumannii*

Factors associated with the carriage of *Acinetobacter baumannii* are complex and multifactorial, involving both host-related and environmental factors. Understanding these factors is crucial for effective infection control strategies and the prevention of *A. baumannii* transmission in healthcare settings. Comprehensive research has been carried out globally to explore the determinants of *A. baumannii* carriage, but there is still a need for further research, especially in specific regions like Kenya.

One of the key host-related factors influencing *A. baumannii* carriage is the immune status of individuals. Immune-compromised patients, such as those with underlying medical conditions, immunosuppression, or prolonged hospital stays, are more predisposed to *A. baumannii* colonization. The weakened immune defenses make these individuals more susceptible to acquiring the bacteria and subsequent infections. Prior antibiotic exposure is another important factor associated with *A. baumannii* carriage. Patients who have received previous antibiotic therapy are at an increased risk, as antibiotics can disrupt the normal microbial flora, creating a favorable environment for the colonization of *A. baumannii*.

Invasive procedures and the use of invasive devices are significant contributors to *A. baumannii* carriage. Ventilators, urinary catheters, and central venous catheters provide entry points for the bacteria to colonize and potentially cause infections. These devices are commonly used in intensive care units, making ICU patients more vulnerable to *A. baumannii* carriage. The duration of stay in the hospital is also a key factor in *A. baumannii* colonization. Prolonged

hospitalization provides more opportunities for exposure to the bacteria, increasing the risk of colonization.

The severity of illness is another determinant of *A. baumannii* carriage. Patients with more severe underlying conditions, especially those admitted to intensive care units, are more predisposed. The combination of a compromised immune system, invasive procedures, and prolonged hospitalization in critical care settings creates an environment conducive to *A. baumannii* colonization.

In addition to host-related factors, the hospital environment plays a significant role in the transmission and carriage of *A. baumannii.* The bacterium is well-adapted to survive on various surfaces, making hospital settings particularly conducive to its persistence and transmission. Nosocomial infections, more so in intensive care units, are often linked to *A. baumannii* outbreaks. While there have been numerous studies exploring the factors responsible for *A. baumannii* carriage in various healthcare settings globally, there is still a need for more research, especially in regions like Kenya. Understanding the specific risk factors prevalent in different geographic locations and healthcare facilities can help tailor infection control measures and antimicrobial stewardship programs to curb the circulation of *A. baumannii*.

In Kenya, limited data on *A. baumannii* carriage and its associated risk factors hinder the development of evidence-based strategies for infection control. Conducting comprehensive studies to assess the prevalence and trends of *A. baumannii* carriage in Kenyan hospitals is

crucial. Such studies can identify specific risk factors in the local context and provide insights into the epidemiology of *A. baumannii* in the country.

Comparative studies across different regions and healthcare settings can shed light on the dynamics of *A. baumannii* carriage and identify potential risk factors for its spread. Understanding the genetic basis and mechanisms of *A. baumannii* resistance can also provide valuable insights into potential targets for new antimicrobial agents. Exploring alternative treatment options, such as combination therapies or novel agents, may offer new avenues for combating *A. baumannii* infections.

2.7 Antibiotic Susceptibility Patterns of *A. baumannii*

Antibiotic susceptibility patterns of *Acinetobacter baumannii* have become a critical area of research and concern as a result of the rising prevalence of strains that are resistant to multiple strains (Rodriguez *et al*., 2018). Understanding the susceptibility profiles of *A. baumannii* is crucial for guiding targeted antibiotic therapy and infection mitigation strategies. Numerous studies have been carried out worldwide to investigate the antibiotic susceptibility profiles of *A. baumannii* isolates, but gaps still exist, particularly in the context of specific regions like Kenya.

Acinetobacter baumannii is notorious for its tendency to exhibit resistance to multiple antibiotics, including carbapenems, which are considered as last-resort treatment options for multidrug-resistant Gram-negative bacteria. Carbapenems, as β-lactam antibiotics, were once highly effective against *A. baumannii*, but the emergence of carbapenem resistance has significantly limited their clinical utility (Djahmi *et al*., 2014). Resistance to carbapenems is

through carbapenemase activity and alterations in bacterial permeability, rendering these antibiotics ineffective in treating *A. baumannii* infections (Rodriguez *et al*., 2018).

In addition to carbapenems, *A. baumannii* has shown resistance to various other classes of antibiotics, such as fluoroquinolones, aminoglycosides, and cotrimoxazole (Souli et al., 2008). This extensive resistance poses a significant challenge for healthcare providers, as limited treatment options are available for infections caused by multidrug-resistant *A. baumannii* strains. Comparative studies on antibiotic susceptibility patterns have revealed regional variations in the prevalence and distribution of resistant *A. baumannii* isolates. A review by Uwingabiye *et al.* (2016) documented varying infection rates across different regions: 17.1% in Eastern Europe, 19.2% in Asia, 5.6% in Western Europe, 3.7% in North America, 4.4% in Oceania, 13.8% in the Caribbean and South America, and 14.8% in Africa. The variations in resistance rates may be attributed to differences in antibiotic usage, infection mitigation strategies, and local antimicrobial stewardship efforts.

However, in the Kenyan context, comprehensive data on the antibiotic susceptibility profile of *A. baumannii* is limited or completely lacking. There is a critical need for well-designed studies to assess the prevalence of antibiotic resistance in *A. baumannii* isolates from Kenyan hospitals. Understanding the local resistance patterns can aid in tailoring empiric antibiotic therapy and implementing effective infection mitigation strategies to curb the spread of resistant strains. Furthermore, investigating the mechanisms of antibiotic resistance in *A. baumannii* strains in Kenya can provide valuable insights into the genetic basis of resistance and identify potential targets for novel antimicrobial agents. Comparative studies between Kenyan isolates and those

from other regions can shed light on the factors contributing to regional variations in antibiotic susceptibility patterns.

The emergence and circulation of antibiotic resistance tendencies in *A. baumannii* are global concerns, and efforts to combat this threat require collaborative efforts from the international scientific community. Investigating alternative treatment options, combination therapies, and novel agents may offer new avenues for managing infections caused by multidrug-resistant *A. baumannii* strains beyond carbapenems. *Acinetobacter baumannii* has demonstrated resistance to other crucial classes of antibiotics, such as fluoroquinolones, aminoglycosides, and cotrimoxazole, further complicating treatment strategies for complications associated with this pathogen (Souli *et al*., 2008). This extensive resistance creates an urgent need for novel therapeutic approaches and infection mitigation strategies to combat the growing threat of multidrug-resistant *A. baumannii* strains.

A wealth of research has been carried out worldwide to examine the antibiotic susceptibility profiles of *A. baumannii* isolates. Comparative studies across different regions have revealed significant regional variations in the prevalence and distribution of resistant strains (Uwingabiye *et al*., 2016). In Eastern Europe, infection rates were reported at 17.1%, while in Asia, it was 19.2%. Western Europe exhibited a lower rate at 5.6%, North America at 3.7%, Oceania at 4.4%, the Caribbean and South America at 13.8%, and Africa at 14.8% (Uwingabiye et al., 2016). Such discrepancies may be attributed to differences in antibiotic prescribing practices, infection control measures, and the implementation of local antimicrobial stewardship programs.

However, within the context of Kenya, comprehensive data on the antibiotic susceptibility patterns of *A. baumannii* isolates remain scarce or non-existent. This critical gap in knowledge necessitates well-designed studies to assess the prevalence of antibiotic resistance in *A. baumannii* isolates from Kenyan hospitals. Understanding the local resistance patterns is imperative to tailor empiric antibiotic therapy as well as putting in place of effective infection control measures to arrest the circulation of strains that are resistant in Kenyan healthcare facilities.

Furthermore, delving into the mechanisms of resistance towards antibiotics among *A. baumannii* strains in Kenya can offer valuable insights into the genetic basis of resistance and identify potential targets for novel antimicrobial agents. Comparative studies between Kenyan isolates and those from other regions can provide crucial information on factors contributing to regional variations in antibiotic susceptibility patterns, which can inform targeted interventions and enhance global efforts to combat antimicrobial resistance.

CHAPTER THREE: MATERIALS AND METHODS

3.1 Study Area

This study was carried out in the ICU section of Moi teaching and Referral hospital (MTRH). The facility is the second largest public hospital in Kenya. It is located 0°31′N 35°17′E along Nandi Road in Eldoret, Uasin Gishu county (311 kilometers Northwest of Nairobi), Kenya (MTRH, 2022). It serves residents from 24 counties in Kenya, Southern Sudan, parts of Eastern Uganda and Democratic Republic of Congo. At the time of this study, MTRH had a bed capacity of 1020 serving as a level six referral hospital. It offers inpatient, outpatient and specialized care services such as the ICU (MTRH, 2022). The intensive care unit had a bed capacity of 20 beds at the time of study. The ICU capacity may have increased due to the pressure occasioned by Covid 19 pandemic in the country recently. These hospital demographics made the facility more ideal for the current study.

3.2 Study Design

This study adopted a cross-sectional study design among patients admitted to the ICU at MTRH between July 2019 and July, 2020.

3.3 Study Population

Patients admitted in the ICU at MTRH constituted the study population for this research. This cohort serves as high-risk individuals for *A. baumannii* co-infection in the hospital setup and ICU environs have been shown to be reservoirs of transmission of *A. baumannii* infection within hospital settings (Shamsizadeh *et al.,* 2017).

3.3.1 Inclusion Criteria

i. Patients admitted to the ICU at MTRH

ii. Patients who would have been admitted to the MTRH – ICU section for a minimum of 48 hours preceding this study.

iii. MTRH – ICU section patients on ventilator support since admission

iv. Patients who consent (self or by caregiver) to participate in the study.

3.3.2 Exclusion Criteria

i. Patients admitted to the general care wards at the study hospital.

ii. Patients whose admission to the MTRH – ICU section would be less than 48 hours by the time of the study

iii. Patients who declined consensual participation in the study.

3.4 Sample Size Determination

The study sample size was calculated according to the Chow *et al*. (2007) formula. The prevalence rate used was 9.5% (Rudan *et al.*, 2008) as follows:

$$n = \frac{z^2 \hat{p}(1-\hat{p})}{m^2}$$

Where:

N : Desired minimal sample size.

Z : Standard normal deviation = 1.96 (from the tailed normal table).

P : Prevalence rate

M : the desired degree of accuracy at 95% confidence level= 0.05

N : 1.96^2 x0.095 (1-0.095) / 0.052 = 132

n :132 samples

3.5 Sampling Technique

Purposive sampling technique according to Palinkas *et al*. (2013) was used to select patients admitted in the ICU at MTRH who constituted the target population. Sampling interval Kth was calculated as; where, MTRH has intensive care units (ICUs) services with an annual capacity of 1,500 patients with a sample size (n=132), giving a sampling interval (K) of 12. Every day for the year of study, intervals of 12 was used to sample participants. The recruitment process was done continuously until 132 study participants were recruited.

3.6 Data Collection

Demographic data, such as gender, age and hospital stay duration, comorbidities, and treatment outcomes, were collected using a standardized questionnaire. The questionnaire was carefully designed and standardized to capture essential variables and clinical information of the study subjects.

3.7 Sample Collection

Clinical samples, including tracheal aspirates, blood samples, urine, and nasopharyngeal swabs, were collected by trained and registered nurses following standard bacteriological procedures. Tracheal aspirates were obtained using a sterile suction catheter, collected in sterile containers, and transported to the microbiology laboratory. Blood samples were collected aseptically using venipuncture techniques directly into BD BACTEC™ Blood Culture Media (Becton, Dickinson

and Company, United States). Urine samples were collected in sterile containers using clean-catch techniques and for the patients in a coma, urine was aspirated directly from the urinary bladder while nasopharyngeal swabs were obtained using sterile swabs and placed in Stuart's transport medium.

3.8 Transportation and Storage of Samples

All samples got to be delivered to the microbiology laboratory within the Moi Teaching and Referral hospital in cold boxes at a temperature of 2-8°C. Immediate analysis was performed within a specified holding time, typically within 2 hours of collection, to ensure sample integrity and accurate results (Lee et al. (2017). Blood samples were used to investigate *A. baumannii-associated* bacteremia, urine samples to assess for presence of urinary tract infections with *A. baumannii* as the core etiological agent, while; tracheal aspirates and nasopharyngeal swabs were used to probe for *A. baumannii* associated respiratory tract infections.

3.9 Laboratory Analysis

3.9.1 Culture

Laboratory isolation of *A. baumannii* was done as per the procedure laid out by Lee *et al*. (2017). Details of the collected samples and the forms they were brought with were confirmed if they match. Samples were then assigned accession numbers for laboratory identification and record keeping. Three blood agar culture media and three Bromocresol purple (BCP) lactose agar culture media were prepared and sterilized by autoclaving at 121^0 C for 15 minutes. Direct inoculation of samples was performed aseptically under a biosafety cabinet. Each of the three

samples was cultured on one blood agar medium and one BCP medium making a total of six culture media.

The tracheal aspirates were cultured on blood agar and MacConkey agar plates and incubated at a temperature of 35-37°C in ambient air for 24-48 hours. Biochemical tests, including oxidase and catalase tests, were conducted to aid in identification. Blood samples were initially inoculated into enriched broth media. Subsequently, for the isolation of *Acinetobacter baumannii*, they were also subcultured on blood agar plates along with other selective and differential media such as MacConkey agar, cetrimide agar, and chocolate agar. These additional media allow for the specific identification and isolation of *Acinetobacter baumannii* based on its growth characteristics and biochemical reactions. Incubation was carried out at 35-37°C either in a candle jar (5-10% carbon dioxide) or under aerobic conditions for a period of 24-48 hours (Lee *et al*., 2017).

Subsequent to inoculation and sub culturing, biochemical tests such as catalase production, oxidase activity, urease test, citrate utilization, and the API 20NE system were conducted to facilitate the identification of *Acinetobacter baumannii*. Urine samples were streaked on Cysteine Lactose Electrolyte Deficient (CLED) agar plates and incubated at 35-37°C in ambient air for 24-48 hours. Colony morphology examination and biochemical tests such as indole and citrate utilization were conducted. Nasopharyngeal swabs were streaked on either MacConkey agar or Cetrimide agar plates and incubated at 35-37°C in ambient air for 24-48 hours. Colonies were then subjected to oxidase and urease tests for further identification. Antibiotic resistant

Acinetobacter baumannii isolates were then subjected to antibiotic susceptibility testing (Lee *et al*., 2017).

3.9.2 Antibiotic Susceptibility Testing

Drug susceptibility testing was done for all isolates of *A. baumannii* as per the CLSI recommended guidelines (CLSI, 2018). This was done using VITEK-2 Compact system with updated Advanced Expert System (bioMerieux, Marcy l'Etoile, France), where the AST-GN76 and AST-N282 cards were utilized to determine the susceptibility of the isolates. The tested antibiotics included Imipenem (IPM), Meropenem (MPM), Ertapenem (EPM), Doripenem (DPM), Biapenem (BPM), Tigecycline (TIG), Colistin (COL), Polymyxin (POL), Aminoglycosides (AMI), carbapenems (CAR) and Trimethoprim-sulfamethoxazole (TRI) and Piperacillin (PIP). Control strains, *Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853, were used to ensure the validity and quality assurance of the tests.

Clinical breakpoints whether resistant, intermediate or sensitive were interpreted with reference to the CLSI (2018) guidelines. Isolates of *Acinetobacter baumannii* that were resistant to three or more classes of antibiotics were termed multidrug resistant (Uwingabiye *et al.*, 2016). The E-test was used to ascertain the minimum inhibitory concentrations for colistin (Biomérieux Marcy l'Etoile France).

3.10 Ethical Considerations and Permit

The study was conducted with approval from the School of Medicine, Moi University and the superintendent at Moi Teaching and Referral Hospital (ELD/MTRH/R&P/10/2/V.2/2010), while

ethical clearance was granted by the Institutional Research and Ethics Committee (IREC) at Moi University under reference number (IREC/2019/126 - 0003392). The National Commission of Science Technology and Innovation (NACOSTI) also issued a permit for data collection under licensure number (NACOSTI/P/19/75649/29865). Prior to sample collection, informed consent was obtained from all participants or their representatives, and they were given the opportunity to opt-out of the study at any time. To ensure confidentiality, data relating to patient characteristics were anonymized with codes. Samples were disposed off/ safely through the established hospital system after analysis, and all data collected will be deleted and shredded three years after the completion of the study.

3.11 Data Analysis

Mean values and standard deviations were used to present data in tables. Statistical analysis was carried out using SPSS Statistics version 25.0 (IBM, 2017). Percentages and proportions were utilized to characterize the social and clinical demographics of the subjects. Additionally, odds ratios (ORs) were computed to assess the associations between social and clinical demographics and the presence or absence of *Acinetobacter baumannii* carriage, as well as hospitalization outcomes (died or discharged). Furthermore, antibiotic susceptibility profiles and phenotypes were analyzed using high multiple antibiotic resistance index (MARI). Statistical significance was set at $p \leq 0.05$.

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CHAPTER FOUR: RESULTS

4.1 Socio-demographic and clinical characteristics of the study population

A total of 132 patients were enrolled in the study. Majority of the participants (51.5%, 68/132) were male. The median age was 52 (IQR =36 – 58) years with (38.6%, 51/132) of the participants aged between 45 and 59 years. Most of the participants (74.2%, 98/132) were married. In investigating education level, (39.4%, 52/132) had primary level of education with equal percentage having secondary level education. Almost half of the participants, (44.7%, 59/132) were self-employed. The median BMI was 24.0(IQR: 21 – 26). Majority of the participants (87.9%, 116/132) were referred. All of the participants had at least one comorbidity with renal related conditions (50.8%, 67/132) and respiratory related conditions (42.4%, 56/132). Almost half of the participants (45.5%, 60/132) had specimen obtained from urine. The median hospital stay duration was 32.5(IQR=22 – 52.8) days with most of them (93.9%, 124/132) had more than 10 days of hospital stay. Many of the participants were discharged (70.5%, 93/132) as shown in Table 4.1.

Table 4.1: Socio-demographic and clinical characteristics of the study population

	Frequency	Percent
Gender		
Male	68	51.5
Female	64	48.5
Age (Median, IQR)	**52.0(36 – 58.0)**	
<24	10	7.6
25 – 44	42	31.8
45 – 59	51	38.6
=>60	29	22.0
Marital status		
Single	34	25.8
Married	98	74.2
Education level		
No formal education	17	12.9
Primary level	52	39.4
Secondary level	52	39.4
Tertiary level	11	8.3
Occupation		
Unemployed	50	37.9
Self employed	59	44.7
Employed	23	17.4
BMI (Median, IQR)	**24.0(21 – 26)**	
<18.5	12	9.1
18.5 - 24.9	64	48.5
25 - 29.9	56	42.4
Referral status		
Referral	116	87.9
Non-referral	16	12.1
Comorbidities		
Respiratory related conditions	56	42.4
Renal related conditions	67	50.8
CNS related conditions	10	7.6
Autoimmune related conditions	14	10.6
Metabolic disorder	11	8.3
Asthmatic	10	7.6
Burns	6	4.5
Injuries	8	6.1
Blood stream conditions	8	6.1
Other Conditions	20	15.2
Sample type		
Blood	23	17.4
Tracheal aspirate	49	37.1
Urine	60	45.5
Length of hospital stay (Median, IQR)	**32.5(22 – 52.8)**	
<=5 days	2	1.5
6 - 10 days	6	4.5
>10 days	124	93.9
Outcome		
Discharged	93	70.5
Died	39	29.5

Key: IQR - interquartile range, **LOS** - Length of stay

4.2 The prevalence of Multidrug and carbapenem resistant *Acinetobacter baumannii* among patients admitted to the ICU at MTRH

4.2.1 *Acinetobacter baumannii* infections among patients

Out of the total of 132 patient samples that were collected and analyzed, non-replicate *Acinetobacter baumannii* isolates were detected in 30 samples. This observed prevalence accounted for approximately 22.7% of the sampled population, indicating the presence of *A. baumannii* in a substantial proportion of the analyzed samples.

4.2.2 Distribution of *Acinetobacter baumannii* isolated from the clinical samples

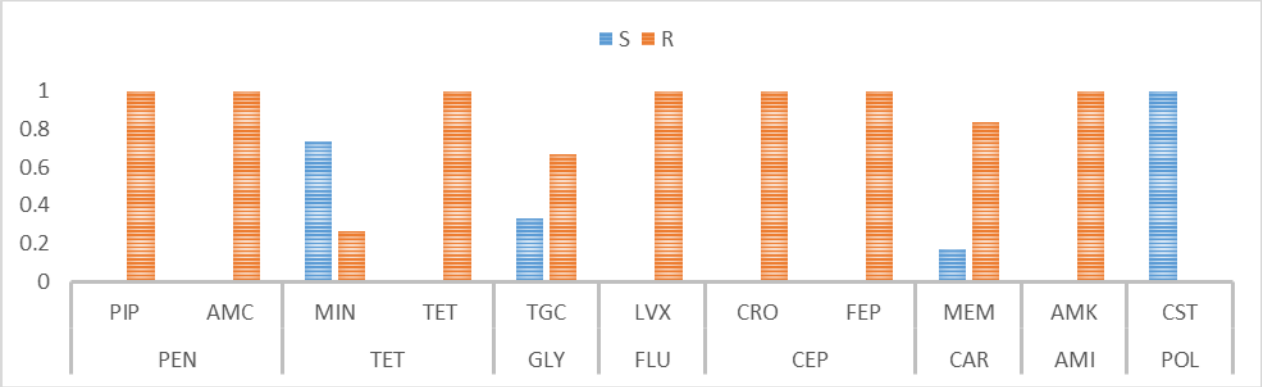
A majority of the non-replicate *Acinetobacter baumannii* isolates were specifically obtained from urine samples, constituting a prevalence of 12.1%. Tracheal aspirates represented the second most common source, yielding an isolation rate of 8.3%. Comparatively, blood samples exhibited the lowest frequency of isolates, accounting for only 2.3% of the isolates as shown in **Table 4.2.**

Table 4.2: Distribution of *Acinetobacter baumannii* isolated from the clinical samples

Sample	Isolates (n)	Percentages (%)
Urine	16	12.1
Tracheal aspirates	11	8.3
Blood	3	2.3

4.3 Antibiotic susceptibility patterns of *A. baumannii* among patients admitted to the ICU at MTRH.

Isolates of *Acinetobacter baumannii* were resistant to all tested drugs except Colistin. They displayed 100% resistance to Piperacillin, Amoxicillin-clavulanic acid, Tetracycline, Levofloxacin, Ceftriaxone, Cefepime, and amikacin. Carbapenem resistance was 83.3%, and the *A. baumannii* isolates were more susceptible to minocycline among the drugs tested (**Figure 4. 1).**



PIP *piperacillin,* **AMC** *amoxicillin-clavulanic acid,* **MIN** *minocycline,* **TET** *tetracycline,* **LVX** *levofloxacin***, TGC** *tigecycline,* **CRO** *ceftriaxone***, FEP** *cefepime***, /AMK** *amikacin***, MEM** *meropenem,* **PEN** *penicillin***, TET** *tetracyclines***, GLY** *glycylcyclines***, FLU** *fluoroquinolones***, CEP** *cephalosporins***, CAR** *carbapenems***, AMI** *aminoglycosides***, POL** *polymyxins,* **S** *susceptible,* **R** *resistant.*

Figure 4.1: Antibiotic susceptibility patterns of A. baumannii among patients admitted to ICU

4.3.1 Drug-resistant phenotypes of *A. baumannii*

All the *Acinetobacter baumannii* were resistant to multiple antibiotics, dominated by carbapenem-resistant isolates (83.3%) and MDR phenotype PIP, AMC/TET/LVX/TGC/CRO, FEP/AMK/MEM, sensitive to only minocycline and colistin among the antibiotics tested (Table 4.3). All the MDR *Acinetobacter baumannii* (MDRAB) were resistant to third-generation and fourth-generation antibiotics tested and amikacin but were susceptible to colistin. The bacterium

displayed a high multiple antibiotic resistance index (MARI), ranging from 0.64 to 0.91as shown in Table 4.3 below.

Table 4.3: Drug-resistant phenotypes of *A. baumannii*

Drug resistance profile	No. abs R	MARI	No. of abs class R	MDR (≥3 absc) n (%)
CSAB				***5 (16.7)***
PIP, AMC/TET/LVX/CRO, FEP/AMK	7	0.64	5	2 (6.7)
PIP, AMC/TET/LVX/CRO, FEP/AMK	7	0.64	5	2 (6.7)
PIP, AMC/MIN, TET/LVX/CRO, FEP/AMK	8	0.73	5	1 (3.3)
CRAB				***25 (83.3)***
PIP, AMC/TET/LVX/CRO, FEP/AMK/MEM	8	0.73	6	3 (10.0)
PIP, AMC/MIN, TET/LVX/CRO, FEP/AMK/MEM	9	0.82	6	2 (6.7)
PIP, AMC/TET/LVX/TGC/CRO, FEP/AMK/MEM	9	0.82	7	15 (50.0)
PIP, AMC/MIN, TET/LVX/TGC/CRO, FEP/AMK/MEM	10	0.91	7	5 (16.7)

PIP *piperacillin,* **AMC** *amoxicillin-clavulanic acid,* **MIN** *minocycline,* **TET** *tetracycline,* **LVX** *levofloxacin,* **TGC** *tigecycline,* **CRO** *ceftriaxone,* **FEP** *cefepime,* **/AMK** *amikacin,* **MEM** *meropenem,* **CSAB** *carbapenem-sensitive Acinetobacter baumannii,* **CRAB** *carbapenem-resistant Acinetobacter baumannii, R, abs, MDR, absc, MARI*

4.3.2 Carbapenem-Resistant *Acinetobacter baumannii* isolates

There were high rates of resistance (83.3%, n=25) of CRAB infections among the sampled subjects. Of the total isolates, (83.3%, n=25) were resistant to carbapenem antibiotics, including IPM (70%), MPM (70%), DPM (86.7), EPM (93.3%), and BPM (96.7%). However, alternative antibiotics, such as COL (16%) and TIG (30%), demonstrated relatively lower resistance rates. Hospital stays of more than 10 days (aOR =2.11, 95% CI:1.31 – 5.12, p =0.002) and presence of

comorbidities (aOR =2.26, 95% CI, 0.63 - 8.17, P =0.212) were significantly associated with resistance to carbapenems (Table 4.4).

Table 4.4: Carbapenem-Resistant *Acinetobacter baumannii* isolates

Antibiotic	R (%)	S (%)
IPM	70	30
MPM	70	30
DPM	86.7	13.3
EPM	93.3	6.7
BPM	96.7	3.3
COL	16	84
TIG	30	70

Imipenem (IPM), Meropenem (MPM), Ertapenem (EPM), Doripenem (DPM), Biapenem (BPM), Tigecycline (TIG), Colistin (COL), R resistant, S sensitive

4.4 Factors associated with MDR and CR *Acinetobacter baumannii* among ICU patients hospitalized at Moi Teaching and referral hospital

4.4.1 Factors associated with *A. baumannii* carriage among patients admitted to the ICU at

Bivariable analysis showed that employed participants were 3.4 times more likely to have *A. baumannii* compared to the unemployed (cOR =3.38, 95%, CI: 1.09 – 10.43, p =0.035), and patients referred to the study site was 83% less likely to have infection compared to non-referral (cOR =0.17, 95%, CI: 0.06 – 0.51, p =0.002). Multivariable analysis showed an independent association between *A. baumannii* carriage with occupation and referral status, where the employed patients were 4.4 times more likely to harbor *A. baumannii* (aOR =4.41, 95%, CI: 1.32 – 14.79, p=0.016), while those referred from other facilities were 86% less likely compared to non-referred patients (aOR =0.14, 95%, CI: 0.05 – 0.45, p =0.001). Patients who were having

high BMI were likely to be infected by *A. baumannii* compared to those who had normal/low BMI (aOR =11.2, 95%, CI: 3.57 – 21.11, p =0.004). However, gender, age, marital status and education factors were not significantly associated with *A. baumannii* carriage among patients admitted to the ICU (Table 4.5).

Table 4.5: Factors associated with *A. baumannii* carriage among patients admitted to the ICU at MTRH

Factor	*A. baumannii* present n (%)	*A. baumannii* absent n (%)	*cOR(95%CI)*	p-value	*aOR (95% CI)*	p-value
Gender						
Male	16(53.3)	52(51.0)	1.10(0.47 - 2.48)	0.839		
Female	14(46.7)	50(49.0)	*Ref*			
Age						
<24	2(6.7)	8(7.8)	1.27(0.22 - 7.45)	0.789		
25 - 44	12(40.0)	30(29.4)	0.80(0.27 - 2.35)	0.679		
45 - 59	9(30.0)	42(41.2)	1.49(0.49 - 4.52)	0.487		
≥60	7(23.3)	22(21.6)	*Ref*			
Marital Status						
Single	10(33.3)	24(23.5)	1.63(0.67 - 3.94)	0.343		
Married	20(66.7)	78(76.5)	*Ref*			
Education level						
No formal	5(16.7)	12(11.8)	0.53(0.08 - 3.40)	0.506		
Primary level	10(33.3)	42(41.2)	0.93(0.17 - 5.01)	0.936		
Secondary level	13(43.3)	39(38.2)	0.67(0.13 - 3.49)	0.631		
Tertiary level	2(6.7)	9(8.8)	*Ref*			
Occupation						
Unemployed	8(26.7)	42(41.2)	*Ref*		*Ref*	
Self employed	13(43.3)	46(45.1)	2.28(0.81 - 6.43)	0.121	2.66(0.89 - 7.93)	0.080
Employed	9(30.0)	14(13.7)	3.38(1.09 - 10.43)	**0.035**	4.41(1.32 - 14.79)	**0.016**
BMI						
<18.5	4(13.3)	8(7.8)	0.44(0.11 - 1.73)	0.237		
18.5 - 24.9	16(53.3)	48(47.1)	*Ref*			
25 - 29.9	10(33.3)	46(45.1)	0.65(0.27 - 1.58)	0.345		**0.004**
Referral status						
Referral	21(70.0)	95(93.1)	0.17(0.06 - 0.51)	**0.002**	0.14 (0.05 - 0.45)	**0.001**
Non-referral	9(30.0)	7(6.9)	*Ref*		*Ref*	
Sample type						
Urine	16(53.3)	44(43.1)	1.51(0.67 - 3.41)	0.405		
Tracheal aspirate	11(36.7)	38(37.3)	0.98(0.42 - 2.27)	0.566		
Blood	3(10.0)	20(19.6)	0.46(0.13 - 1.65)	0.282		
Outcome						
Discharged	24(80.0)	69(67.6)	1.91(0.71 - 5.13)	0.256		
Died	6(20.0)	33(32.4)	*Ref*			
LOHS	41.8 ±21.3	38.1 ±23.0	0.99(0.98 - 1.01)	0.421		

BMI body mass index, **LOHS** length of hospital stay, **Ref** reference, **CI** confidence interval, **cOR** crude odd ratio**, aOR** adjusted odd ratio.

4.4.2 Factors associated with carbapenem-resistant *Acinetobacter baumannii* (CRAB) among ICU patients hospitalized at Moi Teaching and referral hospital

Bivariable analysis established that those who were aged ≥50 years were 21 times more likely to be carbapenem-resistant *Acinetobacter baumannii*, COR =21.0, 95% CI: 1.83 – 240.52, p =0.011. Those who stayed in ICU for more than 30 days were 16 times more likely to be carbapenem-resistant *Acinetobacter baumannii* compared to those who had been admitted (COR = 16.0, 95%CI:1.45 – 176.45, p =0.019. Those who had underlying comorbidity were 46 times more likely to be carbapenem-resistant *Acinetobacter baumannii* compared to those without underlying comorbidity, COR =46.0, 95% CI:3.33 – 634.88, p=0.003. Variables were subjected to multivariable model where none of the variables were statistically significant (Table 4.6).

Table 4.6: Factors associated with carbapenem-resistant *Acinetobacter baumannii* (CRAB) among ICU patients hospitalized at Moi Teaching and referral hospital

	CRAB resistant					
Factors	**Yes, n(%)**	**No, n(%)**	**cOR(95%CI)**	**P-value**	**aOR(95%CI)**	**P-value**
Age						
<50 years	4(16.0)	4(80.0)	Ref			
≥50 years	21(84.0)	1(20.0)	21.0(1.83 - 240.52)	**0.011**	8.33(0.25 - 278.33)	0.236
Gender						
Male	14(56.0)	2(40.0)	1.91(0.27 - 13.50)	0.642		
Female	11(44.0)	3(60.0)	Ref			
Sample type						
Blood	3(12.0)	0				
Tracheal	8(32.0)	3(60.0)				
Urine	14(56.0)	2(40.0)				
Body mass index						
<18.5	3(12.0)	1(20.0)				
≥25	10(40.0)	0				
Normal	12(48.0)	4(80.0)				
Marital status						
Single	9(36.0)	1(20.0)	2.25(0.22 - 23.32)	0.64		
Married	16(64.0)	4(80.0)	Ref			
Education level						
Primary or lower	13(52.0)	2(40.0)	1.63(0.23 - 11.46)	0.595		
Secondary or higher	12(48.0)	3(60.0)	Ref			
Employment status						
Unemployed	7(28.0)	1(20.0)	1.56(0.15 - 16.45)	0.595		
Employed	18(72.0)	4(80.0)	Ref			
Length of ICU stay						
≤30 days	5(20.0)	4(80.0)	Ref			
>30 days	20(80.0)	1(20.0)	16.0(1.45 - 176.45)	0.019	6.90(0.23 - 211.55)	0.269
Presence of comorbidity						
Yes	23(92.0)	1(20.0)	46.0(3.33 - 634.88)	**0.003**	4.91(0.12 - 205.73)	0.404
No	2(8.0)	4(80.0)	Ref			
ICU admission outcome						
Died	5(20.0)	1(20.0)	1.0(0.09 - 11.03)	0.746		
Discharged	20(80.0)	4(80.0)	Ref			

***CRAB**: Carbapenem-resistant Acinetobacter baumannii**, ICU:** Intensive Care Unit, **cOR:** Crude Odds Ratio, **aOR**: adjusted Odds Ratio, **CI:** Confidence interval*

4.5 The hospitalization outcomes of ICU admitted patients with MDR and CR *A. baumannii* infections at MTRH

4.5.1 The hospitalization outcomes of ICU admitted patients with MDR *A. baumannii* infections at MTRH

Multivariable analysis for variables with p≤0.2, revealed that those who were married were 8.6 times more likely to die compared to those who were single (aOR =8.56, 95%CI:2.37 – 15.82, p =0.011). Patients who were overweight/obese were 11 times more likely to die when compared to those who had normal BMI (aOR =11.2, 95%, CI: 3.57 – 21.11, p =0.004). The likelihood of death was twice more with the increasing the duration of stay in the hospital (aOR =2.11, 95%, CI: 1.31 – 5.12, p =0.002) as shown in Table 4.7.

Table 4.7: The hospitalization outcomes of ICU admitted patients with *A. baumannii* infections at MTRH

	Discharged n (%)	**Died n (%)**	***cOR (95%CI)***	**p-value**	***aOR (95%CI)***	**p-value**
Gender						
Male	47(50.5)	21(53.8)	0.88(0.41 - 1.85)	0.849		
Female	46(49.5)	18(46.2)	Ref			
Age						
<24	8(8.6)	2(5.1)	0.35(0.06 - 1.97)	0.236	5.61(0.23 - 12.08)	0.319
25 – 44	33(35.5)	9(23.1)	0.39(0.14 - 1.10)	0.074	0.32(0.03 - 4.16)	0.321
45 – 59	35(37.6)	16(41.0)	0.65(0.25 - 1.67)	0.368	0.42(0.06 - 3.24)	0.408
=>60	17(18.3)	12(30.8)	Ref		Ref	
Marital status						
Single	30(32.3)	4(10.3)	Ref		Ref	
Married	63(67.7)	35(89.7)	4.17(1.36 - 12.80)	**0.009**	8.56(2.37 - 15.82)	**0.011**
Education level						
No formal education	7(7.5)	10(25.6)	3.81(0.74 - 19.66)	0.110	1.82(0.12 - 28.75)	0.669
Primary level	36(38.7)	16(41.0)	1.19(0.28 - 5.06)	0.819	0.34(0.03 - 3.31)	0.351
Secondary level	42(45.2)	10(25.6)	0.64(0.14 - 2.83)	0.552	0.44(0.07 - 2.91)	0.397
Tertiary level	8(8.6)	3(7.7)	Ref		Ref	
Occupation						
Unemployed	36(38.7)	14(35.9)	1.85(0.53 - 6.40)	0.333	0.48(0.06 - 3.99)	0.498
Self employed	38(40.9)	21(53.8)	2.63(0.79 - 8.74)	0.116	2.87(0.63 - 13.16)	0.174
Employed	19(20.4)	4(10.3)	Ref			
BMI						
Normal (18.5 - 24.9)	48(51.6)	16(41.0)	Ref			
Underweight (<18.5)	5(5.4)	7(17.9)	0.83(0.37 - 1.87)	0.659	1.45(0.54 - 3.90)	0.462
Overweight/obese(>25.0)	40(43.0)	16(41.0)	3.50(1.12 - 12.66	**0.005**	11.2(3.57 - 21.11)	**0.004**
Referral status						
Referral	79(84.9)	37(94.9)	0.31(0.07 - 1.41)	0.148	0.33(0.05 - 2.11)	0.243
Non-referral	14(15.1)	2(5.1)	Ref		Ref	
Presence of infection						
Yes	24(25.8)	6(15.4)	1.91(0.71 - 5.13)	0.14	2.26(0.63 - 8.17)	0.212
No	69(74.2)	33(84.6)	Ref		Ref	
LOHS (Mean ±SD)	**34.9 ±20.1**	**48.6±25.3**	**1.41(1.01 - 3.41)**	**0.002**	**2.11(1.31 - 5.12)**	**0.002**

BMI body mass index, **LOHS** length of hospital stay, **Ref** reference, **CI** confidence interval, **cOR** crude odd ratio, **aOR** adjusted odd ratio.

4.5.2 Factors associated with ICU mortality in patients with *Acinetobacter baumannii* colonization/infection

Bivariable analysis revealed that there were no statistically significant factors associated with ICU mortality ($p>0.05$). Further, multivariable analysis was done for variables with $p\leq0.2$, with the findings revealing no statistically significant association between variables and ICU mortality as shown in Table 4.8.

Table 4.8: Factors associated with ICU mortality in patients with Ab colonization

Factors	Outcome					
	Died, n(%)	Discharged, n(%)	COR(95%CI)	P-value	aOR(95%CI)	P-value
Age						
<50 years	3(50.0)	5(20.8)	3.80(0.58 - 24.88)	0.175	6.98(0.50 - 96.77)	0.148
≥50 years	3(50.0)	19(79.2)	Ref			
Gender						
Male	4(66.7)	12(50.0)	2.0(0.31 - 13.06)	0.657		
Female	2(33.3)	12(50.0)	Ref			
Marital status						
Single	1(16.7)	9(37.5)	0.33(0.03 - 3.33)	0.633		
Married	5(83.3)	15(62.5)	Ref			
Education level						
Primary or lower	4(66.7)	11(45.8)	2.36(0.36 - 15.46)	0.651		
Secondary or higher	2(33.3)	13(54.2)	Ref			
Employment status						
Unemployed	2(33.3)	6(25.0)	1.50(0.22 - 10.36)	0.645		
Employed	4(66.7)	18(75.0)	Ref			
BMI						
<18.5	2(33.3)	2(8.3)	0.14(0.01 - 1.67)	0.121	0.06(0.002 - 1.80)	0.106
≥25	2(33.3)	8(33.3)	0.57(0.07 - 4.88)	0.609	0.36(0.03 - 5.32)	0.459
Normal	2(33.3)	14(58.3)	Ref			
Sample type						
Blood	1(16.7)	2(8.3)	0.13(0.01 - 3.08)	0.209	0.10(0.002, 4.42)	0.23
Tracheal	4(66.7)	7(29.2)	0.12(0.01 - 1.25)	0.075	0.11(0.01 - 1.49)	0.096
Urine	1(16.7)	15(62.5)	Ref			
Presence of comorbidity						
Yes	4(66.7)	20(83.3)	0.40(0.05 - 2.98)	0.571		
No	2(33.3)	4(16.7)	Ref			
Referral status						
Yes	6(100)	19(79.2)				
No	0	5(20.8)				
Carbapenem resistant						
Yes	5(83.3)	20(83.3)	1.0(0.09 - 11.03)	0.702		
No	1(16.7)	4(16.7)	Ref			
ICU LOS						
≤30 days	2(33.3)	7(29.2)	1.21(0.18 - 8.22)	0.6		
>30 days	4(66.7)	17(70.8)	Ref			

BMI *body mass index,* ***LOS*** *length of stay,* **Ref** *reference,* **CI** *confidence interval,* ***c*****OR** *crude odd ratio****,*** **aOR** adjusted odds ratio.

CHAPTER FIVE: DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS

5.1 Discussion

5.1.1 The prevalence of Multidrug and carbapenem resistant *Acinetobacter baumannii* among patients admitted to the ICU at MTRH.

This study revealed a significant prevalence of *Acinetobacter baumannii* colonization among the study population, with 22.7% of the individuals carrying *A. baumannii* isolates. These results are consistent with previous literature documenting the high colonization rates of *A. baumannii* in healthcare settings (Ayobami *et al.,* 2019; Mathai *et al.,* 2012). It was interesting to note that in the current study, most participants had at least one comorbidity, with renal conditions prevailing among 50.8% of the participants and respiratory related conditions prevailing among 42.4% of the participants.

These findings are also consistent with those of a similar study carried out in the United States on trends in resistant *Acinetobacter* and enterobacteriaceae species (Gupta *et al.,* 2019). Most of the *A.baumannii isolates* (12.1%) were from urine samples, indicating the potential for *A. baumannii* to cause urinary tract infections in this patient population, while tracheal samples and blood sample yielded 8.3% and 2.3% of the isolates respectively.

5.1.2 Antibiotic susceptibility patterns of *A. baumannii* among patients admitted to the ICU at MTRH

5.1.2.1 Antibiotic susceptibility test patterns of *A.baumannii* on first-resort antibiotics

The *A. baumannii* isolates from this study exhibited resistance to all tested first resort antibiotics including Piperacilin, Amoxicilin-clavulanic acid, Tetracycline, Levofloxacin, Ceftriaxone, Cefipime and Amikacin except Minocycline and Tigecycline. This explains the level of adamancy of this bacteria against these commonly prescribed antibiotics. It is the tendency of this bacteria's ability to resist treatment with first resort antibiotics that has earned it WHO's attention as one of the ESKAPE pathogens of interest, with regard to antimicrobial stewardship particularly (WHO, 2018). The multidrug-resistant phenotype observed in all *A. baumannii* isolates is a significant challenge for effective treatment outcomes. This study uncovered that all MDRAB isolates exhibited resistance to both third-generation and fourth-generation antibiotics, as well as amikacin. Interestingly, however, these isolates-maintained susceptibility to Colistin, positioning it as a potential last-resort treatment option. This noteworthy result aligns with the increasing role of Colistin in treating infections caused by MDRAB, emphasizing its significance in addressing the worrying trend of insensitivity to commonly prescribed antibiotics.

In the current study, a notable range of multiple antibiotic resistance index (MARI) values among the recovered *A. baumannii* isolates was observed, ranging from 0.64 to 0.91. The MARI serves as a vital metric reflecting the extent of antibiotic exposure and selection pressure. High MARI values signify a broader resistance profile due to cumulative antibiotic use, suggesting the imperative for stringent antimicrobial stewardship programs. These programs play a pivotal role in optimizing antibiotic utilization, curbing the progression of resistance, and preserving the

effectiveness of available treatment options. The high multiple antibiotic resistance index (MARI) values indicate extensive exposure to antibiotics and suggest the need for stringent antimicrobial stewardship programs (Asif *et al.,* 2018; Cai *et al.,* 2012).

Furthermore, the observed variability in MARI values aligns with the notion that antibiotic resistance is a multifactorial outcome influenced by factors such as antibiotic exposure patterns, infection control practices, and local healthcare infrastructure. Studies by Patel *et al.* (2017) and Kock *et al*. (2018) provide context-specific insights into MARI variations, underlining the importance of region-specific antimicrobial stewardship strategies.

5.1.2.2 Antibiotic susceptibility test patterns of *A.baumannii* on last-resort antibiotics

Colistin and carbapenemes like Meropenem and Imepenem are crucial as antibiotics of last resort in treatment of infections arising from pathogens that are resistant to multiple antibiotics. They are also highly active against the adamant ESKAPE pathogens like *A. baumannii* and *Pseudomonas* spp. among many other multidrug resistant bacteria (Djahmi *et al.,* 2014).

A. baumannii isolates from the current study were all sensitive to Colistin. However, the isolates displayed an overwhelming overall 83.3% resistance to the carbapenems that they were tested against. The high prevalence of carbapenem resistance is consistent with global reports of increasing resistance rates among *A. baumannii* isolates (Nguyen & Joshi, 2021; Vahhabi *et al.,* 2021). This trend poses a critical concern, as carbapenems, alongside Colistin are categorized among antibiotics of highest priority and critical importance, hence the rising numbers of bacteria strains that portray resistance to them, either concurrently or individually is a global

concern (WHO, 2018). This is because in overall, resistance to these critically important antibiotics is linked to poor clinical outcomes, prolonged stays in the hospital, increased mortality rates and overall cost of healthcare (Howard *et al.*, 2012).

5.1.3 Factors associated with MDR and CR *Acinetobacter baumannii* among ICU patients hospitalized at Moi Teaching and referral hospital.

5.1.3.1 Factors associated with carriage of multidrug and carbapenem resistant *A.baumannii*

This study found that employed participants exhibited a 4.4-fold higher likelihood of harboring *A. baumannii*, suggesting occupational exposure's potential role in colonization. Consistent findings emerged in previous studies across various healthcare settings, employing retrospective cohort designs and cross-sectional surveys. These investigations consistently reported increased *A. baumannii* colonization rates among healthcare workers, supporting the notion that occupation may influence colonization risk in hospital environments (Asif *et al.*, 2018; Manchanda, Sinha & Singh, 2010).

Participants referred to MTRH were at a lower risk of being colonized with *A. baumannii* as compared to those that were initially being treated at MRTH. This is because, in most cases, patients referred to the study's site had already been managed with a course of antibiotics without positive outcomes, necessitating their referral to MTRH. The prior management with a course of antibiotics lessens the probability of referral patients to be colonized with bacteria such as *A. baumannii* as at the time of screening. Moreover, this may be attributed to differences in

patient populations, infection control practices, or colonization patterns in different healthcare settings (Mody *et al*., 2015).

Patients with a high BMI were more likely to be colonized with *A. baumannii* as compared to those who had low or normal BMI. This is consistent with the knowledge that a high BMI predisposes an individual to having a weakened immune system and common health complications like hypertension and diabetes among many others. Gender, age, marital status and a participant's level of education were found to have no significant association with carriage of *A. baumannii* among patients admitted to the ICU, explainable by the fact that *A. baumannii* is an opportunistic pathogen that will almost randomly colonize any suitable host, without regard to either Gender, age, marital status and a participant's level of education (Howard *et al.,* 2012).

5.1.3.2 Factors associated with carbapenem resistance among ICU patients

This study established that participants with a longer ICU stay such as that of more than 30 days were 16 times more likely to be colonized with carbapenem-resistant *A. baumannii* compared to those who had just been recently admitted to the ICU. This is because patients with long stays in the hospital generally are more predisposed to contracting hospital acquired infections that are adamant to treatment by commonly prescribed drugs, as the causative pathogens circulating within the hospital environment are better adapted for survival even against agents designed to eliminate them (Gupta *et al.,* 2019).

It was also interesting to note that participants that had underlying comorbidities were 46 times more likely to harbor isolates of *A. baumannii* that were resistant to carbapenems as compared to

those without underlying comorbidities. This is because underlying comorbidities complicate treatment of the target disease, as the clinician has to most often than not consider the drug interactions of the primary disease with the underlying conditions, which most often leads to use of superior drugs of higher critical activity. This, when often done even in undeserving situations goes a long way to cause the increase in numbers of bacteria strains that exhibit insensitivity to the highly active antibiotics like Colistin and Carbapenems (WHO, 2018).

5.1.4 The hospitalization outcomes of ICU admitted patients with MDR and carbapenem resistant Acinetobacter baumannii infections at MTRH

Acinetobacter baumannii's multidrug resistance poses a significant threat in treatment outcomes of patients in the intensive care units. Hence, this study did not only aim at assessing the impact of these resistant strains on patient outcomes but also identify effective infection mitigation strategies to curb the spread of *A. baumannii* in ICU settings.

5.1.4.1 Association of socio- demographic factors with patients' hospitalization outcomes

Analysis considering variables with $p \leq 0.2$ identified socio- demographic related factors associated with patient outcomes. Married individuals had an increased risk of mortality in comparison to single individuals. The crude odds ratio (cOR) of 4.17 indicated a 4.17-fold increased risk of mortality among married patients. The crude odds ratio (cOR) of 4.17 indicated a 4.17-fold increased risk of mortality among married patients. This finding is contrary to that of most previous studies that have reported lower mortality rates among married individuals compared to their single counterparts. The possible reasons for the current association could be attributed to differences in social support and increased responsibilities among married individuals hence consequently poor quality of life, leading to poorer treatment outcomes

(Vahhabi *et al.,* 2021; Mody *et al.,* 2015). With regard to a participant's level of education, those that had non-formal education had a 3.81 fold increased risk of mortality as compared to those who had formal education. This finding is also consistent with the fact that those who are self-employed, a majority of who lack formal education, had a 2.63 fold risk of mortality compared to the employed and unemployed, majority of who had formal education. Those employed tend to be more at risk in acquiring the bacteria probably due to more exposure to individuals whio are infected compared to the self-employed.

Age and gender were not significantly associated with the hospitalization outcomes of ICU admitted patients with *A.baumannii* infections. However, male participants had a higher mortality rate compared to their female counterparts; crude odds ratio (cOR) of 0.88, indicating a 0.88-fold increased risk of mortality among males. This is attributable to behavioral factors like alcoholism and excessive smoking which contribute to a weakened immune system, hence easier colonization and complication of existing infections even by opportunistic pathogens like *A.baumannii* (Gedefie *et al.,* 2021).

Elderly participants that were above 45 years were more likely to have poor prognosis and consequently die, with a crude odds ratio of 0.65 as compared to the much younger participants who had a crude odds ratio of 0.39. This is due to the fact that the immune system weakens with increasing age (Gedefie *et al.,* 2021).

5.1.4.2 Factors associated with patients' ICU hospitalization outcomes

Patients who had an underlying condition had a 1.91 increased risk of mortality compared to those that did not have any underlying condition. This is due to the already weakened immune system and hence poor prognosis. Patients who were referred to MTRH had a 0.31 fold increased risk of mortality compared to their counterparts who had primarily been admitted at MTRH. This is explainable by the fact that referred patients have already probably undergone treatment at their primary institution of care, without any positive outcome, which necessitated their referral to a tertiary institution for further management. The additional care at this tertiary facility does not necessarily overlook the fact that the immune system has totally been compromised over time, hence further poor prognosis and consequently death is inevitable (Ngbede *et al.,* 2021).

Body mass index was found to be significantly associated with treatment outcome. Overweight or obese patients had a higher likelihood of death compared to those with normal BMI. The cOR of 3.50 suggests a 3.50-fold increased risk of mortality among overweight or obese individuals, emphasizing the adverse impact of elevated BMI on treatment outcomes. These findings align with previous research indicating that higher BMI is a risk factor for adverse treatment outcomes. The underlying mechanisms linking higher BMI to poor prognosis may involve increased inflammation, impaired immune function, and comorbidities associated with obesity, such as cardiovascular diseases and diabetes (Ngbede *et al.*, 2021).

Additionally, the length of stay in the hospital was identified as a significant factor affecting treatment and hospitalization outcome of ICU patients. The association between length of hospital stay and mortality consistently increased, with a two-fold increased risk of death for

each additional day of hospitalization (aOR = 2.11). Prolonged hospitalization has been consistently associated with poor treatment outcomes in various studies. This could be attributed to the increased risk of healthcare-associated infections, unprecedented health complications, and the potential for nosocomial transmission of multidrug-resistant pathogens (Ngbede *et al.,* 2021).

5.2 Conclusions

1. Among the patients admitted to the intensive care unit at MTRH, 22.7% of them were colonized with *Acinetobacter baumannii.*
2. All *Acinetobacter baumannii* isolates from ICU admitted patients were insensitive to all first-resort antibiotics and some carbapenems, but sensitive to Colistin. This suggests Colistin as the most potentially active antibiotic of last-resort for treatment of multidrug resistant *A.baumannii* infections.
3. Increased length of hospital stay, obesity and marital status were the factors found to be significantly associated with *A.baumannii* infections among ICU admitted patients.
4. On the other hand, gender, age, level of education, occupation, referral status and presence of infection were found to have no significant association with *A.baumannii* infections among ICU admitted patients.

5.3 Recommendations

1. All patients admitted to the intensive care units should be screened for colonization with *A.baumannii*, owing to the poor treatment outcomes associated with carriage of this multidrug resistant pathogen.

2. Proper infection control in the ICU settings should be upheld to mitigate the spread of *A.baumannii* in the intensive care units.
3. Stringent antimicrobial stewardship programs should be conducted to ensure that no circulating bacteria strains are resistant to the highly active antibiotics of last resort (carbapenems and Colistin).
4. To improve treatment outcomes, special attention should be given to patients noted to have predisposing factors established to have significant association with *A.baumannii* colonization while in the ICU. This should be done without overlooking the quality of healthcare and attention given to the rest of the ICU admitted patients.

5.3.1 Recommendation for Further Studies

1. Continuously monitoring of Colistin susceptibility patterns in A. baumannii isolates, given its potential as a last-resort treatment option for multidrug-resistant infections should be done.

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APPENDICES

Appendix I: Consent Form

Title of Study: Multidrug-Resistant *Acinetobacter Baumannii* Among Patients Admitted To Intensive Care Unit At Moi Teaching And Referral Hospital, Uasin Gishu County, Kenya.

Institutions: Kenyatta University and the Moi Teaching and Referral Hospital

Principle Investigator: Mr. Fred Kipsang, (P150/CTY/PT/34014/2017) Department of Medical Laboratory Sciences, Kenyatta University, Kenya.

1st Co principal Investigator: Dr. Abednego Musyoki, Department of Medical Laboratory Sciences, Kenyatta University, Kenya.

2st Co principal Investigator: Dr. Nelson Menza, Department of Medical Laboratory Science, Kenyatta University, Kenya

Investigators Statement

This is an educational research study that will be carried out by a researcher from Kenyatta University. This consent form will provide for you information that you will need to help you decide whether to participate in the study or not. The researcher will administer it to you. You may ask any question concerning the purpose of the research, procedures that will be followed, your rights as a participant in the study, risks and benefits of the study.

Purpose of the Study

The purpose of the study is to determine multidrug-Resistant *Acinetobacter Baumannii* among Patients Admitted to Intensive Care Unit at Moi Teaching and Referral Hospital, Uasin Gishu County, Kenya.

Procedures

Samples including blood, tracheal aspirates, urine and swabs for microbiological analysis will be collected aseptically by a trained phlebotomist. Microbiological analyses for drug susceptibility was done using Vitex machine at the Microbiology Laboratory Department at MTRH while molecular characterization will be done at Egerton University Department of Microbiology.

Risks

A minimal point pain will be experienced while drawing blood using a syringe.

Benefits

The data obtained will be helpful in policy formulations for *A. baumannii* antibiotic treatments. Data will also inform on the best course of action in designing antibiotics to be used in treatment of *A. baumannii* infections.

Unable to Consent

Since ICU patients are in a state where they cannot consent, the researcher will notify the next of kin or the guardian who will consent on behalf of the patient or seek further clarifications from the medical practitioner on attendance to give an appropriate direction.

Assurance of Confidentiality

Any information relating to your participation in this study will remain private. Your name will not be used in any report resulting from this study. The consent form will be safely kept and laboratory specimens will have only a study number not your name. If you have more questions regarding the study, feel free to contact me, the principal investigator on 0722234229 or the ethical committee at MTRH on …….....

Subject Statement and Signature

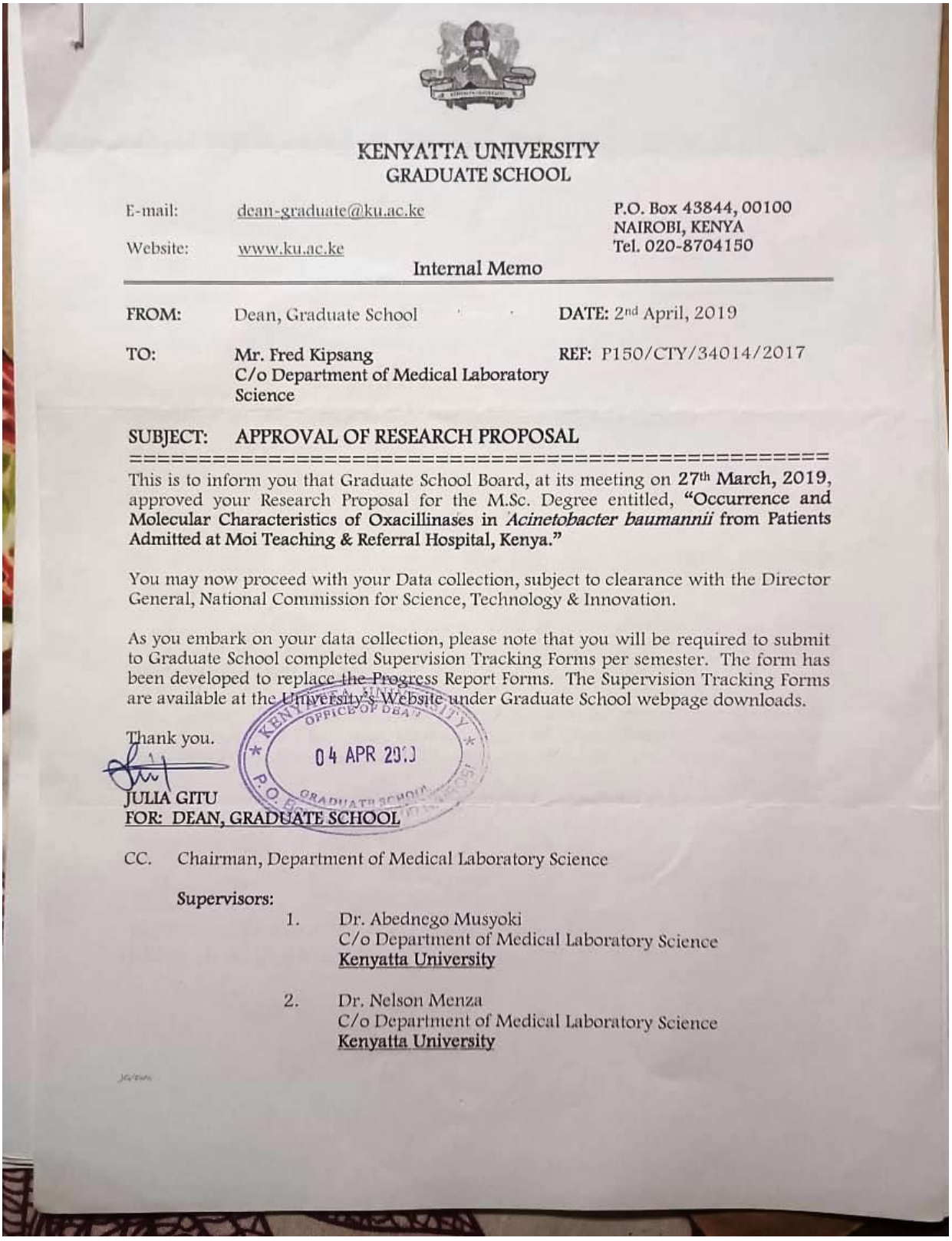
The study has been explained to me. I volunteer to take part in this study.

Name of the participant……..

Name of next of Kin/Guardian……..

Signature or fingerprint ……..……...

Appendix II: Graduate school Proposal Approval



KENYATTA UNIVERSITY
GRADUATE SCHOOL

E-mail: dean-graduate@ku.ac.ke
Website: www.ku.ac.ke

P.O. Box 43844, 00100
NAIROBI, KENYA
Tel. 020-8704150

Internal Memo

FROM: Dean, Graduate School
DATE: 2nd April, 2019

TO: Mr. Fred Kipsang
C/o Department of Medical Laboratory Science
REF: P150/CTY/34014/2017

SUBJECT: APPROVAL OF RESEARCH PROPOSAL

This is to inform you that Graduate School Board, at its meeting on 27th March, 2019, approved your Research Proposal for the M.Sc. Degree entitled, **"Occurrence and Molecular Characteristics of Oxacillinases in *Acinetobacter baumannii* from Patients Admitted at Moi Teaching & Referral Hospital, Kenya."**

You may now proceed with your Data collection, subject to clearance with the Director General, National Commission for Science, Technology & Innovation.

As you embark on your data collection, please note that you will be required to submit to Graduate School completed Supervision Tracking Forms per semester. The form has been developed to replace the Progress Report Forms. The Supervision Tracking Forms are available at the University's Website under Graduate School webpage downloads.

Thank you.

04 APR 2019

JULIA GITU
FOR: DEAN, GRADUATE SCHOOL

CC. Chairman, Department of Medical Laboratory Science

Supervisors:

1. Dr. Abednego Musyoki
   C/o Department of Medical Laboratory Science
   Kenyatta University

2. Dr. Nelson Menza
   C/o Department of Medical Laboratory Science
   Kenyatta University

Appendix III: Research Authorization

KENYATTA UNIVERSITY
GRADUATE SCHOOL

E-mail: dean-graduate@ku.ac.ke
Website: www.ku.ac.ke

P.O. Box 43844, 00100
NAIROBI, KENYA
Tel. 020-8704150

Our Ref: P150/CTY/PT/34014/2017

DATE: 2nd April, 2019

Director General,
National Commission for Science, Technology
and Innovation
P.O. Box 30623-00100
NAIROBI

Dear Sir/Madam,

RE: RESEARCH AUTHORIZATION FOR MR. FRED KIPSANG – REG. NO. P150/CTY/PT/34014/17

I write to introduce Mr. Fred Kipsang who is a Postgraduate Student of this University. He is registered for M.Sc. degree programme in the **Department of Medical Laboratory Science.**

Mr. Kipsang intends to conduct research for a M.Sc. thesis Proposal entitled, **"Occurrence and Molecular Characteristics of Oxacillinases in *Acinetobacter baumannii* from Patients Admitted at Moi Teaching & Referral Hospital, Kenya."**

Any assistance given will be highly appreciated.

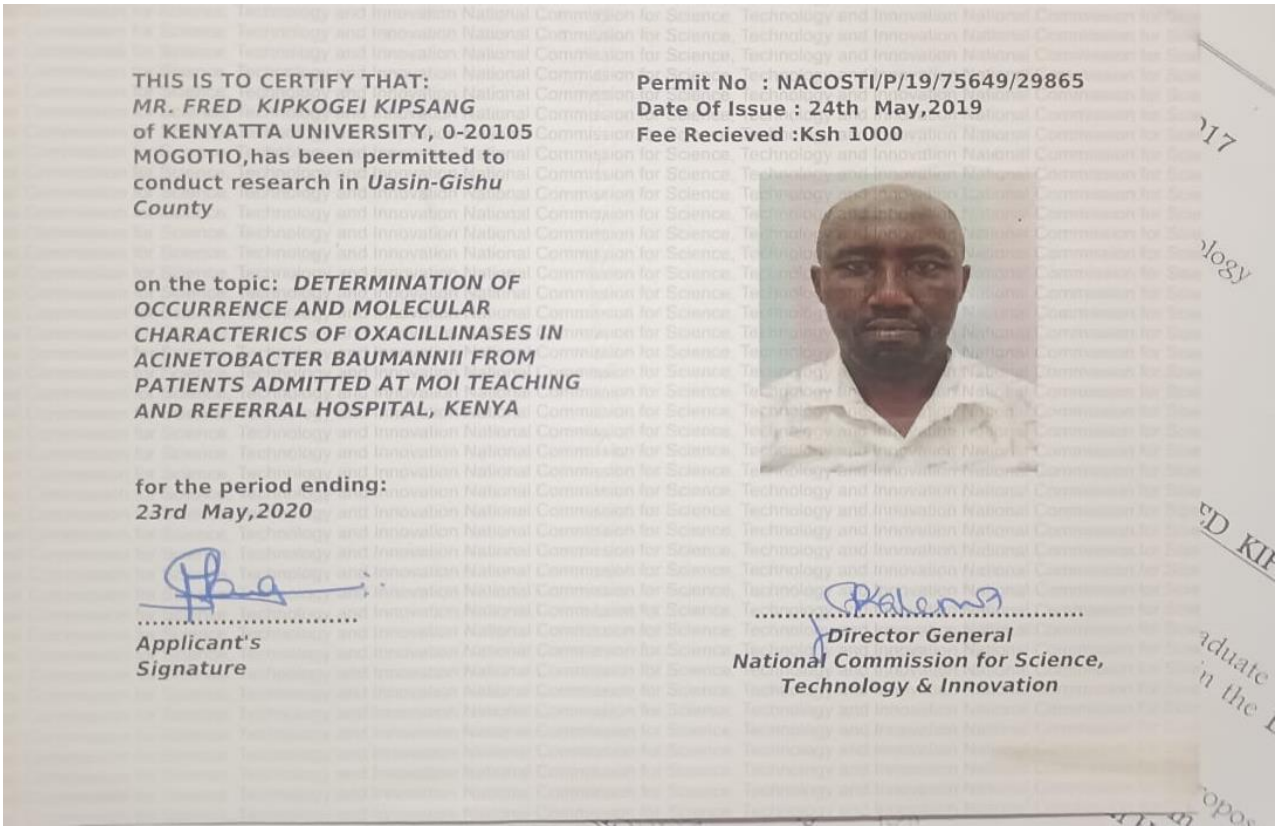
Yours faithfully,

KENYATTA UNIVERSITY OFFICE OF DEAN 04 APR 2019 GRADUATE SCHOOL P.O. Box 43844-00100 NAIROBI

PROF. ELISHIBA KIMANI
DEAN, GRADUATE SCHOOL

JG/ttwn

Appendix IV: Research Permit



THIS IS TO CERTIFY THAT:
MR. FRED KIPKOGEI KIPSANG
of KENYATTA UNIVERSITY, 0-20105
MOGOTIO,has been permitted to
conduct research in *Uasin-Gishu County*

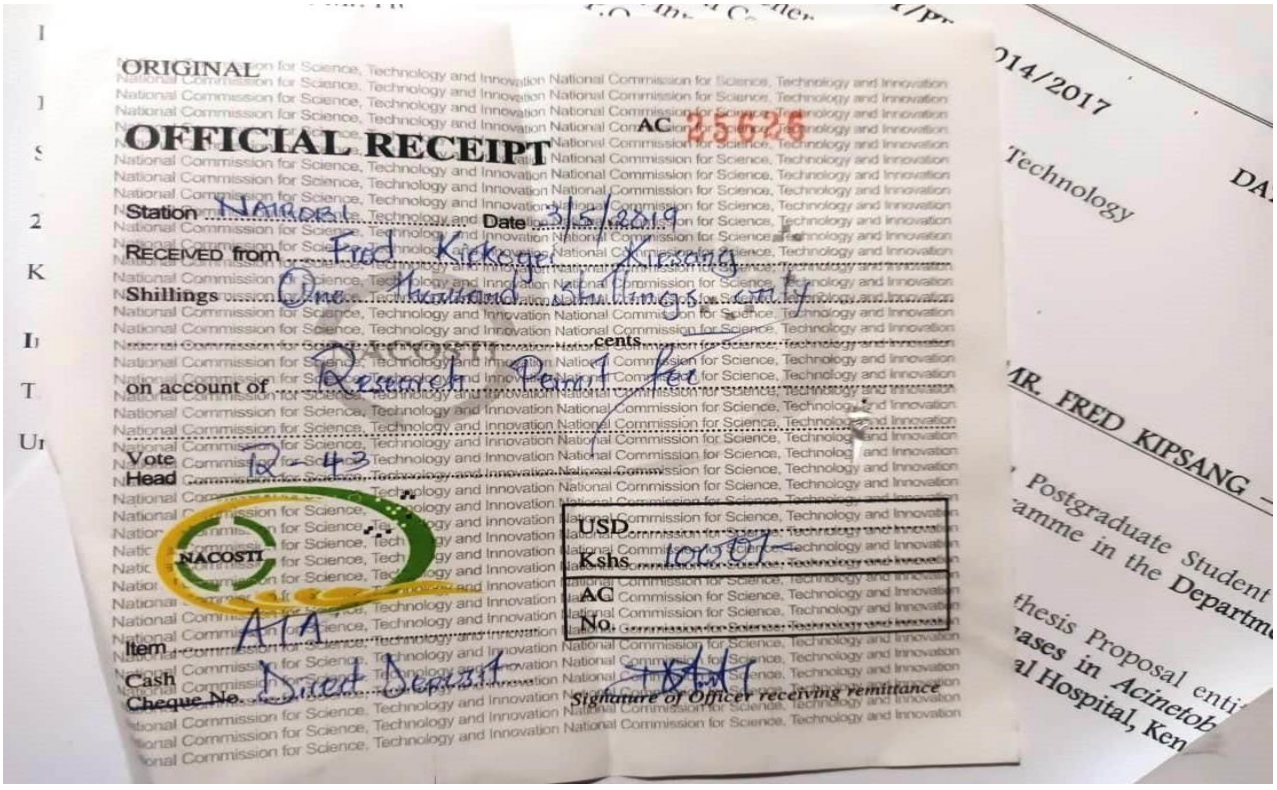
on the topic: *DETERMINATION OF OCCURRENCE AND MOLECULAR CHARACTERICS OF OXACILLINASES IN ACINETOBACTER BAUMANNII FROM PATIENTS ADMITTED AT MOI TEACHING AND REFERRAL HOSPITAL, KENYA*

for the period ending:
23rd May,2020

Applicant's
Signature

Permit No : NACOSTI/P/19/75649/29865
Date Of Issue : 24th May,2019
Fee Recieved :Ksh 1000

Director General
National Commission for Science,
Technology & Innovation



ORIGINAL

OFFICIAL RECEIPT

AC 25626

Station Nairobi Date 3/5/2019

Received from Fred Kipkogei Kipsang

Shillings One Hundred and Thirty Five cents

on account of Research Permit Fee

Vote 12-43

Head

NACOSTI

Item A14

Cash

Cheque No. Direct Deposit

USD

Kshs 1000/=

AC

No.

Signature of Officer receiving remittance

...014/2017

...Technology

...R. FRED KIPSANG –

...Postgraduate Student
...amme in the Departm

...thesis Proposal enti
...ases in Acinetob
...al Hospital, Ken

Appendix V: Ethical Approval

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471//2/3

MOI UNIVERSITY
COLLEGE OF HEALTH SCIENCES
P.O. BOX 4606
ELDORET
Tel: 33471/2/3

Reference: IREC/2019/ 126
Approval Number: 0003392

25th July, 2019

Mr. Fred Kipsang,
Kenyatta University,
School of Medicine,
P.O.Box-43844-00100,
NAIROBI-KENYA.

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
25 JUL 2019
APPROVED
P. O. Box 4606 - 30100 ELDORET

Dear Mr. Kipsang,

DETERMINATION OF OCCURRENCE AND MOLECULAR CHARACTERISTICS OF *Oxacillinases In Acinetobacter Baumannii* FROM PATIENTS ADMITTED AT MOI TEACHING AND REFERRAL HOSPITAL, KENYA

This is to inform you that ***MU/MTRH-IREC*** has reviewed and approved your above research proposal. Your application approval number is ***FAN:0003392.*** The approval period is ***25th July, 2019 – 24th July, 2020.***

This approval is subject to compliance with the following requirements;

i. Only approved documents including (informed consents, study instruments, MTA) will be used.
ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by ***MU/MTRH-IREC***.
iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to ***MU/MTRH-IREC*** within 72 hours of notification.
iv. Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to ***MU/MTRH-IREC*** within 72 hours.
v. Clearance for export of biological specimens must be obtained from relevant institutions.
vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. Attach a comprehensive progress report to support the renewal.
vii. Submission of an executive summary report within 90 days upon completion of the study to ***MU/MTRH-IREC.***

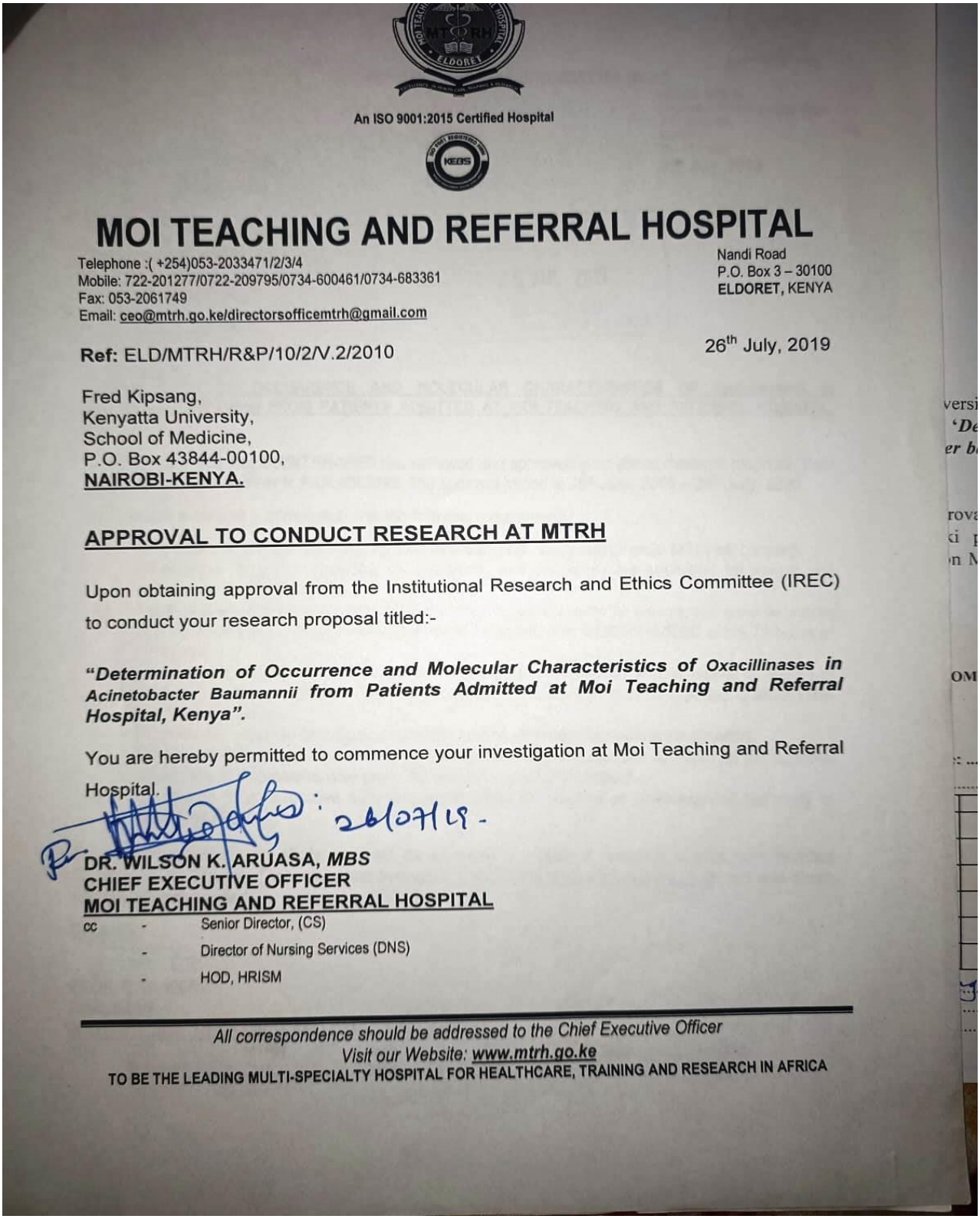
Prior to commencing your study, you will be expected to obtain a research license from National Commission for Science, Technology and Innovation (NACOSTI) https://oris.nacosti.go.ke and also obtain other clearances needed.

Sincerely,

PROF. E. O. WERE
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc CEO - MTRH Dean - SOP Dean - SOM
Principal - CHS Dean - SON Dean - SOD

Appendix VI: Research Permission from MTRH



An ISO 9001:2015 Certified Hospital

MOI TEACHING AND REFERRAL HOSPITAL

Telephone :(+254)053-2033471/2/3/4
Mobile: 722-201277/0722-209795/0734-600461/0734-683361
Fax: 053-2061749
Email: ceo@mtrh.go.ke/directorsofficemtrh@gmail.com

Nandi Road
P.O. Box 3 – 30100
ELDORET, KENYA

Ref: ELD/MTRH/R&P/10/2/V.2/2010

26th July, 2019

Fred Kipsang,
Kenyatta University,
School of Medicine,
P.O. Box 43844-00100,
NAIROBI-KENYA.

APPROVAL TO CONDUCT RESEARCH AT MTRH

Upon obtaining approval from the Institutional Research and Ethics Committee (IREC) to conduct your research proposal titled:-

"Determination of Occurrence and Molecular Characteristics of Oxacillinases in Acinetobacter Baumannii from Patients Admitted at Moi Teaching and Referral Hospital, Kenya".

You are hereby permitted to commence your investigation at Moi Teaching and Referral Hospital.

26/07/19.

DR. WILSON K. ARUASA, *MBS*
CHIEF EXECUTIVE OFFICER
MOI TEACHING AND REFERRAL HOSPITAL

cc - Senior Director, (CS)
- Director of Nursing Services (DNS)
- HOD, HRISM

All correspondence should be addressed to the Chief Executive Officer
Visit our Website: www.mtrh.go.ke
TO BE THE LEADING MULTI-SPECIALTY HOSPITAL FOR HEALTHCARE, TRAINING AND RESEARCH IN AFRICA