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ANALYSIS OF BLOODSTREAM INFECTIONS AND ANTIMICROBIAL RESISTANCE PATTERNS IN PATIENTS ATTENDING LANCET CLINICAL LABORATORIES, 2023-2024

BY

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Abstract

Bloodstream infections (BSI) are a primary global health concern, especially in developing countries including Zimbabwe. In Zimbabwe, the delayed turnaround of blood culture results and lack of data on antibiotic resistance patterns emphasize the need for improved empirical treatment guidelines. This study aimed to identify the bacteria isolates in positive blood cultures and their antimicrobial resistance patterns in patients clinically suspected of bloodstream infections. This study was a retrospective cross-sectional study, analyzing 385 blood culture records from patients clinically suspected of bloodstream infections at Lancet Clinical Laboratory. The BACTEC blood culture system was used for the incubation of blood culture bottles followed by biochemical identification of bacteria plus antimicrobial susceptibility testing on cultures that would have shown positive growth. The patient records of blood culture results were collected from the laboratory's information system (MedTech) covering the period from January 2023 to December 2024. A list of blood culture patient results was created in an Excel sheet using data from MedTech. Using the systematic random sampling method, a sample size of 385 blood culture records was retrieved, systematically organized, and analyzed into tables. Of the 130 culture-positive samples, 86 (66%) were adults and 44 (34%) were pediatric patients. Amongst the culture-positive blood cultures, 69 (53.1%) Gram-positive organisms were isolated and 61 (46.9%) Gram-negative bacteria were isolated. Isolated bacteria were *Coagulase-negative Staphylococcus species* (CoNS) (46.9%), *E. coli* (16.9%), *Pseudomonas aureginosa* (9.2%), *Klebsiella pneumoniae* (7.7%), *S. aureus* (6.2%), *Enterococcus* (6.2%), *Acinetobacter baumanni* (4.6%) and *Panteo* (2.3%). Gram-negative isolates showed high resistance to gentamicin (32.0%), cotrimoxazole (43%), and ceftriaxone (28.3%). Also, Gram-negative bacteria *E.coli, K.pneumoniae,Pseudomonas aureginosa, Acinetobacter baumanni* and *Panteo species* showed consistent susceptibility with (0.0%) resistance to doripenem, meropenem, and imipenem collectively known as carbapenems. Whilst *Coagulase-negative Staphylococcus (CoNS*) and *S. aureus* showed resistance to the commonly used antibiotics cotrimoxazole (39.1%), cloxacillin (34.8%), ceftriaxone (29.0%), tetracycline (29.0%), gentamicin (24.7%), cefoxitin (24.6%), and amoxicillin-clavulanate (20.8%). This study emphasized that *CoNS, E.coli, Pseudomonas aureginosa, Klebsiella spp, S.aureus, Enterococcus spp,* and *Acinetobacter* are responsible for bloodstream infections in patients attending Lancet and their antibiotic resistance pattern. A broader sampling across multiple healthcare facilities particularly in public hospitals to ensure a representative population would assist in the guidance of effective BSI empiric antimicrobial treatment in patients.

Keywords: **Bloodstream infections**, **antimicrobial resistance patterns**, **empirical treatment**

Declaration

I, Hope T Mutandwa student number 210519 do hereby declare that this dissertation is my original work except where sources have been cited and acknowledged. The work has never been submitted, nor will it ever be submitted to another university for the award of a Bachelor of Science degree.

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23/03/2025

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23/03/25

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Dedication

I dedicate this dissertation proposal to my parents Mr. and Mrs. Mutandwa for being there for me always with their unwavering support and prayers.

List of Acronyms and Abbreviations

AMR Anti-microbial Resistance

BSI Bloodstream Infection

CoNS *Coagulase-negative Staphylococcus*

ESKAPE *Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae,* Acinetobacter *baumannii, Pseudomonas aeruginosa, Enterobacter species*

MRSA Methicillin Resistant *Staphylococcus aureus*

PSA *Pseudomonas aureginosa*

PCR Polymerase Chain Reaction

WHO World Health Organization

Definition of terms

Antimicrobial resistance(AMR): occurs when bacteria, viruses, or fungi no longer respond to antimicrobial medicines hence medicines become ineffective and infections become very difficult to treat (Murray et al., 2022).

Bacteremia: can be defined as the presence of viable bacteria in the bloodstream without any multiplication (Birru et al,.2021).

Bloodstream infections: can be defined as the growth of microorganisms from a blood culture sample obtained from patients having systemic signs in which contamination has been ruled out (Timsit et al., 2020).

Septicemia: is a condition in which bacteria multiplies and produces toxins in the bloodstream that end up harming organs of the body (Birru et al,.2021).

Morbidity: is the state of having a specific illness or condition, it often refers to chronic conditions such as cancer, diabetes, etc.

Mortality: refers to the number of deaths due to a specific illness or condition.

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CHAPTER 1 INTRODUCTION

1.1 Introduction

Bloodstream infections pose a significant public health challenge globally contributing to significant morbidity and mortality. While they remain prevalent in developed countries, their burden is severe in the least developed and developing countries. Despite their severity in these developing countries, bloodstream infections often go unreported hence they pose a major health problem worldwide and cause morbidity and mortality in many countries (Maharath & Ahmed, 2021).

Blood is considered a sterile site because it does not have normal microbial flora. In a healthy state blood is free from any bacteria, fungi, virus or other microorganism. The presence of microorganisms in the circulating blood suggests that a bloodstream infection has occurred.

Bloodstream infections (BSI) can be broadly defined as infections of the blood caused by the presence of viable microorganisms in the circulating blood. According to studies BSIs can be defined as the growth of microorganisms from a blood culture sample obtained from patients showing systemic signs in which contamination has been ruled out (Timsit et al., 2020). If left untreated microbial invasion of the bloodstream may lead to immediate consequences such as shock, multiple organ failure, disseminated intravascular coagulation (DIC), and death. Therefore, timely detection and identification of microorganisms in the microbiology laboratory is crucial.

The burden of bloodstream infections is significant and poses challenges in the health sector by raising morbidity and mortality rates, extending hospital stays, and increasing costs as well. This burden of BSIs goes beyond health affecting social and economic systems, particularly in developing nations. For instance, in Zimbabwe, bloodstream infections are major contributors to maternal and child morbidity and mortality (Khan et al., 2025). The high rate of BSIs is caused by factors such as an increased rate of invasive procedures, an aging population, immunosuppressive treatment, and mostly the emergence of multi-drug resistant organisms (Haitao Zhao, 2024). Research has shown that the rise of multi-drug-resistant bacteria and fungi has made it more difficult to effectively treat bloodstream infections in Zimbabwe (Chinowaita et al., 2020).

Bloodstream infections (BSI) show variations in epidemiological patterns and microorganism profiles across different geographical regions. For instance, according to population-based studies in developed countries such as America and European countries, the most isolated pathogens in BSI are *Streptococcus pneumonia, Escherichia coli* and *Staphylococcus aureus*. In contrast, *Enterobacteriacea* and *Coagulase negative Staphylococcus* are the prominent pathogens in BSIs in Africa and Asia (Marchello et al., 2019).

Another gap is challenges in the diagnosis of Bloodstream infections, particularly in low-income countries. Often there are delays in receiving the blood culture results due to the long periods of incubation and culturing processes required in processing blood culture results. This results in delayed initiation of appropriate treatment leading to clinicians resorting to empirical treatment. In developing countries, there is a lack of knowledge of local antimicrobial resistance patterns which is crucial for effective

empirical treatment. Hence there is a need for local studies to investigate the local pathogens causing BSI and their resistance patterns.

The study primarily aimed to determine the common bacterial organism associated with bloodstream infections and analyze their antibiotic resistance patterns in patients attending Lancet Clinical Laboratories from the period 1 January 2023 to 1 December 2024. This study focused on Lancet Clinical Laboratories patients which is the leading diagnostic laboratory in Harare, Zimbabwe situated near big hospitals and healthcare facilities. The study also sought to review the existing literature on the bacterial organisms isolated and the possible clinical manifestations they cause in patients. This study establishes a foundation for investigating local BSI-causing pathogens in Zimbabwe and their resistance patterns to generate antibiograms which are laboratory reports that summarize the susceptibility of isolates. These antibiograms will assist in guiding the administration of empirical therapy.

1.2 Background to the study

Bloodstream infections have become a major global concern as of late and the increasing drug-resistant bacteria is worsening the related morbidity and mortality rates (Birru et al., 2021). Bloodstream infections are infectious diseases caused by the presence of viable bacteria, fungi, viruses, and protozoa in the bloodstream. Bacteria accounts for most bloodstream infections and it is called bacteremia. Bacteremia can be defined as the presence of viable bacteria in the bloodstream without any multiplication. A complication that results from bacteremia if no immediate treatment is administered is septicemia. Septicemia is a condition in which bacteria multiply and

produce toxins in the bloodstream that end up harming multiple organs of the body (Birru et al., 2021). Clinicians often use the terms bacteremia and septicemia interchangeably.

Several risk factors can lead to bloodstream infections which are immunosuppressive treatments, widespread use of broad-spectrum antibiotics that disrupt normal flora and increase the emergence of resistant strains, invasive procedures that increase the risk of bacteria entering into the bloodstream and also in immunocompromised individuals (Kurt et al., 2022). In 2018 at the World Hygiene Day celebrations at Wilkins Hospital, Zimbabwe, Dr Parirenyatwa in a speech advised good hygiene practices and infection control in hospitals as more cases of neonatal sepsis a complication of bacteria in the bloodstream developed as a result of Healthcare-associated infections (HAIs) (Michael Gwarisa, 2018).

Studies have shown that *Staphylococcus aureus*, *Coagulase negative Staphylococcus*, and *Enterococci* are among the most common Gram-positive bacteria that cause bloodstream infections. *Pseudomonas aeruginosa, Acinetobacter species, Klebsiella pneumoniae*, and *Escherichia coli* are the common Gram-negative bacteria that cause bloodstream infections (Birru et al., 2021). If no immediate treatment is given, invasion of the bloodstream by the above-mentioned microbial can result in fatal complications such as disseminated intravascular coagulopathies (DIC), septic shock, multiple organ failure, and death (Kurt et al., 2022). These possible clinical manifestations are caused by exotoxins and endotoxins produced by the bacteria. A blood culture is the laboratory gold standard test used to identify the presence of

bacteria in the bloodstream and positive blood cultures confirm suspicions of bacteremia in patients (Rhodes et al., 2017).

Research has demonstrated a concerning global trend of increasing incidence of bloodstream infections with bacterial BSI being the most prevalent. Studies have shown that BSI accounts for 4-41.5 percent of mortality. With a prevalence of 14.6% in Africa, 7.3% in Asia, 2.9% in Europe and 7.3% in the Americas (Birru et al., 2021). According to research, the mortality rates associated with BSI in hospitals in Sub-Saharan Africa are high reaching about 39%. Furthermore, the prevalence of BSIs in Eastern African countries has been documented to be 11% to 28%. The extensive and inappropriate use of antimicrobial drugs has led to a concerning increase in the prevalence of antimicrobial-resistant bacteria, especially the *Staphylococci species* as well as the *Pseudomonas* and *Klebsiella species*. This alarming trend poses significant challenges in the effective management of infections, as the available treatment options become increasingly limited.

Zimbabwe faces a growing threat from antimicrobial resistance due to the widespread access to over-the-counter antibiotics, lack of drug resistance knowledge, and unregulated antimicrobial sales for self-treatment exacerbated by economic and social factors. This alarming rise in multidrug-resistant bacteria requires immediate attention and intervention from the healthcare system and policymakers. This research aimed to determine the bacterial profile of bloodstream infections and antimicrobial susceptibility patterns to aid in empirical treatment.

1.3 Statement of Problem

Studies have shown that bloodstream infections are a major public health concern in both developed and developing countries due to their prevalence in healthcare settings. Despite the establishment of medications and drugs, treatment of bloodstream infections is extremely challenging for clinicians in most developing African countries, Zimbabwe included. This is caused by an increase in multidrug-resistant bacteria caused by widespread over-the-counter access to antibiotics, lack of drug resistance knowledge, unregulated antimicrobial sales for self-treatment, and lack of updated information on appropriate empiric antibiotic therapy.

Studies have shown that the microbial profile of BSIs and the threat posed by antimicrobial resistance (AMR) of bloodstream infections (BSIs) are ever-changing from one geographical region to another, hence it is essential to regularly generate, analyze, and use local microbiological data to create and update local facility-based treatment guidelines for the common local pathogens isolated in bloodstream.

In my two months of training at the Lancet Clinical Laboratories Microbiology department, I noticed that high volumes of blood culture samples were received and that many of them tested positive between 1 and 5 days using the BACTEC instrument. This reflects that in many developing countries like Zimbabwe, advanced methods for detecting bacteria in blood cultures like Polymerase Chain Reaction (PCR) which are more accurate and faster are not available due to high cost.

Therefore, blood culture results usually take time to come out in laboratories due to the longtime of incubation of blood culture bottles monitor growth. Delays in blood culture results often necessitate empirical therapy to keep the patient alive. In the

context of antibiotics, empirical therapy refers to the initial antibiotic regimen selected before definitive pathogen identification and susceptibility testing. The absence of a thorough understanding of local bacteria associated with bloodstream infections and the proportion of these causative bacteria that are resistant to or sensitive to widely used antibiotics is the problem statement for this study. Addressing this knowledge gap by analyzing BSI data and resistance patterns retrospectively could help pharmacists make the necessary adjustments to their drug stock and assist clinicians in giving appropriate empirical treatment.

1.4 Research objectives

1.4.1 Broad objective

- The broad objective of this study was to identify the bacteria isolates in positive blood cultures and their antimicrobial resistance patterns in patients attending Lancet Clinical Laboratories from 2023 to 2024.

1.4.2 Specific objectives

1. To determine the proportion of bloodstream infections in patients attending Lancet Clinical Laboratories.
2. To carry out laboratory identification of the bacteria found in positive blood cultures of bloodstream infections patients attending Lancet Clinical Laboratories and their possible clinical manifestations.
3. To determine the antimicrobial resistance patterns of bacteria found in bloodstream infections in patients attending Lancet Clinical Laboratories.

1.5 Research questions

1. What is the proportion of bloodstream infections in patients attending Lancet Clinical Laboratories?
2. What are the bacterial species found in positive blood cultures of patients attending Lancet Clinical Laboratories and their possible clinical manifestations?
3. What are the antimicrobial resistance patterns of bacteria found in bloodstream infections in patients attending Lancet Clinical Laboratories?

1.6 Significance of the study

Although there is a global burden of bloodstream infections and AMR, there is limited local research specific to Harare, Zimbabwe, the data is scarce in the study area. Moreover, research has shown that the microbiological profile of BSI and the threat posed by antimicrobial resistance (AMR) of bloodstream infections (BSIs) are ever-changing regularly, hence there is a need to generate, analyze, and use local microbiological data to create and update facility-based treatment guidelines for infectious diseases (Lwigale, 2024). Clinicians must have data on antimicrobial resistance patterns and bacterial profiles to choose the right drugs for patients and the correct empirical therapy. This in turn reduces the number of hospitals stay hence reducing hospital-acquired infections, hospital expenses, and the mortality rate.

1.7 Delimitation of the study

The study population was limited to patients attending Lancet Clinical Laboratories from January 2023 to December 2024.

1.8 Limitation

The main limitation is that the study was conducted at a single center only to patients attending Lancet Clinical Laboratories which limits its generalizability to the broader population of Zimbabwe. Another limitation was that the researcher relied on others for good laboratory identification of bacteria since this research was a retrospective study. Blood cultures which are the gold standard test for detecting bloodstream infections are subject to false positive and false negative errors. Contamination may have occurred in which blood cultures are infected with normal flora or the environment which will give a false impression that the organisms are there. Lastly, most drugs are expensive locally in Zimbabwe since they need to be imported hence limited variety of drugs were used for antimicrobial susceptibility testing.

CHAPTER 2 LITERATURE REVIEW

2.1 Introduction

Bloodstream infections (BSI) represent a significant global health concern, with an estimated 30 million people affected annually, resulting in approximately 6 million deaths worldwide (Santella et al., 2020). These infections are characterized by the presence of viable bacteria in the bloodstream. The ESKAPE group of bacteria, known for their propensity to "escape" the effects of antibiotics, are the most frequently identified pathogens in BSI.

This chapter reviews literature related to bloodstream infections and their antimicrobial resistance patterns. It aims to contribute to the body of knowledge already available on bloodstream infections and provide valuable insights to researchers and medical professionals to help mitigate the problem of bloodstream infections and the emergence of antimicrobial resistance.

2.2 Conceptual framework

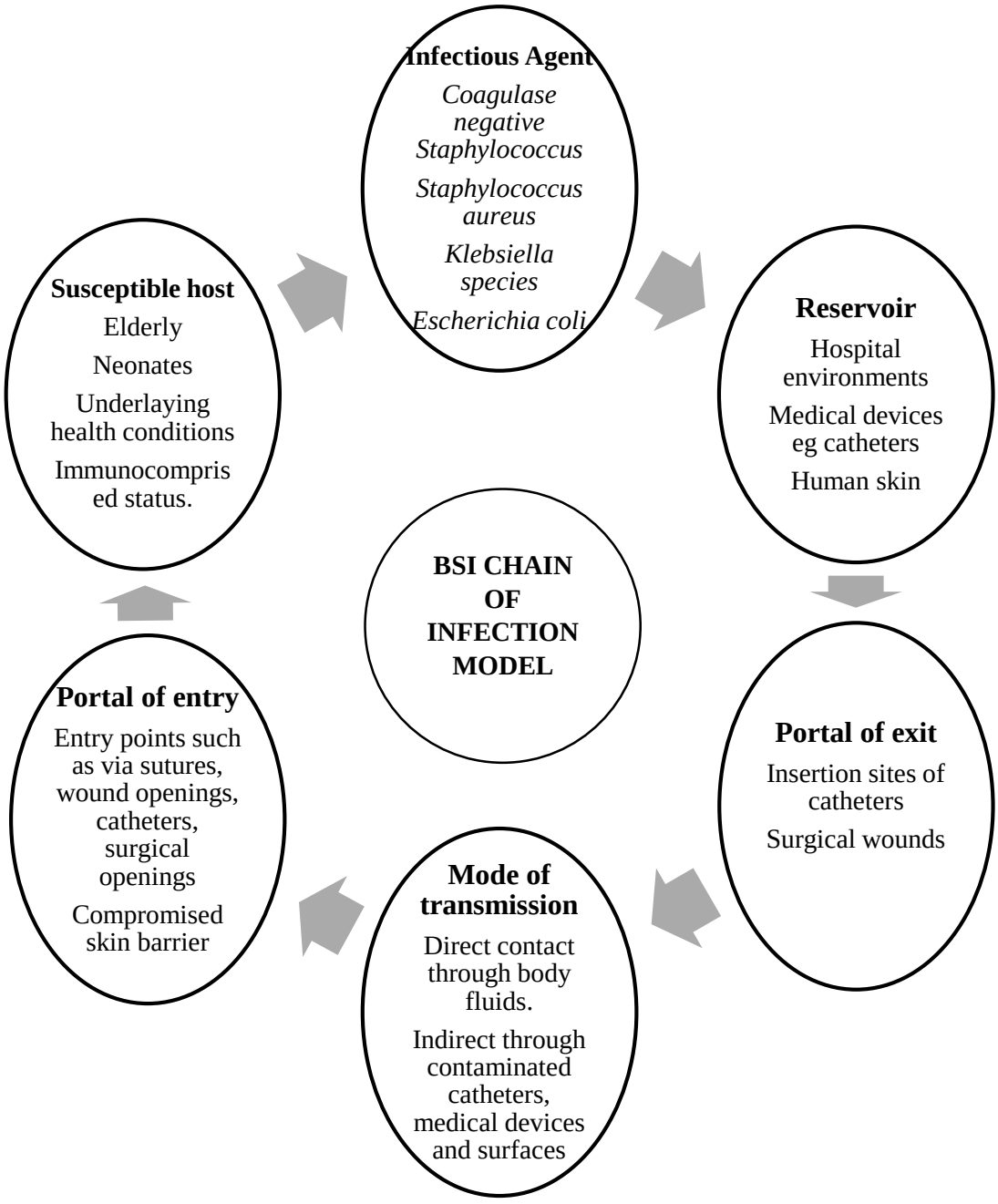

Figure 1: Bloodstream infections (BSI) chain of infection model

2.3 Relevance of the Conceptual Framework to the Study

This study used the above-illustrated Bloodstream infections chain of infection conceptual model. The chain of infection model is more appropriate because it is a well-established framework used in epidemiology and infection control. It explains the factors for an infection to occur and spread. In the context of BSI, it explains how the infectious microorganisms enter into the bloodstream and also how the infection spreads from one host to another. Understanding these steps will enable healthcare workers to devise or come up with ideas to break the infection chain cycle to reduce the number of bloodstream infections and AMR.

The chain of infection model consists of six components that are the infectious agent, reservoir, portal of exit, mode of transmission, portal of entry, and susceptible host (CDC, 2012; APIC, 2015). The chain starts with an infectious agent which refers to the microorganism causing bloodstream infection in the context of BSI. According to related studies, these can be the ESKAPE group of bacteria which consists of *Escherichia coli, Klebsiella species, Acinetobacter species, Pseudomonas aeruginosa,* and another common BSI agent the MRSA(*Methicillin Resistant Staphylococcus aureus* (Marturano & Lowery, 2019). The bacteria need a place to live and multiply which is the reservoir. The potential reservoirs for BSI pathogens are either hospital-contaminated surfaces, medical equipment, human skin, or other chronically ill patients who harbor the bacteria. Studies reviewed that neonates are more at risk of central-line associated BSI which is often linked to skin colonizers like *Coagulase-negative Staphylococcus* (García et al., 2019).

The portal of exit refers to how the infectious agent exits the reservoir (hospital settings or chronically ill patients with BSI). These can be body fluids like pus, blood which can exit through surgical wounds, or invasive operating procedures. The mode of transmission is the route by which the bacteria is transferred from the reservoir to the susceptible host. There are two types direct contact and indirect contact (APIC, 2015; CDC, 2012). Direct contact is infection from one person to another by infectious body fluid. While indirect this involves contamination through contaminated medical equipment, surfaces, and catheters. The portal of entry is the route through which bacteria enter the susceptible hosts. Studies have shown that there are various routes in which bacteria enter the bloodstream which are catheter insertions, surgical procedures, and other medical treatments due to poor practices of insertion, maintenance, and removal of the catheters to patients (World Health Organization).

Susceptible hosts are the patients who are at risk of getting infections due to various factors such as age: geriatrics and pediatrics, the immunocompromised, those suffering from chronic diseases, and those undergoing chemotherapy. According to a study done at Children's Hospital in Bulawayo in 2018, there were about 40.8% cases of neonatal sepsis showing it is one of the causes of illness and death in newborn babies (Mathela et al., 2022). Studies in Zimbabwe in 2020 have shown that one of the main risk factors for sepsis is cancer; patients with cancer have a relatively higher chance of getting sepsis than people without cancer (Chinowaita et al., 2020).

2.4 Literature review of objectives

2.4.1 Prevalence of Bloodstream Infections

A population-wide retrospective cohort study was done in Ontario in 2017 which provides insights into the prevalence and mortality associated with bloodstream infections. The study revealed that out of 531,065 blood cultures, 22 935 positive blood cultures for BSI were identified in 19 326 patients showing an incidence of 150 per 100 000population. The most isolated pathogens were *Escherichia coli, Klebsiella species*, and *Staphylococcus aureus*. The study concluded that the BSI was associated with a 17.0% mortality rate (Verway et al., 2022).

Similar results were obtained in a systematic study conducted among patients hospitalized with fever in Africa and Asia. The study found that the median prevalence of bloodstream infections in Africa and Asia was 12.5%. The most isolated pathogen was *Escherichia coli* (8.8%). The study concluded with emphasis on continued monitoring and implementing strategies to mitigate the problem of BSI and antimicrobial resistance (Marchello et al., 2019).

A cross-sectional study was done at 6 lower-tier South African hospitals. The study investigated culture-confirmed bloodstream infections (BSI) in neonates (0-27 days) from October 2019 to September 2020. The study identified 907 cases of neonatal bloodstream infections (BSI). The Gram-negative pathogens were predominant (63.2%) with *Klebsiella pneumonia* (25.7%) being the predominant pathogen isolated. The study also found a mortality rate of 25.5% among neonates with BSI (Susan Meiring et al., 2025).

According to a cross-sectional study conducted at Children's Hospital in Bulawayo, Zimbabwe in 2018, a total of 98 mothers with sick neonates were enrolled and 40 (40.8%) babies were confirmed to have sepsis (a complication of bacteria in the bloodstream) showing a high prevalence of clinically confirmed neonatal sepsis being caused mostly by low birth weight and poor hand hygiene practiced by the mothers (Mathela et al., 2022).

In 2016, a similar study was also conducted at Parirenyatwa group of Hospitals in Neonatal Intensive Care Unit (NICU). The NICU experienced a surge in neonatal sepsis (a complication of bacteria in bloodstream) incidences recording 108 cases and 41 deaths in five months. The study aimed to determine the source of infection and factors leading to increase in incidence of sepsis (Tsitsi Juru, 2018).

According to a study done in Africa in 2010 by Dr. Elizabeth, the study emphasized the major impact of bloodstream infections in Africa, although the data regarding their occurrence and causation is scarce. The study examined 22 eligible studies, which included 58,296 patients hospitalized in hospitals throughout Africa. According to the statistics, 13.5% (2,051 out of 15,166) of adults had bloodstream infections, while 8.2% (3,527 out of 43,130) of children did. The common pathogens were *Streptococcus pneumoniae*, most prevalent in children, accounting for 18.3% of infections, *Staphylococcus aureus* for 9.5% of infections, and *Escherichia coli* for 7.3%. The in-hospital case fatality rate for individuals with bloodstream infections was 18.1%. This research highlights the prevalence and severity of bloodstream infections in Africa, emphasizing the need for enhanced clinical microbiology services (Reddy et al., 2010).

A comprehensive study conducted from 2015 to 2019 at the San Giovanni di Dio e Ruggi d'Aragona Hospital in Salerno, Italy, provided valuable insights into the prevalence, causative agents, and antibiotic resistance patterns of BSIs. The research revealed a significant average annual incidence of 16.4%. Among the identified pathogens, *Coagulase-negative Staphylococci (CoNS)* were the most prevalent at 17.4%, followed by *Staphylococcus aureus* (12.8%), Escherichia *coli* (10.9%), and *Klebsiella pneumoniae* (9.4%).

Notably, Gram-negative bacteria exhibited the most concerning antimicrobial resistance (AMR) patterns, with increasing resistance to critical antibiotics such as carbapenems and Vancomycin. These findings underscore the alarming trends in BSI epidemiology and antibiotic resistance, highlighting the urgent need for enhanced antimicrobial surveillance. The study emphasizes the importance of optimizing empirical therapy strategies for BSIs to combat this growing threat effectively (Santella et al., 2020).

According to a study conducted by Costa and Carvalho (2022), they were reviewing the burden caused by bloodstream infections and also enlightening on the current diagnostics methods being used to diagnose bloodstream infections. According to their studies, 90% of bloodstream infections are caused by bacteria mostly bacteria belonging to the ESKAPE group(*Enterococcus faecium, S. aureus, K. pneumoniae, Acinetobacter baumannii, P. aeruginosa*, and *Enterobacter species*) and fewer infections by fungi, parasites, and viruses(Banik et al., 2018). The authors then further went on to compare different types of bloodstream infections which are community-acquired, healthcare-associated, and hospital-acquired. Their study also highlighted

the challenges in treating and diagnosing bloodstream infections. Culture-based methods using blood culture are regarded as the gold standard but the challenge is that they require 12 hours post-culture to identify the pathogens and also the detection of some microorganisms is impaired by the administration of antimicrobials before blood collection which leads to false negatives (Thorndike & Kollef, 2020).

The study also describes the new technologies introduced which include PCR(Polymerase Chain Reaction) (Regina Margherita Children's Hospital Bloodstream Infections Study Group participants et al., 2016) and also the Fluorescence in situ Hybridization. These methods have proved to reduce hospital stays, and costs and enable effective therapy treatment. However, in developing countries, more research is needed to develop more sensitive and cost-effective diagnostic methods to enable quicker antimicrobial therapy in bloodstream infections (Costa & Carvalho, 2022).

2.4.2 Bacterial isolates found in Bloodstream infections

Establishing the bacteria profile of the frequently encountered bacteria in bloodstream infections helps in the understanding of bacteria that are causing most of the bloodstream infections and their antibiotic susceptibility patterns is useful to physicians in providing empirical treatment to patients (Kaur et al., 2024).

A retrospective cohort study was done in Ethiopia which aimed to determine the prevalence of bacterial isolates among patients with BSI. The estimated pooled prevalence of Gram-positive and Gram-negative bacterial isolates was 15.5% and 10.48% respectively. The two most common gram positive bacteria are *Coagulase negative Staphylococcus* and *Staphylococcus aureus.* The most frequently isolated

Gram-negative bacteria were *Salmonella species* 1.09%, *Pseudomonas species* 0.39%, *Klebsiella species* 7.04 %, and *E. coli* 1.69% (Alemnew et al., 2020).

Similar results were obtained in another retrospective study, the study examined data from 3150 patients. Out of the samples submitted, 1026 (35.5%) were positive for pathogens. The most common bacteria isolated in decreasing frequencies were *Coagulase-negative Staphylococcus (CoNs),* 189 (28.6%), *Klebsiella spp*., 120 (18.2%), *Escherichia coli,* 66 (10.0%), *Citrobacter spp.,* 48 (7.3%), *Staphylococcus aureus,* 47 (7.1%), *Pseudomonas aeruginosa,* 34 (5.1%), *Salmonella spp.,* 33 (5.1) (Andemichael et al., 2025).

In similarity, other authors also quoted that for BSIs in cancer patients, gram-positive bacteria were more frequently the causative agent. The most common bacteria were *S. aureus, CoNS, K. pneumoniae*, and *P. aeruginosa*(Worku et al., 2022). In another study done in Zimbabwe, *CoNS, E. coli, K. pneumonia, E. faecalis,* and *S. aureus* were the major microbial drivers of sepsis among cancer patients (Chinowaita et al., 2020). Another study conducted by (Thomer et al., 2016) suggested that *S. aureus* is the leading cause of bloodstream infections in the United States of America. This is giving rise to the *Methicillin-Resistant Staphylococcus aureus MRSA* (Thomer et al., 2016).

A retrospective study was conducted at the Microbiology department in India over eight months to estimate the prevalence of *Coagulase-negative Staphylococcus (CoNS*) in bloodstream infection cases. The study analyzed data of blood culture patients which were clinically suspected of bloodstream infection (BSI). The CoNS was found in most patients with 90% of *Coagulase-negative Staphylococcus* resistant

to methicillin. Among the *Coagulase-negative Staphylococcus the S.haemolyticus* was the most common species of *CoNS* followed with *S.epidermidis* (Patil et al., 2024).

Gram-negative bacterial isolates which are *Escherichia coli (E. coli), Klebsiella species*, and *Pseudomonas aeruginosa (PSA*). These bacterial isolates produce endotoxin lipopolysaccharides (LPS), which cause fever and inflammation as early signs and septic shock in severe cases. E. coli can cause septic shock in severe cases, along with diarrhea in enterotoxigenic strains. Klebsiella spp. are also associated with septic shock, particularly in immunocompromised patients, and can lead to pneumonia and abscess formation (Andemichael et al., 2025).

These studies are similar in several ways, such as the prevalence of Gram-positive bacteria (especially CoNS and S. *aureus*) in bloodstream infections (BSIs), the regular presence of K. *pneumoniae* and E. *coli* among the most commonly isolated Gram-negative bacteria, and the focus on BSIs in cancer patients, which may indicate a special vulnerability in this population. Together, these findings emphasize the significance of further research and surveillance into blood-stream infections (BSIs), especially in vulnerable groups. They also show how widespread this healthcare issue is and how coordinated efforts in infection control and antimicrobial management are required.

2.4.3 Antimicrobial resistance patterns of bacteria isolates found in Bloodstream infections (BSI)

Antimicrobials are medicines used to prevent and treat infectious diseases in humans, while antimicrobial resistance(AMR) occurs when bacteria, viruses, or fungi no longer

respond to antimicrobial medicines hence medicine becomes ineffective and infections become very difficult to treat (Murray et al., 2022). This is usually due to abuse and unnecessary use of antimicrobials by individuals and a lack of knowledge about antimicrobial susceptibility patterns in patients with bacteremia. According to studies, 4.95 million fatalities from AMR are expected in 2019, and up to 10 million deaths annually are predicted by 2050, AMR poses a worldwide health problem as the leading cause of death (Kaur et al., 2024).

In a study by Alonso-Menchen et al which examined bloodstream infections in Europe. According to the study Methicillin-resistant *Staphylococcus aureus* and Vancomycin-resistant *E. faecium* bloodstream infections were more frequently reported in Southern and Western Europe. While Carbapenems-resistant *Pseudomonas aeruginosa* BSI were more common in Northern and Western Europe. They concluded that decreased resistance percentages were associated with community-acquired infections in contrast to healthcare-associated infections (Maria Diletta Pezzani et al., 2024).

Another study was conducted (Akova, 2016) about AMR being a global health threat with millions of deaths resulting from AMR due to mostly resistant pathogens. The ESKAPE group of bacteria (*Enterococcus faecium, S. aureus, K. pneumoniae, Acinetobactor baumannii, P. aeruginosa and Enterobacter species*) is the most common group causing more hospital-acquired infections.

Another study conducted at the Tertiary Care Nephrology Teaching Institute in India examined 1440 blood samples that were drawn from patients suspected of having bacteremia. Gram-positive bacteria accounted for 58.3% of cases with a majority of *Staphylococcus aureus*, 40.2% of the bacteria were gram-negative, with

Enterobacteria predominating; fungal isolates made about 1.5% of the total. Vancomycin, Teicoplanin, daptomycin, linezolid, and Tigecycline were the most successful medications in treating Gram-positive infections, while carbapenems, colistin, aminoglycosides, and Tigecycline were the most successful in treating Gram-negative isolates. Vancomycin resistance was present in 21.6% of cases and *methicillin-resistant Staphylococcus aureus (MRSA)* in 70.6% of cases (Gohel et al., 2014).

In another study conducted about Gram-negative bacteria in bloodstream infections, the study pointed out an increase in antimicrobial resistance in Gram-negative bacteria. This is due to their ability to produce Extended-spectrum beta-lactamase (ESBL) hence an increase in carbapenems resistance. The use of cefepime drug was still being debated (Alcántar-Curiel et al., 2023)

Therefore this study which aims to give access to current epidemiological data on antibiotic resistance of commonly encountered bacterial infections will help develop an efficient antimicrobial surveillance program in hospitals as well as for selecting empirical treatment approaches (Akova, 2016).

2.5 Summary

This chapter outlines the theoretical literature review about objectives for bloodstream infections and antimicrobial resistance patterns to identify gaps in the existing literature and add knowledge to the already body of knowledge.

CHAPTER 3. METHODOLOGY

3.1 Introduction

This study used a retrospective cross-sectional design. In a retrospective study, the outcomes for each participant are already known at the time of enrollment, and data is gathered from existing records and documentation. This chapter outlines the study's context, including the setting, population, duration, sample size, and the sampling methods employed. It also details the data collection instruments used and the analytical techniques applied to the data. Additionally, ethical considerations will be addressed in this section.

3.2 Research design

This study was a retrospective cross-sectional study of blood cultures processed at Lancet Clinical Laboratories, in Harare from January 2023 to December 2024. A retrospective cross-sectional study is a research design that analyzes past data from a defined population at a single point in time to identify patterns or correlations (Julia Simkus, 2023). In this context, the term retrospective indicates that we examined records from the past while cross-sectional signifies that the analysis focuses on a specific timeframe rather than tracking changes over time. The records are then used to conclude relationships within the data. The information and data collected from these records were analyzed and organized into tables and graphs allowing for a clear visual representation of the findings.

3.3 Study site

The primary data for this study was collected from the head office of Lancet Clinical Laboratories, situated in Harare the capital city of Zimbabwe at number 22 Corner Fife and Blakiston. Lancet Laboratories is renowned as the leading private diagnostic laboratory in Zimbabwe and hence plays a crucial role in the healthcare system. In addition to its headquarters in Harare, Lancet operates outstation laboratories across all ten provinces of Zimbabwe ensuring there is coverage for diagnostic services. The Harare location was chosen for this study due to it being a central testing point for blood culture samples collected from patients throughout the country. All samples from the various provincial laboratories are sent to the Harare headquarters for analysis making it the ideal site for gathering data relevant to our research objectives.

3.4 Study population

The study looked at blood culture records from patients of all ages and genders who attended Lancet Clinical Laboratories in Harare from January 2023 to December 2024.

3.4.3 Inclusion criteria

Blood culture records from patients of all ages and genders who visited Lancet Clinical Laboratories in Harare from January 1, 2023, to December 31, 2024, were included in the study.

3.4.4 Exclusion criteria

Patients admitted outside the defined study period and blood cultures growing nonpathogenic isolates.

3.5 Study period

This study focused on the period between January 2023 and December 2024.

3.6 Sample size

The formula below was used to calculate the sample size:

$$\boldsymbol{N} = \frac{Z^2\ \alpha \mathrm{p}(1-\mathrm{p})}{\boldsymbol{d^2}}$$

Where

- N=Sample size
- Zα= a constant found in normal variate tables (level of confidence) 1.96 for a 95% confidence level
- P= prevalence expected 0.5(50%)
- d=precision of the estimate 0.05 (5%)

Calculate the sample size using the above formula. N=385

3.8 Sampling procedure

Sampling can be defined as selecting units/subsets from the population of interest so that by studying the sample we may fairly generalize our results back to the population

from which they were chosen (A&1, 2018). In this study, a simple random sampling method was used. Systematic random sampling means choosing participants from a group so that everyone has an equal chance of being picked. A list of blood culture patient results who were clinically suspected of bloodstream infection was generated on an Excel sheet from the Lancet laboratory's information system MedTech. The total number of eligible entries of blood cultures (10,779) was divided by the sample size calculated above 385 to get a sampling interval based on the determined sample size of 385. Until we obtained the necessary sample size of 385, we chose every 28^{th} record (where the 28^{th} record is the sampling interval) starting from the first sample. This sampling method used reduced selection bias.

3.9 Data collection instruments

The Lancet Clinical Laboratories MedTech Laboratory Information System (LIS) which contains comprehensive medical records of all the patient information, was used to collect data on all positive blood culture results including the bacteria identified and their associated antimicrobial patterns.

3.10 Pretesting tools

A pilot study is a smaller version of a research project conducted to determine whether the full study should be pursued. It is conducted to look for any problems so they can be resolved before the whole study is done. Pretesting of data extraction tool and data extraction procedures and data collection procedure was done using the Lancet

Clinical Laboratories MedTech LIS. It was used get the detailed patient data and tests results.

3.11 Data collection procedures

The study participants were picked by first compiling a list of all the blood cultures clinically suspected of bloodstream infection received in the microbiology department of Lancet Clinical Laboratories during the period of January 2023 to December 2024. After that a total of 385 blood culture patients' results were sampled from the list using the systematic random sampling procedure as follows.

A total of 10,779 blood cultures were processed from January 2023 to December 2024. The BACTEC blood culture system (BD, Franklin Lakes, and NJ) was used to identify the presence of pathogens in blood cultures. The blood cultures were incubated into the BACTEC at 37ºC for at least 7 days or until the BACTEC machine detects the growth of the pathogen. If growth was detected by the machine, the positive blood cultures were cultured/inoculated on Blood agar and MacConkey agar plates. The inoculated culture plates were incubated at 37ºC for 24 hours. The grown bacterial isolates were identified using biochemical tests following the standard operating procedure.

The antimicrobial susceptibility testing was done using the disk diffusion method on Mueller Hinton agar. The disk diffusion method is also known as the Kirby-Bauer test. A bacterial culture picked was evenly spread on Mueller Hinton agar plate to create a lawn of bacteria. Small disks impregnated with specific antibiotics (mentioned below) were then placed on the agar surface and the plates were incubated at 37 degrees Celsius for 24-48 hours to allow bacterial growth. After incubation, the presence of

clear zones around the antibiotic disks, known as inhibition zones, was measured. The size of these zones indicated the effectiveness of the antibiotics; a large zone suggested susceptibility, while a small or absent zone indicated resistance. The antibiotics used in this study are amoxicillin-clavulanate, piperacillin-tazobactam, cephalexin, cefuroxime, cefotaxime, ceftazidime, ceftriaxone, cefepime, imipenem, meropenem, gentamicin, tobramycin, amikacin, ciprofloxacin and cotrimoxazole.

A list of blood culture patient results was created in an Excel sheet using data from the MedTech information system at Lancet Laboratories. We had a total of 10 779 eligible blood culture entries. To determine the sampling interval, we divided this total by the calculated sample size of 385 which gave us an interval of 28. To collect our required sample of 385 we selected every 28th record starting with the first sample until we reached the desired number of 385. Only patients who attended the Lancet clinical laboratory during this period were included in the list of participants for the study.

When the list of 385 participants had been completed, the results of each participant were retrieved and a table was made in Microsoft Excel to display the patient's age, sex, bacteria identified in positive blood cultures, and the antibiotics tested on the bacteria. Microsoft Excel table was then used to analyze the data and the data was further arranged according to the proportion of positive blood cultures, the bacteria identified in the positive blood cultures, and their antimicrobial resistance patterns. The data was checked to ensure accuracy and completeness.

The primary purpose of the study was to identify the bacteria isolates found in the positive blood cultures and evaluate the proportion of bacteria isolates across different age groups. As blood stream infections present differently in neonates, adults and the

elderly. The percentage proportions of each bacteria isolate were calculated as well as the number of culture positives among different age groups.

After identifying the bacteria isolates in positive blood cultures, we linked the bacteria isolates found to the already existing literature to understand the clinical implications and manifestations these bacteria have on humans. The study of the literature helped us contextualize our findings by shedding light on significant issues about the isolated bacteria, including their virulence, resistance patterns, and toxins that they may produce in humans.

A comprehensive examination of the bacteria isolates found in positive blood cultures, their related health consequences, and the findings from the literature review were conducted. The Lancet Clinical Laboratories laboratory manager and the appropriate authorities will be informed of our findings. It is crucial to share this knowledge in order to influence future research, guide treatment regimens, and perhaps have applications in practice.

3.12 Data management and analysis

This section describes the methods that were used to analyze the data that was collected. After the collection of data onto the tables the data was analyzed using statistical software. Pie charts and bar graphs were then created to visually represent the results, showing the patterns of antibiotic resistance and the frequency of positive blood cultures. The understanding and dissemination of the research findings are aided by these visual representations and profiles, which offer easily understandable insights into the patterns of BSIs and AMR in the population under study.

3.13 Ethical consideration

Ethical approval to conduct the study was sought from The Africa University Research and Ethics committee (AUREC) and this was granted. Before collection of the data from Lancet Laboratories, consent was sought for from the laboratory manager and was granted. The names of the patients were not included in the study and all the results were kept confidential.

The study took into account and maintained the ethical values of research, which include autonomy, non-maleficence, beneficence, justice, advocacy, and secrecy**.**

3.14 Summary

This study was a retrospective study of blood culture samples received in the microbiology department of Lancet Clinical Laboratories between January 2023 and December 2024. The calculated sample size for this retrospective study was 385. The data from 385 patient records was collected on the data extraction sheet. Permission to collect data was obtained from the Laboratory Manager of Lancet Clinical Laboratories as well as permission to carry out the study was obtained from AUREC. Microsoft Excel and statistics were used to analyze the data and confidentiality of patients' identity was done.

CHAPTER 4 DATA PRESENTATION, ANALYSIS AND INTERPRETATION

4.1 Introduction

This chapter presents the findings obtained from this study. The information in this section was originated by organizing and analyzing the raw data, as described in chapter 3 and then analyzed using the graphs and pie charts.

4.2 Data presentation, analysis, and interpretation

4.2.1 Proportion of positive blood cultures in patients attending Lancet Clinical Laboratories, 2023-2024.

A total of 385 blood culture patient results were obtained and analyzed. Out of 385 blood culture results 130 blood cultures were positive while 255 were negative. The total 130 positive blood cultures consist of 72 positive blood cultures in 2023 and 58 positive blood cultures in 2024 as shown in **table 1.**

Table 1. Proportion of positive blood cultures in patients attending Lancet Clinical Laboratories, 2023-2024.

Blood cultures	Proportion of blood cultures n (%)
Positive	130 (44)
Negative	255 (66)
Total *	385 (100)

Note: Positive refers to blood cultures that yielded growth of pathogenic bacteria after 24-48 hours of incubation, and Negative refers to blood cultures that did not yield any growth of bacteria after 48 hours of incubation. *= total sample size of blood cultures analyzed, number

4.2.2 Proportion of positive blood cultures in different age groups of patients attending Lancet Clinical Laboratories, 2023-2024.

As illustrated by Table 2, two distinct age groups had positive blood cultures the pediatric and adults. According to age categories neonates (n =18), infants (n =9), Children (n = 7), adults (n =34), and elderly (n =52). Over the two years of data collection, a higher percentage of adult patients (66%) were diagnosed with bloodstream infections (BSI) compared to pediatric patients (34%). Among the pediatric group, the neonates had the highest proportion of culture-positive blood cultures (14%) as compared to the infants (7%) and children (13%). The elderly comprised of higher proportion of positive blood cultures (40%) than the adults with 26%. However the elderly had the highest percentage of culture-positive blood cultures with a percentage of 40%.

Table 2. Proportion of positive blood cultures in different age groups of patients attending Lancet Clinical Laboratories, 2023-2024.

Patient group	Age category	Proportion with positive culture n (%)
Pediatrics	Neonates (<28days)	18 (14)
	Infants (>28days-1)	9 (7)
	Children (1-15years)	17 (13)
Adults	Adults (16-65years)	34 (26)
	Elderly (>65years)	52 (40)

Note: Total blood cultures with positive culture =130

4.2.3 Gram reactions of bacteria isolate in positive blood cultures in patients attending Lancet, 2023-2024.

Out of 130 culture-positive blood culture samples, 69(53.1%) were gram-positive organisms isolated and 61(46.9%) were gram negative organisms' isolated. As shown in table 3 the gram-positive bacteria were most isolated bacteria in this study as compared to the gram-negative bacteria.

Table 3. Gram reactions of bacteria isolates in positive blood cultures

	Gram-positive	**Gram-negative**
Bacteria isolates n (%)	69 (53.1)	61 (46.9)

Note: Total bacteria isolates=130

4.2.4 Proportion of bacteria isolates in positive blood cultures in patients attending Lancet, 2023-2024.

Table 4 shows the percentage distributions of bacteria isolated from the blood cultures during the two-year period of 2023-2024. *Coagulase-negative Staphylococcus (CoNS*) (46.9%) was the most isolated bacteria from blood cultures in this study, followed by *Escherichia coli* (16.9%). The predominant bacteria isolates among Gram-positive isolates were *Coagulase-negative Staphylococcus (CoNS)* (46.9%), *Staphylococcus aureus* (6.2%), and *Enterococcus species* (6.2%). Among the Gram-negative isolates,

the most predominant was *E.coli 22(16.9%)* followed by *Pseudomonas spp. 12 (9.2%), Klebsiella species 10(7.7%)* and *Acinetobacter species 6(4.6).*

Table 4. Bacteria isolated from positive blood cultures

Bacterial isolates	**Frequency n (%)**
Gram-positive isolates	69 (53.1) **a**
Coagulase-negative Staphylococcus	61 (46.9)
Staphylococcus aureus	8 (6.2)
Enterococcus species	8 (6.2)
Gram-negative isolates	61 (46.9) **b**
Escherichia coli	22 (16.9)
Pseudomonas aeruginosa	12 (9.2)
Klebsiella pneumonia	10 (7.7)
Acinetobactor baumannii	6 (4.6)
Pantoea species	3 (2.3)

Note: **a**= Total Gram-positive bacteria isolates and frequency percentage. **b**=Total Gram-negative bacteria isolates and frequency percentage.

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4.2.5 Antimicrobial resistance of Gram-positive bacteria isolates from positive blood cultures in patients at Lancet, 2023-2024

Table 5 below shows the pattern of antimicrobial resistance in Gram-positive isolates over the two years of the study period. *Coagulase-negative Staphylococcus* showed high resistance to several antibiotics cotrimoxazole (39.3%), cloxacillin (34.4%), ceftriaxone (29.5%), tetracycline (29.5%), gentamycin (24.6%), cefoxitin (24.6%), amox-clavulonic acid (19.7%), 1st generation cephalosporins (19.7%), cefuroxime

(15.0%), eryth/azithromycin (15.0%), Clindamycin (9.8%), Rifampicin (5.0%). CoNS showed no resistance to linezolid.

Staphylococcus aureus showed resistance to similar antibiotics in *CoNS* but the frequency is smaller as compared to CoNS due to few isolates found in Staphylococcus as compared to CoNS. It displayed high resistance in cotrimoxazole (37.5%).Also no resistance was observed in linezolid (0.0%) and rifampicin (0.0%). The *enterococcus species* showed resistance to a few tested drugs in the study. Gentamycin (25.0%), amox-clavulonic acid (25.0%), levofloxacin (25.0%). *Enterococcus species* showed no resistance to linezolid (0.0%), vancomycin (0.0%), and teicoplanin (0.0%).

Table 5. Antimicrobial resistance of Gram-positive bacteria isolates from positive blood cultures in patients at Lancet, 2023-2024.

Drug	Proportion with drug resistance %			
	Coagulase negative staphylococcus **freq (%)**	***Staphylococcus aureus*** **freq (%)**	***Enterococcus Species*** **freq (%)**	**Total Resistance freq (%)**
Cotrimoxazole	24 (39.3)	3 (37.5)	-	**27 (39.1%)**
Cloxacillin	21 (34.4)	3 (37.5)	-	**24 (34.8%)**
Ceftriaxone	18 (29.5)	2 (25.0)	-	**20 (29.0%)**
Tetracycline	18 (29.5)	2 (25.0)	-	**20 (29.0%)**
Gentamycin	15 (24.6)	2 (25.0)	2 (25.0)	19 (24.7%)
Cefoxitin	15 (24.6))	2 (25.0)	-	17 (24.6%)
Amox-clavulonic acid	12 (19.7)	2 (25.0)	2 (25.0)	16 (20.8%)
1st generation of cephalosporins	12 (19.7)	2 (25.0)	-	14 (20.3%)
Cefuroxime	9 (15.0)	-	-	9 (13.0%)
Eryth/azithromycin	9 (15.0)	1 (13.0)	-	10 (14.5%)
Clindamycin	6 (9.8)	1 (12.5)	-	7 (10.1%)
Rifampicin	3 (5.0)	0 (0.0)	-	3 (4.3%)
Linezolid	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0%)
Vancomycin	-	-	0 (0.0)	0 (0.0%)
Teicoplanin	-	-	0 (0.0)	0 (0.0%)
Levofloxacin	-	-	2 (25.0)	2 (25.0%)

Key: Freq=frequency (resistance frequency which is the proportion of Gram-positive isolates that exhibited resistance to the drugs used). (-) means the drug was not used on the bacteria isolate. Bold texts highest drug resistance

4.2.6 Antimicrobial resistance of Gram-negative bacteria isolates from positive blood cultures in patients at Lancet, 2023-2024

Table 6 below shows the pattern of antimicrobial resistance in Gram-negative isolates over the two years of the study period. *Escherichia coli* isolates exhibited high resistance to cotrimoxazole (40.9%), ciprofloxacin (36.4%), gentamicin (31.8%), and ceftriaxone (31.8%). It showed no resistance in meropenem and doripenem. *Klebsiella* species isolates showed high resistance to cotrimoxazole (50.0%), ciprofloxacin (40.0%), and ceftriaxone (40.0%). It showed no resistance to meropenem, imipenem, and doripenem. *Pseudomonas* species isolates exhibited resistance to ciprofloxacin (33.3%), gentamicin (25.0%), ceftazidiam (25.0%) and piperacillin/tazobactam (25.0%). *Pseudomonas* species displayed no resistance to imipenem (0.0%), meropenem (0.0%) and doripenem (0.0%)

Acinetobacter species isolates showed high resistance to the tested drugs. Ciprofloxacin (66.7%), gentamicin (50.0%), ceftriaxone (50.0%), cefepime (33.3%), ceftazidiam (33.3%), piperacillin/tazobactam (33.3%), amikacin (16.7%). No resistance was observed to imipenem (0.0%), meropenem (0.0%), and doripenem (0.0%). *Pantoea* species isolates showed resistance to the following drugs, ciprofloxacin (33.3%), gentamicin (33.3%), and ceftriaxone (33.3%).

Table 6. Antimicrobial resistance of Gram-negative bacteria isolates from positive blood cultures in patients at Lancet, 2023-2024

Drug	Proportion with drug Resistance (%)					
	Escherichia coli **freq (%)**	***Klebsiella species*** **freq (%)**	***Pseudomonas species*** **freq (%)**	***Acinetobacter species*** **freq (%)**	***Pantoea species*** **freq (%)**	**Total resistsnce freq (%)**
Cotrimoxazole	9 (40.9)	5 (50.0)	-	-	-	**14 (43%)**
Ciprofloxacin	8 (36.4)	4 (40.0)	4 (33.3)	4 (66.7)	1 (33.3)	**21 (39.6%)**
Gentamicin	7 (31.8)	3 (30.0)	3 (25.0)	3 (50.0)	1 (33.3)	**17 (32.0%)**
Ceftriaxone	7 (31.8)	4 (40.0)	-	3 (50.0)	1 (33.3)	**15 (28.3%)**
Cefuroxime	6 (27.3)	3 (30.0)	-	-	-	9 (17%)
Cefepime	4 (18%)	3 (30%)	2 (16.7)	2 (33.3)	0 (0)	11 (20.8%)
Ceftazidiam	3 (14%)	2 (20%)	3 (25.0)	2 (33.3)	0 (0)	10 (18.9%)
Piperacillin/tazobactam	2 (9.1)	2 (20)	3 (25.0)	2 (33.3)	0 (0.0)	9 (17%)
Amikacin	2 (9.1)	2 (20)	1 (8.3)	1 (16.7)	-	6 (12%)
Amox-clavulonic acid	1 (5%)	1 (10%)	-	-	-	2 (6.25%)
Ertapenem	1 (5%)	1 (10%)	-	-	-	2 (6.25%)
Tigecycline	1 (4.5)	1 (10.0)	-	-	-	2 (6.25%)
Imipenem	1 (4.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.9%)

Meropenem	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0%)
Doripenem	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0%)
Tobramycin	-	-	2 (16.7)	-	-	2 (16.7%)

Key: Freq=frequency (resistance frequency which is the proportion of Gram-negative isolates that exhibited resistance to the drugs used). (-) the drug was not used on the bacteria isolate. Bold texts; highest drug resistance

4.2.7 Clinical manifestations resulting from exotoxins produced by the Gram-positive bacterial isolates in positive blood cultures

Table 7 outlines the possible clinical manifestations in relation to literature resulting from exotoxins produced by Gram-positive bacterial isolates from positive blood cultures. *Staphylococcus aureus* produces *Staphylococcus* Enterotoxins (SE), which can cause food poisoning, a painful but typically self-limiting illness. However, Toxic Shock Syndrome (TSS), which is far more severe and can lead to major consequences such as fever, septic shock, multiple organ failure, and skin rash, can also be produced by S. *aureus. Coagulase Negative Staphylococcus* also produces SE, which is associated with skin diseases, folliculitis, and furuncles but it's not severe.

The table 7 below shows some Gram-positive bacteria isolated in clinical manifestations investigated.

Table 7. Possible clinical manifestations found in the Gram-positive bacteria isolated

Bacterial isolates	Exotoxins	Effect of exotoxins
S.aureus	SE	Food poisoning
	TSS	Fever, septic shock, multiple organ failure and skin rash
CoNS	SE	Skin diseases, folliculitis, and furuncle.

Key*: CoNS=Coagulase-Negative Staphylococci; S.aureus=Staphylococcus aureus;* SE= *Staphylococcus* Enterotoxins; TSS=Toxic Shock Syndrome**.**

4.2.8 Clinical manifestations resulting from endotoxins produced by the Gram-negative bacterial isolates in positive blood cultures

Table 8 outlines the possible clinical manifestations in relation to literature resulting from endotoxins produced by Gram-negative bacterial isolates which are *Escherichia coli (E. coli*), *Klebsiella species*, and *Pseudomonas aeruginosa (PSA*). The endotoxins produced by the three bacterial isolates are lipopolysaccharides (LPS), which cause fever and inflammation as early signs and septic shock in severe cases. *E. coli* can cause septic shock in severe cases, along with diarrhea in enterotoxigenic strains. *Klebsiella spp*. are also associated with septic shock, particularly in immunocompromised patients, and can lead to pneumonia and abscess formation, which may complicate recovery. *Pseudomonas aeruginosa* has similar effects on septic shock being especially severe in patients with burns or chronic lung diseases.

Table 8. Possible clinical manifestations found in the Gram-negative bacteria isolated

Bacterial isolates	**Endotoxins**	**Effect of endotoxins**
Escherichia coli	LPS	Septic shock Inflammation Fever Diarrhea
Klebsiella species	LPS	Septic shock Pneumonia and abscess formation Inflammation Fever
Pseudomonas aeruginosa	LPS	Septic shock Inflammation Fever

Key: LPS= Lipopolysaccharide.

4.3 Summary

This chapter outlined the results obtained in this study on blood cultures at Lancet Clinical Laboratories for 2023-2024, with respect to each of the study objectives. A total of 385 blood cultures were analyzed and 130 were found positive. Adult patients had more positive blood cultures proportion (66%) than pediatric patients (34%), and the largest proportion percentage of positive cultures (40%) was seen in the elderly. Of the bacteria isolates 46.9% were Gram-negative Escherichia coli being the predominant and 53.1% were Gram-positive Coagulase-Negative Staphylococcus being the predominant Gram-positive isolate. Both Gram-positive and Gram-negative isolates exhibited antimicrobial resistance, with notable resistance to common drugs such as ciprofloxacin and cotrimoxazole.

CHAPTER 5 DISCUSSION, CONCLUSION AND RECOMMENDATIONS

5.1 Introduction

This chapter discusses the study findings in chapter 4 and makes comparison with existing literature on bloodstream infections. This will be carried out in relation to the literature review and research objectives. The findings of this study will be compared and contrasted with those of other research of a similar nature. The study's limitations, public health implications, suggestions and possible next steps will also be discussed.

5.2 Discussion

This study analyzed data from 385 blood culture results of patients attending Lancet Clinical Laboratories, 2023-2024. From the total data of 385 blood culture, 130 were found positive. Adult patients had more positive blood cultures proportion (66%) than pediatric patients (34%), and the largest proportion percentage of positive cultures (40%) was seen in the elderly.

5.2.1 Proportion of bloodstream infections in patients attending Lancet Clinical Laboratories.

In this study, the data revealed differences in bloodstream infections (BSI) across age groups. The elderly represented the largest group with culture-positive cases (40%) as compared to the adults. In the pediatric group, a significant percentage of culture-positive cases (14%) were in neonates. However, risk factors for the development of bloodstream infections were not investigated in this study, hence it is unclear why there are blood culture-positive samples at such extremes of ages. This finding is almost similar to the one noted in the study by Susan Meiring et al., (2025) in six lower-tier hospitals. The study reviewed a high proportion of bloodstream infections

among neonates with 907 cases identified in a period of one year with a mortality of 25.5%. In similarity, studies have shown that neonates are at a higher risk for central line-associated bloodstream infections, caused by healthcare-related infections. Neonates are at risk of developing bloodstream infection due to factors like weakened immune systems since their immune system will still be developing, less breastfeeding from the mother, low birth weight, and poor hygiene by the mothers (Mathela et al., 2022).

5.2.2 Bacterial isolates found in positive blood cultures of patients attending Lancet Clinical Laboratories.

In this study, 53.1% of bloodstream infections were caused by Gram-positive bacteria and 46.9% by Gram-negative bacteria. These findings are similar to a retrospective cohort study done in Ethiopia which aimed to determine the prevalence of bacterial isolates among patients with BSI. The estimated pooled prevalence of Gram-positive and Gram-negative bacterial isolates was 15.5% and 10.48% respectively (Alemnew et al., 2020). Also studies by Thomer et al., 2016 and Worku et al., 2022 showed similar findings.

In this study, *Coagulase-negative Staphylococcus (CoNS*) was identified as the most common bacterial pathogen causing bloodstream infections (BSI) among Gram-positive organisms, accounting for 46.9%. This is in agreement with the findings of Patil et al in 2024 done at the Microbiology laboratory in India. Patil et al found that *Staphylococcus haemolyticus* and *Staphylococcus epidermidis* were the most common *Coagulase-negative Staphylococcus* species found in bloodstream infections(Patil et al., 2024). *Coagulase-negative staphylococcus* is mostly isolated in bloodstream

infection due to their presence as normal skin flora hence they used to be considered contaminants. Studies have now changed and recognized *Coagulase-negative Staphylococcus (CoNS)* as an established pathogen causing bloodstream infections (BSI) (Patil et al., 2024).

Staphylococcus aureus (8%) was the second most commonly isolated organism in the Gram-positive which concurs with findings of similar studies that estimated pooled prevalence of Gram-positive and Gram-negative bacterial isolates were 15.5% and 10.48% respectively. The two most common Gram-positive bacteria were *Coagulase-negative Staphylococcus* and *Staphylococcus aureus* (Alemnew et al., 2020). In similarity, other authors also quoted that for BSIs in cancer patients, Gram-positive bacteria were more frequently the causative agent. The most common bacteria were *Staphylococcus aureus* and *Coagulase-negative Staphylococcus* (Worku et al., 2022). Studies have also shown that CoNS is associated with immunocompromised people.

Escherichia coli (16.9%) was the predominant organism isolated among Gram-negative bacteria, followed by *Pseudomonas aeruginosa* (9.2%), Klebsiella spp. (7.7%), *Acinetobacter* spp. (4.6%) and *Panteoa spp* (2.3%). Similarly, in another study done in Zimbabwe, *CoNS, E. coli, K. pneumoniae, E. faecalis,* and *S. aureus* were the major microbial drivers of sepsis among cancer patients (Chinowaita et al., 2020). This study also concurs with the findings of similar studies such as those by Costa and Carvalho (2022), they were reviewing the burden caused by bloodstream infections and also enlightened on the current diagnostics methods being used to diagnose bloodstream infections. According to their studies, 90% of bloodstream infections are caused by bacteria mostly bacteria belonging to the ESKAPE group(*Enterococcus*

faecium, S. aureus, K. pneumoniae, Acinetobacter baumannii, P. aeruginosa, and *Enterobacter species)* and fewer infections by fungi, parasites, and viruses (Banik et al., 2018).

Linking to existing literature from various authors, the Gram-negative bacteria isolates found in patients attending Lancet, particularly *E. coli, Klebsiella species,* and *Pseudomonas aeruginosa,* are known to produce endotoxins in the bloodstream. Septic shock is one of the serious complications that these endotoxins can cause. Septic shock is a life-threatening condition resulting from severe sepsis. It is characterized by persistent low blood pressure leading to inadequate blood flow to organs and potential organ failure. *E. coli* is particularly threatening since certain strains can cause diarrhea and septic shock. Additionally, *Klebsiella species* pose serious hazards because they can result in abscesses, pneumonia, and septic shock, which can make recovery more difficult, especially for people with compromised immune systems. Similarly, *Pseudomonas aeruginosa* can cause tissue destruction and can cause severe septic shock, especially in patients with burns or long-term lung diseases. All things considered; the results of this investigation highlight the grave risks to human health that these Gram-negative bacteria represent.

In reviewing existing literature on Gram-positive bacterial isolates from positive blood cultures, we find that exotoxins produced from Gram-positive isolates cause notable clinical symptoms. Notably, food poisoning is largely associated with *Staphylococcal* Enterotoxins (SE), which are produced by *Staphylococcus aureus*. Toxic Shock Syndrome (TSS) and other more serious illnesses can also be brought on by *S. aureus*.

TSS is particularly concerning, as it can result in serious complications, including fever, septic shock, multiple organ failure, and skin rashes.

There is need to emphasize the grave risks to health that these Gram-negative bacteria and Gram-positive bacteria represent and the significance of careful observation and efficient treatment plans for those who are impacted.

5.2.3 Antimicrobial resistance of bacteria isolates from positive blood cultures among patients at Lancet

When comparing the significant antimicrobial resistance trends, it can be seen that most of the bacterial isolates demonstrated high resistance to ciprofloxacin, cotrimoxazole, and gentamicin as shown in Tables 7 and 8 provided in Chapter 4. Among the Gram-positive isolates, *Coagulase-negative Staphylococcus (CoNS)* showed resistance to the commonly used antibiotics cotrimoxazole (37.5%), cloxacillin (37.5%), ceftriaxone (25.0%), tetracycline (25.0%), gentamicin (25.0%), cefoxitin (25.0%), and amoxicillin-clavulanate (25.0%). These results were in partial agreement with the study conducted by Gohel et al in 2014. This is of concern since *CoNS* is no longer being considered as a contaminant in bloodstream infections but actually as one of the major causing pathogens in BSI. Their high resistance to drugs like cephalosporins can be due to the widespread use of these beta-lactam antibiotics which in turn render them resistant to ESBL-positive bacteria.

Staphylococcus aureus also showed high resistance to the same classes of antibiotics as in *Coagulase-negative Staphylococcus*. Both *Staphylococcus aureus* and *Coagulase-negative Staphylococcus* showed no resistance to linezolid (0.0%). This is in agreement with a study conducted by Patil et al in 2024 where all the *Coagulase-*

negative Staphylococcus (CoNS) were susceptible to linezolid. Linezolid is an important and effective drug for treating infections but it's very expensive since it is imported from foreign countries most patients cannot afford it.

The Gram-negative isolates, *Klebsiella species*, *Pseudomonas aeruginosa*, *Acinetobacter*, and *Escherichia coli* showed high resistance to the commonly used antibiotics in empiric therapy such as cotrimoxazole (43.0%), ciprofloxacin (39.6%), gentamicin (32.0%) and ceftriaxone (28.3%). This is in agreement with the study conducted by Alcántar-Curiel et al in 2023 in which most Gram-negative bacteria showed resistance to beta-lactam antibiotics. The resistance to third-generation cephalosporins such as ceftriaxone is caused by the enzymes called extended-spectrum beta-lactamases (ESBL) in *Klebsiella* and *E.coli.* These enzymes break the beta-lactam drugs hence they show high resistance.

Lastly, all the Gram-negative isolates showed a consistent susceptibility to the carbapenems class of drugs which consists of meropenem, doripenem, and imipenem. The Gram-negative isolates showed 0.0% resistance to meropenem and doripenem. Hence these drugs can now be used as last-line antibiotics for treating infections. These results were in agreement with the findings from Gohel et al in 2014 where carbapenems, colistin, aminoglycosides, and tigecycline were the most successful in treating Gram-negative isolates. .

5.3 Implications

This study showed that *Coagulase negative staphylococcus* contributes to most of the bloodstream infections. This finding aligns with numerous similar studies in the literature that identify *CoNS* as a prevalent causal agent, often due to contamination

since CoNS is a skin pathogen or a higher incidence in immunosuppressed individuals. There is a pressing need for increased public and healthcare provider education regarding the risk factors associated with bloodstream infections. This education could focus on hygiene practices, especially in healthcare settings, to minimize contamination risks. Training staff on proper protocols for handling intravenous lines and other invasive devices could further reduce infection rates.

The study will help generate, analyze, and use local microbiological data to create and update facility-based treatment guidelines for bloodstream infections. Clinicians will have updated data on antimicrobial resistance patterns and bacterial profiles to choose the right drugs for patients and the correct empirical therapy. This in turn reduces the number of hospital stays hence reduced hospital-acquired infections, hospital expenses and the mortality rate.

5.4 Limitations of the study

There were some limitations when conducting this study. This study was conducted at a single center during a specific time frame, which limits its generalizability to the broader population of Zimbabwe. In addition, the Lancet clinical laboratory is a private facility and most of the samples come from private doctors hence as a result, the study predominantly included financially privileged patients leading to a potential bias in the findings.

5.5 Conclusion

This study found that Gram-positive bacteria were responsible for more bloodstream infections than Gram-negative bacteria. *Coagulase-negative Staphylococcus* was the most common bacteria detected in positive blood cultures from patients at Lancet Clinical Laboratory during 2023-2024. This study also emphasized that *CoNS, E.coli, Pseudomonas aureginosa, Klebsiella spp, S.aureus, Enterococcus spp,* and *Acinetobacter* are responsible for bloodstream infections in patients attending Lancet. This study analyzed these bacteria in existing literature which will help understand the severity of these organisms in the bloodstream. The high resistance rate of pathogens like *CoNS*, *E.coli* and *Staphylococcus aureus* to antibiotics is alarming. The susceptibility of Gram-negative bacteria to carbapenems and linezolid in Gram-positive isolates offers an alternative treatment option for patients.

5.6 Recommendations and further suggestions for research

For future studies, the researcher suggests broader sampling across multiple healthcare facilities particularly in public hospitals to ensure a representative population. Also, further studies involving larger sample sizes and multiple centers are needed to provide a more comprehensive understanding of antimicrobial resistance patterns in this region. Furthermore, developing antibiotic stewardship programs based on local resistance patterns will optimize antibiotic use to help reduce the problem of Antimicrobial Resistance. Additionally, it would be highly advantageous if techniques such as the Polymerase Chain Reaction could be applied to the identification of bacteria, as this would be more accurate and efficient in terms of time.

5.7 Dissemination of results

Lastly, it is important to share the data collected from studies like this one with healthcare facilities. This way, hospitals can use the information to find ways to reduce bloodstream infections. By providing this feedback, healthcare providers can better understand infection patterns and take specific actions to improve patient care.

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APPENDICES

Appendix 1: Application to conduct study and approval from the study site

Hope Tafadzwa Mutandwa

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Seke

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mailto:mutandwah@africau.edu

LANCET
CLINICAL LABORATORIES
22 FIFE AVE / Cnr BLAKISTONE ST.
P.O. BOX BW260
BORROWDALE, HARARE

Approved
01/10/24

30 September 2024

The Laboratory Manager

Lancet Clinical Laboratories

Blakiston Street 22 Fife Ave

Harare

RE: APPLICATION FOR PERMISSION TO COLLECT DATA FROM THE MICROBIOLOGY LABORATORY AT LANCET FOR A RESEARCH PROJECT

Dear Mr Magaisa

My name is Hope Tafadzwa Mutandwa. I am studying Medical Laboratory Sciences at Africa University. I am in my final year's first semester of study and am currently attached to your Lancet Laboratories Harare branch.

I am writing to request permission to use data that I plan to get from the Lancet Clinical Laboratories microbiology department. My research project topic is **A retrospective analysis of bloodstream infections and antimicrobial resistance patterns among patients attending Lancet Clinical Laboratories 2023-2024**.

The information retrieved will consist of blood culture findings (the bacteria identified in positive blood cultures and their patterns of resistance). Also, patients' confidentiality will be ensured since no names or other identifying characteristics will be used.

Please find attached to this letter my research proposal.

Looking forward to your response

Yours sincerely

Hope Tafadzwa Mutandwa

Appendix 2: Approval Letter from AUREC

"Investing in Africa's future"
AFRICA UNIVERSITY RESEARCH ETHICS COMMITTEE (AUREC)

P.O. Box 1320 Mutare, Zimbabwe, Off Nyanga Road, Old Mutare-Tel (+263-20) 60075/60026/61611 Fax: (+263 20) 61785 Website: www.africau.edu

Ref: AU 3494/24 5 November, 2024

HOPE TAFADZWA MUTANDWA
C/O Africa University
Box 1320
MUTARE

RE: **A RETROSPECTIVE ANALYSIS OF BLOODSTREAM INFECTIONS AND ANTIMICROBIAL RESISTANCE PATTERNS AMONG PATIENTS ATTENDING LANCET CLINICAL LABORATORIES 2023-2024**

Thank you for the above-titled proposal you submitted to the Africa University Research Ethics Committee for review. Please be advised that AUREC has reviewed and approved your application to conduct the above research.

The approval is based on the following.

a) Research proposal

- **APPROVAL NUMBER** AUREC 3494/24
  This number should be used on all correspondences, consent forms, and appropriate document
- **AUREC MEETING DATE** NA
- **APPROVAL DATE** November 5, 2024
- **EXPIRATION DATE** November 5, 2025
- **TYPE OF MEETING**: Expedited
  After the expiration date, this research may only continue upon renewal. A progress report on a standard AUREC form should be submitted a month before the expiration date for renewal purposes.
- **SERIOUS ADVERSE EVENTS** All serious problems concerning subject safety must be reported to AUREC within 3 working days on the standard AUREC form.
- **MODIFICATIONS** Prior AUREC approval is required before implementing any changes in the proposal (including changes in the consent documents)
- **TERMINATION OF STUDY** Upon termination of the study a report has to be submitted to AUREC.

AFRICA UNIVERSITY RESEARCH ETHICS COMMITTEE (AUREC) APPROVED P.O. BOX 1320, MUTARE, ZIMBABWE

Yours Faithfully

MARY CHINZOU
ASSISTANT RESEARCH OFFICER: FOR CHAIRPERSON
AFRICA UNIVERSITY RESEARCH ETHICS COMMITTEE

Appendix 3: Budget for the project

ITEM	COSTS (ZIG$)
Travelling cost	100.00
Printing cost	42.00
Stationery cost	56.00
Internet cost	0.00
Total cost	198.00

Appendix 4: Timeline for the research project

2024 to 2025						
Activities	**September 2024**	**October 2024**	**November 2024**	**December 2024**	**January 2025**	**Feb 2025**
Submit a project proposal to the supervisor						
Submit a project proposal to AUREC.						
Data collection						
Data analysis						
Project writing						
Submit a project to the African University						