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DETERMINANTS OF ANTIMICROBIAL RESISTANCE OF GRAM-NEGATIVE BACTERIA IN PAEDIATRIC PATIENTS AT VICTRORIA CHITEPO PROVINCIAL HOSPITAL, 2024

BY

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A DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF BACHELOR OF MEDICAL LABORATORY SCIENCES IN THE COLLEGE OF HEALTH, AGRICULTURE AND NATURAL SCIENCES

2025

Abstract

Antimicrobial Resistance in Gram-negative bacteria is a pressing global health issue, particularly affecting vulnerable populations such as pediatric patients. It has become an important threat to international health which is potentially undermining nearly a century of gains since antibiotics were discovered. This study investigates the determinants of Antimicrobial Resistance at Victoria Chitepo Provincial Hospital. A cross-sectional study design was employed, using retrospective clinical and laboratory data from 250 pediatric patients. A systematic random sampling method was used. The analysis involved descriptive statistics and binary logistic regression to assess the influence of potential determinants on the likelihood of antimicrobial resistance. Visual tools such as bar charts and forest plots were also utilized to enhance interpretation. Key findings revealed that Gram-negative bacteria accounted for 60% of the isolates, with the highest prevalence observed among infants aged 0–23 months. Age was found to be significantly associated with GNB infection, while gender was not. The antimicrobial resistance patterns showed widespread resistance to commonly used antibiotics such as Amoxicillin-Clavulanate and TMP-SMX, particularly among Acinetobacter baumanni and Pseudomonas aeruginosa. Even Gentamicin, the most effective antibiotic in this study, showed only moderate susceptibility rates. Logistic regression analysis identified several significant determinants of antimicrobial resistance with the most influential factor being prior antibiotic use with an Odds Ratio of 3.2 followed by history of urinary tract infections (OR=2.4), HIV-positive status(OR=1.9), and behavioral factors such as purchasing antibiotics without a prescription(OR=2.1) and early discontinuation of treatment(OR=1.8). Younger age was also found to be associated with antimicrobial resistance most probably due to the underdeveloped immune systems of babies. Socio-demographic factors including residence in high-density areas and low parental education also showed significant associations with resistance. Overall, the study provided a comprehensive and statistically supported assessment of the prevalence, resistance trends, and drivers of AMR in Gram-negative infections among young children by highlighting the interplay between biomedical vulnerabilities and modifiable behavioral factors. These results advocate for immediate action in public health policy and clinical practice, emphasizing the importance of targeted educational interventions for caregivers and stricter regulations on antibiotic prescriptions.

Key words: Determinants, Antimicrobial, Resistance, Pediatrics, Antibiotics

Declaration Page

I Shingisai Maenzanise student number 210484 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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Acknowledgements

First and foremost, l humbly thank God for the wisdom, resilience and grace that sustained me throughout this journey. To my supervisor, Professor Maibouge Tanko Mahamane Salissou, l am deeply grateful for your mentorship, intellectual guidance and the unwavering support which shaped this work into its current form. I would also like to thank the nurses and the laboratory manager at Victoria Chitepo Provincial Hospital for their contributions to the data collection procedures. Thank you to my best friend, Monalisa Dhlamini for the technical expertise, patience, emotional support and unwavering trust that has been my anchor during this challenging yet rewarding process. Finally l acknowledge the financial support from my parents which enabled the realization of this project

Dedication

This work is a dedication to my family whose unwavering love and huge sacrifices have been the bedrock of my journey. Their rentless encouragement and trust in my potential have shaped me into the scholar l am today. I also honor my friend, Nyasha Mubure whose influence has inspired my commitment to this field. May this work reflect the resilience and hope that you have instilled in me and may it contribute meaningfully to the world we strive to build together.

List of Acronyms

AMR : Antimicrobial Resistance

TSP-TX : Trimethoprim-Sulfamethoxazole

E.coli : Escherichia coli

GNB :Gram negative Bacteria

GPB : Gram Positive Bacteria

OR : Odds Ratio

CKD :Chronic Kidney Disease

Definition of Key Terms

Antibiotics-A class of drugs used to treat bacterial infections by killing bacteria or inhibiting their growth.

Determinants- Factors that influence the occurrence, distribution and outcomes of health-related events.

Bacteria- Single celled microorganisms that can exist in various environments and can be beneficial or pathogenic.

Intervention- Actions taken to improve health prevent disease or enhance quality of life.

Pediatric- Branch of medicine that deals with the health of medical care of infants, children and adolescents.

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CHAPTER ONE: INTRODUCTION

1.1 Introduction

Antimicrobial resistance has emerged as a great challenge in recent years, particularly affecting vulnerable populations such as pediatrics. This chapter serves as a critical issue of Antimicrobial resistance (AMR) in Gram-negative bacteria amongst pediatrics at Victoria Chitepo Provincial Hospital located in Mutare, Zimbabwe. It begins by outlining the significance of AMR as a public health threat and emphasizing its potential to undermine nearly a century of medical advancements achieved through the development and use of antibiotics. The chapter will delve into the background of the study, detailing the prevalence of Gram-negative bacteria infections in pediatric patients and the associated risk factors that contribute to the development and spread of AMR. It will also articulate the specific research questions guiding this study, aiming to investigate the determinants of AMR in GNB among pediatric patients. Furthermore, the introduction will also outline the assumptions and justifications for the study, emphasizing the urgent need for targeted interventions to mitigate the rising of AMR. The research intends to fill existing gaps in the knowledge and inform public health policies and practices that can enhance patient outcomes and promote effective antimicrobial stewardship.

1.2 Background of the Study

Antimicrobial resistance has become a looming global health crisis that is threatening to undermine antibiotic effectiveness, the primary defense against bacterial infections. AMR occurs when microorganisms evolve mechanisms that protect them from drugs designed to treat infections (De Kraker et al., 2016)This resistance can arise naturally through genetic mutations or can be accelerated by human activities like the misuse and overuse of antimicrobials in the healthcare and agriculture. As a result, it becomes harder to treat infections and there is risk of disease spread, severe illness, disability and death (Zankari et al.,2012)The pediatric population particularly children is more vulnerable to the consequences of AMR, experiencing higher rates of morbidity and mortality due to their underdeveloped immune systems which make them more susceptible to infectious diseases like pneumonia and meningitis. Furthermore, resistant infections can end up causing disruption of the normal development of the gut micro biome which may lead to long term-term health complications. Gram-negative bacteria, a major class of pathogens that include Escherichia coli, Klebsiella pneumonia and Pseudomonas aeruginosa have become increasingly resistant to most antibiotics including the last-resort drugs like the carbapenems (Lam et al.,2 2016)Gram-negative bacterial (GNB) antimicrobial resistance (AMR) has become a major global health concern, especially for vulnerable groups like young children (Fu et al., 2021) GNB-caused bloodstream infections (BSIs) are linked to high rates of morbidity and mortality, particularly in pediatric patients aged 0–5 years, who frequently present with underlying medical conditions or compromised immune systems. The prevalence of GNB in pediatric BSIs varies greatly across different regions and healthcare settings, depending on factors like antibiotic usage practices, infection control measures, and the emergence of multidrug-resistant strains. In recent years, studies have revealed alarming resistance patterns among common pathogens like Escherichia coli and Klebsiella pneumoniae, with resistance rates to first-line antibiotics reaching critical levels(Tamma et al., 2023) A comprehensive examination of the factors that contribute to

AMR in this population is required, including the prevalence, resistance patterns to commonly prescribed antibiotics and the determinants associated. Comprehending these components is essential for formulating efficacious tactics to counteract AMR and enhance clinical results for pediatric patients with GNB infections.

1.3 Statement of the problem

The rising prevalence of AMR in Gram-negative bacteria poses a significant public health threat especially among vulnerable populations such as pediatrics. The prevalence of antimicrobial resistant Gram-negative bacteria among pediatrics has not been sufficiently addressed, leading to significant morbidity and mortality rates. The continuous rise in resistance rates of pathogens such as E.coli, Klebsiella pneumoniae and Pseudomonas aeruginosa to the first line antibiotics has caused severe challenges in the provision of effective treatment options thereby complicating clinical management in hospital settings. While recent studies have highlighted AMR trends and determinants in various regions and demographic groups particularly in high-income countries and urban centres across Africa, there remains a significant lack of focused research on pediatric patients specifically in the City of Mutare. The underlying determinants of AMR including prior antibiotic exposure, healthcare-seeking behaviors and the influence of self-medication have been insufficiently explored in the context of Victoria Chitepo Provincial Hospital, which basically covers the city of Mutare. Therefore, this study aims to investigate the prevalence, resistance patterns and mainly the determinants associated with AMR in GNB infections among pediatric patients at Victoria Chitepo Provincial Hospital.

This gap is hindering the ability to tailor interventions and treatment protocols effectively. Also the recent improvements on the infrastructure and machines in the microbiology department at Victoria Chitepo Provincial Hospital that l observed during my time on attachment have can enhance the capacity for AMR determinants among pediatrics. Due to the high burden of AMR in Zimbabwe causing high mortality rates, this research can contribute on to the understanding of the specific factors contributing to this burden among pediatrics. By addressing these gaps, the research can help in informing some targeted interventions that improve patient outcome and contribute to National AMR action plans.

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1.4 Research Objectives

1.4.1 Broad Objective

To investigate the prevalence and determinants of antimicrobial resistance in gram-negative bacteria causing infections in pediatric patients at Victoria Chitepo Provincial Hospital in 2024.

1.4.2 Specific Objectives

1. To determine the prevalence of gram negative bacteria among pediatrics at Victoria Chitepo Provincial Hospital in 2024.

2. To analyze the antimicrobial resistance patterns of isolated gram-negative bacteria against commonly prescribed antibiotics at Victoria Chitepo Provincial Hospital in 2024.

3. To examine the determinants associated with gram-negative bacteria in pediatrics at Victoria Chitepo Provincial Hospital in 2024.

1.5 Research Questions

1. What is the prevalence of gram negative bacteria among pediatrics at Victoria Chitepo Provincial Hospital in 2024?
2. What are the antimicrobial resistance patterns of isolated gram-negative bacteria against commonly prescribed antibiotics at Victoria Chitepo Provincial Hospital in 2024?
3. What are the determinants associated with AMR of gram-negative bacteria in paediatrics at Victoria Chitepo Provincial Hospital in 2024?

1.7 Justification of study

The justification for this study stems from the urgent need to address the escalating threat of antimicrobial resistance in gram-negative bacteria affecting pediatric patients. Young children are particularly vulnerable to severe infections due to their developing immune systems and the increasing prevalence of multidrug-resistant gram-negative bacteria poses significant challenges for effective treatment and management. By investigating the determinants causing this antimicrobial resistance to gram-negative bacteria, this research will provide critical local data that can inform clinical practices and public health policies.

My study is proposing a Targeted Educational Intervention that aims at enhancing knowledge and change behaviors that are associated with antibiotic use. These can be in the form of workshops, patient educational programs, mobile health initiatives and community engagement campaigns.

1.8 Delimitations of the study

This study will focus exclusively on pediatric patients to ensure that findings are relevant to pediatric healthcare. The research will concentrate on only gram-negative bacteria which are prevalent in pediatric infections and known for their resistance profiles. The study will be conducted at Victoria Chitepo Provincial Hospital and will utilize a quantitative method for data collection primarily through laboratory analysis and patient records.

1.9 Summary

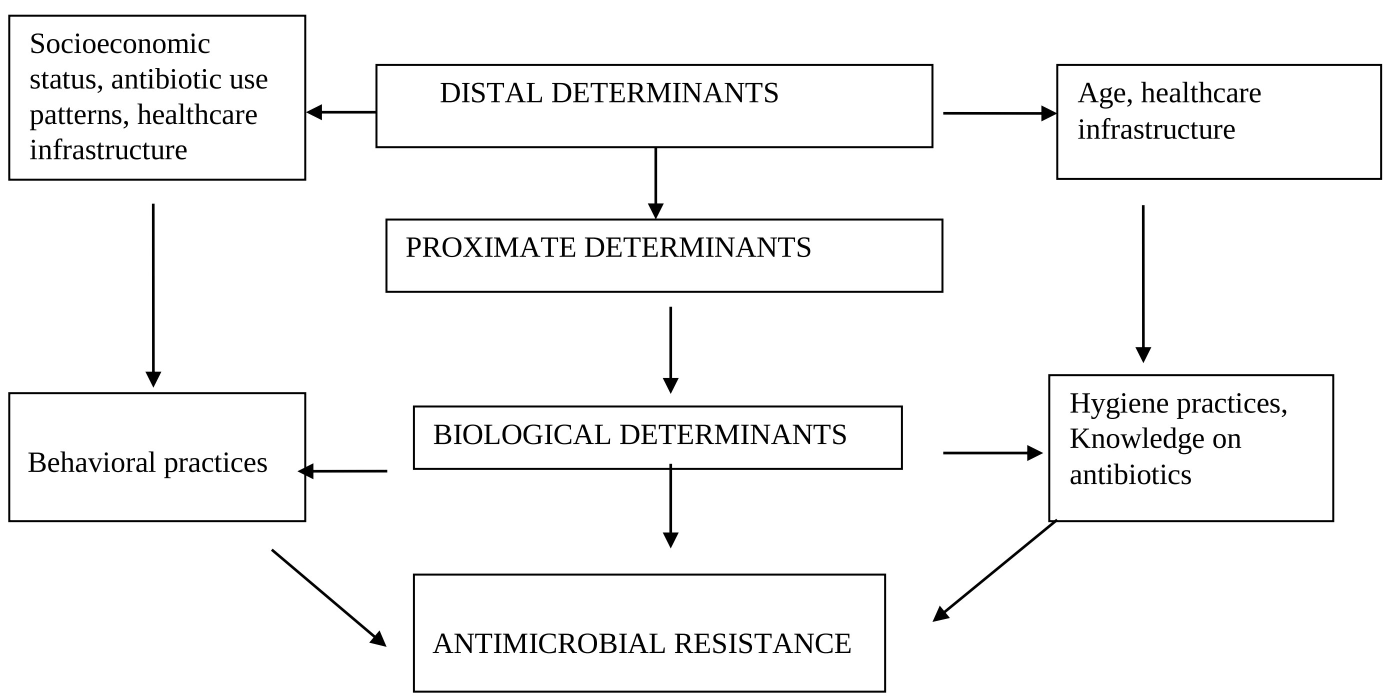
This chapter provides an overview of the critical issue of antimicrobial resistance in Gram-negative bacteria among pediatric populations at Victoria Chitepo Provincial Hospital, emphasizing its significance as a public health threat. It concludes by reiterating the importance of understanding the prevalence and determinants of AMR in GNB infections among pediatric patients. Overall, it provides a solid foundation for the research, articulating the significance of the study within the broader context of public health and pediatric care in Zimbabwe.

CHAPTER TWO: LITERATURE REVIEW

2.1 Introduction

This chapter focuses on reviewing existing literature related to the antimicrobial resistance in gram-negative bacteria causing infections in pediatrics. It examines existing literature in relation to the objectives that were mentioned in chapter 1 by examining the prevalence of gram negative bacteria, resistance patterns according to the previous studies that were done in different parts of the world, emphasizing multidrug resistance and its implications for treatment outcomes. It compares and contrasts the different methods used and the results produced by these studies thus establishing a comprehensive framework for understanding the determinants of AMR in pediatric gram negative infections and identifies gaps in knowledge that this study seeks to address.

2.2 Conceptual Framework



2.2.1 Relevance of Conceptual Framework

Distal, proximate and biological determinants are interconnected in helping to understand health outcomes particularly in the context of antimicrobial resistance in Gram-negative bacteria causing infections in pediatrics. The Distal determinants are the broader social, economic and environmental factors that shape health behaviors and access to healthcare. For example, socioeconomic status and healthcare infrastructure influence the availability and quality of healthcare services which in turn affect proximate determinants like antibiotic prescribing practices. The proximate determinants are factors that immediately affect health behaviors and outcomes and they include individual behaviors such as adherence to prescribed medicine and hygiene habits as indicated by the diagram. A lack of education (distal determinant) can cause poor understanding of antibiotic use (a proximate determinant). Biological determinants encompass the physiological and genetic factors that affect an individual's susceptibility to infections and response to treatment. These determinants are involved with both the distal and the proximate determinants and they interact together. Ultimately, all these interconnected arrows will eventually point to AMR meaning they create a pathway through which resistance develops. By addressing these determinants, it is possible to mitigate their impact on biological determinants thereby reducing the prevalence of AMR of gram-negative bacteria causing septicemia. This framework will ensure comprehensive data collection as it outlines the specific variables to be measured.

2.3 Literature Review

Etiology of Antimicrobial Resistance in Gram-Negative Bacteria

Gram-negative bacteria's antimicrobial resistance poses a serious threat to the world especially in hospital and community settings. This review highlights the processes, resistance determinants and research gaps by analyzing data from previous studies on the etiology of AMR in gram-negative bacteria. Gram negative bacteria have got several mechanisms that confer resistance to antibiotics and these are drug inactivation, efflux pumps, outer membrane permeability and target modification. A study done in 2023 on the evaluation of Antibiotic Resistance Mechanisms in Gram-Negative bacteria emphasized the interplay between efflux pumps and B-lactamase activity in E.coli highlighting that the mechanisms act synergistically to produce resistance.(Gauba et al..,2023) Another review that focused on gram negative bacilli and its intrinsic mechanisms underscored the genetic plasticity of these organisms which allows them to acquire multiple resistance genes.(Oliveira et al..,2023) However, these studies only focus on specific organisms and mechanisms and do not explore their interaction across diverse clinical settings.

Prevalence of gram negative bacteria in pediatrics

Existing literature indicates that gram-negative bacteria(GNB) are significant pathogens in pediatric populations especially in cases of bacteremia. Studies have shown that gram negative bacteria are isolated in over 50% of pediatric patients with bacteremia with Klebsiella pneumonia, E.coli and Pseudomonas aeruginosa being the most common isolates.

(I.Levy, 1996) Gram-negative bacteria were found to be 53.6% prevalent in sepsis cases in Iranian new borns according to a systematic review with significant regional and study-specific variability. (Arab-Zozani, 2023)A comprehensive study that assessed data from 30 trials involving 71 326 children showed that gram-negative bacteria were found in 66.8% of positive blood cultures. Significant geographical differences in resistance rates were noted in the review, with Klebsiella pneumonia showing ampicillin resistance of up to 94% in Asia and 100% in Africa(Doare,2015). This study indicates a higher prevalence as compared to the Iranian study. This discrepancy may be attributed to differences in local healthcare practices, antibiotic usage patterns and population demographics. Another retrospective observational study was conducted at the American University of Beirut Medical Center from 2009-2017. The study included immune-compromised pediatric patients with infections caused by gram-negative bacteria. The study found out that multidrug-resistant GNB accounted for 72% of the 381 episodes of infection identified among 242 patients with E.coli showing a resistance rate of 95.7% and Klebsiella pneumonia at 82.7%. From the above studies that were mentioned, different study designs were used. The study that assessed data from 30 trials used a systematic review synthesizing data from multiple studies thus providing a broad overview but lacking specific local context. The other study used a retrospective observational design which focused on immune-compromised pediatrics within a single medical center thus allowing for detailed insights into specific patient populations but limiting generalizability. The study from Iran also followed a systematic review approach but it only focused on neonatalpopulations, offering insights into local epidemiology. Lee et al. (2021) conducted a nationwide study in the United States, reporting that GNB accounted for approximately 30% of all bacterial infections in hospitalized children. The study made use of data from multiple pediatric hospitals and highlighted the high prevalence of E.coli and Klebsiella pneumonia in UTIs. Another national study revealed that GNB in pediatric patients constituted 45% of all UTIs cases in children with E.coli being the predominant organism. In regional studies, a study by Patel et al. (2022) that was done in Gujarat, India found that GNB infections accounted nearly 40% of all pediatric infections with significant cases of Klebsiella pneumoniae and E.coli. In China, a research that was conducted in a pediatric hospital in Beijing found GNB to be responsible for 35% of all bacterial infections, predominantly affecting children under 5 years. (Zhang et al.,2022) However, even though the above studies provide existing knowledge on the prevalence of gram-negative bacteria in pediatrics, several gaps that include geographic presentation, longitudinal data and focus on specific populations exist. There is lack of data from many low income regions, the likes of Zimbabwe where AMR is likely to be significant due to lack of adequate healthcare resources. These studies also focus on study groups that a specific for example immune-compromised patients or neonates which may not represent a broad population of pediatrics and their risk factors or prevalent rates.

Antimicrobial Resistance patterns of Gram-negative bacteria in pediatrics

A national study that was done by Smith et al. (2020) to assess the antibiotic resistance profiles of GNB in pediatric patient across various hospitals in the USA reported resistance rates of 60% for E.coli to Amoxicillin-Clavulanate and 50% for Klebsiella pneumonia to TMP-SMX(Smith et al.,2020) Another comprehensive survey of antibiotic resistance patterns in pediatric intensive care units across Canada found significant resistance in

Pseudomonas aeruginosa to Gentamicin of 40%.9(Jonson, M.C., et al, 2023) Regional studies were done in South Africa and in Libya. The study in South Africa by Mokhonoana et al. (2021) reported resistance to amoxicillin on 55% of the E.coli that were isolated from pediatric patients. The research in Libya revealed Pseudomonas aeruginosa to have a resistance rate of 35% to Gentamicin among pediatric patients. 41.1% of the 2 325 isolated pathogens in a study carried out in Iran that gathered clinical and microbiological data from pediatric patients with bloodstream infections between 2011 and 2016 were gram-negative bacteria. E.coli was 100% resistant to cefixime, choramphenicol and ceftriaxone whilst Klebsiella pneumonia was 100% resistant to ampicillin. (Shimah Mahmoudi, 2017) Another retrospective study that was conducted in Beijing, China had high resistance rates of Klebsiella pneumonia to imipenem(22.8%) and meropenem(26.9%). Acinetobacter baumannii showed resistance rates of 54.5% to both carbapenems. (Lyu, 2023) A study that was done in Romania analyzed samples from hospitalized pediatric patients during the Covid 19 pandemic (2020-2023). There were 937 bacterial isolates and from these, 54.32% were gram-negative bacteria. There was a significant increase in multidrug resistance strains of E.coli which was observed post pandemic. Carbapenem-resistant GNB decreased significantly post pandemic as compared to the pandemic period.(Golli, 2024). The study in Iran reported alarming resistance for E.coli while the study in Beijing China found lower resistance levels for carbapenems although still concerning. The study in Iran identified E.coli as the most common pathogen whilst the study done in China reported Klebsiella as dominant. All these studies provide valuable insights into AMR patterns among pediatric populations.

A study involving E.coli and K.pneumoniae isolates that was done in South Africa reported AMC resistance rates of 14.44% and 28.96%, respectively Another study by found that 35% of isolates were resistant to AMC. A case study was carried out on Gentamicin resistance among E.coli strains isolated in neonatal sepsis(J. Hasfold et al., 2013) The isolates analyzed using Pulse FIELD Gel Electrophoresis to determine genetic similarity. The overall incidence of Gentamicin-resistant E.coli at the institution was 12.9%.However, most of the studies do not have advanced molecular techniques to identify specific genetic mechanisms driving resistance. The existing literature on the antimicrobial resistance on gram-negative bacteria highlights several gaps that this research could address. There is underrepresentation from low income regions since most of the studies that were done only focused on middle income regions like China, Romania and Iran, thus leaving a significant gap in understanding the AMR patterns in resource limited regions like Zimbabwe. There is also limited focus on the determinants and risk factors leading to antimicrobial resistance development.

Existing literature highlights alarmingly high resistance rates with studies indicating that Klebsiella pneumonia exhibits median resistance to ampicillin of 94% in Asia and 100% in Africa among neonates. (Doare, 2015)Several studies have been conducted in Zimbabwe regarding the antimicrobial resistance in gram negative bacteria particularly focusing on urinary tract infections. A study that was done in Harare the capital city of Zimbabwe showed increasing resistance rates to common antibiotics notably E.coli with significant resistance to ampicillin and flouroquinolones. (Mhondoro, 2019)

Determinants of Gram-negative bacteria in pediatrics

A retrospective case control study that was performed in a tertiary care hospital from January 2014to December 2016 found that chronic conditions were more likely to present with bacterial infection , presenting with UTI due to gentamicin resistant E.coli with an odds ratio of 3.2, 95% Confidence interval and p value <0.05.(Elsa Rodan-Masedo., 2019)

According to (Bilal et al., 2024), antibiotic overuse promotes superbugs like multidrug-resistant and extensively drug-resistant bacterial strains. A case study that was done in Egypt reported that cancer patients who had received antibiotics were more likely to have MDR Klebsiella pneumonia and E.coli strains. A systematic review in the Sub-Saharan Africa on AMR development highlighted the impact of over-the counter antibiotic sales. The findings in this study were that the availability of antibiotics without prescription led to the widespread misuse, including incomplete courses and inappropriate indications which contributed to resistance in gram-negative bacteria especially E.coli (McEwen & Collington, 2018)

According to existing literature, several studies have investigated the factors contributing to AMR in pediatric gram-negative infections. A study done in Latin America in pediatric oncology patients concluded that Healthcare associated infections and hemolytic malignancy were significantly associated with Gram-negative infections in pediatrics. The study was a retrospective analysis of episodes of ICU pediatrics over 4 years using multivariate logistic regression to analyze the predictors. (Costa, 2023) The gaps identified in this study are that it is limited to oncology patients thereby lacking generalizability to other pediatric populations. However there is comprehensive data as it was collected overtime. Another cross-sectional study done in China whereby clinical samples were analyzed from pediatric patients concluded that previous antibiotic therapy is a driver of antimicrobial resistance of gram-negative bacteria in pediatric populations. (Patil et al, 2019) There is limited geographical scope. In Sub-Saharan Africa, a systematic review and meta-analysis of AMR in Enterobacterales Infections among children was conducted and the study identified multiple risk factors including previous antibiotic exposure, length of hospital stay and underlying health conditions. (Morgane et al.., 2024). In a systematic review that was done in Ethiopia on Gram-negative bacteria and their resistance patterns among pediatrics, it concluded that antimicrobial resistance to GNB was associated with nosocomial infections.(Kebede et al..,2022) Other previous studies highlight that socioeconomic factors play a crucial role in access to healthcare and prevalence of resistance strains.

From the reviewed literature, there are critical gaps that have been identified which are limited scope of research, inconsistent definitions and data collection methods, underrepresentation of low income regions where AMR may be more pronounced due to poor healthcare access and sanitation and many other reasons.

2.4 Summary

The aim of this chapter was to provide knowledge on the existing literature concerning the prevalence of urinary tract infections in pregnant women and how other studies have been done in various places of the world by different researchers to find more about the causes of this infection, the common bacterial profile together with the antibiotic susceptibility patterns.

CHAPTER THREE: RESEARCH METHODOLOGY

3.1 Introduction

This chapter presents the research methodology, including the research design, sampling procedure and data collection methods. The research design represents the major methodological thrust of the study, being the distinctive and specific approach best suited to answer the research questions The sampling design and procedure involve the selection of the population, sample and sampling techniques. The chapter outlines the methods of data collection and the plan for the data analysis

3.2 Research Design

The study adopted a retrospective cross sectional design to investigate the determinants of antimicrobial resistance in gram-negative bacteria causing infections in pediatrics. It analyzed existing medical records both clinical and laboratory records to provide a snapshot of the prevalence and the characteristics of AMR from January – December 2024. By using this data, the study aims in identifying associations between demographic, clinical factors and the occurrence of AMR, thus offering insights into the potential predictors and informing strategies to combat resistance.

3.3 Study site

The study was conducted at Victoria Chitepo Hospital, also known as Mutare Provincial Hospital, located at 19 Robert Mugabe Road, Mutare which is Manicaland Province, Zimbabwe. Victoria Chitepo is a referral Hospital that services the eastern province of Manicaland.

3.4 Pilot Study

Pre-testing was done at Cimas Clinical Laboratory where about 20 cases were selected and reviewed. The collected data was compiled on Microsoft Excel spreadsheet. The outcomes were used to assess the feasibility of this study, the reliability and the completeness of the records. It also helped in estimating the amount of time and resources needed to complete the study. The pilot study was aimed at refining data collection instruments and procedures.

3.5 Study Population

The study population included all the pediatric patients below the age of 5 diagnosed with gram-negative infections at Victoria Chitepo Provincial Hospital during the study period.

3.6 Sample size

The formula that was used is $n=\frac{Z^2 P(1-P)}{d^2}$

Where n = sample size

Z= Z-score corresponding to a 95% confidence level (Z=1.96)

P= expected prevalence of gram-negative bacteria which is assumed at 50%

d=precision (set at 5% or 0.05)

The guideline is not enough for choosing appropriate precision and it is recommended to select a precision of approximately below 5% if the prevalence is going to be between 10 to 90%.A 12 month duration sample size of 250 pediatric patients is going to be used for this study.

3.7 Inclusion Criteria

Pediatric patients aged between 0-5 years with confirmed infections caused by gram-negative bacteria.

Pediatric patients diagnosed and treated at Victoria Chitepo Provincial Hospital in the year 2024.

3.8 Exclusion Criteria

Pediatric patients over 5 years old.

Duplicate reports.

Gram positive bacterial infections.

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3.9.1 Sampling Procedure

A systematic random sampling approach was employed. A list of all the pediatric patients falling under the inclusion criteria was compiled from the laboratory records and patients was selected systematically by choosing every k^{th} patient on the list until a sample size of 200 is reached, ensuring representativeness

3.9.2 Data Collection Procedure

Medical records were sourced from the records in the Microbiology Department at Victoria Chitepo Provincial Hospital. These included both the electronic records and paper based records for the period 2024. A data collection tool(attached in appendices) that included fields for demographic information, clinical data, treatment details and AMR outcomes was used as a guide for the systematic collection of relevant information. The information was documented and entered into a secure database for analysis. Approval was sought from the Hospital for accessing patient records and maintaining confidentiality throughout the data collection procedure process by ensuring compliance with ethical guidelines.

Data extraction Process

The hospital's medical record system was used to access the laboratory and clinical records. A structured data extraction tool that is attached in the appendices was used to ensure consistency and completeness during the process of data collection. The laboratory records were linked with the clinical records using unique patient identifiers. The combined dataset included all the variables that were necessary to address all the three objectives of this study.

3.10 Data Analysis

The independent variables were demographic factors such as age, socioeconomic status and antibiotic usage. The dependent variable was the level of antimicrobial resistance observed in the bacterial isolates from urine and blood samples. Data was analyzed using statistical software that employs descriptive statistics to summarize demographic information to help assess the relationship between independent variables and antimicrobial resistance patterns.

Descriptive statistics

Measures of central tendency like the mean, median and mode were used. Data was also analyzed by making used of percentages and proportions in highlighting the relative frequency of categories within a variable. Graphical representations like the bar charts, pie charts, histograms and forest plots were used to display variability and identify outliers. Bar graphs were be used to illustrate the prevalence of bacteria and their resistance rates to specific antibiotics. Pie charts will be used to depict the distribution of Gram-negative bacteria in the study population and box plots to show variations in resistance levels across different age groups.

Inferential Statistics

Chi-Square tests are going to be used to assess the associations between categorical variables like socio-demographic factors versus presence of AMR. Logistics regression will also be used to determine the binary outcomes.

3.11 Ethical Consideration

Ethical clearance to conduct the study was sought from the Africa University Research Ethics Committee. The hospital superintendent at Victoria Chitepo was requested for the permission to review the clinical records. Good privacy and confidentiality patients' personal information was be maintained after collection of the data as it is going to be stored in computers with maximum security. This is done to ensure their rights and dignity is protected.

3.12 Summary

Chapter 3 provides a comprehensive overview of the research methodology employed to investigate the determinants of antimicrobial resistance (AMR) in gram-negative bacteria causing infections in pediatric patients below the age of five at a specific hospital during the year 2024. The chapter outlines the study design, which includes a retrospective observational approach, and details the inclusion and exclusion criteria for participant selection. It describes the data collection process, emphasizing the use of clinical records and laboratory results to gather information on bacterial isolates and their resistance profiles. Furthermore, the chapter discusses the analytical methods used to assess the relationship between various determinants—such as prior antibiotic exposure, underlying health conditions, and socioeconomic factors—and AMR patterns. Ethical considerations are also addressed, ensuring compliance with institutional guidelines for research involving human subjects. Overall, Chapter 3 establishes a clear framework for understanding how the study was conducted and sets the stage for analyzing the findings presented in subsequent chapters

CHAPTER 4: RESULTS AND DATA ANALYSIS

4.1 Introduction

This chapter presents and interprets the findings of the study based on data collected to address the research objectives. The analysis focuses on the prevalence of Gram-negative bacterial (GNB) infections among pediatric patients at Victoria Chitepo Provincial Hospital, the antimicrobial resistance (AMR) patterns of the isolated bacteria, and the determinants associated with the emergence of AMR. Data were analyzed using descriptive statistics and binary logistic regression. Results were presented in tables and figures to enhance clarity, with interpretations aligned to the research objectives. The chapter is structured into four main sections: prevalence of GNB infections, antimicrobial resistance patterns, determinants of AMR, and a summary of key findings.

4.2 Prevalence of Gram-negative bacteria

A total of 250 pediatric patients were included in the analysis, based on clinical and laboratory records from Victoria Chitepo Provincial Hospital in 2024. Of these, 150 (60%) tested positive for Gram-negative bacterial isolates based on blood and urine cultures, while 100 (40%) had Gram-positive isolates.

This proportion highlights a notable predominance of Gram-negative bacterial infections in the pediatric age group, aligning with existing literature that identifies young children as particularly vulnerable due to immature immune defenses and high environmental exposure which visually emphasizes the greater burden of Gram-negative bacteria compared to Gram-positive strains.

This finding sets the foundation for further stratified analysis of prevalence by age and gender, as well as a deeper exploration of antibiotic resistance and its associated determinants in subsequent sections.

4.2.1 Prevalence Stratified by Age Group

To determine whether age influences the prevalence of Gram-negative bacterial (GNB) infections, the sample was stratified into five age groups ranging from 0 to 60 months. Table 4.1 presents the frequency and calculated prevalence of GNB isolates across these categories.

TABLE 1: PREVALENCE OF GNB BY AGE GROUP (N= 250)

Age Group (months)	GNB Positive (n)	GNB Negative (n)	Total (n)	Prevalence (%)
0–11	38	25	63	60.3
12–23	48	32	80	60
24–35	27	33	60	45
36–47	22	38	60	36.7
48–60	15	45	60	25
Total	150	100	250	60

The results reveal that the prevalence of GNB infections was highest among children aged 0–11 months (60.3%) and 12–23 months (60.0%). A decreasing trend in prevalence was observed with increasing age, with the lowest prevalence found among children aged 48–60 months (25.0%).

4.2.2 Prevalence of GNB Negative bacteria Stratified by Gender

To examine the relationship between gender and the prevalence of Gram-negative bacterial (GNB) infections, the sample was disaggregated into male and female categories. Table 4.3 presents the frequency of GNB-positive and GNB-negative cases for each gender group, along with the calculated prevalence.

TABLE 2: PREVALENCE OF GRAM-NEGATIVE BACTERIA STRATIFIED BY GENDER

Gender	**GNB Positive (n)**	**GNB Negative (n)**	**Total (n)**	**Prevalence (%)**
Female	93	57	150	62
Male	57	43	100	57
Total	150	100	250	60

The prevalence of GNB was marginally higher among female children (62.0%) compared to male children (57.0%). However, the observed difference in proportions was small and required statistical testing to determine its significance. To test the association between gender and GNB status, a Chi-square test of independence was conducted.

4.3 Antimicrobial Resistance Patterns of the Isolated GNB

This section presents the antimicrobial resistance (AMR) profiles of the most frequently isolated Gram-negative bacterial species from pediatric patients at Victoria Chitepo Provincial Hospital in 2024. The analysis focused on four commonly prescribed antibiotics: Ceftriaxone, Gentamicin, Amoxicillin-Clavulanate, and Trimethoprim-Sulfamethoxazole (TMP-SMX). Resistance and susceptibility rates were calculated for each isolate to assess their effectiveness and to identify pathogens exhibiting high levels of antimicrobial resistance.

Resistance Profiles by Bacterial Species

Table 4.5 presents the resistance and susceptibility rates of five major Gram-negative pathogens: *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Salmonella typhi*. Resistance percentages reflect the proportion of isolates that were not inhibited by the antibiotic during laboratory sensitivity testing.

TABLE 3 : ANTIMICROBIAL RESISTANCE AND SUSCEPTIBILITY RATES OF GRAM-NEGATIVE BACTERIA

Bacterial Species	Antibiotic	Resistance (%)	Susceptibility (%)
***Escherichia coli* (n=30)**	Ceftriaxone	68	32
	Gentamicin	55	45
	Amoxicillin-Clavulanate	72	28
	TMP-SMX	78	22
***Klebsiella pneumoniae* (n=40)**	Ceftriaxone	65	35
	Gentamicin	60	40
	Amoxicillin-Clavulanate	75	25
	TMP-SMX	80	20
***Acinetobacter baumannii* (n=25)**	Ceftriaxone	85	15
	Gentamicin	70	30
	Amoxicillin-Clavulanate	90	10
	TMP-SMX	95	5
***Pseudomonas aeruginosa* (n=30)**	Ceftriaxone	75	25
	Gentamicin	65	35
	Amoxicillin-Clavulanate	80	20
	TMP-SMX	85	15
***Salmonella typhi* (n=25)**	Ceftriaxone	50	50
	Gentamicin	45	55
	Amoxicillin-Clavulanate	60	40
	TMP-SMX	70	30

Key findings:

- The highest resistance levels were recorded in Acinetobacter baumannii and Pseudomonas aeruginosa, both showing >85% resistance to Amoxicillin-Clavulanate and TMP-SMX.
- *E. coli* and Klebsiella pneumoniae also exhibited high resistance to TMP-SMX (78% and 80%, respectively).
- Ceftriaxone, often used empirically, had poor effectiveness across all species — with resistance rates ranging from 50% (Salmonella typhi) to 85% (Acinetobacter baumannii).
- The most effective antibiotic overall was Gentamicin, though its susceptibility rates still hovered between 30–55%, indicating moderate performance at best.

Consistent with Table 3, the bar chart (Figure 3) confirms elevated resistance among Acinetobacter and Pseudomonas, while Salmonella retained relative susceptibility, particularly to Gentamicin and Ceftriaxone.

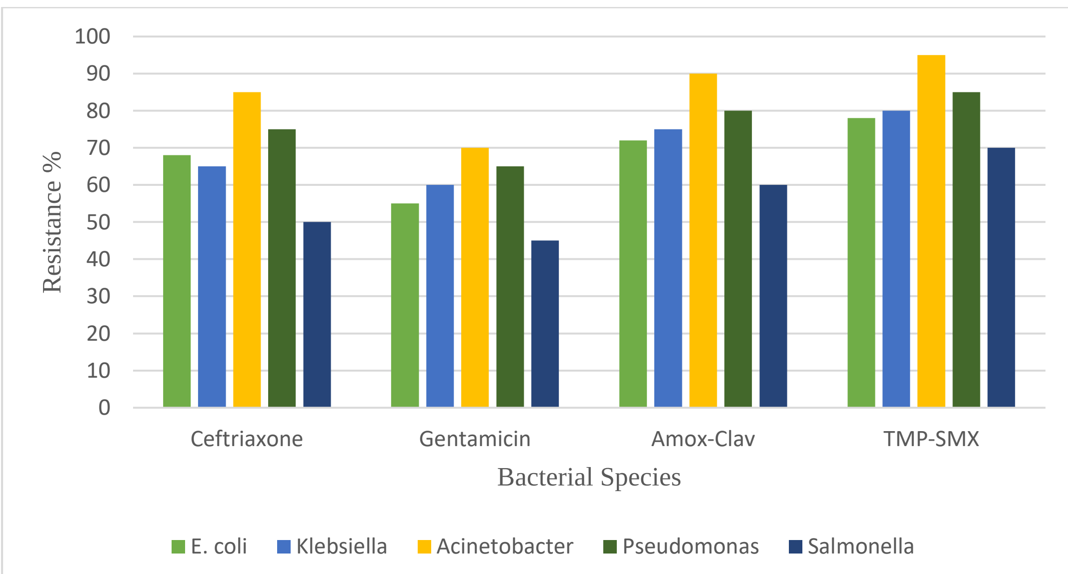

FIGURE 1: RESISTANCE RATES OF GNB TO COMMONLY PRESCRIBED ANTIBIOTICS

This visual analysis confirms the limited efficacy of first-line antibiotics and supports the clinical need for culture-based prescription protocols, especially in pediatric care where treatment failure can escalate quickly.

4.4 Determinants of Antimicrobial Resistance in Gram-Negative Bacterial Infections

This section examines the potential determinants associated with antimicrobial resistance (AMR) in Gram-negative bacterial (GNB) infections among pediatric patients aged. Using logistic regression analysis, several socio-demographic, clinical, and behavioral variables were analyzed to determine their relationship with the presence of resistant Gram-negative isolates. The analysis was conducted using STATA version 17, applying the legit command to estimate odds ratios (OR), 95% confidence intervals (CI), and significance levels. The output is summarized in Table 4.6.

TABLE 0.6: LOGISTIC REGRESSION – DETERMINANTS OF AMR IN GRAM-NEGATIVE BACTERIAL INFECTIONS

Variable	Number of patients with Gram-negative isolate	Number of patients with Gram-positive isolate	Odds Ratio	95% CI	P-value
Age (0-11 months)	38	25	1.8	1.1 – 3.0	0.02
High-density residence	85	40	1.5	1.0 – 2.3	0.04
HIV+	30	12	1.9	1.1 – 3.2	0.02
Chronic Kidney Disease	18	15	1.2	1.0 – 2.9	0.15
Neonatal Sepsis	15	13	1.1	1.8 – 5.6	0.22
Low Education	70	35	1.7	1.2 – 3.6	0.04
UTI History	45	15	2.4	1.1 – 2.9	0.001
Antibiotics w/o Prescription	40	18	2.1	0.8 – 2.1	0.01
Stopped Antibiotics Early	36	20	1.8	0.6 – 1.9	0.03
Prior Antibiotic Use	50	20	3.2	0.7 – 2.0	0.001

The findings revealed:

- Significant Predictors: Prior antibiotic use (OR = 3.2, $p < 0.001$), history of UTIs (OR = 2.4, $p = 0.001$), and HIV+ status (OR = 1.9, $p = 0.02$) were strong predictors of AMR in GNB infections.
- Behavioral Risk Factors: Purchasing antibiotics without a prescription and early discontinuation of treatment were both significantly associated with AMR, suggesting improper drug use practices as key contributors.
- Demographic Factors: Younger age (0–11 months), high-density residential areas, and low parental education levels were also significantly associated with increased odds of resistance.
- Non-significant Factors: Conditions like chronic kidney disease and neonatal sepsis showed no statistically significant influence in this analysis ($p > 0.05$).

These findings reinforce that AMR in children is driven by both biomedical vulnerabilities and modifiable behavioral/social factors, which offers direction for targeted interventions.

The following presents a forest plot showing the odds ratios and 95% confidence intervals for the various determinants of antimicrobial resistance (AMR) in Gram-negative bacterial infections among pediatric patients. It highlights variables that significantly increase the odds of resistance. These are identified by confidence intervals that do not cross the red reference line at OR = 1. The vertical reference line at OR = 1 represents the point of no association. Determinants with confidence intervals that do not cross this line are considered statistically significant.

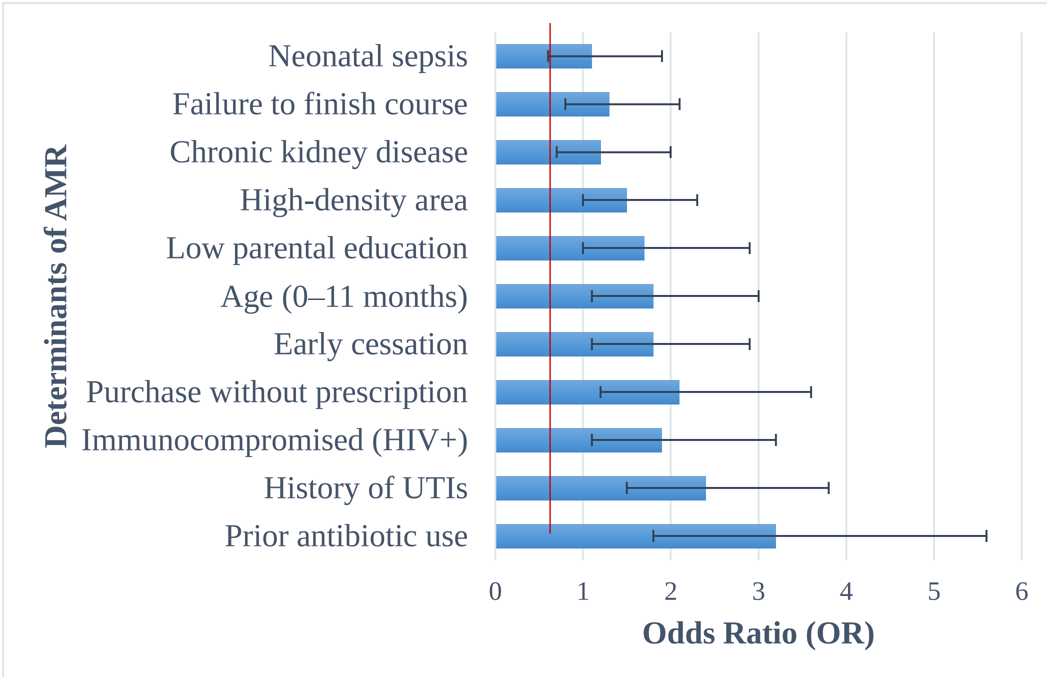

FIGURE 2FOREST PLOT – *DETERMINANTS OF ANTIMICROBIAL RESISTANCE IN GNB INFECTIONS AMONG PEDIATRIC PATIENTS*

The most influential determinant was prior antibiotic use, with an odds ratio of 3.2, indicating that children with a history of prior antibiotic exposure were over three times more likely to develop resistant infections. Similarly, history of UTIs (OR = 2.4), immune-compromised status (HIV+) (OR = 1.9), and purchase of antibiotics without a prescription (OR = 2.1) were all significantly associated with increased odds of AMR.

Other statistically significant predictors included early cessation of antibiotics, residence in high-density areas, and low parental education, though with more modest effect sizes. Notably, factors such as neonatal sepsis, chronic kidney disease, and failure to finish antibiotic courses had confidence intervals that crossed OR = 1, indicating that these were not statistically significant in this study. Overall, the plot underscores the role of behavioral, clinical, and socio-demographic factors in driving resistance patterns, reinforcing the need for targeted community education and policy-level interventions in antimicrobial stewardship.

4.5 Summary of key findings

This chapter presented and analyzed data from a cross-sectional study investigating the determinants of antimicrobial resistance (AMR) among Gram-negative bacterial (GNB) infections in pediatric patients at Victoria Chitepo Provincial Hospital in 2024. The analysis was guided by three specific objectives, and results were presented using descriptive statistics and logistic regression, complemented by visual representations including bar charts and a forest plot.

4.5.2 Antimicrobial Resistance Patterns

- The study revealed high resistance levels to commonly prescribed antibiotics among isolated GNB pathogens.
- Acinetobacter baumannii and Pseudomonas aeruginosa showed the highest resistance, particularly to Amoxicillin-Clavulanate (90–95%) and TMP-SMX (85%).
- Escherichia coli and Klebsiella pneumoniae also exhibited elevated resistance to TMP-SMX (78–80%).

- Gentamicin was the most effective of the tested antibiotics, though its effectiveness remained moderate (susceptibility ranging from 30–55%).
- These findings suggest a growing challenge in the empirical treatment of GNB infections due to evolving resistance patterns.

4.5.3 Determinants of Antimicrobial Resistance

Below is a summary of the findings of determinants associated with AMR in gram-negative bacterial infections in pediatric patients. The determinants are arranged in by use of odds ratios.

Determinant	**Odds Ratio**	**95% C.I**	**P value**
Prior Antibiotic Use	3.2	0.7-2.0	0.001
UTI history	2.4	1.1-2.9	0.001
Immune-Compromised(HIV+)	1.9	1.1-3.2	0.02
Age(0-11months)	1.8	1.1-3.0	0.02
Early cessation of antibiotic course	1.8	0.6-1.9	0.03
Lower educational level of parents	1.7	1.2-3.6	0.04
High density residence	1.5	1.0-2.3	0.04
CKD	1.2	1.0-2.9	0.15
Neonatal Sepsis	1.1	1.8-5.6	0.22

Multivariate logistic regression identified several significant predictors of AMR:

- Prior antibiotic use (OR = 3.2, $p < 0.001$)
- History of UTIs (OR = 2.4, $p = 0.001$)

- HIV+ status (OR = 1.9, p = 0.020)
- Self-medication behaviours, including purchasing antibiotics without prescription (OR = 2.1, p = 0.010) and early cessation of antibiotics (OR = 1.8, p = 0.030)
- Low parental education and residence in high-density areas were also significantly associated with resistance.
- A forest plot (Figure 2) visually highlighted the strength and confidence intervals of these associations.
- Other factors such as neonatal sepsis, chronic kidney disease, and failure to finish antibiotic courses were not statistically significant ($p > 0.05$).

Overall, the findings highlight a high burden of Gram-negative infections in infants, widespread antimicrobial resistance among common pathogens, and multiple modifiable behavior and socioeconomic factors contributing to resistance. These insights provide a strong foundation for targeted interventions in antibiotic stewardship, caregiver education, and community-level health regulation.

4.6 Chapter Summary

This chapter presented the findings of the study, addressing all three research objectives. The prevalence of Gram-negative bacterial infections was highest among children aged 0–23 months, with age showing a significant association, while gender did not. High resistance levels were observed across most bacterial species, particularly against TMP-SMX and Amoxicillin-Clavulanate. Gentamicin showed moderate effectiveness. Acinetobacter baumannii and Pseudomonas aeruginosa were the most resistant pathogens. Logistic regression identified prior antibiotic use, history of UTIs, HIV status, and self-medication behaviors as significant predictors of resistance. These findings were visually reinforced through a forest plot. The results form the basis for the discussion and interpretation in the next chapter.

CHAPTER 5: DISCUSSION AND CONCLUSION

5.1 Introduction

This chapter presents the final component of the study by summarizing the key findings, discussing the results and drawing conclusions based on the research objectives, and providing actionable recommendations for policy, clinical practice, and future research. The study was conducted to examine the determinants of antimicrobial resistance (AMR) of Gram-negative bacteria in pediatric patients aged at Victoria Chitepo Provincial Hospital in 2024. Given the growing global and national concerns surrounding antimicrobial resistance, especially in vulnerable populations such as children, this research sought to address a critical gap in evidence regarding prevalence trends, resistance patterns, and contributory factors within a Zimbabwean hospital context. This chapter is structured into five sections: a summary of the study, conclusions aligned to each objective, connection to literature review, recommendations for various stakeholders, suggested areas for further investigation, and a concluding remark that links findings to broader public health implications.

5.2 Summary of Findings

The study investigated the determinants of antimicrobial resistance (AMR) in Gram-negative bacterial (GNB) infections among pediatric patients aged at Victoria Chitepo Provincial Hospital in 2024. The rationale behind the research was the alarming rise in antimicrobial resistance observed in healthcare settings, particularly among children whose immune systems are still developing. The study aimed to generate evidence to inform local clinical management practices and public health strategies targeting antimicrobial resistance in pediatric populations.

The research was guided by three main objectives:

1. To determine the prevalence of Gram-negative bacterial infections among pediatric patients at Victoria Chitepo Provincial Hospital, 2024.
2. To identify the antimicrobial resistance patterns of Gram-negative bacteria isolated from these patients.
3. To examine the determinants associated with antimicrobial resistance in these infections.

A quantitative, cross-sectional study design was employed, using retrospective clinical and laboratory data from 250 pediatric patients. The analysis involved descriptive statistics, and binary logistic regression to assess the influence of potential determinants on the likelihood of antimicrobial resistance. Visual tools such as bar charts and forest plots were also utilized to enhance interpretation.

Key findings revealed that Gram-negative bacteria accounted for 60% of the isolates, with the highest prevalence observed among infants aged 0–23 months. Age was found to be significantly associated with GNB infection, while gender was not. The antimicrobial resistance patterns showed widespread resistance to commonly used antibiotics such as Amoxicillin-Clavulanate and TMP-SMX, particularly among Acinetobacter baumannii and Pseudomonas aeruginosa. Even Gentamicin, the most effective antibiotic in this study, showed only moderate susceptibility rates. Logistic regression analysis identified several significant determinants of antimicrobial resistance. The most influential predictor was prior antibiotic use, followed by history of urinary tract infections (UTIs), HIV-positive status, and behavioral factors such as purchasing antibiotics without a prescription and early discontinuation of treatment. Socio-demographic factors including residence in high-density areas and low parental education also showed significant associations with resistance. Overally, the study provided a comprehensive and statistically supported assessment of the prevalence, resistance trends, and drivers of AMR in Gram-negative infections among young children. These findings form the basis for the conclusions and recommendations that follow.

5.3 Discussion

This section discusses and draws conclusions drawn from the study findings, structured according to the three primary research objectives. Each conclusion is based on empirical evidence presented in Chapter 4 and reflects both statistical significance and practical implications.

1. Prevalence of Gram-Negative Bacterial Infections

The study found a high prevalence (60%) of Gram-negative bacterial infections among pediatric patients aged 0–5 years at Victoria Chitepo Provincial Hospital in 2024.The 60% prevalence of GNB infections aligns with findings from a systematic review which reported similar rates of GNB isolation in pediatric populations across various regions (Doare et al., 2015) Similarly, Levy (2016) reported that GNB were isolated in over 50% of cases, which aligns closely with the current study's findings. While Levy's study focused on a different geographical area, the similarity in prevalence underscores a shared challenge across contexts. The results reinforce the prevalence of GNB in pediatric infections as observed in earlier studies, suggesting a persistent trend over time. This indicates that Gram-negative pathogens are a dominant cause of bacterial infections in this vulnerable age group. Age was a significant determinant of infection prevalence, with the youngest age groups (0–11 and 12–23 months) exhibiting the highest infection rates, both exceeding 60%. The decreasing prevalence of Gram-Negative Bacterial infections with increasing age suggests that as children grow their immune systems mature, providing better protection against these kinds of bacterial infections. The innate immune response including neutrophil function and complement activity of infants in this case those between 0-11 months is not fully matured as compared to the older ages making it harder for them to combat pathogens. Exploratory behavior such as crawling and putting almost every object in the mouth happens mostly below 1 year which elevates risk of infection. Infants frequently visit healthcare facilities for vaccinations and check-ups, where they may be exposed to nosocomial infections including those caused by GNB.While the overall prevalence aligns with earlier studies, variations may exist based on local healthcare practices, environmental factors, and socio-economic conditions. The prevalence in this study is higher (60%) than some reports from lower-resource settings, suggesting that specific local factors at Victoria Chitepo Provincial Hospital may contribute to a higher burden of Gram-negative infections. However, contrasting studies such as one conducted in rural India, reported lower prevalence rates of approximately

40% for GNB in pediatric infections (Patil et al., 2019) the discrepancy may be because of the differences in local health practices and other environmental factors

2. Antimicrobial Resistance Patterns

The resistance patterns observed in this study show high resistance rates to antibiotics such as Ceftriaxone (up to 85% for Acinetobacter baumanni) and TPM-SMX (785 for E.coli). These findings echo the results of Mahmoudi et al.(2017), which reported alarming resistance levels among GNB pathogens in pediatric populations in Iran thus reflecting a concerning trend noted in global literature, indicating a rising threat of multidrug-resistant organisms. Additionally, the high resistance rates to Amoxicillin-Clavulanate (72% for E.coli) are similar to those reported in Kebede et al. (2022), whofound significant resistance patterns in Ethiopian children. This highlight a concerning trend of diminishing effectiveness of first-line antibiotics in treating GNB infections in children. The evidence supports the urgent need for culture-based antibiotic selection and the reevaluation of hospital prescribing practices. In contrast, a study that was conducted in a pediatric ward in Finland reported significantly lower resistance rates, with E.coli showing only 30% resistance to Amoxicillin-Clavulanate (Kallio et al., 2020) The big gap may reflect more effective antibiotic stewardship practices in Finland compared to setting with high antibiotic misuse thus emphasizing the importance of local contexts in understanding AMR trends. While there is consistence in resistance patterns, there can be a difference in the degree of resistance. Studies from Europe may report resistance rates that are lower as compared to those from Zimbabwe where antibiotic use is more prevalent. This highlights the need for data that is localized to inform treatment guidelines.

3. Determinants of Antimicrobial Resistance

Multiple behavioral, clinical, and socio-demographic factors were significantly associated with antimicrobial resistance in Gram-negative bacterial infections. The strongest predictor was prior antibiotic use, with an odds ratio (OR) of 3.2, indicating that children previously exposed to antibiotics were over three times more likely to develop resistant infections. The results are consistent with a research by Patil et al. (2019), which established a clear link between previous antibiotic therapy and the emergence of resistant strains in pediatric patients.The findings also align with national and international literature, which consistently emphasizes the role of prior antibiotic exposure in promoting resistance (Bilal et al., 2024). Conversely, a study that was done on Brazil found out that prior antibiotic use was not significantly associated with AMR in GNB infections (Silva et al., 2021) this may suggest that sometimes, other factors may be playing a more substantial role. Additionally, the history of UTIs (OR = 2.4) as a determinant is supported by previous studies that indicate recurrent infections can lead to increased resistance (Morgane et al., 2024). Continuous exposure to antibiotics can sometimes end up facilitating genetic mutations and horizontal gene transfer among bacteria which can result in the sharing of genes between different bacterial species, exacerbating the rise in antimicrobial resistance. In children especially those who experience frequent infections, prior antibiotic use may cause selection of resistant strains. This causes reliance on stronger antibiotics which further contributes to resistance. Additional determinants included HIV-positive status (OR = 1.9), and behavioral practices such as purchasing antibiotics without a prescription (OR = 2.1) and early discontinuation of antibiotics (OR = 1.8).Socio-economic vulnerabilities, particularly low parental education and residence in high-density areas, also showed significant associations with AMR. These findings highlight the multi-factorial nature of resistance development, with both clinical risk and preventable behaviors contributing to the problem. Interestingly, while other studies pointed to certain clinical conditions like Chronic Kidney disease as key determinants of AMR (Morgane et al, 2024); this study did not find these to be statistically significant. This suggests that in the specific context, modifiable factors such as behavioral practices like purchase of antibiotics without prescription play more critical role compared to underlying health conditions. The study found low parental education and high-density living areas to be significant socio-demographic factors associated with AMR. This aligns with McEwen & Collington (2018), who noted that socio-economic status significantly affects health outcomes and access to healthcare. However, a study conducted in a high-income country concluded that socio-demographic factors were less influential on AMR patterns than previously thought with clinical factors like invasive procedures being more critical.(Thompson et al., 2022) Studies from higher-income countries may not report such strong associations, indicating that socio-economic determinants play a more pronounced role in lower-resource settings. The findings regarding self-medication like purchasing antibiotics without prescription underscore a growing concern in many low-income countries. Similar findings in the literature were reflected by this study where self-medication was identifies as a determinant of AMR (Kebede et al., 2022). The study also found out that early discontinuation of antibiotics was significantly associated with AMR, reinforcing findings from previous studies that emphasize the importance of adhering to prescribed treatment regimens. In contrast to studies that were done in developed countries has improved antibiotic use behaviours, this study highlights the urgent need for educational interventions in Zimbabwe.

5.4 Conclusion

In sum, the study concludes that AMR among Gram-negative bacteria in pediatric patients is both prevalent and influenced by modifiable risk factors. This offers a clear opportunity for targeted interventions through antimicrobial stewardship, caregiver education, and regulatory enforcement to curb inappropriate antibiotic use.

5.5 Implications for Practice

There are several implications for clinical practice and public health policy derived from the findings of this study. The high prevalence and resistance rates observed necessitate enhances antibiotic stewardship, public education campaigns and targeted interventions. The implementation of guidelines that are strict for antibiotic prescription in pediatric care is useful in preventing unnecessary exposure and subsequent resistance. Awareness should be spread among caregivers on the dangers of self-medication and the importance of completing prescribes antibiotic courses.

5.6 Recommendations

Drawing from the findings and conclusions of this study, the following detailed recommendations are proposed. These are directed toward key stakeholders including government policymakers, healthcare professionals, caregivers, and researchers, with the aim of reducing antimicrobial resistance among Gram-negative bacterial infections in pediatric patients.

Recommendations to the Ministry of Health and Child Care (MoHCC)

There is an urgent need to reinforce legal and regulatory frameworks governing the sale of antibiotics. The ministry should implement stricter controls that prevent pharmacies, clinics, and informal drug vendors from dispensing antibiotics without a valid prescription. This can be done through random inspections, licensing reviews, and penalties for non-compliance. Doing so would directly reduce the availability of antibiotics for self-medication, which this study identified as a major determinant of resistance. The ministry should invest in the expansion of a nationwide antimicrobial resistance surveillance programmed. This includes equipping laboratories at provincial and district hospitals with standard diagnostic tools, training personnel, and creating digital platforms for reporting AMR trends. Such a system would enable timely detection of resistance outbreaks and inform evidence-based adjustments to national treatment guidelines, especially in pediatric settings. Policies should be introduced to encourage or mandate routine culture and sensitivity testing before initiating antibiotic treatment in hospitalized patients. For pediatric units, where empiric treatment is common, this approach ensures that antibiotics are only prescribed when appropriate and based on actual susceptibility results, which minimizes unnecessary or ineffective drug use.

Recommendations to Healthcare Providers

Clinicians should transition from empirical prescribing to evidence-based antibiotic treatment by relying on microbiology results. This is particularly crucial in cases where the patient does not respond to initial therapy. Culture-guided therapy not only improves treatment outcomes but also helps curb the development of resistance by avoiding unnecessary broad-spectrum antibiotic use.

Healthcare workers, particularly nurses and pediatricians, should use every clinical encounter as an opportunity to educate caregivers on antimicrobial use. This includes emphasizing the need to complete the full course of antibiotics, not to share medications, and the importance of returning for follow-up care. This study showed that premature cessation of antibiotics and prior unsupervised antibiotic use was significant contributors to resistance. Hospital antibiotic formularies and treatment protocols must be updated to reflect local resistance patterns. Empirical treatment guidelines should be revised to reduce reliance on antibiotics with high resistance rates (e.g., TMP-SMX and Amoxicillin-Clavulanate) and incorporate agents with higher efficacy, such as Gentamicin, where appropriate. This should be done in consultation with microbiology departments and informed by local antibiograms.

Recommendations to the Community and Caregivers

Public health education initiatives should be implemented using culturally appropriate media, including local radio, community outreach programs, and posters in clinics. These campaigns should focus on explaining the risks of antimicrobial resistance, the importance of using antibiotics only when prescribed by a health professional, and the dangers of interrupting treatment early. Messaging should be tailored to reach low-literacy and rural populations, especially in high-density areas where resistance was shown to be higher. Households should be educated on basic hygiene practices that can significantly reduce the incidence of infections such as UTIs and gastrointestinal illnesses. This includes consistent hand-washing with soap, safe water storage, clean food handling, and regular cleaning of children's items and play areas. Preventing infections naturally reduces antibiotic consumption and, by extension, resistance. Caregivers of children with compromised immunity, particularly HIV-positive children, should be given specialized education and support. This includes early recognition of infection symptoms, timely healthcare seeking, and adherence to prescribed treatments. Clinics should consider routine screening and counseling sessions for such families to reduce the risk of resistant infections.

Recommendations for Future Researchers and Academics

Future studies should track patients over time to determine how resistance patterns evolve, especially after repeated antibiotic exposure. This would provide insight into the long-term impacts of antibiotic misuse and help in developing predictive models for AMR in pediatric populations. There is a need for future research to investigate additional factors not covered in this study, such as nutritional status, breastfeeding practices, traditional medicine usage, access to healthcare facilities, and caregiver health literacy. These could unveil deeper behavioral and environmental drivers of AMR in children. More comparative studies should be conducted between urban and rural hospitals, and between public and private healthcare institutions. Such comparisons could help assess the role of infrastructure, staffing, and resource availability in influencing antimicrobial stewardship and resistance outcomes. This can also aid in creating location-specific interventions.

5.7 Areas for Further Research

While this study provided valuable insights into the prevalence, resistance patterns, and determinants of antimicrobial resistance (AMR) in Gram-negative bacterial infections among pediatric patients, several areas remain underexplored. The following are suggested for future research.

This study was cross-sectional in design and therefore could not track the evolution of resistance over time. Future research should adopt longitudinal or cohort-based approaches to monitor changes in resistance patterns, treatment outcomes, and recurrent infections in the same patients over an extended period. This would offer a clearer picture of the dynamics of AMR progression and the long-term impact of interventions. Conducting similar studies across multiple provinces or districts in Zimbabwe, with larger sample sizes, would enhance the generalizability of findings. Comparing urban, peri-urban, and rural settings may reveal contextual differences in AMR drivers, healthcare access, and treatment practices that could inform regional strategies.

This study focused specifically on Gram-negative bacteria. Future studies should include Gram-positive pathogens and explore specific resistance mechanisms (e.g., Extended-Spectrum Beta-Lactamases, carbapenem resistance). Molecular characterization of resistance genes could also help identify emerging strains with high public health risks. Although behavioral factors like early discontinuation of antibiotics and self-medication were analyzed, the study did not assess caregiver knowledge, attitudes, or beliefs about antibiotics. Future research should use qualitative methods or mixed approaches to explore how caregiver understanding influences antibiotic practices in households. Future studies should assess the effectiveness of current antimicrobial stewardship programs and policy interventions implemented at hospitals or community levels. This includes evaluating the impact of health education campaigns, prescription audits, or pharmacy regulation on antibiotic use and resistance rates.

5.8 Chapter Summary

This chapter provided a summary of key findings; conclusions aligned to the study objectives, and targeted recommendations. The study revealed a high prevalence of Gram-negative bacterial infections in children under five, with infants under 24 months most affected. Significant resistance to commonly used antibiotics was observed, especially in Acinetobacter baumannii and Pseudomonas aeruginosa. Key determinants of resistance included prior antibiotic use, HIV status, history of UTIs, self-medication, and low parental education. Recommendations were directed at the Ministry of Health, healthcare providers, communities, and researchers, focusing on regulation, stewardship, and public awareness. The chapter concluded by identifying future research needs to better address AMR in pediatric care.

APPENDIX1: DATA COLLECTION TOOL

SECTION 1: DEMOGRAPHIC INFORMATION (DISTAL DETERMINANTS)

Patient ID (for confidentiality)

Age

Income level of parents/guardians

Education level of parents/guardians

Residence: High/Low Density

SECTION 2: CLINICAL DATA (PROXIMATE DETERMINANTS)

Symptoms of UTI

Diagnosis Method

Bacterial Identification

Severity of infection (mild, moderate, severe)

Previous Antibiotic Use: Yes/No

History of bacterial infections: Yes/No

Underlying health conditions? If yes specify

SECTION 3: TREATMENT INFORMATION

Antibiotics Prescribed: Yes/No

Treatment Duration

Was the whole course finished: Yes/No

Treatment Outcomes: Successful/Unsuccessful

Complications

Mortality

SECTION 4: AMR DATA

Presence of AMR:Yes/No

Antibiotic Susceptibility Test Results(Specify antibiotics tested and results)

AMR pattern(Specify which antibiotics the bacteria are resistant to)

APPENDIX 2: BUDGET

CATEGORY	SUBCATEGORY	COSTS(USD$)
PERSONNEL	Data analyst, medical assistant, project coordinator	100
RESEARCH COSTS	Printing and postage, travel expenses, stationery	30
DATA ANALYSIS AND SOFTWARE	Internet access, phone expenses, office supplies, statistical techniques to identify trends and relationship among variables	150
Participant incentives	Snacks, drinks, token of appreciation	20
TOTAL COSTS		300

TABLE 2: BUDGET

Please note that this budget is just a rough estimation and actual costs may vary depending on different factors.

APPENDIX 3 : TIMELINE

	MONTH (2024-2025)	AUG-SEPT	Oct	Nov	Dec	Jan	Feb	Mar	April	MAY
Activity										
Identification, presentation And approval of research Topic										
Proposal Writing										
Pretesting										
Data collection										
Data processing and analysis										
Report Writing										
Submission of dissertation and study report presentation										

APPENDIX 4: STUDY CITE APPROVAL LETTER

Reference:

Telephone: 263-020-64321
Fax: +263-020-67048
E-mail: mphosp@syscom.co.zw

ZIMBABWE

Victoria Chitepo Provincial Hospital
P.O. Box 30
Mutare
MANICALAND
ZIMBABWE

10 February 2025

Att: Shingisai Maenzanise
Victoria Chitepo Provincial Hospital
Box 30
Mutare

Re: APPLICATION FOR SUBMISSION OF PROJECT PROPOSAL FOR SHINGISAI MAENZANISE: VICTORIA CHITEPO PROVNCIAL HOSPITAL

In reference to the above subject matter:

I have no objection to your request.

You can go ahead with your research.

Hope you will find this institution helpful in your research.

VICTORIA CHITEPO PROVINCIAL HOSPITAL
MEDICAL SUPERINTENDENT
11 FEB 2025
P.O. BOX 30, MUTARE
ZIMBABWE

DR H. Makiwa
ACTING MEDICAL SUPERINTENDENT

APPENDIX 5: AUREC APPROVAL LETTER

"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 3704/25

12 March, 2025

SHINGISAI MAENZANISE
C/O Africa University
Box 1320
MUTARE

RE: ***DETERMINANTS OF ANTIMICROBIAL RESISTANCE OF GRAM-NEGATIVE BACTERIA IN PAEDIATRICS PATIENTS (0-5YEARS) AT VICTORIA CHITEPO PROVINCIAL HOSPITAL,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 3704/25
  This number should be used on all correspondences, consent forms, and appropriate document
- **AUREC MEETING DATE** NA
- **APPROVAL DATE** March 12, 2025
- **EXPIRATION DATE** March 12, 2026
- **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.

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Yours Faithfully

Mchinzou

MARY CHINZOU
FOR CHAIRPERSON
AFRICA UNIVERSITY RESEARCH ETHICS COMMITTEE

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