# ENSIGN GLOBAL COLLEGE, KPONG EASTERN REGION, GHANA

ASSESSMENT OF ANTIBIOTIC RESISTANCE PATTERNS AMONG PATIENTS

PRESENTING WITH WOUND INFECTION AT THE HO TEACHING HOSPITAL IN

THE VOLTA REGION OF GHANA: A SIX (6) -YEAR RETROSPECTIVE STUDY

 $\mathbf{BY}$ 

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A THESIS SUBMITTED TO THE DEPARTMENT OF COMMUNITY HEALTH,
FACULTY OF PUBLIC HEALTH, ENSIGN GLOBAL COLLEGE IN PARTIAL
FULFILLMENT OF THE REQUIREMENTS FOR THE
MASTER OF PUBLIC HEALTH DEGREE

#### **DECLARATION**

I, hereby certify that except for references to other people's work, which I have duly cited, this project submitted to the Department of Community Health, Ensign Global College, Kpong is the result of my own investigation, and has not been presented for any other degree elsewhere.

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## **DEDICATION**

This work is dedicated to my caring wife Seraphine Afedzi, my son Jedidiah Jenkins Nukunu Gbemu, then to my Supervisor Dr. Stephen Manortey and the entire family for their moral support during the entire period of study. May the Almighty God bless you all.

#### ACKNOWLEDGEMENT

Several persons have contributed to the successful completion of my Master of Public Health programme. I am grateful to my wife Seraphine Afedzi and Son Jedidiah Jenkins Nukunu Gbemu for their Support. I express my gratitude to The Kenneth R. Young Memorial Scholarship for partly sponsoring me during my studies. I am also appreciative of the Management and staff of the Ho Teaching Hospital whose facility was the target of the research, for their support and contributions.

I acknowledge the guidance of my supervisor Dr. Stephen Manortey for his unique supervision and encouragement have been beneficial to this project and an experience for life.

The support of my Parents Mr. and Mrs Joseph and Josephine Gbemu and siblings has been great and I thank them for their patience, encouragement and love.

I appreciate all my friends who have in one way or the other supported me during my thesis work especially to Obed Kweku Amenyo, Loretha B.B. Mensah, Enoch Kwame Obuobi, and Samuel Mawunyo Adams who were very instrumental during my data collection.

Finally, whatever I have been able to achieve has been enhanced by Christ Jesus (Philippians 4:13) and for that I am grateful to God Almighty.

#### **ABSTRACT**

Introduction: Antibiotics are the backbone of the treatment of infections in wounds. Its resistance is problematic. Information on the prevalence and antibiotic susceptibility of common bacteria responsible for wound infections in the Volta region and to a large extent the whole country of Ghana is scanty. **Objective:** To assess antibiotic resistance patterns among patients presenting with wound infection at the Ho Teaching Hospital in the Volta Region of Ghana. Methods: We performed a retrospective descriptive study using data collected on bacterial Isolates from wounds based on clinical suspicion of wound infection between January 1st 2018 and June 30th 2023. Bacteria were cultured on both enrichment and selective media including blood agar supplemented with 5% sheep blood and MacConkey agar, and identified by Gram stain, routine biochemical tests and VITEK 2 system. Data on routine culture and sensitivity tests performed on bacterial isolates from patients samples were retrieved from the hospital's health information system. Data were then entered into and analysed using IBM Statistical Package for Social Sciences Version 26 (IBM SPSS; Armonk, New York). Results: A total of 1065 bacterial isolates were identified from wounds of patients suspected of wound infection between 2018 and 2023 at the facility representing a wound infection prevalence of 63.94% among the 1,665 suspected cases. Pseudomonas aeruginosa accounts for 21.3% of the total isolates identified. This was followed by Escherichia coli (18.1%), Pseudomonas spp (11.5%), Staphylococcus aureus (9.4%), Klebsiella spp (8.8%) and Proteus mirabilis (5.8%) which represented the top six (6) most isolated wound pathogen in the facility. Trends and patterns in ABR saw meropenem drastic reduction to resistant, from an alarming 91.67% in 2018 to a much-improved 11.90% in 2023. Cotrimoxazole resistance exhibited a cyclical pattern while Chloramphenicol, Ampicillin, and Ciprofloxacin, resistance remained relatively stable over the study period. Conclusion/Recommendations: The study uncovers high antibiotic-resistant wound infection rates influenced by demographics and climate, with Pseudomonas aeruginosa as a significant pathogen. While meropenem resistance shows a positive trend, challenges persist, notably in cotrimoxazole resistance. Recommendations emphasize the importance of antibiotic stewardship, surveillance, targeted awareness campaigns for males, seasonal preparedness, customized treatment guidelines, genetic research on resistance mechanisms, individualized antibiotic selection, and regular guideline updates.

**Keywords:** Antibiotic Resistance, Wounds, Ho Teaching Hospital, Volta Region, Ghana

#### **GLOSSARY OF ABBREVIATIONS**

ABR - Antibiotic Resistance

AMR - Antimicrobial Resistance

CDC - Centers for Disease Control and Prevention

CLSI - Clinical and Laboratory Standard Institute

HTH - Ho Teaching Hospital

IPC - Infection Prevention and Control

LHIMS - Lighwave Health Information Management System

LMIC - Low and Midddle income countries

MDR - Multi Drug Resistance

MOH - Ministry of Health

MRSA - Methicillin Resistance Staphylococcus aureus

PH - Hydrogen ion Concentration

SSA - Sub-Saharan Africa

UK - United Kingdom

WASH - Water, Sanitation and Hygiene

WHO - World Health Organisation

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#### **CHAPTER ONE**

#### INTRODUCTION

#### 1.1 Background Information

Antimicrobial resistance, or the inability of bacteria to respond to widely prescribed antibiotics, is a developing global public health concern (Lnarayan et al., 2016). Antimicrobial resistance is predicted to be the cause of 10 million deaths globally each year by 2050, according to a report commissioned by the Wellcome Trust and the UK Department of Health (O'Neill J. 2016). Sub-Saharan Africa bears a disproportionate share of the world's infectious illness burden (Murray et al., 2012), however comprehensive data on antibiotic resistance from this region is still lacking. The bulk of sub-Saharan African nations' data, as well as information on priority diseases like Methicillin-Resistant Staphylococcus aureus (MRSA), were absent from a recent World Health Organization (WHO) worldwide report on the surveillance of antibiotic resistance (WHO 2014). Researchers in underdeveloped nations should take note of this findings and intensify their research in these areas to enhance patient outcomes and support the database for ongoing surveillance.

It is impossible to overstate the growing financial burden that wound infections and the accompanying mortality rates impose on society. Wound infections are a developing medical concern on a global scale. Damage to the integrity of biological tissue, such as skin, mucous membranes, and organ tissues, is what is referred to as a wound. These can result from a variety of trauma types, and in order to prevent infection and additional harm, wounds must be cleaned and dressed properly (Wilkins, 2013). Four groups of wound statuses make up the classification criteria developed by the Centers for Disease Control and Prevention (CDC);

Class 1 wounds are considered to be clean. They are mostly closed, lack irritation, and are not infected. A closed draining technique is required if these wounds need to be drained.

Furthermore, the respiratory, alimentary, vaginal, or urinary tracts are not penetrated by these lesions.

Class 2 wounds are considered to be clean-contaminated. There is no rare contamination in these wounds. Wounds classified as class 2 penetrate the urinary, vaginal, alimentary, or respiratory systems. These wounds have, nevertheless, undergone regulated entry into these tracts.

Class 3 wounds are considered to be contaminated. These are recently opened wounds that may have been caused by a sterile procedure breach or gastrointestinal tract leaks. Furthermore, class 3 wounds are defined as incisions that cause acute inflammation or do not exhibit purulent inflammation.

Class 4 wounds are considered to be dirty-infected. Usually, trauma wounds that are not appropriately cared for lead to these wounds. According to Onyekwelu et al. (2017), Class 4 wounds show devitalized tissue and are typically caused by germs present in the surgical field or in perforated viscera. Numerous variables or origins of a wound may cause it to worsen into a chronic condition once the usual healing time has passed.

These variables may include advanced age, malnourishment, hypovolemia, obesity, diabetes, steroid usage, malignancy, smoking, and concurrent infection at a distant location, among other patient risk states. Procedure-related risk factors for surgical wounds include the following: the development of a hematoma; the use of foreign materials, such as drains; leaving dead space; infection history; length of surgical scrub; shaving before surgery; poor skin preparation; lengthy surgery; poor surgical technique; hypothermia; contamination from the operating room; and extended hospital stay following surgery (Vitiello et al., 2020). Injuries have the ability to harbor several dangerous germs, making them susceptible to infection if appropriate treatment is not provided. When a wound is infected, healing takes significantly longer,

increasing treatment costs and the amount of pain and discomfort that patients experience. The mainstay of treatment for bacterial wound infections is the administration of antibiotics, in the right dosages for the right length of time. Wound-infecting bacteria have diverse identities and distributions across individuals, sites, and temporal dimensions. The antibiotic susceptibility of bacteria detected in wounds varies by region and is constantly changing as a result of the establishment of antibiotic resistance (Lai et al., 2017).

Because wounds require more resources to manage and patients are typically ostracized because of the stink they carry, this also has a negative impact on the carers. The main factor impeding the healing process is the presence and quantity of bacteria. When these bacteria don't react to antibiotic therapy, the condition gets worse (Lipsky et al., 2016). In other to gain insights into antibiotics resistance among wound-related issues in clinical conditions or situations, this study assessed patterns of antibiotic resistance among patients who present wound infection at the Ho Teaching Hospital retrospectively.

#### 1.2 Problem statement

Antibiotic resistance is a "global security threat," hurting food security, development, and global health, and it is just as significant as terrorism and climate change, according to the World Health Organization (WHO, 2020). 700,000 people perish from resistant diseases each year. According to the Wellcome Trust and the British Government's final report, 10 million people would die from AMR by the year 2050 if the current pace of rise continues (O'Neill J. 2016). Eight.2 million cancer deaths in 2019 would be surpassed by ten million deaths in 2050 (Bassetti et al., 2017).

In any country, people of all ages can be impacted by antibiotic resistance. It is estimated that treatable infectious diseases claim the lives of 5.7 million people annually, the majority of whom reside in low- and middle-income countries (LMICs). If antibiotics had been effective

and widely available, many lives might have been spared. This figure is significantly higher than the 700,000 fatalities globally attributed to ABR each year (Wall 2020).

The emergence of resistance highlights the fact that the world's poorest people are still more impacted by antibiotic shortages than by resistance, even if it threatens our legally guaranteed right to the finest care. It is therefore morally required to maintain the efficacy of antibiotics while guaranteeing their accessibility to all (Daulaire et al., 2015). Present research indicates that little is understood about the common bacteria that cause wound infections in many developing nations, particularly in sub-Saharan Africa (SSA), in terms of their susceptibility to antibiotics (Lai et al., 2017).

Ghana as one of the Sub-Saharan African countries is also in the same lime light in that little or no much information about antibiotic resistance profiling of wound infection is known nationwide, and the Volta Region is no exception to this. Understanding the patterns of antibiotic resistance and the epidemiology of wound infections is crucial for advising doctors on the best course of action when it comes to choosing antibiotics for patients' empirical treatment. Time-varying spatial variations in antibacterial sensitivity patterns and bacterial spectra emphasize the significance of local surveillance data (Lai et al., 2017). There is no known studies that have been carried out in the etiologic wound infections and their antibiotic profiling at the Teaching hospital and the whole of the Volta Region. It is based on this premise and the findings from (Akova 2016), concerning morbidities and mortality increase due to lacerations, delayed hospitalization and the economic drain of scarce health resources and burden it posed to patients and their relatives that incite this study. In response to this problem, this project sought to assess antibiotic resistance patterns among patients presenting with bacteria wound infection at the Ho Teaching Hospital.

#### 1.3 Rational of the study

Although the hospital records from 2017 to mid-2023, reviewed is not representative of the region or the nation; there was a need for analysis of resistant pattern in wound infection within this period to ascertain the current prevalence in the hospital for references and analysis. Comparison with the worldwide findings as well as comparison with resistant patterns in other areas of Ghana and Africa. The resultant effect would be the review of the guidelines for wound management as provided by the Ministry of Health (MoH) and make available local antibiograms for proper wound treatment, prevention and management by clinicians at the Ho Teaching Hospital and its environs.

#### 1.4 Conceptual framework

A conceptual framework of wound bacteria isolates and the establishment of antibiogram at the Ho Teaching Hospital in the Volta Region of Ghana. The dependent variables being the results of antibiotics susceptibility testing and information for patient care and choice of antibiotic. The independent variables are the conditions necessary for bacterial growth and isolations such as the appropriate nutrients required, the right pH, and the ambient temperature. The standard protocol for bacteria identification and antibiotic susceptibility testing as laid down by the Clinical and Laboratory Standard Institute (CLSI) was applied. Data generated from results will provide local guidelines for bacterial wound infections, surveillance and policy. (Figure. 1)

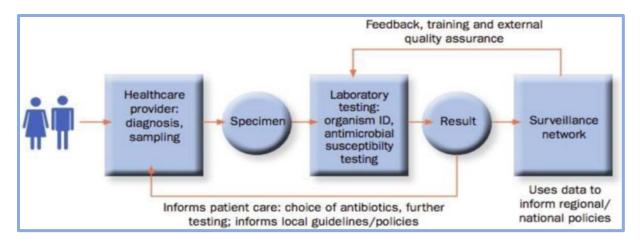


Figure 1; Conceptual framework for the study

Source: Littlejohn et al., 2016

#### 1.5 Research question

- 1. What are the prevalence and the trend of antibiotic resistance among patients with bacteria wound infection at the Ho Teaching Hospital?
- 2. What are the etiologic agents in wound infection at Ho Teaching Hospital?
- 3. Is there any specific and reliable local antibiogram for wound infection treatment and management at the Ho Teaching Hospital.

#### 1.6 General objective

This project seeks to assess antibiotic resistance patterns among patients presenting with bacteria wound infection at the Ho Teaching Hospital.

#### 1.7 Specific objectives

- 1. To determine the prevalence and trend of antibiotic resistance among patients with bacterial wound infection at the Ho Teaching Hospital.
- 2. To identify the types of etiologic agents in wound infection at Ho Teaching Hospital
- To develop a local antibiogram for wound infection treatment and management at Ho
   Teaching Hospital

#### 1.8 Profile of Study Area

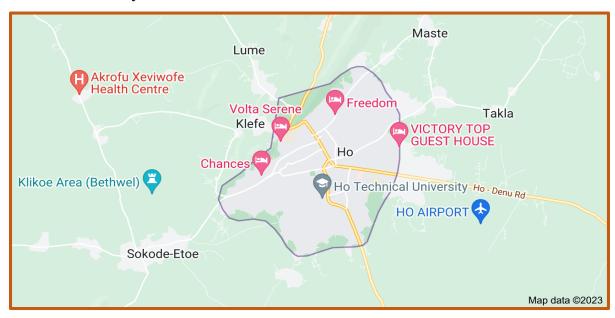


Figure 2: Map of the Study Area

Source: Map data © 2023.

Ho is one of the four (4) Municipalities out of the twenty (20) districts in the Volta Region of Ghana. The Region is one of the 16 regions of the country located at latitudes 50°45"N and 80°45"N in the southeastern part of the country. The Volta Region is bounded by Togo on the east and Lake Volta on the west. It has a population of about 180,420, according to the Ghana Statistical Service 2021Census report, and is the administrative and commercial capital of the Volta Region. Ho lies between latitude 6 degrees 20 1N and 60 degrees 55 1N and longitudes 0 degrees 12 1E and 0 degrees 53 1E and covers an area of 11.65 square kilometres. Generally, mean monthly temperatures range between 22 °C and 32 °C while annual mean temperature ranges from 16.5 °C to 37.8 °C.

The two rainy seasons—known as the major and minor seasons—define the rainfall pattern. The main season runs from March through June, and the secondary one lasts from August through November. The term "dry season" refers to the final five (5) months of the year. The yearly precipitation ranges from 20.1 mm to 192 mm. June records the highest mean rainfall of 192 mm, while December records the lowest mean rainfall of 0.1 mm. The agricultural

economy is a result of the pattern of rainfall and the high fertility of the soil. The majority of Ho is covered with savannah woodland, which is the city's vegetation. Nonetheless, semi-deciduous forest patches do exist; these are primarily found in the highlands. The city's growing population as a result of increased migration has the biggest impact on the vegetation.

2. Stress on housing stock and housing infrastructure. 3. The Ho District Assembly (2002) initiated the fast commercialization of the economy, which began in the early years of the Ghanaian government's structural adjustment program.

#### 1.9 Scope of Study

The scope of the study was limited to all patients presented with wound infection at the Ho Teaching Hospital between January 1<sup>st</sup> 2018 to June 30<sup>th</sup>, 2023. The age range was between 0 and 100 years whose samples were collected for the purposes of diagnosis, treatment and management. This data collection period lasted for 3 months and ended when the last data entry was done.

#### 1.10 Organization of Report

There are six chapters in this report on the research study. The study's setting, including the background, problem statement, justification, conceptual framework, research questions, and objectives, are outlined in Chapter One, the introduction. A review of relevant literature pertaining to the topic is presented in Chapter 2. The research design and methodology used to conduct the study are presented in Chapter Three. This section also covers research instruments, data gathering methodologies, data processing techniques, and sample strategies. The findings of the examination of the created study data are the main topic of Chapter Four. Chapter Six offers a conclusion and specific recommendations for the study, while Chapter Five addresses the major findings in the context of the available literature.

#### **CHAPTER TWO**

#### LITERATURE REVIEW

#### 2. 1 Introduction

Data on antibiotic resistance in wound infection are scarce in sub-Saharan Africa (SSA) and most of the developing countries, with the story not different in Ghana (WHO, 2014) (Yevutsey *et al.*, 2017). Hospital based analysis of antibiotic resistance in wound infection becomes important and can help assess the burden of diseases, quality of health-care delivery, and help to prevent an approximate measure of infections leading to death (Arodiwe *et al.*, 2014).

#### 2.2 Wound and its Healing Process

Wounds can affect any part of the human body and take a different and considerable amount of time to heal depending on the level of damage and treatment offered and at what time and circumstance. The healing also depends on the level of resistance to antibiotics that the patient's anatomic system can accommodate. There are different types of wounds as shown in figure 1 below

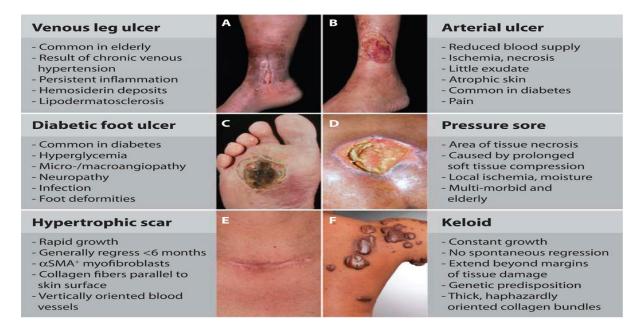


Figure 3: A diagrammatic presentation of types of wound

As previously mentioned, a wound is an impairment to the structural integrity of biological tissue, such as the skin, mucous membranes, and organ tissues. In the shortest amount of time,

it would mend via the regular physiological process. Hemostasis, inflammation, proliferation, and tissue remodeling or resolution are the four primary integrated and transecting phases of the wound-healing process, according to Guo and Dipietro (2010) (Source 2016).



Figure 4: A diagrammatic Presentation of the four stages of wound Healing

According to Mathieu et al. (2006), these phases and the biophysiological processes they support must take place in the right order, at the right time, and at the right intensity during the entire length. Numerous variables can impede one or more stages of the wound healing process, leading to inadequate or hampered tissue restoration. Reduced-healing wounds—delayed acute and chronic wounds, in particular—have typically not healed through the stages that are typical for healing. These wounds often progress into a pathologic inflammatory state as a result of a delayed, inefficient, or disorganized healing process. Many factors can contribute to poor wound healing. Repair is often impacted by two different kinds of factors: systemic and local.

The physical characteristics of a wound are directly influenced by local factors like oxygenation, infection, foreign bodies, and venous sufficiency; on the other hand, systemic factors like age and gender, sex hormones, stress, ischemia, diseases (like diabetes, keloids, fibrosis, hereditary healing disorders, jaundice, uraemia, obesity), medications (like glucocorticoids, non-steroidal anti-inflammatory drugs, chemotherapy), alcoholism and smoking, immune-compromised conditions (like cancer, radiation therapy, AIDS), and nutrition have a cumulatively detrimental effect on an individual's health or capacity to recover from a disease. Many of these variables are interrelated, and systemic variables affect local impacts, which in turn affect wound healing (Guo and Dipietro 2010).

#### 2.3 Wound Infections

Microorganisms that are normally trapped at the skin's surface become accessible to the underlying tissues as soon as the skin is wounded, according to research by Vicar et al. (2021) and Edwards R. (2004). The degree of infection and the ability of the bacteria to replicate determine whether a wound is classified as having contamination, colonization, spreading invasive infection, local infection/critical colonization, or both. In contrast to contamination, which is the presence of non-replicating organisms on the wound, colonization is the presence of bacteria that reproduce without causing tissue harm. Local infection/critical colonization is an intermediate stage that involves the microbial replication and the start of local tissue reactions. Invading infections, according to Edwards R. (2004), occur when organisms that reproduce inside a wound also cause harm to the host. Bioburden has been found to be one of the primary barriers to wound healing (Rhoads et al., 2012). Pathogens colonizing the wound site greatly increase the chronicity of the wound (Rahim et al., 2017; Kirketerp-Moller et al., 2008). Previous studies have shown that wounds caused by diabetes, hypertension, venous disorders, surgery, and surgical site infections (SSIs) are more likely to harbor harmful bacteria

than primary skin infections (Calina et al., 2017). According to Guan et al. (2021), among these, surgical site infections (SSI) account for around 15% of all nosocomial infections and are notoriously hard to treat because of their resistance to numerous medications.

Pseudomonas aeruginosa, Enterococcus faecalis, Escherichia coli, Proteus mirabilis, and Staphylococcus aureus are the most often found bacteria in chronic wounds, according to multiple lines of evidence on the prevalence of pathogenic bacteria in chronic wounds (Rahim et al., 2017) (Wu et al.2018). However, a number of variables, including geographic location and the reasons for wounds, influence the dissemination of diseases (Dowd et al., 2008). (Guan et al. 2021). Since their discovery and advancement, antibiotics have proven to be very beneficial and significant in the treatment of bacterial isolates from wound sources as well as pathogenic infections (Hutchings et al., 2019).

#### 2.4 Antibiotic and its Resistance

Antibiotics are drugs that are used to prevent or cure bacterial infections (Hutchings, 2019). When used appropriately, they can save lives. Antibiotics have been utilized in recent decades to enable modern medical treatment, which includes the ability to treat cancer, perform operations, and replace organs. We are headed for a continuous selection pressure on bacteria for resistance to evolve due to the concomitant pressures of high rates of nosocomial infections in aging populations with increased time spent in long-term health-care settings and the persistent burden of infectious disease in many low-income and lower-income countries. For the past eight decades, antibiotics in particular have been the cornerstone of contemporary medicine (Aljeldah 2022). According to Laxminarayan et al. (2016), penicillin decreased mortality from 20–40% to 5% for pneumococcal pneumonia and from 50–80%4 to 18–20% for pneumococcal bacteraemia. But antibiotic resistance is becoming a bigger problem. It happens when bacteria adjust to the effects of an antibiotic and develop resistance to them.

Resistant bacteria may continue to grow and proliferate. It's possible that the germs will get resistant to the medications you take. It can be difficult and often impossible to treat resistant infections (CDC 2019a).

#### 2.5 Mechanisms of Antibiotic Resistance

ABR genes (DNA) can be horizontally or vertically transferred between bacteria at the cellular level. When a bacteria divides, its DNA is passed from parent to daughter cells, resulting in vertical spread. DNA can travel horizontally between bacteria belonging to the same species or to distinct species within their microenvironment. This happens through three different mechanisms: transduction, which involves the transfer of genes between bacteria via a bacteriophage, a virus that infects the bacteria; conjugation, which involves the transfer of plasmids between bacteria; transformation, which involves the uptake of DNA from dead bacteria in the environment (Dantas G 2014). (Wall 2020).

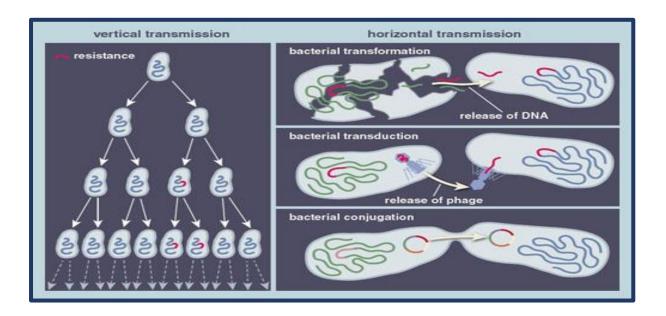


Figure 5: A diagrammatic presentation of vertical and horizontal transmission Illustration by Barbara Aulicino

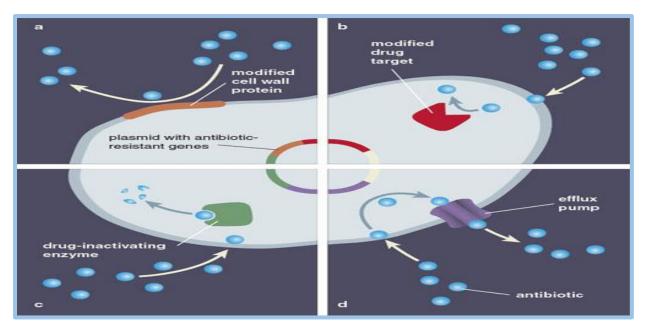


Figure 6: A diagrammatic presentation of resistance mechanism

Illustration by Barbara Aulicino

Our resistance mechanisms: Antibiotics (blue spheres) are blocked by impermeable barrier (a) because the medicine can no longer pass through the bacterial cell membrane. By changing the proteins that the antibiotic inhibits, target modification (b) prevents the medication from binding correctly. The process of antibiotic modification (c) yields an enzyme that renders the antibiotic inactive. Genes coding for enzymes that actively pump the antibiotic out of the cell are used by Efflux (d).

#### 2.6 Factors Influencing Antibiotic Resistance

Antibiotic resistance has historically been shown to be a natural process that allows the bacteria to survive, but it has also been fueled by human activities such as overuse, inappropriate prescription, overprescription, excessive use of antibiotics as growth supplements in livestock, and the scarcity of new antibiotics (Ventola, 2015, Aljeldah, 2022). The World Health Organization (WHO, 2021) lists the following as the primary causes of antimicrobial resistance: improper and excessive use of antibiotics; inadequate access to clean water, sanitation, and hygiene (WASH) for both humans and animals; inadequate infection and

disease prevention and control in hospitals and agricultural settings; and limited availability of high-quality, reasonably priced medications. Wound infections, which are common in environments with inadequate infection prevention and control (IPC) measures, are among the most common indications for antimicrobial treatment (Delamou et al., 2019).

Another important aspect in ABR is the production of biofilm. Because of the innate antibiotic resistance imposed by its lifestyle, pathogenic microbial biofilm is regarded as a global concern (Ribeiro et al,2016). In a clinical setting, bacteria that reside in a community are the source of severe and serious infections. To counteract this cell arrangement, significant dosages of antibiotics must be administered over a lengthy period of time. These approaches often fail, which contributes to the infection's persistence. When biofilms develop in medical devices, they can cause infections in addition to its therapeutic limitations. Researchers from all around the world have been inspired by the challenge posed by biofilms to suggest or create methods for controlling biofilms. In this review, the authors outlined the novel approaches that may be applied in clinical settings to stop or get rid of harmful biofilms (Ribeiro et al,2016).

#### 2.7 Impact of Antibiotic Resistance on Patient Outcomes

Antimicrobial resistance poses an immediate threat to public health around the world, accounting for at least 1.27 million deaths globally and approximately 5 million fatalities in 2019. Every year, around 2.8 million antibiotic-resistant illnesses happen in the United States. As a result, around 35,000 people pass away, according to (CDC 2019a). The combined U.S. toll of all the risks in the report approaches 3 million infections and 48,000 deaths when Clostridium difficile, a bacteria that is not usually resistant but can cause severe diarrhea and is linked to antibiotic usage, is added (CDC 2019b). People at any stage of life, as well as the veterinary, agricultural, and healthcare sectors, may be impacted by antibiotic resistance. This puts it among the most pressing public health issues facing the entire globe.

Serious issues may arise if an antibiotic is resistant. For instance, patients may suffer from major side effects, such as organ failure, and extended care and recovery, often lasting months, as a result of antimicrobial-resistant infections that necessitate the use of second- and third-line treatments (CDC 2019b). Due to the persistence of AMR trends, which will reduce the effectiveness of antibiotics, doctors should resort to last-resort medication classes like carbapenems and polymyxins. These medications are expensive, difficult to obtain in developing nations, and have a wide range of adverse effects (WHO, 2015). Every year, substantial death rates are linked to Methicillin resistance in Staphylococcus aureus (MRSA), one of the most well-known incidences of antimicrobial resistance (AMR) worldwide (Founou et al., 2017). According to Bassetti et al. (2019), the treatment of many illnesses, such as pneumonia and urinary tract infections, has become increasingly difficult due to the presence of multi-drug resistant gram-negative bacteria (MDR-GNB).

#### 2.8 Prevalence of Wound Infections and Antibiotic Resistance

According to Ahmed et al. (2023), polymicrobial wound samples predominated. The pathogens that were isolated most frequently were S. aureus and P. aeruginosa. Among S. aureus isolates, a significant MRSA rate was found. The most potent medications against S. aureus were vancomycin and linezolid, while the most potent medication against P. aeruginosa was ciprofloxacin. A significant escalation in bacterial resistance and challenges in identifying treatment options for all infections are shown by the fact that many isolates had MDR characteristics for every tested class of antibiotic. Numerous epidemiological analyses have indicated that a range of Gram-positive and Gram-negative bacterial species are responsible for nosocomial infections (Khawaja et al., 2018). The overuse of antimicrobial agents in various healthcare units to treat different infectious diseases is one of the main factors contributing to the rise in nosocomial infections among patients and antibiotic resistance in

hospitals (Baym et al., 2016, Scaglione et al., 2022). Notably, antibiotic resistance—which has lately developed as a result of the COVID-19 pandemic—is one of the most significant health issues affecting people worldwide (Livermore 2021). During the COVID-19 outbreak, self-medication with antibiotics, empirical antibiotic therapy, and antibiotic prescriptions from general practitioners were all associated with increased levels of antibiotic resistance. In 2022, Sulayyim et al. Anxiety and inappropriate antibiotic use have a direct impact on the availability of antibiotics without a prescription in low- and middle-income countries with lax antibiotic control policies. 2022; Warda et al.

In addition, the worldwide usage of biocides increased significantly during the COVID-19 pandemic. These biocides most likely raised the amount of indirect pressure that led to antibiotic resistance (Getahun et al., 2020). Longer hospital stays for patients and greater healthcare costs are the outcome of the prevalence of multidrug-resistant (MDR) microorganisms, which become resistant to several antibiotics through innate or acquired mechanisms (Huang et al., 2018). Therefore, in order to execute a treatment approach that effectively avoids the transmission of these infections among patients, especially in an institutional setting, it is imperative to determine the frequency of microbial pathogens and their patterns of antibiotic susceptibility (Hassan et al., 2022).

#### 2.9 Emperical Review

On a global scale, the issue of wound infections remains a substantial and pressing concern within the healthcare landscape. Numerous studies conducted worldwide have consistently sounded an alarm by revealing a deeply concerning surge in the prevalence of antibiotic-resistant wound infections (Zaman *et al.*, 2017; Baloch *et al.*, 2020; Inusah *et al.*, 2021). This worrying trend is intricately linked to an intricate web of factors that collectively contribute to the amplification of antibiotic resistance. Among these contributing factors, overuse and misuse of antibiotics stand out as primary culprits. The injudicious use of these powerful drugs

has been documented in various clinical settings, including both inpatient and outpatient care, fueling the development of antibiotic resistance.

Across different countries, research consistently identifies common wound pathogens, including *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa*. However, these pathogens exhibit varying levels of antibiotic resistance, emphasizing the need for tailored treatment approaches. The emergence of multidrug-resistant strains further complicates effective treatment strategies (Guan *et al.*, 2021)

In a cross-country analysis, it becomes evident that research consistently pinpoints the presence of common wound pathogens, with *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa* being frequently encountered culprits (Prestinaci, Pezzotti and Pantosti, 2015; Baloch *et al.*, 2020; Guan *et al.*, 2021). However, what is equally apparent is the stark disparity in the antibiotic resistance profiles exhibited by these pathogens across different regions. This divergence in resistance patterns underscores the essential requirement for precisely tailored treatment approaches to address wound infections effectively in diverse global contexts.

As detailed by Prestinaci, Pezzotti and Pantosti (2015), the emergence of multidrug-resistant strains within these common pathogens further adds complexity to the therapeutic landscape. These formidable strains possess resistance to multiple classes of antibiotics, posing a significant challenge for healthcare providers. This not only diminishes the efficacy of conventional treatment regimens but also necessitates the development of innovative and specialized strategies to combat these highly resistant wound infections (Baloch *et al.*, 2020). This global and regional variation in resistance highlights the imperative for healthcare systems to adopt a nuanced, adaptable, and data-driven approach in managing wound infections, acknowledging that a one-size-fits-all solution is often ineffective in the face of diverse resistance profiles.

### **CHAPTER THREE**

#### **METHODOLOGY**

#### 3.1 Study Design

A hospital-based descriptive retrospective study was conducted at the Ho Teaching Hospital (HTH) in the Volta Region of Ghana.

#### 3.2 Study Site

In November 1998, the Ho Teaching Hospital (HTH) was founded. The hospital is a tertiary care center with 14 wards, 306 beds, and over 1200 staff members. In the Volta Region, it serves as the primary referral facility. 12,872 is the annual average for both inpatient admissions and outpatient attendance. The hospital's microbiology department gets laboratory requests for a range of microbiological tests from the hospital's departments, wards, and surrounding healthcare facilities as well as the surrounding area.

#### 3.3 Data Collection Techniques

Data for this study was generated according to the following thematic areas;

#### 3.4 Sample Culturing

Consideration was given to specimens that had been gathered, handled, and examined in the HTH microbiology unit in accordance with the standards for microbial identification and culture. Both enrichment and selective media, such as blood agar enriched with 5% sheep blood for Grampositive cocci and MacConkey agar for Grampositive bacilli, were used to cultivate the bacteria. The cultures were kept for a whole day at 35±2°C.

#### 3.5 Isolates Identification

Cultures that did not grow were labeled as "no bacteria growth." On the other hand, cultures that did develop were identified as Gram-positive or Gram-negative using microscopy, the VITEK 2 system, and standard biochemical tests such as the coagulase and catalase tests for Gram-positive cocci. Repeat isolates from the same individual were removed from the study to prevent duplication, and both culture-positive and culture-negative isolates were included. Antibiotic sensitivity tests were conducted on the bacterial isolates found in these samples.

#### 3.6 Antibiotic Susceptibility Test

Sensitivity or resistance to antibiotics using the disk diffusion techniques developed by (Bauer 1961) following (CLSI 2021) standards were determined and recorded in the hospital's information management system, Lightwave Health Information Management System (LHIMS), as susceptible, intermediate or resistant.

#### **3.7 Study Population**

The study included data collected on bacterial Isolates from wounds based on clinical suspicion of wound infection between January 1<sup>st</sup> 2018 and June 30<sup>th</sup> 2023.

#### 3.8 Sample Size Calculation

Sample size calculation was not applicable since the study used secondary data and the entire data size generated within the stipulated period for the study was censored.

#### 3.9 Inclusive and Exclusive Criteria

#### 3.9.1 Inclusion Criterion

- All patients with complete records demographic within the stipulated period were reviewed and included in the study.
- 2. All patients who had their wounds cleaned per the standard protocol before sample collection were included.

#### 3.9.2 Exclusion Criteria

- All wound swab reports with incomplete patient data, e.g., age, gender, and test results were excluded.
- 2. Patients who were on antibiotics prior to the test were excluded.
- 3. Patients who had their wound dressed prior to sample collection were excluded.

#### 3.10 Pre-Testing

The data-collecting instrument, thus the Microsoft Excel spreadsheet developed was tested on about five (5) data sets of patients in the study site (HTH) before the main work begins

#### 3.11 Data Handling

The data was extracted from the hospital's information management system into Microsoft Excel 2019. The Principal Investigator (PI) was responsible for data cleaning and management. The original entry from laboratory documents and the Laboratory Information Management System were used as source data. Soft copies of all datasets and work done were saved in a special folder of PI's personal computer with password-protected, e-mail, and an external drive served as a backup. The PI kept the data for a maximum period of five years after the completion of the study.

#### 3.12 Data Analysis

Microsoft Office Excel 2016 was used to enter, clean, and manage the data. IBM Statistical Package for Social Sciences Version 26 (IBM SPSS; Armonk, New York) was used to analyze the data. Frequencies and proportions were used to represent categorical variables such as age

group, sex, climate season, positive and negative results from bacterial culture tests, and the types of bacteria. Fisher's exact probability test and Pearson's chi-squared test were used to compare the categorical variables. To ascertain trends in medication resistance and infection prevalence, the Cochrane-Armitage test for Trend was run for the ordinal variables, such as year and age group. P-values were deemed statistically significant if they were less than 0.05. Tables and figures were used to display the analysis's findings. To maintain a minimal degree of precision in the calculation, the resistance percentage was only calculated when the denominator contained at least 30 isolates.

#### 3.13 Ethical Consideration

The Ensign Global College Ethical Review Committee granted ethical approval. The Ho Teaching Hospital's Ethical Committee on Human Research granted permission to gather data from the hospital system. Patient records information was kept private and utilized exclusively for research.

#### 3.14 Limitations of Study

- The study may be limited by its sample size and diversity as the sample was drawn
  from a single healthcare facility. This limits the generalizability of the findings to
  broader populations and healthcare settings. Future studies with larger and more diverse
  samples would provide a more comprehensive understanding of wound infection
  patterns.
- The study was conducted at the Ho Teaching Hospital, and the findings may be influenced by regional factors, such as local healthcare practices, patient demographics, and environmental conditions. These results may not be applicable to other regions or countries.

- 3. The study covered a period from 2018 to June 2023. While this provides valuable insights into temporal trends, it may not capture longer-term changes in antibiotic resistance patterns. A more extended study period could provide a more comprehensive view.
- 4. The accuracy and reliability of the findings depend on the quality of data collection and laboratory procedures. Any errors or inconsistencies in data collection, storage, or analysis could impact the validity of the results.
- 5. The study's retrospective nature limits the ability to control variables and the collection of additional data that might have been relevant to understanding the antibiotic resistance patterns.
- 6. While the study identified seasonal variations in wound infections, it may not have considered specific environmental factors, such as temperature or humidity, which could influence the prevalence of certain pathogens.
- 7. The study focused primarily on the prevalence of antibiotic resistance patterns but did not delve into the genetic or molecular mechanisms behind resistance. Understanding these mechanisms could offer deeper insights into the issue of resistance.

#### 3.15 Assumptions

- Adequate sample size: The study assumes that the number of wound cultures and
  microbial isolates available for analysis over the five-year period is sufficient to draw
  meaningful conclusions about antibiotic resistance patterns. Insufficient sample size
  may limit the statistical power and precision of the findings.
- 2. Representativeness of wound cultures: The assumption is made that the wound cultures obtained during the study period are representative of the overall population of patients

- with wound infections in the teaching hospital. However, some cases may go unreported or uncultured, leading to potential underestimation or selection bias.
- 3. Consistency in antibiotic prescribing practices: The study assumes that the antibiotic prescribing practices for wound infections remained relatively consistent over the five-year period. Changes in guidelines, clinical protocols, or antimicrobial stewardship programs during the study duration may impact the observed resistance patterns.
- 4. Appropriate documentation: The study assumes that the medical records contain accurate and complete information regarding patient demographics, wound characteristics, and antibiotic susceptibility test results. Inadequate documentation or missing data may introduce information bias and affect the validity of the study findings.
- 5. Generalizability: While efforts are made to provide valuable insights, the study assumes that the antibiotic resistance patterns observed in this teaching hospital can be extrapolated to similar healthcare settings. However, variations in patient populations, local antimicrobial usage patterns, and healthcare practices may limit the generalizability of the findings.

# CHAPTER 4 RESULTS

### **4.1 Demographic Characteristics**

A total record of 1,665 suspected cases of wound infection was identified at the Ho Teaching Hospital within the period of 2018 and June 2023. Out of the total suspected cases, 842 representing 50.6% were from males and 823 representing 49.4% were females. Individuals aged 60 years and above constituted the highest proportion of the suspected cases accounting for 20.4% of the suspected cases. The number of suspected cases of wound infection tested at the facility rose from a least of 104 (6.2%) in 2018 increasing across the years and peaking in 2022 with a count of 559 suspected cases representing 33.6% of the total suspected cases within the 6 years period. The rainy season in the study time tends to have more suspected infection cases than the dry period. See **Table 1**.

**Table 1: General Description of Study Characteristics** 

Parameter	Frequency	Percentage
Total	1665	100.0
Sex		
Female	823	49.4
Male	842	50.6
Age group		
<18 years	270	16.2
18 - 29 years	263	15.8
30 - 39 years	297	17.8
40- 49 years	251	15.1
50 - 59 years	244	14.7
60 years and above	340	20.4
YEAR		
2018	104	6.2
2019	129	7.7
2020	227	13.6
2021	264	15.9
2022	559	33.6

2023	382	22.9
Climatic season		
Dry season	664	39.88
Rainy season	1001	60.12

A total of 1,065 bacterial isolates were identified from wounds of patients suspected of wound infection between 2018 and 2023 at the facility representing a wound infection prevalence of 63.96% among suspects.

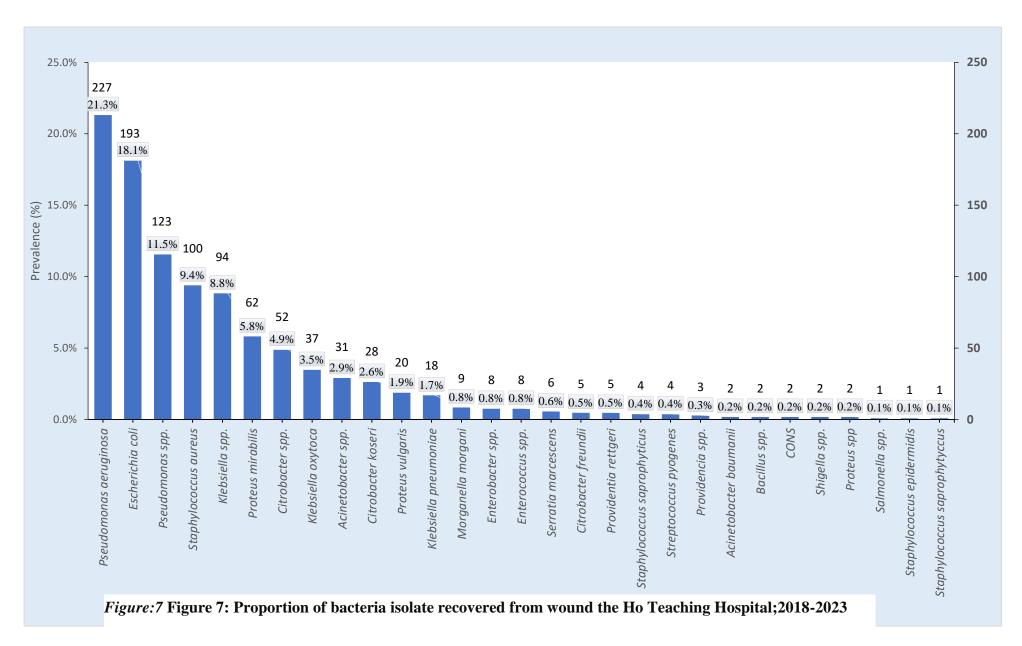
# 4.2 Bivariate Analysis of Wound Infection with Selected Correlates

It was observed that demographic factors such as age group and sex were associated with the occurrence of wound infection among suspected cases. The occurrence of positive culture among male suspects was significantly higher among males (66.86%) than females (61.00%) (p=0.014). Also, the preponderance of wound infection among suspected cases varied significantly across age groups rising from the least age group [< 18 years (52.96%)] through the age groups 18 - 29 years (58.17%) and 30 - 39 years (64.98%) to individuals in their forties having the highest burden of infection. This trend of increasing prevalence of wound infection among suspects across increasing age groups was observed to be significant (p-value for trend <0.001). Furthermore, climatic seasons were identified to be associated with the occurrence of bacterial wound infection with a higher prevalence seen in the rainy season 679(67.83%) than in the dry season 386(58.13%), (p<0.001). See **Table 2**.

Table 2: Prevalence of Wound Infection among Suspected Cases and its Association with Demographic and Seasonal Factors

Factor	Total	No bacterial pathogen isolated	Pathogen isolated	P-value	
Total	1665	600(36.06)	1065(63.94)		
Age group					
<18 years	270	127(47.04)	143(52.96)	<0.001	
18 - 29 years	263	110(41.83)	152(58.17)		
30 - 39 years	297	104(35.02)	193(64.98)		
40- 49 years	251	75(29.88)	176(70.12)		
50 - 59 years	244	80(32.79)	164(67.21)		
60 years and above	340	104(30.59)	236(69.41)		
Sex					
Female	823	321(39.00)	502(61.00)	0.014	
Male	842	279(33.14)	563(66.86)		
Year					
2018	104	35(33.65)	69(66.35)	0.001	
2019	129	41(31.78)	88(68.22)		
2020	227	76(33.48)	151(66.52)		
2021	264	127(48.11)	137(51.89)		
2022	559	199(35.60)	360(64.40)		
2023	382	122(31.94)	260(68.06)		
Dry season	664	278(41.87)	386(58.13)	< 0.001	
Rainy season	1001	322(32.17)	679(6 7.83)		

As presented in Figure 5, the most frequently isolated species of wound infection at the Ho Teaching Hospital was *Pseudomonas aeruginosa* accounting for 21.3% of the total isolates identified. This was followed by *Escherichia coli* (18.1%), *Pseudomonas spp* (11.5%), Staphylococcus *aureus* (9.4%), *Klebsiella spp* (8.8%) and *Proteus mirabilis* (5.8%) which represented the top 6 most isolated wound pathogen in the facility with each accounting for more than 5% of the total number of isolate recovered from the wound infections at the facility within the 6years period. See **Figure 7**.



A year-on-year resistance trend analysis of frequently used antibiotic agents against wound pathogens was used in identifying temporal trends in the occurrence of drug resistance to isolates from wound infection. It was observed that the burden of drug resistance to Meropenem saw a steeply decreasing trend of drug resistance over the study period from a resistance of 91.67% in 2018 to 11.90% in 2023. This trend in decreasing the burden of drug resistance wound isolates to Meropenem was observed to be statistically significant (p<0.0001). Similarly, a significant declining trend in drug-resistant isolates to Cotrimoxazole antibiotic was observed from a peak of 100% in 2018 to 50% in 2021 (p=0.0036). However, there was a resurgence of drug resistance from the trough of 50% in 2021 to 83.33% in 2023. Also, among the aminoglycosides class of antibiotics, there was a significant trend in drug resistance year on year for the two antibiotics assessed. While an increasing trend of drug resistance was observed for Amikacin, a decreasing trend in resistance to Gentamicin was generally seen across the years. For Chloramphenicol, Ampicillin and Ciprofloxacin, the burden of drug resistance to these antibiotic agents was stable across the 6 years (p>0.05). See Figure 8.

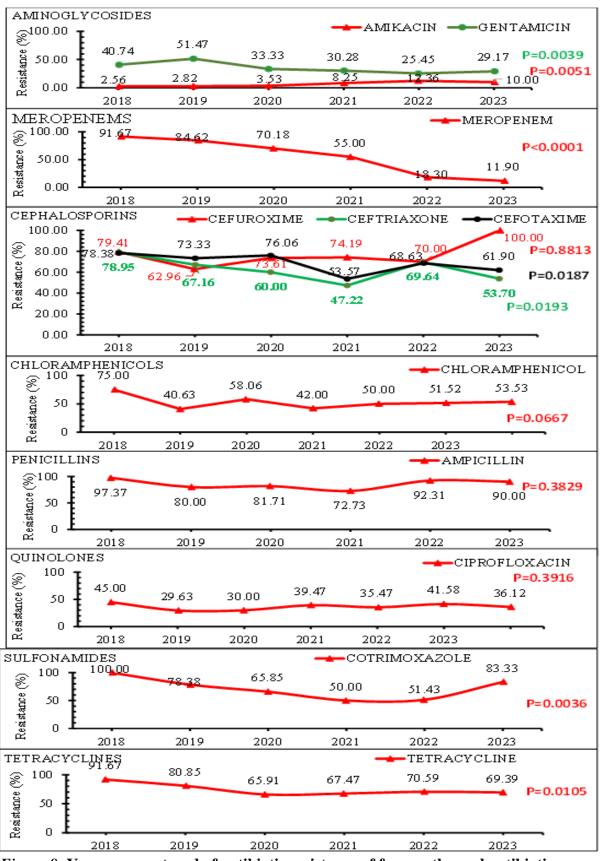


Figure 8: Year-on-year trend of antibiotic resistance of frequently used antibiotics against wound pathogens at Ho Teaching Hospital, 2018-2023

For antibiotics tested against gram-positive isolates, Ciprofloxacin was identified as the most sensitive drug with a resistance rate of 12.82% against gram-positive isolates. This was followed by Gentamicin with a resistance rate of 20.25%. Gram-positive isolates were identified to be least sensitive to Penicillin with about 81.13% and 73.53% of the isolates being resistant to Penicillin and Ampicillin respectively. See Figure 9.

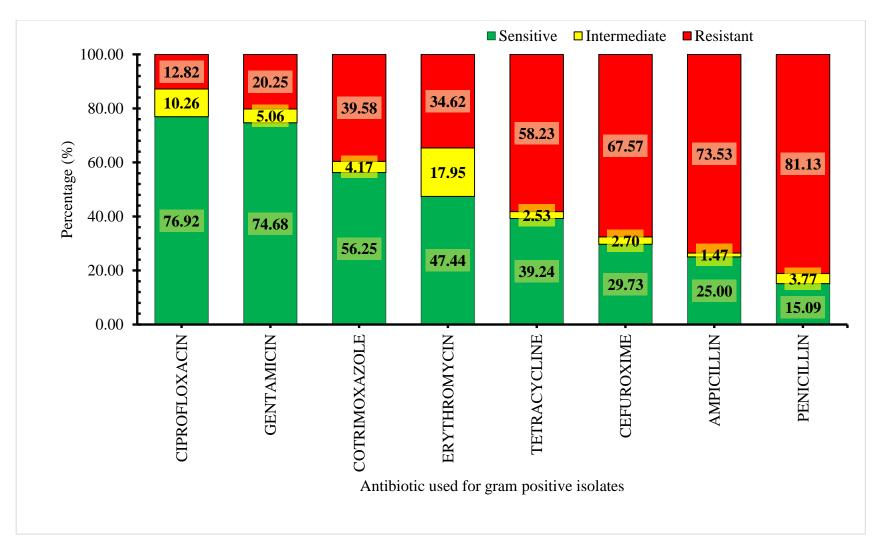


Figure 9: Antibiotic susceptibility pattern of gram-positive isolates from wounds at the Ho teaching hospital, 2018-2023

The susceptibility pattern of gram-negative isolates to frequently tested antibiotic agents is described in Figure 10. Gram-negative isolates cumulatively had a high sensitivity to Amikacin with a sensitivity rate of 90.22%. Similar to that seen among the gram-positive isolates, the cumulative resistance of gram-negative isolates to antibiotic agents was highest in the Penicillin drug Ampicillin. Except for resistance to Cefoxitin, Cefetetan and the 4<sup>th</sup> generation cefepime where the gram-negative isolates had resistance rates of less than 50%, all the 2<sup>nd</sup> and 3<sup>rd</sup> generation cephalosporins (Cefuroxime, Ceftazidime, Cefixime and Ceftriaxone, and Cefotaxime) had more than 50% of the gram-negative isolates showing resistance against them.

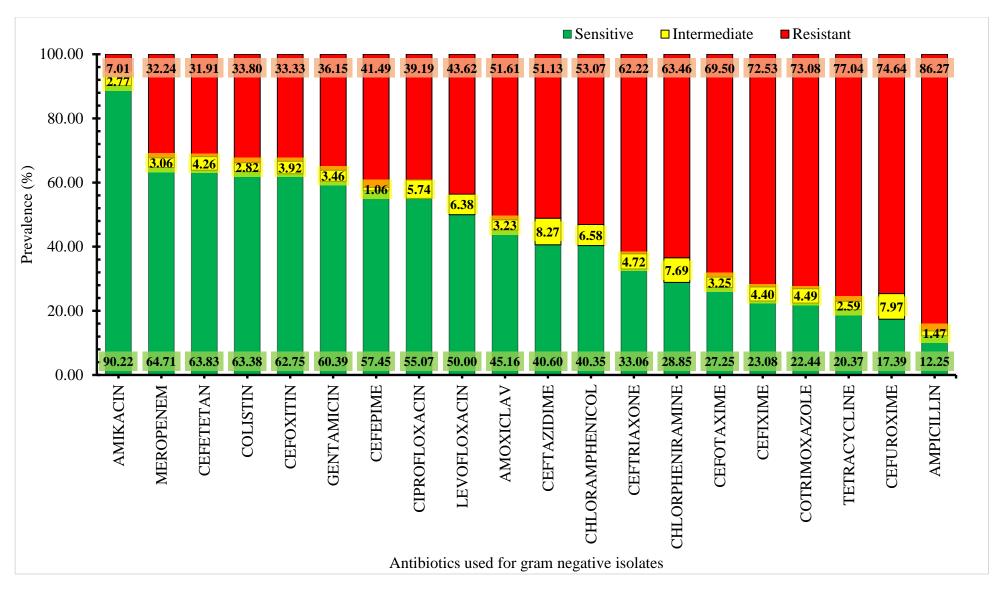


Figure 10: Antibiotic susceptibility pattern of gram-negative isolates from wounds at the Ho Teaching Hospital, 2018-2023

Table 3 describes the antibiotic resistance rates of various pathogenic bacterial specie of wound infection at the Ho Teaching Hospital between 2018 and 2023. *P. aeruginosa* which is the most frequent isolate of wound infection had resistance rates of greater than 50% against Ampicillin (93.55%), Tetracyclin (69.44%), Ceftriaxone (69.57%). Cefotaxime (79.73%) and Chloramphenicol (73.53%). *P. aeruginosa* was most susceptible to Amikacin with a resistance rate of 5.84%. A similar pattern was seen for *E.coli* except that unlike seen in *P. aeruginosa* there was a resistance rate of 62.83% against Ciprofloxacin. *Pseudomonas spp* had resistance rates of 8.93% against Amikacin, 25.42% against Meropenem 33.33% against Ciprofloxacin with the highest resistance rate seen against Gentamicin (35.42%

Table 3: Antibiotic resistance patterns of frequently isolated wound pathogens at the Ho Teaching Hospital;2018-2023

Antibiotic agent	Escherichia coli	Klebsiella spp.	Proteus mirabilis	Pseudomonas aeruginosa	Pseudomona s spp.	Citrobacter spp.	Staphylococus aureus
<b>Total isolates</b>	193	94	62	227	123	52	100
CHLORAMPHENICOL	31/52(59.62)	-	-	25/34(73.53)	-	-	-
AMIKACIN	6/107(5.61)	3/58(5.17)	3/36(8.33)	8/137(5.84)	5/56(8.93)	-	
CIPROFLOXACIN	71/113(62.83)	3/53(5.17)	8/39(20.51)	32/156(20.51)	27/81(33.33)	11/34(32.35)	9/66(13.64)
GENTAMICIN	32/88(36.36)	20/44(45.45)	10/43(23.26)	34/113(30.09)	17/48(35.42)	-	14/71(19.72)
CEFUROXIME	-	-	-	-	-	-	22/34(64.71)
CEFOXITIN	13/59(22.03)	-	-	-	-	-	-
ERYTHROMYCIN	-	-	-	-	-	-	24/66(36.36)
MEROPENEM	20/90(22.22)	11/41(26.83)	8/31(25.81)	37/106(34.91)	15/59(25.42)	-	-
CEFTAZIDIME	-	-	-	13/32(40.63)	-	-	-
CEFTRIAXONE	47/77(61.04)	29/44(65.91)	14/41(34.15)	48/69(69.57)	-	-	-
COLISTIN				10/34(29.41)	-	-	-
AMPICILLIN	38/39(97.44)			29/31(93.55)	-	-	44/57(77.19)
TETRACYCLINE	55/64(85.94)		25/34(73.53)	25/36(69.44)	-	-	38/67(56.72)
CEFOTAXIME	59/9065.56)	42/51(82.35)	17/41(41.46)	5/749(79.73)	-	21/30(70.00)	-
COTRIMOXAZOLE	-	-	-	-	-	-	18/44(40.91)
PENICILLIN	-	-	-	-	-	-	39/45(86.67)

Data presented as number of resistant isolate over isolates tested with the percentage in parenthesis.

# CHAPTER FIVE DISCUSSION

### 5.1Introduction

The rising prevalence of antibiotic resistance among bacterial pathogens presents a significant challenge to modern healthcare. This study sought to investigate the antibiotic resistance patterns and trends of bacterial isolates obtained from wound samples at the Ho Teaching Hospital over six years (2018-2023), with the aim of revealing insights on the occurrence, etiology and state of antibiotic resistance in wound infections. These results have several noteworthy implications for wound care, antimicrobial stewardship and public health.

## 5.2 Prevalence, Risk and Etiologic Agent of Wound Infection

A total of 1,665 suspected cases of wound infection were identified and from these 1065 bacterial isolates were identified revealing a wound infection prevalence of 63.94% among suspects. The high occurrence of positive culture in tested cases is in tandem with the relatively high (86%) occurrence of positive cultures in tested cases for bacteriologic wound infection among patients in another teaching hospital in Ghana (Bediako-Bowan *et al.*, 2020).

Demographic factors, including age and gender, were found to be associated with wound infections among suspected cases. Males exhibited a significantly higher occurrence of positive cultures (66.86%) compared to females (61.00%), a trend which is in contrast to a previous study in a different teaching hospital in Ghana where females were more burdened with wound infection (Forson *et al.*, 2017). This finding suggests a potential geography or social-culturally oriented gender-based susceptibility to wound infections. Additionally, age played a substantial role in infection prevalence, with the prevalence increasing with increasing age. This aligns with research by (Bediako-Bowan *et al.*, 2020) in Ghana that highlight age as a significant predictor of surgical site wound infection risk. Ejaz (2019) also observed a trend of increasing wound infection prevalence across increasing age groups among children in Pakistan. These

findings emphasize the importance of considering demographic factors when assessing wound infection risk and tailoring preventive strategies accordingly.

This study revealed a significant association between climatic seasons and the occurrence of bacterial wound infections. The prevalence of infections was notably higher during the rainy season (67.83%) compared to the dry season (58.13%) (p<0.001). A study by Sagi *et al.*, (2015) also observed a significant association between climatic seasons and the occurrence of wound infection with preponderance of infection in spring and summer which correspond with the rainy or wet season of the jurisdiction of the present study. This observation suggests that environmental factors related to seasonal changes may influence wound infection rates, warranting further investigation into the specific factors driving this variation. Seasonal variations in wound infection area less discussed dimension that needs attention and further studies to identify the mechanisms involved to develop policies and strategies to enhance wound care and management.

The most frequently isolated species of wound infection at the Ho Teaching Hospital was *Pseudomonas aeruginosa*, accounting for 21.3% of the total isolates. This was followed by *Escherichia coli* (18.1%), *Pseudomonas spp* (11.5%), *Staphylococcus aureus* (9.4%), *Klebsiella spp* (8.8%), and *Proteus mirabilis* (5.8%). This pattern of aetiologic agents to wound infection with high occurrence of *Pseudomonas spp* has also been described in other parts of the country (Forson *et al.*, 2017). The frequent occurrence of Pseudomonas aeruginosa has also been reported in a Tertiary health facility in neighboring Nigeria (AYE *et al.*, 2011). This notwithstanding, the spectrum of frequently isolated bacteria seen in this study reflects similar patterns seen in Korle-Bu Teaching Hospital (Forson *et al.*, 2017). These findings provide valuable insights into the local prevalence of wound pathogens and can guide clinicians in selecting appropriate empirical treatments for wound infections.

#### 5.3 Patterns and trends of antibiotic resistance in wound infection

One of the most striking observations in this study was the substantial reduction in resistance to meropenem, from an alarming 91.67% in 2018 to a much-improved 11.90% in 2023. This trend aligns with broader global efforts to address carbapenem-resistant bacteria. It echoes findings from previous studies that have also reported decreasing resistance to meropenem, underscoring the positive impact of targeted interventions and the importance of this antibiotic in treating severe infections caused by multidrug-resistant Gram-negative bacteria (Horikoshi *et al.*, 2017; Hu *et al.*, 2016)

In contrast, cotrimoxazole resistance exhibited a cyclical pattern. It initially stood at 100% resistance in 2018, decreased to 50% in 2021, but then experienced a resurgence to 83.33% in 2023. This cyclical pattern has been documented in prior research and is often attributed to changes in antibiotic prescribing practices and usage patterns (Neupane *et al.*, 2023). It highlights the need for continued vigilance in antibiotic stewardship to maintain and enhance the effectiveness of antibiotics like cotrimoxazole.

The study also explored resistance trends within the aminoglycoside class, revealing distinct patterns for Amikacin and Gentamicin. Amikacin resistance increased, while Gentamicin resistance decreased. This variation in resistance within a single antibiotic class underscores the dynamic nature of antibiotic resistance and the importance of distinguishing between specific antibiotics when assessing resistance trends. Previous studies have also reported similar diversity in resistance patterns within antibiotic classes, emphasizing the complex interplay of factors influencing resistance (Ranjbar & Farahani, 2019).

In the case of Chloramphenicol, Ampicillin, and Ciprofloxacin, resistance remained relatively stable over the study period. While this study did not directly compare these findings with prior research, it aligns with the notion that certain antibiotics may exhibit consistent resistance

patterns over time. However, it is essential to recognize that resistance can evolve, and ongoing surveillance is crucial to detect any emerging trends or shifts in resistance patterns.

Ciprofloxacin emerged as the most effective drug against gram-positive isolates, with a resistance rate of only 12.82%. Conversely, Penicillins (Penicillin and Ampicillin) demonstrated the highest resistance rates among gram-positive isolates. Among gram-negative isolates, Amikacin displayed the highest sensitivity, with a rate of 90.22%. However, the cephalosporins showed resistance rates of over 50%, indicating a need for careful antibiotic selection when treating gram-negative wound infections. The finding of the present study compares with a study on gram-negative isolates from Komfo Anokye Teaching Hospital (KATH) where the gram-negative isolates showed high resistance to ampicillin (94.4%), cefuroxime (79.0%) and cefotaxime (71.3%) but low resistance to ertapenem (1.5%), meropenem (3%) and amikacin (11%) (Agyepong *et al.*, 2018).

Further analysis of antibiotic resistance rates by specific bacterial species revealed variations in resistance patterns. P. aeruginosa, the most frequently isolated pathogen, exhibited resistance rates of over 50% against several antibiotics, including Ampicillin, Tetracycline, Ceftriaxone, Cefotaxime, and Chloramphenicol. Conversely, *P. aeruginosa* displayed relatively low resistance to Amikacin (5.84%). *E. coli* demonstrated a similar pattern but exhibited resistance to Ciprofloxacin (62.83%). (Bediako-Bowan *et al.*, (2020) also described a similar pattern of *E. coli* resistance to Ampicillin and Ciprofloxacin at the Korle-Bu Teaching Hospital. Other *Pseudomonas spp* showed moderate resistance rates to antibiotics, with the highest resistance observed against Gentamicin (35.42%) which compares with findings from a study among 6 African countries where each country reported similar resistance rates (Lai *et al.*, 2018).

The indiscriminate use of antibiotics may be responsible for the observed patterns of prevailing antibiotic resistance to frequently used antibiotics (Morgan *et al.*, 2011).

# **CHAPTER SIX**

## CONCLUSIONS AND RECOMMENDATIONS

#### **6.1 Conclusions**

In conclusion, this study uncovered critical insights into wound infections, concerning prevalence and trends of antibiotic-resistant wound infections at the Ho Teaching Hospital from 2018 to 2023. The prevalence of positive cultures to wound infections was notably high. Demographic factors and climatic seasons were found to influence infection rates, emphasizing the need for targeted prevention strategies. Pseudomonas aeruginosa emerged as a prominent pathogen, guiding empirical treatments. Encouragingly, reductions in meropenem resistance is promising and reflects global efforts against carbapenem-resistant bacteria.

However, cyclical cotrimoxazole resistance underscores ongoing stewardship challenges. Varying resistance patterns within antibiotic classes emphasize the intricate nature of antibiotic resistance. Moving forward, sustained vigilance and tailored antibiotic strategies are vital to mitigate the impact of antibiotic resistance in wound care and healthcare at large.

#### 6.2 Recommendations

- There is a need for management in collaboration with Ghana Health Service to implement and strengthen antibiotic stewardship programs within the Ho Teaching Hospital and other healthcare facilities in and around Ho Municipality. These programs should focus on promoting the judicious use of antibiotics, regular monitoring of resistance patterns, and educating healthcare providers on appropriate prescribing practices to improve antibiotic resistance.
- 2. The Management at the Ho Teaching Hospital should establish a comprehensive surveillance system for monitoring antibiotic resistance in wound infections. Regular data collection and analysis can help identify emerging resistance patterns, enabling timely interventions.

- 3. The Management at the Ho Teaching Hospital in collaboration with Ghana Health Service should conduct awareness campaigns and educational programs aimed at males, who exhibited a higher susceptibility to wound infections in the study. These programs should emphasize wound care, hygiene, and early detection.
- 4. Healthcare facilities in and around Ho Municipality should prepare for an increased burden of wound infections during the rainy season. Adequate staffing, resources, and infection prevention measures should be in place to manage the seasonal surge effectively.
- 5. The Management at the Ho Teaching Hospital should institute treatment guidelines that consider the predominant wound pathogens identified in the study, particularly Pseudomonas aeruginosa and Escherichia coli. Tailor empirical antibiotic therapies to local resistance patterns.
- 6. The Ministry of Health should enact policies that support further research to investigate the genetic mechanisms underlying antibiotic resistance among wound isolates. This research can provide insights into the molecular basis of resistance and guide the development of targeted therapies.
- 7. The Ministry of Health in collaboration with the Management of the hospital should promote the practice of choosing antibiotics based on individual patient susceptibility and wound culture results whenever possible, rather than relying solely on empirical treatments.
- 8. Conduct regular reviews of hospital antibiotic guidelines in light of evolving resistance patterns. Ensure that these guidelines are evidence-based and up-to-date.

By implementing these recommendations, healthcare facilities can improve wound infection management, reduce antibiotic resistance, and ultimately enhance patient care outcomes. Additionally, ongoing research and collaboration will be essential in addressing the complex issue of antibiotic resistance in wound infections effectively

#### REFERENCES

- Agyepong, N., Govinden, U., Owusu-Ofori, A., & Essack, S. Y. (2018). Multidrug-resistant gram-negative bacterial infections in a teaching hospital in Ghana. *Antimicrobial Resistance & Infection Control*, 7(1), 37. https://doi.org/10.1186/s13756-018-0324-2
- AYE, E. C., Omoregie, R., OHIORENUAN, I. I., & Onemu, S. (2011). Microbiology of wound infections and its associated risk factors among patients of a Tertiary hospital in Benin City, Nigeria.
- Bediako-Bowan, A. A., Kurtzhals, J. A. L., Mølbak, K., Labi, A.-K., Owusu, E., & Newman, M. J. (2020). High rates of multi-drug resistant gram-negative organisms associated with surgical site infections in a teaching hospital in Ghana. *BMC Infectious Diseases*, 20(1), 890. https://doi.org/10.1186/s12879-020-05631-1
- Bediako-Bowan, A., Owusu, E., Debrah, S., Kjerulf, A., Newman, M. J., Kurtzhals, J. A. L., & Mølbak, K. (2020). Surveillance of surgical site infection in a teaching hospital in Ghana: a prospective cohort study. *Journal of Hospital Infection*, 104(3), 321–327. https://doi.org/https://doi.org/10.1016/j.jhin.2020.01.004
- Ejaz, H. (2019). Determination of bacterial profile and spectrum of antimicrobial drug resistance in pediatric wound infections. *Journal of Pure and Applied Microbiology*, 13(4). https://doi.org/10.22207/JPAM.13.4.21
- Forson, O. A., Ayanka, E., Olu-Taiwo, M., Pappoe-Ashong, P. J., & Ayeh-Kumi, P. J. (2017). Bacterial infections in burn wound patients at a tertiary teaching hospital in Accra, Ghana. *Annals of Burns and Fire Disasters*, 30(2), 116.
- Horikoshi, Y., Suwa, J., Higuchi, H., Kaneko, T., Furuichi, M., Aizawa, Y., Fukuoka, K., Okazaki, K., Ito, K., & Shoji, T. (2017). Sustained pediatric antimicrobial stewardship program with consultation to infectious diseases reduced carbapenem resistance and infection-related mortality. *International Journal of Infectious Diseases*, 64, 69–73. https://doi.org/https://doi.org/10.1016/j.ijid.2017.09.012
- Hu, F.-P., Guo, Y., Zhu, D.-M., Wang, F., Jiang, X.-F., Xu, Y.-C., Zhang, X.-J., Zhang, C.-X., Ji, P., & Xie, Y. (2016). Resistance trends among clinical isolates in China reported from CHINET surveillance of bacterial resistance, 2005–2014. *Clinical Microbiology and Infection*, 22, S9–S14.
- Lai, P. S., Bebell, L. M., Meney, C., Valeri, L., & White, M. C. (2018). Epidemiology of antibiotic-resistant wound infections from six countries in Africa. *BMJ Global Health*, 2(Suppl 4), e000475. https://doi.org/10.1136/bmjgh-2017-000475
- Morgan, D. J., Okeke, I. N., Laxminarayan, R., Perencevich, E. N., & Weisenberg, S. (2011). Non-prescription antimicrobial use worldwide: a systematic review. *The Lancet Infectious Diseases*, 11(9), 692–701.
- Neupane, R., Bhathena, M., Das, G., Long, E., Beard, J., Solomon, H., Simon, J. L., Nisar, Y. B., MacLeod, W. B., & Hamer, D. H. (2023). Antibiotic resistance trends for common

- bacterial aetiologies of childhood diarrhoea in low-and middle-income countries: A systematic review. *Journal of Global Health*, 13.
- Ranjbar, R., & Farahani, A. (2019). Study of genetic diversity, biofilm formation, and detection of Carbapenemase, MBL, ESBL, and tetracycline resistance genes in multidrug-resistant Acinetobacter baumannii isolated from burn wound infections in Iran. *Antimicrobial Resistance & Infection Control*, 8(1), 172. https://doi.org/10.1186/s13756-019-0612-5
- Ahmed, Eman Farouk, Asia Helmi Rasmi, Abdou M A Darwish, Gamal Fadl, and Mahmoud Gad. 2023. "Prevalence and Resistance Profile of Bacteria Isolated from Wound Infections among a Group of Patients in Upper Egypt: A Descriptive Cross-Sectional Study," 1–11.
- Akova, Murat. 2016. "Epidemiology of Antimicrobial Resistance in Bloodstream Infections." *Virulence* 7 (3): 252–66. https://doi.org/10.1080/21505594.2016.1159366.
- Aljeldah, Mohammed M. 2022. "Antimicrobial Resistance and Its Spread Is a Global Threat."
- Arodiwe, E.B., Nwokediuko, S.C. & Ike, S.O. 2014. "Medical Causes of Death in a Teaching Hospital in South-Eastern Nigeria: A 16 Year Review." *Nigerian Journal of Clinical Practice* 17(6).
- Bassetti M, Peghin M, Vena A, Giacobbe DR. 2019. "Treatment of Infections Due to MDR Gram-Negative Bacteria." *Front Med.* 6: 74. https://doi.org/10.3389/fmed.2019.00074.
- Bassetti M, Poulakou G, Ruppe E, Bouza E, Sebastian J V H, Adrian B. 2017. "Antimicrobial Resistance in the next 30 Years, Humankind, Bugs and Drugs: A Visionary Approach." *Intensive Care Med* 43: 1464–1475.
- Bauer, W. Kirby and A. 1961. "Disk Diffusion Test for Antibiotics' Standardized by World Health Organization." WHO, 134.
- Baym, M.; Stone, L.K.; Kishony, R. 2016. "Multidrug Evolutionary Strategies to Reverse Antibiotic Resistance." *Science*, 1;351(6268):aad3292. doi: 10.1126/science.aad3292.
- Calina D, Docea AO, Rosu L, Zlatian O, Rosu AF, Anghelina F. 2017. "Antimicrobial Resistance Development Following Surgical Site Infections." *Mol Med Rep.* 15: 681–88. https://doi.org/10.3892/mmr.2016.6034.
- CDC. 2019a. "Antibiotic Resistance, A Threat in the United States"
- CLSI. 2021. "Performance Standards for Antimicrobial Susceptibility Testing'." 31ST Information Supplement. CLSI M100-S31.
- Dantas G, Sommer MOA. 2014. "How to Fight Back against Antibiotic Resistance." Am Sci

- 102: 42–51.
- Daulaire N, Bang A, Tomson G, Joan N K, Otto C. 2015. "Universal Access to Effective Antibiotics Is Essential for Tackling Antibiotic Resistance." *J Med Law Ethics* 43: 17–21.
- Delamou A., Camara B.S., Sidibé S., Camara A., Dioubaté N., El Ayadi A.M., Tayler-Smith K., Beavogui A.H., Baldé M.D., Zachariah R. 2019. "Trends of and Factors Associated with Cesarean Section Related Surgical Site Infections in Guinea." *J. Public Health Afr.* 10: 818. https://doi.org/10.4081/jphia.2019.818.
- Dowd SE, Sun Y, Secor PR, Rhoads DD, Wolcott BM, James GA. 2008. "Survey of Bacterial Diversity in Chronic Wounds Using Pyrosequencing, DGGE, and Full Ribosome Shotgun Sequencing." *BMC Microbiol*. 8: 43. https://doi.org/10.1186/1471-2180-8-43.
- Edwards R, Harding KG. 2004. "Bacteria and Wound Healing." *Curr Opin Infect Dis* 17: 91–96.
- Founou RC, Founou LL, Essack SY. 2017. "Clinical and Economic Impact of Antibiotic Resistance in Developing Countries: A Systematic Review and Meta-Analysis." *PLoS One*. 12(12): e0189621. https://doi.org/10.1371/journal.
- pone.0189621Getahun, H.; Smith, I.; Trivedi, K.; Paulin, S.; Balkhy, H.H. 2020. "Tackling Antimicrobial Resistance in the COVID-19 Pandemic. Bull." *World Health Organ.* 98: 442-442A.
- Guan, Haonan, Wei Dong, Yechen Lu, Minfei Jiang, and Di Zhang. 2021. "Distribution and Antibiotic Resistance Patterns of Pathogenic Bacteria in Patients With Chronic Cutaneous Wounds in China" 8 (March): 1–13. https://doi.org/10.3389/fmed.2021.609584.
- Guo, S, and L A Dipietro. 2010. "Factors Affecting Wound Healing," no. Mc 859: 219–29. https://doi.org/10.1177/0022034509359125.
- Hassan, M.A.; El-Aziz, S.A.; Elbadry, H.M.; El-Aassar, S.A.; Tamer, T.M. 2022. "Prevalence, Antimicrobial Resistance Profile, and Characterization of Multi-Drug Resistant Bacteria from Various Infected Wounds in North Egypt." *Saudi J. Biol. Sci.* 29: 2979–88.
- Huang, H.; Chen, B.; Liu, G.; Ran, J.; Lian, X.; Huang, X.; Wang, N.; Huang, Z. A. 2018. "Multi-Center Study on the Risk Factors of Infection Caused by Multi-Drug Resistant Acinetobacter Baumannii." *BMC Infect. Dis.* 18: 11.
- Hutchings, M.I.; Truman, A.W.; Wilkinson, B. 2019. "Antibiotics: Past, Present, and Future." *Curr. Opin Microbio* 51: 72–80.
- Khawaja, A.; Arshad, F.; Munir, S. 2018. "Acinetobacter Species: Prevalence and Sensitivity Pattern of Acinetobacter Species among Clinical Isolates of Tertiary Care Hospital." *Prof. Med. J.* 25: 1949–53.

- Kirketerp-Moller K, Jensen PO, Fazli M, Madsen KG, Pedersen J, Moser C, Tolker-Nielsen T, Hoiby N, Givskov M, and Bjarnsholy T. 2008. "Distribution, Organization, and Ecology of Bacteria in Chronic Wounds." *Clin Microbiol* 46: 2717–22. https://doi.org/10.1128/JCM. 00501-08.
- Lai, Peggy S., Lisa M. Bebell, Carron Meney, Linda Valeri, and Michelle C. White. 2017. "Epidemiology of Antibiotic-Resistant Wound Infections from Six Countries in Africa." *BMJ Global Health* 2: 1–7. https://doi.org/10.1136/bmjgh-2017-000475.
- Laxminarayan, Ramanan, Precious Matsoso, Suraj Pant, Charles Brower, John Arne Røttingen, Keith Klugman, and Sally Davies. 2016. "Access to Effective Antimicrobials: A Worldwide Challenge." *The Lancet* 387 (10014): 168–75. https://doi.org/10.1016/S0140-6736(15)00474-2.
- Lipsky, Benjamin A, Matthew Dryden, Finn Gottrup, Dilip Nathwani, Ronald Andrew Seaton, and Jan Stryja. 2016. "Antimicrobial Stewardship in Wound Care: A Position Paper from the British Society for Antimicrobial Chemotherapy and European Wound Management Association," no. July: 3026–35. https://doi.org/10.1093/jac/dkw287.
- Livermore, D.M. 2021. "Antibiotic Resistance during and beyond COVID-19." *JAC-Antimicrob. Resist.* 3: i5–16.
- Mathieu D, Linke J-C, Wattel F. 2006. Non-Healing Wounds. In: Handbook on Hyperbaric Medicine.
- Murray, Christopher J.L., Theo Vos, Rafael Lozano, Mohsen Naghavi, Abraham D. Flaxman, Catherine Michaud, Majid Ezzati, et al. 2012. "Disability-Adjusted Life Years (DALYs) for 291 Diseases and Injuries in 21 Regions, 1990-2010: A Systematic Analysis for the Global Burden of Disease Study 2010." *The Lancet* 380 (9859): 2197–2223. https://doi.org/10.1016/S0140-6736(12)61689-4.
- Onyekwelu I, Yakkanti R, Protzer L, Pinkston CM, Tucker C, Seligson D. 2017. "Surgical Wound Classification and Surgical Site Infections in the Orthopaedic Patient." *J Am Acad Orthop Surg Glob Res Rev*, Jun;1(3):e022. [PMC free article] [PubMed].
- Rahim K, Saleha S, Zhu X, Huo L, Basit A, Franco OL. 2017. "Bacterial Contribution in Chronicity of Wounds." *Microb Ecol.* 73: 710–21. https://doi.org/10.1007/s00248-016-0867-9.
- Rhoads DD, Wolcott RD, Sun Y, Dowd SE. 2012. "Comparison of Culture and Molecular Identification of Bacteria in Chronic Wounds." *Int J Mol Sci.* 13: 2535–50. https://doi.org/10.3390/ijms13032535.
- Ribeiro SM, Felício MR, Boas EV, Gonc alves S, Costa FF, Samy RP. 2016. "New Frontiers for Anti-Biofilm Drug Development." *Pharmacol Ther* 160: 133–44.

- Scaglione, V.; Reale, M.; Davoli, C.; Mazzitelli, M.; Serapide, F.; Lionello, R.; La Gamba, V.; Fusco, P.; Bruni, A.; Procopio, D. 2022. "Prevalence of Antibiotic Resistance Over Time in a Third-Level University Hospital." *Microb. Drug Resist.* 28.
- Source, Wound. 2016. "The Four Stages of Wound Healing."
- Sulayyim, H.J.A.; Ismail, R.; Al Hamid, A.; Ghafar, N.A. 2022. "Antibiotic Resistance during COVID-19: A Systematic Review." *Int. J. Environ. Res. Public Health* 19: 11931.
- Ventola, C.L. 2015. "The Antibiotic Resistance Crisis." *Pharm. Ther.* 40: 277–83.
- Vicar, Ezekiel Kofi, Samuel E. K. Acquah, Walana Williams, Eugene D. Kuugbee, Courage K. S. Saba, and Gloria Ivy Mensah. 2021. "Antibiotic Resistant Bacteria Infecting Wounds of Rural Community Dwellers in Northern Ghana." *European Journal of Medical and Health Sciences* 3 (1): 112–17. ttps://doi.org/10.24018/ejmed.2021.3.1.678.
- Vitiello R, Perna A, Peruzzi M, Pitocco D, Marco G. 2020. "Clinical Evaluation of Tibiocalcaneal Arthrodesis with Retrograde Intramedullary Nail Fixation in Diabetic Patients." *Acta Orthop Traumatol Turc* 54(3):255-.
- Wall, Stig. 2020. "Prevention of Antibiotic Resistance An Epidemiological Scoping Review to Identify Research Categories and Knowledge Gaps" 12 (2019). https://doi.org/10.1080/16549716.2020.1756191.
- Warda, Ahmed E Abou, Fatma Molham, Heba F Salem, Gomaa Mostafa-hedeab, Bashayer F Alruwaili, Ayman N Moharram, Mohamed Sebak, and Rania M Sarhan. 2022. "Emergence of High Antimicrobial Resistance among Critically Ill Patients with Hospital-Acquired Infections in a Tertiary Care Hospital," 1–18.
- WHO. 2014. "Global Report on Surveillance 2014." WHO 2014 AMR Report, 1–8. http://www.who.int/drugresistance/documents/AMR\_report\_Web\_slide\_set.pdf.
- Wilkins RG, Unverdorben M. 2013. "Wound Cleaning and Wound Healing." A Concise Review; Adv Skin Wound Care, Apr; 26(4):160-3. [PubMed].
- Wu M, Pan H, Leng W, Lei X, Chen L, Liang Z. 2018. "Distribution of Microbes and Drug Susceptibility in Patients with Diabetic Foot Infections in Southwest China." *Diabetes Res* 2018: 9817308. https://doi.org/10.1155/2018/9817308.
- Yevutsey, Saviour Kwame, Kwame Ohene Buabeng, Moses Aikins, Berko Panyin Anto, Richard B. Biritwum, Niels Frimodt-Møller, and Martha Gyansa-Lutterodt. 2017. "Situational Analysis of Antibiotic Use and Resistance in Ghana: Policy and Regulation." *BMC Public Health* 17 (1): 1–7. https://doi.org/10.1186/s12889-017-4910-7.