PRESENCE OF METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* AMONGST PATIENTS ADMITTED TO THE INTENSIVE CARE UNITS OF SIX KWAZULU-NATAL HOSPITALS, 2018 TO 2022

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DECLARATION

I, Sizolwethu Abitious Cebekhulu, declare that this is my original work, the project was only carried out for the purpose of completing and achieving the master's degree at Central University of Technology, and that the work was reviewed and approved by HSREC (Approval letter attached in the appendix section). I declare that the work has never been submitted to another university for the award of a degree.

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Signature

18/08/24

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Date

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ABSTRACT

BACKGROUND

The rate of nosocomial infection is detrimental to the health system, exacerbating the management costs, mortality, and morbidity globally. *Staphylococcus aureus* accounts for community and nosocomial infections associated with humans, including bacteraemia, pneumonia and bloodstream infection. Methicillin-resistant *Staphylococcus aureus* is a major contributor to infections linked to healthcare, especially in the intensive care unit. It is also a major public health concern around the world due to its resistance to routinely used antibiotics and associated with severe infections. There is no study that has recently determine the presence of MRSA strain from patients admitted to ICU ward of six Kwazulu-Natal hospitals, which are the King Edward VIII Hospital, Inkosi Albert Luthuli Central Hospital, Addington Hospital, Mahatma Gandhi Memorial hospital, Prince Mshiyeni Memorial Hospital and Northdale Hospital during the pandemic period.

AIM

The aim of the study was to determine the prevalence and antimicrobial profile of MRSA identified at King Edward VIII, Inkosi Albert Luthuli Central Hospital, Addington, Mahatma Gandhi Memorial, Prince Mshiyeni Memorial Hospital, and Northdale hospitalised patients older than 18 years of age, for a period of five years.

METHOD

This retrospective study was conducted from six KZN hospitals from 2018 to 2022, utilising data obtained from National Health Laboratory Services (NHLS). The initial plan was to concentrate more on ICU patients above 18 years of age. Data received from the CDW for MRSA isolates were detected from 2018 to 2022 for patients in the ICU of the six hospitals. However, due to the very limited ICU data received, since one of six hospitals (Mahatma Gandhi) does not have an ICU ward and the ICU admits fewer patients compared to other hospital wards, we chose to concentrate on the total MRSA prevalence across all wards because low sample numbers may make statistical analysis unreliable. Data comprised infection rate, test data, and demographic information. MRSA and *Staphylococcus aureus*

cases were compared using descriptive analysis and cross-tabulation. Data was analysed using IBM SPSS version 27.

RESULTS

Amongst 11663 *Staphylococcus aureus* isolated from Six KZN hospitals, 2357 isolated tests were resistant to methicillin. The most prevalent age groups affected by MRSA infection were individuals between the ages of 18 and 29 as well as those aged between 30 and 40 years. More males than females were infected with MRSA in both pre and post-COVID- 19. MRSA was commonly isolated in pus specimens, followed by automated blood culture. Inkosi Albert Luthuli Central hospital is presented with a high number of MRSA compared to other hospitals in pre-COVID-19. In post-COVID-19 high rate of MRSA infection was observed in Northdale hospital. Antimicrobial susceptibility revealed that MRSA is highly sensitive to linezolid, teicoplanin, fusidic acid and vancomycin. High resistance patterns were seen in cefoxitin and penicillin-ampicillin.

CONCLUSION

The results of the study found that there was a 20,2% MRSA prevalence rate over the five-year period across all six hospitals, which is alarming. This clearly calls for drastic measures to curb the spread of this resistant isolate by employing improved infection control strategies and antimicrobial stewardship in healthcare settings. The slight increase in MRSA incidence from pre-COVID-19 (19,46%) to post-COVID-19 (20,84%) implies that COVID-19 had little impact on MRSA transmission. Strategies for control and prevention, such as decolonisation, should be prioritised. Drugs that are found to be of choice for the treatment of MRSA are linezolid, teicoplanin and vancomycin. Continuous monitoring and surveillance should be implemented to ensure drug resistant organisms are identified sooner.

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ABBREVIATIONS

- AARMS : Academic Affairs and Research Management System
- AMR : Antimicrobial Resistance
- CA-MRSA : Community Acquired Methicillin-Resistant *Staphylococcus aureus*
- CDC : Centres for Disease Control and Prevention
- CDW : Corporate Data Warehouse
- GLASS : Global Antimicrobial Surveillance
- HA-MRSA : Hospital-Acquired Methicillin-Resistant *Staphylococcus aureus*
- HIV : Human IMMUNODEFICIENCY VIRUS
- IALCH : Inkosi Albert Luthuli Central Hospital
- ICU : Intensive Care Unit
- KEH : King Edward VIII Hospital
- KZN : Kwa-Zulu Natal
- MIC : Minimum Inhibitory Concentration
- MRSA : Methicillin-resistant *Staphylococcus aureus*
- MSSA : Methicillin-sensitive *Staphylococcus aureus*
- NICD : National Institute for Communicable Diseases
- NHLS : National Health Laboratory Service
- PBP : Penicillin Binding Protein
- PCR : Polymerase Chain Reaction
- SA : South Africa
- *S. aureus* : *Staphylococcus aureus*
- SCCmec : Staphylococcal cassette chromosome mec
- WHO : World Health Organization

CHAPTER 1: INTRODUCTION

Globally high excessive health management costs, mortality, and morbidity result from significant nosocomial infections (Lipsett, 2008, WHO, 2011). *Staphylococcus aureus* (*S. aureus*) accounts for community- (CA) and hospital-acquired (HA) infections associated with humans, including bacteraemia, pneumonia and bloodstream infections (Luzzaro *et al*., 2011). It was first observed in 1878 by Robert Koch in a pus specimen, and the bacteria was given the name *Staphylococcus* by Sir Alexander Ongston in 1881 (Orent, 2006). This bacterium was curable with penicillin, but extensive antibiotic use resulted in the formation of penicillin resistance (Brumfitt & Hamilton-Miller, 1989). A new drug, methicillin, was discovered in the 1950s to replace penicillin in the treatment of penicillin-resistant *S. aureus* (Jevons, 1961; Chambers & Deleo, 2009). However, two years post-introduction, methicillin-resistant *S. aureus* (MRSA) was reported (Jevons, 1961; Rayner & Munckhof*,* 2005; Khoshood *et al.,* 2019).

Methicillin-resistant *Staphylococcus aureus* is a unique strain, which caused a major public health concern because of its resistance to the routinely used penicillin antimicrobial agents, making infection difficult to treat (CDC, 2019). Methicillin-resistant *Staphylococcus aureus* is more dangerous in hospitals, as it can cause severe infections in fragile patients such as those in intensive care units (ICUs) (Washer, Joffe & Solberg, 2006). This hospital-acquired methicillin-resistant *S. aureus* (HA-MRSA) is being reported to account for a high proportion of hospitalised patients infected with *S. aureus* (Stefani *et al*., 2012). Intensive care units are crucial locations in hospitals where patients with serious diseases or injuries receive extensive medical care (Vincent *et al*., 2013). Patients in ICUs are most likely to contract infections like MRSA due to variables such as extended hospital stays, invasive procedures and weakened immune systems.

Over the years, the world, especially sub-Saharan African countries, including South Africa (SA), witnessed HA-MRSA increasing around 20–50% of *S. aureus*-associated infections (Stefani *et al*., 2012). MRSA remained a significant cause of nosocomial infections for more than six decades. Methicillin-resistant *Staphylococcus aureus* caused a lot of morbidity when compared to methicillin-sensitive *Staphylococcus aureus* (MSSA) globally (Cosgrove *et al*.,

2003; Stefani *et al*., 2012). A meta-analysis study found that the risk of mortality due to MRSA bacteraemia was doubled compared to MSSA bacteraemia (Whitby, McLaws & Berry, 2001). Most patients infected with MRSA tend to spend longer in hospital, which results in a three times greater financial burden on the health system, staffing and increased hospital resources in general (Antonanzas *et al*., 2014; Fortuin-de Smidt *et al*., 2015; Thampi *et al*., 2015).

In order to control MRSA, it is important to understand the burden of this disease in KwaZulu-Natal (KZN) public hospitals. Identification of drug resistance patterns associated with *S. aureus* is essential, as it will guide infection control measures. The study aims to contribute to the body of knowledge by describing the presence of MRSA among patients admitted to the ICUs and other wards at six KZN hospitals from 2018–2022**.** The study may contribute to the review of the current *S. aureus* treatment regime in combating the MRSA spread across the province.

1.1 PROBLEM STATEMENT

Antimicrobial-resistant *S. aureus* infections generate major issues in the general population, and they can be especially catastrophic for the very young, the old, and people with impaired immune systems (WHO, 2023). If no effective measures are taken to limit the spread of this pandemic, it is anticipated that by 2050, the world will have lost roughly 10 million people per year (O'Neil, 2016). The drug of choice for MRSA infection is vancomycin, but some studies in SA revealed that some MRSA strains are now resistant to vancomycin and teicoplanin (Ferraz *et al*., 2000). This suggests that the knowledge of antimicrobial resistance in *S. aureus* is essential for making the best choices of formularies and infection control procedures. This will be the first study done in KZN to determine the prevalence of MRSA at six KZN hospitals from 2018 to 2022. Knowledge of local antibiotic resistance patterns of bacterial infection is crucial for practising physicians, clinical microbiologists and public health officials, as it informs empirical and pathogen-specific therapeutic decisions. The findings from this research will be used to educate the public and healthcare staff about the occurrence and prognosis of MRSA infections.

1.2 HYPOTHESIS

Since MRSA is a nosocomial infection, the prevalence of MRSA is expected to have been high in 2020 to 2022 compared to 2018 to 2019, as more patients were admitted to hospitals due to the COVID-19 pandemic and significant focus was given to the pandemic.

1.3 AIM OF THE STUDY

The aim of the study was to determine the prevalence and antimicrobial profile of MRSA identified at King Edward VIII, Inkosi Albert Luthuli Central Hospital, Addington, Mahatma Gandhi Memorial, Prince Mshiyeni Memorial Hospital, and Northdale hospitalised patients older than 18 years of age, from 2018 to 2022.

1.4 OBJECTIVES OF THE STUDY

1. To determine the number of infections due to MRSA in patients from six KZN hospitals using data obtained from the National Health Laboratory Service (NHLS), Corporate Data Warehouse (CDW).
2. To determine the rate of methicillin resistance among identified *S. aureus* isolates from the results of patients at six KZN hospitals indicated above.
3. To establish through data analysis the relationship between sex and age as predisposed to common factors to these infections.
4. To compare the data from the different hospitals for any possible common trend in resistance pattern.

CHAPTER 2: LITERATURE REVIEW

2.1 *STAPHYLOCOCCUS AUREUS*

Staphylococci are Gram-positive cocci resembling grape-like clusters and produce an enzyme called catalase (Lowy, 1998). They are classified based on coagulase production, e.g. coagulase-positive is *S. aureus*, and coagulase-negative could be S. *epidermidis* or *S. saprophyticus* (Becker *et al.,* 2014). *Staphylococcus aureus* is the most frequent cause of pneumonia and bacteraemia in communities and at hospitals (Luzzaro *et al.*, 2011). This Gram-positive pathogen is found in the skin and upper respiratory system as part of the natural flora (King *et al*., 2012). *Staphylococcus aureus* does not usually cause infection on healthy skin, but if these bacteria penetrate the bloodstream or intestinal tissues, they can cause serious infections (Tong *et al.,* 2015).

Endocarditis, food poisoning, cellulitis, toxic shock syndrome, skin and soft-tissue infections, bone and joint infections, pneumonia, and bloodstream infections are among the illnesses *S. aureus* can cause (Boyce, 1997). A higher risk of developing *S. aureus* is also linked to male gender, intravenous drug use, Human Immunodeficiency Virus (HIV) infection, nasal colonisation, past medical history (diabetes mellitus), hospitalisation and frequent interaction with the healthcare system (Morin *et al*., 2001). It is linked to a high death rate, particularly in patients who are extremely sick and admitted to an intensive care unit (ICU) (Lambert *et al.*, 2011; Van Hal *et al*., 2012).

Staphylococcus aureus is a major contributor to bacteraemia in developed and developing countries (Weiner-Lastinger *et al*., 2011). A study conducted in the Netherlands revealed that 20% of people have *S. aureus* in their noses, while 30% are intermittent carriers (Wertheim *et al*., 2005). The Global Antimicrobial Surveillance System (GLASS) regards *S. aureus* as one of the eight important pathogens along with *Shigella spp., Salmonella spp., Streptococcus pneumonia, Klebsiella pneumonia, Neisseria gonorrhoeae, Acinetobacter spp.,* and *Escherichia coli* (Tong *et al*., 2015).

In the early 1940s, penicillin was introduced as a drug to treat infections caused by *S. aureus.* Penicillin was the first drug of choice for the treatment of *S. aureus* infections (Brumfitt & Hamilton-Miller, 1989). However, bacteria started to protect themselves by producing an enzyme called penicillinase (Brumfitt & Hamilton-Miller, 1989). Methicillin was introduced in 1959 as the first semisynthetic penicillin to treat penicillin-resistant *S. aureus* infection. Methicillin is resistant to the enzyme penicillinase, which deactivates the beta-lactam ring of penicillins causing antibiotic deactivation (Chambers & Deleo, 2009, Pichereau *et al*., 2010, Lade, 2003; Kim *et al.,* 2024). When a microorganism is resistant to an antibiotic, it can grow or survive in the presence of a concentration of antibiotics that would normally inhibit or kill organisms of the same species (Behring, 2022). Antimicrobial resistance is regarded as a serious threat to public health systems worldwide, not just in developing countries (Founo *et al*., 2017).

2.1.1 Methicillin-resistant *staphylococcus aureus*

Methicillin was effective when it was first used in clinical therapy in the United Kingdom in 1959 because of its ability to withstand the action of beta-lactamase (Chambers & Deleo, 2009; Jokinen, Maisem & Järvinen, 2017). However 1961, two years after its introduction, Methicillin-resistant *S. aureus* was reported at a British Hospital (Jevons, 1961; Rayner & Munckhof, 2005; Khoshood *et al*., 2019). Methicillin-resistant *S. aureus* infections are more challenging to treat, especially if they are situated in anatomical sites where drug permission is decreased (Duckworth, 2003). It is a global multidrug-resistant human pathogen seen in hospital and community settings (Milheirico, De Lencastre & Tomasz, 2017).

A study done at a tertiary care centre in Riyadh, Saudi Arabia*,* between January 2013 and June 2017 revealed that all isolates tested were susceptible to vancomycin, linezolid, and tigecycline (Alhunaif *et al*., 2021). Most MRSA is resistant to a variety of antimicrobial treatments, including beta-lactam antibiotics (penicillin, cephalosporin), macrolides (erythromycin, azithromycin), fluoroquinolones (ciprofloxacin), aminoglycosides (gentamicin, tobramycin) (Kim *et al.,* 2004). In a hospital context, one of the most common areas of MRSA colonisation and infection is an intensive care unit (Ewans, Ortiz & LaForce, 1990). Therefore, understanding the prevalence and dynamics of MRSA in hospitals is crucial in the fight against AMR and nosocomial infections. It is crucial to notify the infection control team if the number

of isolates in a certain ward or ICU rises. In that case, healthcare worker screening, hand cleanliness, and other infection control techniques should be implemented quickly (CDC, 2019).

Numerous things have changed in the hospitals and community at large with the start of the COVID-19 pandemic. The probability of MRSA transmission decreased as a result of social distancing, hospital hygiene regulations, lockdowns in the general public, and the measures that prevented person-to-person contact (Jeffery *et al*., 2021). This is because MRSA is mostly spread through contact. Like other multidrug-resistant organisms, MRSA spreads between countries through goods or travellers in addition to within the healthcare system. Total travel bans and restrictions on international shipping could affect the transmission of diseases (Rump, Adams & Fischer, 2018).

2.1.2 Hospital-acquired methicillin-resistant *Staphylococcus aureus* infection

Methicillin-resistant *S. aureus* infections are classified as either healthcare-associated (HA-MRSA) or community-associated (CA-MRSA) (Lindsay, 2013). People who have spent time in a healthcare setting, such as a hospital, nursing home, or dialysis centre, are more likely to contract HA-MRSA infection (Fridkin *et al.*, 2005). Antimicrobial resistance from healthcare-associated illnesses is growing (Zhanel *et al*., 2008). Long-term use of broad-spectrum antibiotics, particularly in immunocompromised individuals, increases the incidence of HA-MRSA infection (Kurkowski., 2007). Over the past several decades, Gram-positive cocci have become the most common pathogen responsible for hospital infection worldwide (Jama, 1994). HA-MRSA accounts for a significant proportion of *S. aureus* infections in hospitalised patients (Stefani *et al*., 2012). In most African nations, including South Africa, HA-MRSA represents 20–50% of *S. aureus* infection (Stefani *et al*., 2012). Contact with infected sheets or improperly sterilised surgical instruments can potentially lead to illness. HA-MRSA can result in serious complications such as bloodstream infections and pneumonia (Klevens *et al*., 2007).

Community-acquired MRSA is transmitted by skin-to-skin contact or in crowded environments (CDC, 2019). Community-acquired (CA-MRSA) infections are MRSA infections that affect patients who have never been hospitalised or had no medical procedures (CDC, 2019). CA-MRSA is commonly contracted by people who are otherwise healthy (Fridkin *et al*.,

2005). Community-acquired methicillin resistance is diagnosed within 48 hours of admission in the absence of any medical equipment, indwelling catheter and previous hospitalisation (So, Hawkes & Byers, 2008). This MRSA infection is more common in high school and college athletes and persons in dormitories, jails, and military barracks (Goldstein, 2012).

2.2 EPIDEMIOLOGY OF METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS*

The spread of MRSA has a massive impact on people as well as countries because it significantly increases healthcare expenditure (Capitano, Cirpiano & Freitas, 2003). Patients with MRSA have a worse prognosis than those infected with MSSA (Kopp, Nix & Armstrong, 2004). In 2007, more than 170 000 MRSA infections and 5 400 deaths were noted in Europe, with an estimated economic cost of USD 380 million (European Centre for Disease Prevention and Control, 2010). Methicillin-resistant *S. aureus* infections increase hospital expenditures by prolonging hospital stays and increasing morbidity and mortality (Lee *et al*., 2013). The fact that antibiotics can no longer be effective in treating infection indicates an unknown future for healthcare (Chokshi *et al*., 2019). A multicentre study carried out in China between 2013 and 2015 revealed that MRSA infections were linked with a longer hospital stay, increased mortality rate, and higher hospital cost, compared to MSSA, especially in immunocompromised patients, e.g. patients with malignancy or chronic pulmonary diseases (Zhen, Zhang & Liu*,* 2020).

Methicillin-resistant *S. aureus* is one of the most common nosocomial infections in hospitals, and it is the major cause of hospitalisation and mortality worldwide (Bell *et al.,* 2002). It was first described in the 1960s and has then emerged in the last decade as a cause of nosocomial infections, causing rapidly progressive, potentially fatal diseases such as life-threatening pneumonia, necrotising fasciitis, endocarditis, osteomyelitis, severe sepsis and toxic shock syndrome (Monecke *et al.*, 2011). All MRSA strains are resistant to beta-lactam antibiotics, and most hospitals check/test MRSA infection upon admission as a crucial method of infection control (Gorwitz, 2008). MRSA has been considered the most significant antimicrobial-resistant pathogen by the Public Health Agency of Canada (PHAC) due to its high level of AMR and effect on public health (CCDR, 2016) and is also classified as a “priority pathogen” by the

World Health Organisation (WHO) due to its effective clones and potential to spread life-threatening infections (WHO, 2024).

Methicillin-resistant *S. aureus* is also a global health concern and is not limited to any particular region (Carrl, 2008). Methicillin-resistant *S. aureus* was first identified in clinical isolates from hospitalised patients in the United Kingdom in 1960, but it has spread rapidly in the community since 1990. Its strains are common in many European and American hospitals, accounting for 29–35% of all clinical isolates in 1990 (Vincent *et al*., 1995). According to European Prevalence of Infection in Intensive Care (EPIC) research, 57% of infections caused by MRSA in 1992 were recorded in an ICU (Vincent *et al*., 1995). In Europe, hospital-acquired (HA) infections caused by MRSA in 2008 were high, accounting for about 44% (Kock *et al*., 2010). Methicillin-resistant *S. aureus* is quite common in hospitals around the world, with a high rate (>50%) documented in Asia, Malta, and North and South America in 2012 (Stefani *et al*., 2012). Data from the European Antimicrobials Resistance Surveillance System (EARSS) in Europe in 2022 revealed that the prevalence of HA-MRSA in acute and long-term settings ranged from one to 24%, with significant intercountry variance (Johnson, 2022). According to additional literature from pan-European surveys, MRSA affects over 150 000 patients in the European Union (EU) each year and accounts for 380 million euro In additional hospital costs for the EU healthcare system, with the average excess costs per MRSA-positive patient ranging from 5 700 to 10 000 euro (Kanerva *et al*., 2011).

Methicillin-resistant *S. aureus* in 2014 was the cause of 80% of cases in the African region, 90% in the American region, 60% in the European Region, and 80% in the Western Pacific region (WHO, 2014). Hospital-associated MRSA accounts for about 20–50% of *S. aureus* infections in most African countries, including South Africa (Stefan *et al*., 2011). According to the Asia Pacific Region, 26–73% of *S. aureus* in 2011 were found to be resistant to methicillin in hospital settings (Mendes, Sader & Jones, 2013).

A study done at the Janaki Medical College Teaching Hospital, conducted from January 2016 to December 2017, reported the prevalence of MRSA 39,5% (Yadav & Prakash, 2016). A high prevalence of MRSA of 42% among positive cultures of *S. aureus* was noted in a study that was conducted in Iran from June 2018 to March 2020 (Serrafzadeh *et al.*, 2021). This high incidence of MRSA in Iran could be due to the over-prescription of antibiotics, inadequate

infection control measures in hospitals, improper training and inappropriate use of antibiotics (Serrafzadeh *et al*., 2021). Boston City Hospital in the USA was the first to report MRSA infections in 1968 (Burrett, McGehee & Finland, 1968). In the United States (US), a large proportion of *S. aureus* isolates, which are the leading cause of hospital-acquired infection, are methicillin-resistant (Klevens *et al*., 2007). A prior survey that gathered national hospitalisation and resistance data from 1999–2005 revealed that hospitalisation linked to MRSA doubled from 127 036 to 278 203 (Klein, Smith & Laxminarayan, 2007). There were approximately 95 360 invasive MRSA infections in the USA in 2005, and 18 000 patients died. This proportion was higher than the percentage linked to HIV/AIDS (Klevens *et al*., 2007). National Nosocomial Infection Surveillance Reports report that the incidence of MRSA causing nosocomial infection in the USA increased from 2% in 1974 to 22% in 1995 and then 63% in 2004 (Shresta, Pokhrel & Mohapatra, 2009).

Of hospital-acquired infections in ICU in the USA from 1992 to 2003, 50% were caused by MRSA, according to the National Nosocomial Infection Surveillance System (NNIS) (Fridkin *et al*., 2004). The prevalence of SAB and MRSA in the USA has been found to be elevated due to the frequency of invasive operations, intravascular device usage, and immunocompromised individuals. However, MRSA incidence has been observed to be declining in the UK (Johnson, 2011). In 2005–2016, the prevalence of MRSA infection decreased from 74–40% in the United States (Kourtis, 2019). Despite this decrease, it is estimated that almost 120 000 *S. aureus* bloodstream infections and 20 000 deaths are linked to *S. aureus.* A study conducted in the United States discovered a significant 34% rise in MRSA infection during COVID-19 compared to pre-COVID-19 (Weiner-Lastinger *et al*., 2019). In the United States, an estimated 35 000 deaths that occur each year are due to antimicrobial-resistant infections (CDC, 2019).

A study about the prevalence of MRSA conducted at eight African hospitals and Malta in 2003 showed that the presence of MRSA in Nigeria, Kenya and Cameroon ranged from 21–30%, and none of the isolates was resistant to vancomycin (Kesah *et al*., 2003). A study conducted in Kenya 2017 revealed that out of 25 *S. aureus* isolates, 28% were found to be MRSA (Lohan, Muloiwa & Akech, 2017). In another study conducted in Nigeria to find the presence of MRSA infection among hospitalised wound patients in a tertiary hospital in Enugu Metropolis, MRSA

was found to be 22,3%, and females were more likely to be affected than males, with a percentage of 12,7% and 9,6%, respectively (Chukwueze *et al*., 2022).

A Pan-European Antimicrobial Resistance Using Local Surveillance (PEARLS) study conducted in 2001–2002 revealed that an MRSA prevalence of 33% was reported in South Africa (Bouchillon, Johnson & Stuart, 2004). Marais *et al*. (2009) conducted their research in South Africa to assess the susceptibility of MRSA isolates in the country. The 248 MRSA isolates were gathered from both NHLS and private laboratories. These isolates were evaluated with 17 antibiotics using the disk diffusion method (Marais *et al*., 2009). It was discovered that MRSA was often resistant to similar antibiotics such as ciprofloxacin, erythromycin, gentamicin, tetracycline and trimethoprim, and all MRSA were sensitive to vancomycin (Marais *et al*., 2009). The study conducted in South Africa as part of a national survey by the National Institute for Communicable Diseases (NICD) from 2010 to 2012 showed a significant resistance pattern on amoxicillin-clavulanic acid (Perovic et al., 2012). An important factor to consider in South Africa is that MRSA is mostly HA (26,8%), as opposed to CA-MRSA (2,3%) (Naidoo *et al*., 2011). The prevalence of MRSA in South Africa declined from 36–24% between 2007 and 2011 (Falag, Moshiri & Ziegler, 2013). Exactly the same downward trend was revealed by another study whereby a small number of MRSA isolates were observed in South Africa during the year 2010 to 2012 (Perovic *et al.,* 2015). A study conducted in South Africa at Chris Hani Baragwanath Academic Hospital from January to December 2013 found the prevalence of MRSA to be 19% (Raphulu *et al*., 2023). The occurrence of MRSA during COVID-19 in South Africa has not been thoroughly reported in the available literature, but the study that was done in Australia during the COVID period discovered no significant impact of the pandemic on MRSA rates (Zarfel, Tschiedel & Kummer, 2023). This could suggest that the pandemic also did not have a significant influence on MRSA prevalence in other countries; however, regional variances in healthcare procedures and the epidemiology of MRSA could lead to different findings (Zarfel *et al*., 2023).

Methicillin-resistant *S. aureus* clinical isolates were first reported in Africa in 1978 during a hospital outbreak in Johannesburg in 1986–1987 (Park, 1989), and CA-MRSA infections have been reported in Zimbabwe since the early 1990s (Mason, Kitai & Chigonde, 1991). MRSA rates were found to be 23% in a study of patients with *S. aureus* bacteraemia at two academic

hospitals in Johannesburg (Perovic *et al*., 2006). According to geographic distribution data, Gauteng hospitals have a higher proportion of MRSA compared to other South African hospitals (Perovic *et al.,* 2012). In 2012, a surveillance study in four South African provinces revealed a 40% MRSA prevalence, and this has reduced from 53% in 2010 (Perovic *et al*., 2015). A previous South African study conducted between 2013 and 2016 at five public tertiary hospitals in two provinces (Gauteng and Western Cape) revealed that most MRSA bacteraemia cases were healthcare-associated (Perovic, Zong & Ehlers, 2017).

The first MRSA pandemic was reported in the neonatal intensive care unit in KwaZulu-Natal, South Africa, in 1989, indicating the importance of this organism (Coovadia *et al.,* 1989). In a study that was conducted in 2006, it was discovered that the prevalence of MRSA in KZN Province, South Africa, was roughly 27% (Shittu *et al.,* 2006). It is important to consider the relationship between HIV and MRSA in South Africa, because the study shows that MRSA infections are six to eight times more common in people with HIV than in the general population, and 6,9 % of HIV patients are MRSA carriers (Zervou *et al*., 2014). In a study conducted at the Addington Hospital in KZN for a period of one year, MRSA was found to be 8,04% and more males than females were affected (Dube *et al*., 2024).

2.3 TRANSMISSION OF MRSA

The most prevalent form of transmission is direct and indirect contact. Direct contact, such as contaminated hands of both employees and visitors, touching the skin of someone with MRSA. Indirect contact is interaction with contaminated tools, contact with objects such as MRSA on phones, and touching one's nose or sores (Kavanagh *et al*., 2017). MRSA is predominantly transmitted by the hands of healthcare staff as a result of noncompliance with hand hygiene standards (Fraser *et al*., 2006; Nicol *et al*., 2009). The study utilising data from multiple international studies on MRSA in ICUs revealed that high-touch surfaces (HTS) played a significant role in the transmission of MRSA in hospital settings when appropriate cleaning practices were not followed (Lei *et al*., 2020). A study carried out in a surgical intensive care unit discovered that MRSA might be spread more easily than MSSA between patients and healthcare workers (Naimi *et al*., 2001).

2.4 PREDISPOSING FACTORS

Mostly associated with prolonged hospital stay, people who are immunocompromised, such as people with HIV & AIDS (Fridkin *et al*., 2005). People over 60 years of age are more prone to develop MRSA because the likelihood of hospitalisation increases with age (Siddiqui *et al.*, 2023). Other predisposing factors are the use of a lot of antibiotics, haemodialysis, peripheral malperfusion, indwelling devices, advanced age, insulin-requiring diabetes, and residency in long-term facilities (Teicconelli *et al*., 2008). Chronic disorders frequently impair the immune system, making it more difficult for the body to combat an infection like MRSA (Shah *et al*., 2003).

2.5 MECHANISM OF RESISTANCE

In 1959, methicillin was introduced to treat infection caused by penicillin-resistant *S. aureus* (Jevons, 1961). After being introduced to the clinic in 1959, methicillin proved an effective treatment for penicillin-resistant *S. aureus* infection (Chambers, 2009). However, only two years after the first application for *S. aureus,* a British scientist, Jevons, announced the isolation of an MRSA strain (Jevons, 1961). In *S. aureus,* the peptidoglycan layers are held together by the penicillin-binding protein 2 (PBP2) (Turner *et al*., 2014). This protein holds together the peptidoglycan filament. If there are beta-lactam antibiotics, this antibiotic has a high affinity for the PBP2. Therefore, it will connect to it, and this protein cannot crosslink the peptidoglycan layer. The cell will not have the correct cell wall and eventually die (Turner *et al*., 2014).

Methicillin-resistant *S. aureus* has the same structure, but the difference is that PBP2A is the new form of PBP2; therefore, if there are beta-lactam antibiotics, there is no affinity for the PBP2A. The drug will not interact with anything, and PBP2A will continue crosslinking peptidoglycan layers. Therefore, MRSA can build cell walls in the presence of beta-lactam drugs (Pinho *et al*., 2001). *Staphylococcus aureus* developed resistance to methicillin and most other beta-lactamases-resistant beta-lactam drugs by acquiring a MecA gene. This gene produces PBP2a with a low affinity for beta-lactam antibiotics (Kayse, 1986). MecA gene is found on mobile genetic elements known as staphylococcal cassette chromosome mec

(SCCmec) elements (Kayser, 1986). To the 3' end of the staphylococcal chromosome, SCCmec attaches two essential elements, the Mac gene, which is responsible for methicillin resistance and CCR (Cassette chromosome recombinase), which encodes the recombinase protein (Yuzawa *et al*., 2004). MacA Gene detection by PCR is regarded as the gold standard for the detection of MRSA. Penicillin-binding protein 2 (PBP2) secreted by MRSA binds to beta-lactam antibiotics, rendering them ineffective against *S. aureus* (Munson, 2019).

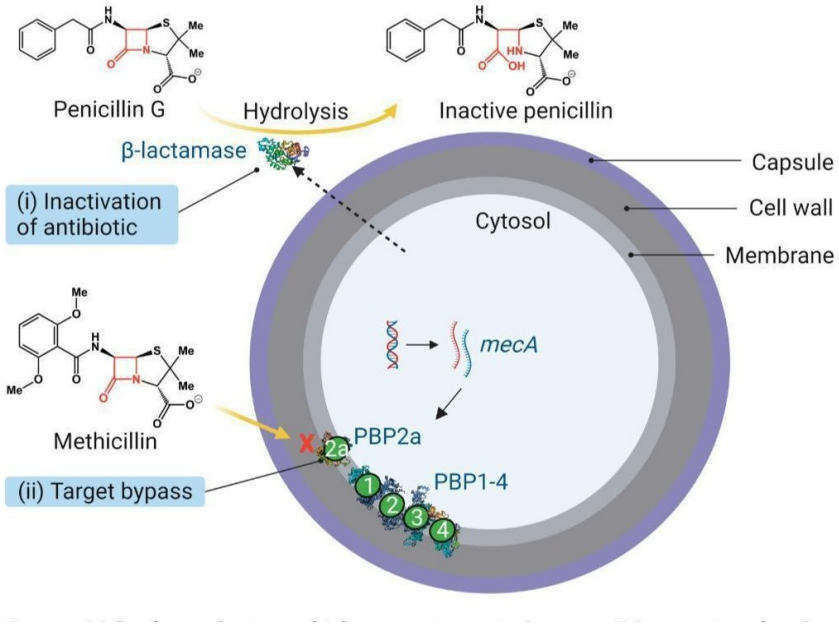


Figure 1: Mechanism of beta-lactam resistance in S. aureus (Lade et al., 2023)

2.6 LABORATORY DIAGNOSIS OF MRSA SAMPLES PROCESSING IN THE MICROBIOLOGY LABORATORIES OF NHLS

Patient samples for Microscopy, Culture and Sensitivities (MC&S) could be pus swabs, CSF, blood culture, urine, sterile fluid, sputum and throat swabs. Gram stain is done on those specimens, and *S. aureus* appeared as gram-positive cocci in clusters. Samples are cultured on mannitol, 5% sheep blood agar and McConkey agar, then incubated aerobically at 37 °C for 18–24 hours. After incubation, bacterial colonies show typical characteristics of *S. aureus* (medium to large) colonies with a convex, creamy appearance. Most strains show a narrow zone of beta haemolysis, while some strains are non-haemolytic on blood agar, with yellow colonies surrounded by a yellow zone on mannitol salt agar. The catalase test is done, and the

positive one is subjected to the coagulase test (confirmation test for *S. aureus*). Confirmed *S. aureus* isolates are subjected to Antimicrobial Susceptibility Testing.

2.7 ANTIMICROBIAL SENSITIVITY TESTING

A Vitek analyser is used to perform and analyse the antimicrobial sensitivity against different organisms. A gram identification card is used to identify MRSA, and cloxacillin came out as resistant from the instrument with a minimum inhibitory concentration (MIC) of greater than 4 micrograms/ml. For the MIC reading of less than 4 micrograms/ml, the Kirby Bauer disk diffusion method was used to confirm. A standard Kirby-Bauer disk diffusion method is performed using the Muller Hinton Agar (MHA) technique. A bacterial suspension equivalent to 0.5 McFarland standard is used for inoculation. The Cefoxitin disk is placed on an inoculated MH plate and incubated overnight at 37 °C. Isolates resistant to cefoxitin are considered MRSA.

2.8 PREVENTION OF MRSA

The prevention and control of MRSA are essential as the COVID-19 pandemic continues to increase globally. More people are admitted to hospitals and may acquire hospital-acquired infections, including MRSA (CDC, 2020). Some of the prevention tips to prevent COVID-19 that health organisations recommend can prevent MRSA infection, such as social distancing, use of sanitiser, and cleaning and bandaging of wounds.

2.8.1 Practise good hygiene

Hands should be washed frequently with soap and running water. Use an alcohol-based hand sanitiser as well. Hand washing is the most effective way to prevent the spread of infection (Reybrouck, 1983). Cuts should be kept clean and covered with a bandage. Avoid coming into direct contact with other people's bandages or wounds. Avoid sharing personal items such as razors and towels (Husney, 2021).

2.8.2 Use antibiotics wisely

It is imperative that the adherence and administration of antibiotics are followed as per the guidelines and exactly as prescribed by the doctor. Patients should continue until the antibiotics course is finished, regardless of how that feels. Antibiotic resistance may grow only if a portion of the drug is used, and that allows the microorganism to manifest resistance mechanisms if a lesser dosage is taken than prescribed. Antibiotic misuse, such as under-dosing, taking numerous or long courses, and using broad-spectrum drugs, are key contributors to the spread of antibiotic resistance in healthcare settings (Husney, 2021). Strong antimicrobial stewardship initiatives are required to maximise therapeutic results while reducing antibiotic-related side effects (Dellit *et al*., 2007).

2.8.3 Screening

Methicillin-resistant *S. aureus* prevention and control solutions that work rely on early detection so that suitable actions can be taken. It is crucial to test individuals in these situations because 2% of people carry MRSA, even if the bacterium is mainly contained in the nostril and the patient does not show any symptoms (Harbarth *et al*., 2011).

2.8.4 Isolation

Isolation is an important method for limiting the spread of MRSA in hospitals. It also reduces the chances of cross-contamination, which can occur through either direct (contacting an infected wound) or indirect (touching MRSA-contaminated surfaces). Patients infected with MRSA must be isolated to prevent the infection from spreading to others. When entering and leaving the isolation room, healthcare staff must wear personal protective equipment (PPE) such as gloves and gowns, as well as practise strict hand hygiene (CDC, 2019).

2.8.5 Education

Education for healthcare professionals is critical for reducing MRSA infections. Studies show that continual education and training programs can considerably lower MRSA infection rate by ensuring that all employees are informed of and follow the most recent infection control protocols (CDC, 2007). Patients and visitors must be educated about the spread of this infection, the need for hygiene, and why some infection control measures such as isolation

are required (Haung *et al*., 2014). Educate the general population, healthcare personnel and athletes about MRSA infection and the value of hygiene.

CHAPTER 3: METHODOLOGY

3.1 STUDY LOCATION

The study was done at the King Edward VIII Hospital laboratory of the NHLS. The King Edward VIII Hospital is a tertiary-level hospital providing regional and tertiary services to the whole of KZN and Eastern Cape, utilising the NHLS inside the premises. The Inkosi Albert Luthuli Central Hospital, a tertiary and quaternary hospital, is a public hospital in Durban, KwaZulu-Natal. The Addington Public Hospital is situated in South Beach, Durban, in KZN. The Mahatma Gandhi Memorial Hospital is a public hospital situated in Phoenix, KZN. The Prince Mshiyeni Memorial Hospital is a public hospital in the Durban district of KZN. Northdale is a public hospital located at Dr Chota Motel Road, Pietermaritzburg (PMB), KZN.

3.2 STUDY POPULATION AND SAMPLE SIZE

The research method was retrospective quantitative, and primary data was collected for the six mentioned hospitals in the study location via Central Data Warehouse (CDW) with permission from Academic Affairs and Research Management System (AARMS). Data was received from the CDW for MRSA isolates detected from 2018 to 2022 for patients in the ICUs of the six hospitals. However, due to the very limited ICU data received, since one of six hospitals (Mahatma Gandhi) does not have an ICU ward and the ICU admits fewer patients compared to other hospital wards, we chose to concentrate on the total MRSA prevalence across all wards because low sample numbers may make statistical analysis unreliable.

3.3 STUDY RATIONALE

No study has been conducted previously to determine the prevalence of MRSA at the six mentioned hospitals in the Durban and PMB areas. This gap encouraged me to conduct this research. The study will have a positive impact, as it will assist healthcare officials in understanding the current infection pattern, taking appropriate action, and even making improvements where possible. The findings from this research will be used to educate the public and healthcare staff about the occurrence and prognosis of MRSA infections.

3.4 DATA COLLECTION AND QUALITY CONTROL

This study comprises data from 1 January 2018 to 31 December 2022 collected from six public hospitals in KwaZulu-Natal, namely the King Edward Hospital, Inkosi Albert Luthuli Central Hospital, Addington Public Hospital, Mahatma Gandhi Memorial Hospital, Prince Mshiyeni Memorial Hospital, and the Northdale Hospital. Before the commencement of the study, ethical approval was granted from the Human Science Research Ethics Committee (HSREC), reference number UFS-HSD2023/0401/2609 (Appendix A) at the University of the Free State (UFS), and data were received following approval from the AARMS, reference number: PR2234961 (Appendix B) from the National Health Laboratory Service (NHLS) from the CDW The data consisted of patients from six hospitals mentioned above. Data included positively identified *S. aureus* and MRSA with their antimicrobial susceptibility information.

3.5 ETHICAL CONSIDERATION

All data used in this study were not traceable to any patient or individual. Before supplying the data, the NHLS and AARMS departments removed all patient identifiers except for episode numbers. The data collected include the age, gender, and all *S. aureus* results with the following tests: microscopy, culture, sensitivity, and the hospital where the patient resided, not the participant names since the data were protected as in “Date storage and backup” in the section below. Therefore, there was a minimum possibility of breaches of patient confidentiality. All data used in the study were from routine clinical care investigations; no further investigations were required specifically for this study. The study commenced after full ethical and institutional approval was obtained. This includes the faculty research and innovation committee (FRIC) at the Central University of Technology (CUT), and final approvals were obtained from the University of the Free State-Health Science Research Ethics Committee (HSREC) and NHLS AARMS.

3.6 DATA SHARING/ACCOUNTABILITY

Only the principal investigator (PI) worked with the original data and shared it with the supervisor to have a duplicate. The biostatistician only received the Excel data and had no

access to any other patient data or information. The PI, the supervisor, and I were responsible for ensuring that the data were managed in accordance with POPIA principles, as mentioned in the data plan and protocol (POPIA,2013). I did not plan to collect information that was considered "Personal Information" or Identifiable. Pseudo-anonymous data that were received/collected will be kept for five years to ensure availability in case of queries after publication. If I leave the NHLS/CUT, data and files under my protection will be deleted, and final control will be with the supervisor/CUT or an employee appointed in the event that the supervisor is no longer available.

3.7 STORAGE AND BACKUP

Data were requested in CSV file format to ensure integrity and stored in a double password-protected file/computer and cloud storage as original. The files received were pseudo-anonymised and were then anonymised in the second file in the Figshare platform, which adheres to all security and POPIA requirements. From Figshare, the analysis was done in Excel files that were password protected on the completely deidentified data and stored with a reference that adheres to all security and POPIA requirements folder different from that with the deidentified and pseudo-anonymous information, although the data were anonymous (POPIA,2013). The number was stored in a different file that does not have the metadata of the original study data and identifier. Data were then captured in a Figshare database, which is also password-protected. From there, the anonymous data were analysed in Excel to create documents with my initials as principal investigator, the date created, and protected with passwords. Passwords were changed monthly and documented in a specific file.

3.8 INCLUSION CRITERIA

The results of tests performed on specimens of patients admitted to all wards from January 2018 to December 2022, with MRSA identified from the specimens. Only patients older than 18 years of age were included in the study.

3.9 EXCLUSION CRITERIA

Data that were duplicates of previous samples and data that were not fully filled in due to wrong patient details.

3.10 DATA ANALYSIS

Data are displayed in the form of tables. All patient identities are kept private. Prevalence was calculated, and percentages were given. Descriptive statistics were used to analyse data.

CHAPTER 4: RESULTS

A total of 11 663 samples from all the wards at the six hospitals were analysed using IBM SPSS version 27 for the descriptive analysis. Initially, the aim was to investigate the prevalence of MRSA in ICU wards individually. However, only 158 isolates were from ICUs, and therefore, the data concentrated on the total MRSA isolates from all wards, as indicated in section 3.2 of the methods. This allowed us to make better use of the available data and present a more comprehensive picture of MRSA prevalence in hospitals. Another analysis was done to establish if a specific age group is more susceptible to or affected by an MRSA infection. Of 11 663, 20% (2 357) of *S. aureus* isolates received were resistant to methicillin.

4.1 RESULTS ON *STAPHYLOCOCCUS AUREUS* AND METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS*

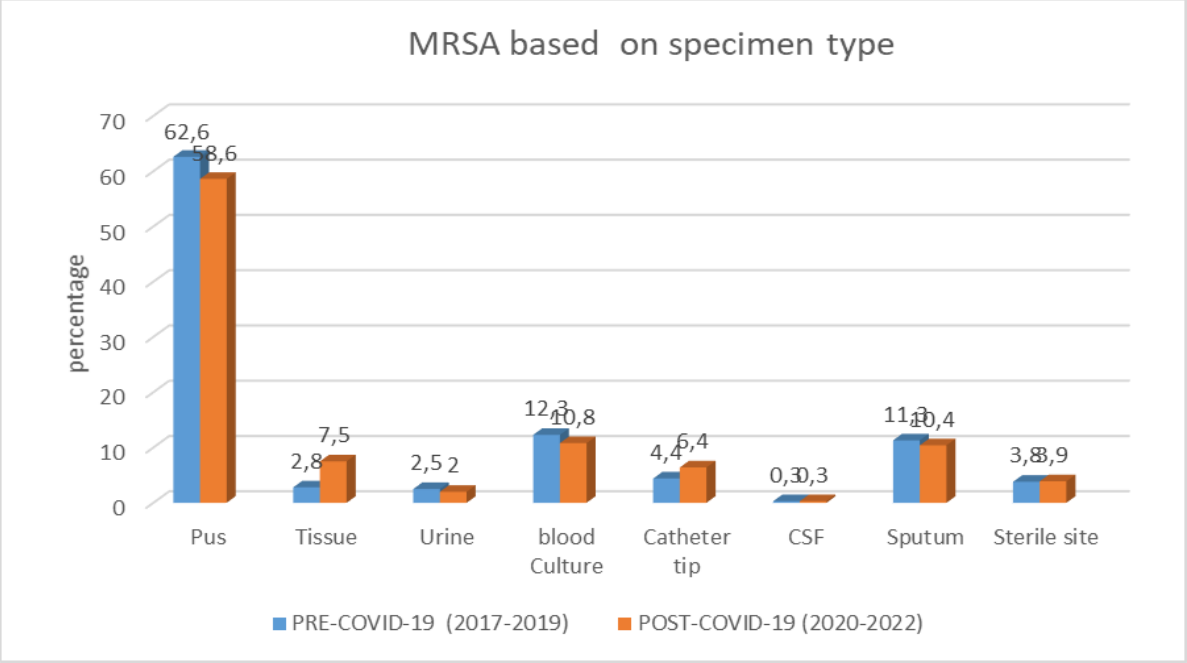
The results in Table 1 and graphs 1 to 3 show the demographic distribution of infections reported in patients across the six KZN hospitals, namely the Inkosi Albert Luthuli Central Hospital, King Edward VIII Hospital, Addington Hospital, Mahatma Gandhi Memorial Hospital, Prince Mshiyeni Memorial Hospital and Northdale over five years from January 2018 to December 2022. Graphs 1 to 3 show a comparison of specimens that showed MRSA infections in patients ages and sex pre-COVID-19 (2018 to 2019) and post-COVID-19 (2020 to 2022).

Table 1: Cross-tabulation methicillin-resistant Staphylococcus aureus and Staphylococcus aureus at hospitals both pre- and post-COVID-19

								phi	p-value
		ADDINGTON HOSPITAL	INKOSI ALBERT LUTHULI CENTRAL HOSPITAL	KING EDWARD VIII HOSPITAL	MAHATMA GANDHI HOSPITAL	NORTHDALE HOSPITAL	PRINCE MSHIYENI MEMORIAL HOSPITAL		
PRE-COVID-19 (2018–2019)	**MRSA Total=1044**	**52**	**329**	**137**	**93**	**315**	**118**	0,388	0,000
		5,0%	**31,5%**	**13,1%**	**8,9%**	**30,2%**	**11,3%**		
Total = 5 364	*STAPH*	*952*	*934*	*317*	*146*	*2771*	*244*		
		17,7%	*17,4%*	*5,9%*	*2,7%*	*51,7%*	*4,5%*		
POST-COVID-19 (2020–2022)	**MRSA Total=313**	**69**	**351**	**143**	**84**	**529**	**137**	0,305	0,000
		5,3%	**26,7%**	**10,9%**	**6,4%**	**40,3%**	**10,4%**		
Total = 6 299	*STAPH*	***1411***	***1047***	***427***	***143***	***2941***	***330***		
		22,4%	*16,6%*	*6,8%*	*2 3%*	*46,7%*	*5,2%*		

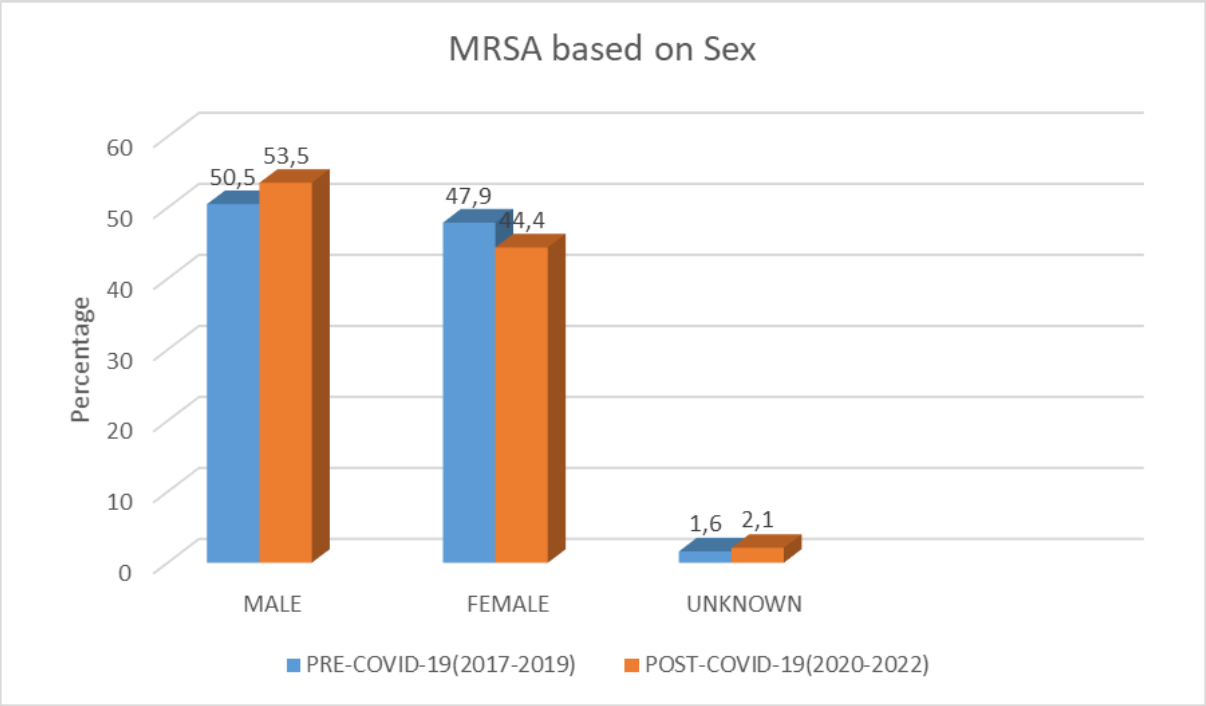
The cross-tabulation results in Table 1 show the prevalence of MRSA against total isolated *Staphylococcus aureus* across individual different hospitals pre- and post-COVID-19 pandemic. Northdale Hospital had the highest rate of *Staphylococcus aureus* infections (51,7%), followed by Addington (17,7%) and Inkosi Albert Luthuli Central Hospital (17,4%). The results show that prior to COVID-19 (2018-2019) MRSA infection cases were the most commonly reported at the Inkosi Albert Luthuli Central Hospital (31,5%) and Northdale Hospital (30,2%), with lower percentages at other hospitals. The phi coefficient of 0.388 and a p-value of 0.000 indicate a strong and statistically significant relationship between hospital names and infection rates throughout this period. Laboratory identification of cases post-COVID-19 reported high incidences at Northdale Hospital (46,7%), with considerable numbers at Addington Hospital (22,4%) and Inkosi Albert Luthuli Central Hospital (16,6%). Despite the decline in the phi coefficient to 0.305, the relationship between hospitals and infection rate after COVID-19 remained statistically significant (p-value of 0.000).

4.2 METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* LABORATORY SPECIMEN AND DEMOGRAPHIC INFORMATION FROM SIX HOSPITALS IN KWAZULU-NATAL PRE- AND POST-COVID-19



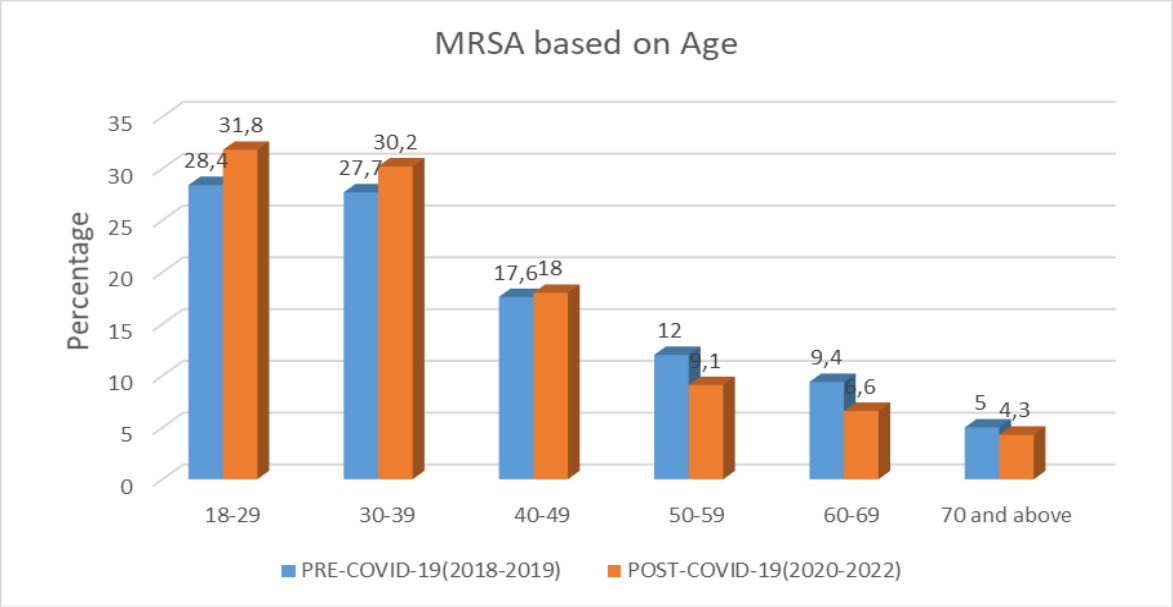
Graph 1: Distribution of methicillin-resistant Staphylococcus aureus isolated from patients attending six KwaZulu-Natal hospitals based on the type of specimen from 2018–2019 (pre-COVID-19) and 2020 to 2022 (post-COVID-19)

Graph 1 shows the results of the specimen types analysed from the six KwaZulu-Natal hospitals in this study. It indicates that 62,6% (654) pre-COVID-19 and 58,6% (769) post-COVID-19 MRSA were isolated from pus, 12,3% pre-COVID-19 and 10,8% post-COVID-19 from blood cultures. Other specimen types yielded 11% and less. Only 0.3% of MRSA was isolated in CSF specimens pre- and post-COVID-19.



Graph 2: Distribution of methicillin-resistant Staphylococcus aureus isolated from patients attending six KwaZulu-Natal hospitals from 2018–2019 (pre-COVID-19) and 2020–2022 (post-COVID-19) based on sex

Methicillin-resistant *Staphylococcus aureus* cases in the study (Graph 2), were closely distributed between males (50,5%) and females (47,9%) prior to the pandemic (2017–2019), and more male (53,5%) hospitalisation was observed in 2020–2022, while a reduction was observed in females post-COVID-19 to 44,4%.



Graph 3: Distribution of methicillin-resistant staphylococcus aureus isolated from patients attending six KwaZulu-Natal hospitals based on age from 2018–2019 (pre-COVID-19) and 2020 to 2022 (post-COVID-19)

Group age determination assists with understanding how the organism spread within the community, taking into consideration the period of the study during the COVID-19 era. The proportion of cases within the 18–29 and 30–39 age categories were 28,4% and 31,8%, respectively, overall 60,2% of all cases. These slowly decreased in both groups post-COVID-19 to 27,7% and 30,2%, respectively.

4.3 METHICILLIN-RESISTANT *STAPHYLOCOCCUS* ANTIBIOTICS BASED ON HOSPITALS ISOLATED AT PRE-AND POST-COVID-19 IN KWAZULU-NATAL

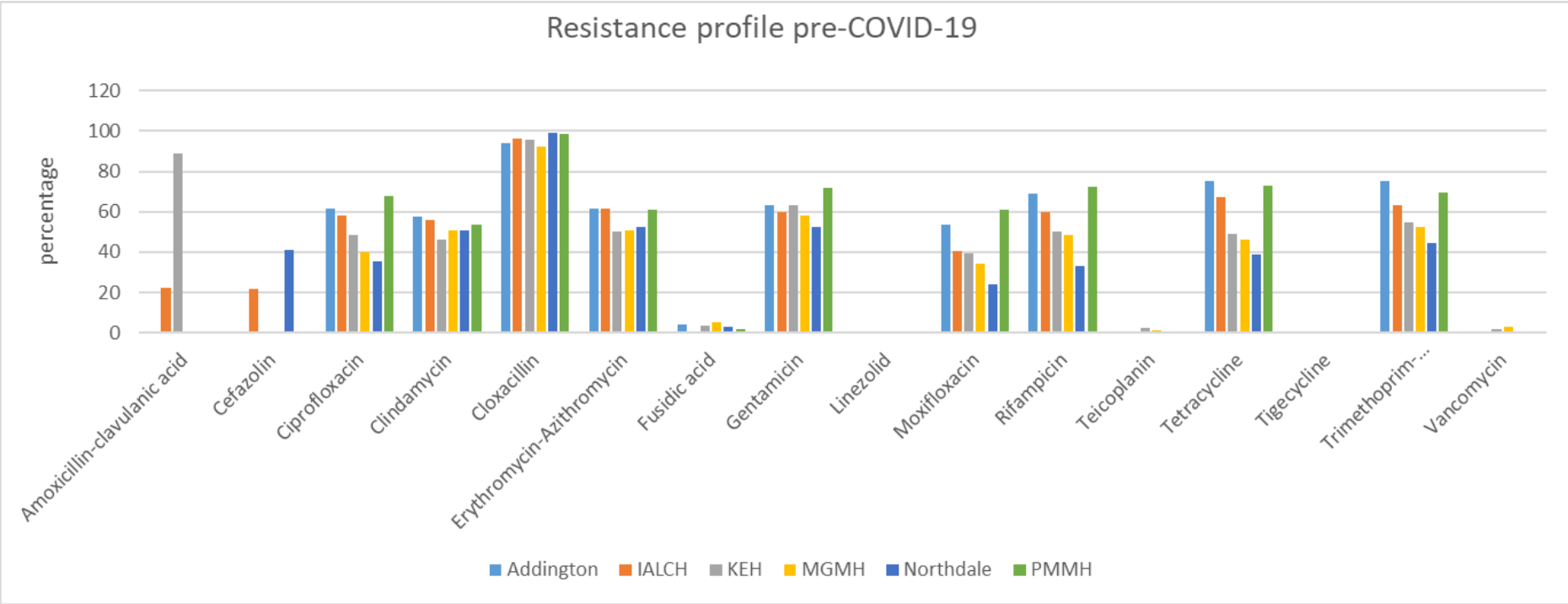
Table 2 compares the antimicrobial susceptibility during 2018 and 2019 to that of the years 2020 to 2022 in data analysed from all six hospitals used for the study. The representation of “null” illustrated in the table accounts for the percentage of antibiotics that were not tested for sensitivity or resistance against MRSA at some of the hospitals.

Table 2: Susceptibility profiles of methicillin-resistant staphylococcus aureus to different antibiotics both pre-COVID-19 and post-COVID-19

	Pre-COVID-19 (2018–2019)				Post-COVID-19 (2020–2022)			
Antibiotic tested	Sensitivity	Intermediate	Resistance	Null	Sensitivity	Intermediate	Resistance	Null
Penicillin-ampicillin	3(0.3%)	1(0.1%)	964(92.3%)	76(7.3%)	2(0.2%)	0	1203(91.6%)	108(8.2%)
Cloxacillin	15(1.4%)	0	1011(96.8)	18(1.7%)	17(1.3%)	0	1293(98.5%)	3(0.2%)
Moxifloxacin	450(43.1%)	128(12.3%)	394(37.7%)	72(6.9%)	541(41.2%)	125(9.5%)	533(40.6%)	114(8.7%)
Ciprofloxacin	422(40.4%)	32(3.1%)	519(49.7%)	71(6.8%)	522(39.8%)	14(1.11%)	671(51.1%)	106(8.1%)
Clindamycin	433(41.5%)	1(0.1%)	547(52.4%)	63(6%)	434(33.1%)	1(0.1%)	792(60.3%)	86(6.5%)
Erythromycin-Azithromycin	390(37.4%)	1(0.1%)	589(56.4%0	64(6.1%)	362(27.6%)	2(0.2%)	849(64.7%)	100(7.6%)
Gentamicin	345(33%)	0	622(59.6%)	77(7.4%)	335(25.5%)	3(0.2%)	863(65.7%)	112(8.5%)
Linezolid	968(92.7%)	0	0	76(7.3%)	1203(91.6%)	0	0	110(8.4%)
Moxifloxacin	450(43.1%)	128(12.3%)	394(37.7%)	72(6.9%)	541(41.2%)	125(9.5%)	533(40.6%)	114(8.7%)
Fusidic Acid	934(89.5%)	0	30(2.9%)	80(7.7%)	1164(88.7%)	0	37(2.8%)	112(8.5%)
Rifampicin	431(41.3%)	1(0.1%)	533(51.1%)	79(7.6%)	619(47.1%)	2(0.2%)	581(44.2%)	111(8.5%)
Trimethoprim-sulfamethoxazole	379(36.3%)	0	594(56.9%)	71(6.8%)	457(34.8%)	0	750(57.1%)	106(8.1%)
Tetracycline	378(36.2%)	0	579(55.5%)	87(8.3%)	561(42.7%) %)	0	638(48.6%)	114(8.7%)
Tigecycline	956(91.6%0	0	0	88(8.4%)	1191(90.7%)	0	0	122(9.3%)
Teicoplanin	963(92.2%)	1(0.1%)	6(0.6%)	74(7.1%)	1181(89.9%)	4(0.3%)	11(0.8%)	117(8.9%)
Vancomycin	1016(97.3)	2(0.2%)	6(0.6%)	20(1.9%)	1293(98.5%)	2(0.2)	4(0.3%)	14(1.1%)

The examination of MRSA susceptibility to antimicrobial agents, particularly in the resistance patterns of the five essential medicines: penicillin, ciprofloxacin/moxifloxacin, clindamycin, erythromycin-azithromycin and gentamicin resistance, was high and increased over the years. Ciprofloxacin resistance increased from 49,7% to 51,1%, showing that resistance levels remain strong. Clindamycin resistance rose from 52,4% to 60,3%. Similarly, erythromycin-azithromycin resistance grows dramatically from 56,4% to 64,7%, resulting in a decrease in sensitivity. Gentamicin resistance also increased from 59,6% to 65,7%, resulting in a decrease in sensitivity. Vancomycin sensitivity increased from 97,3% to 98,5%.

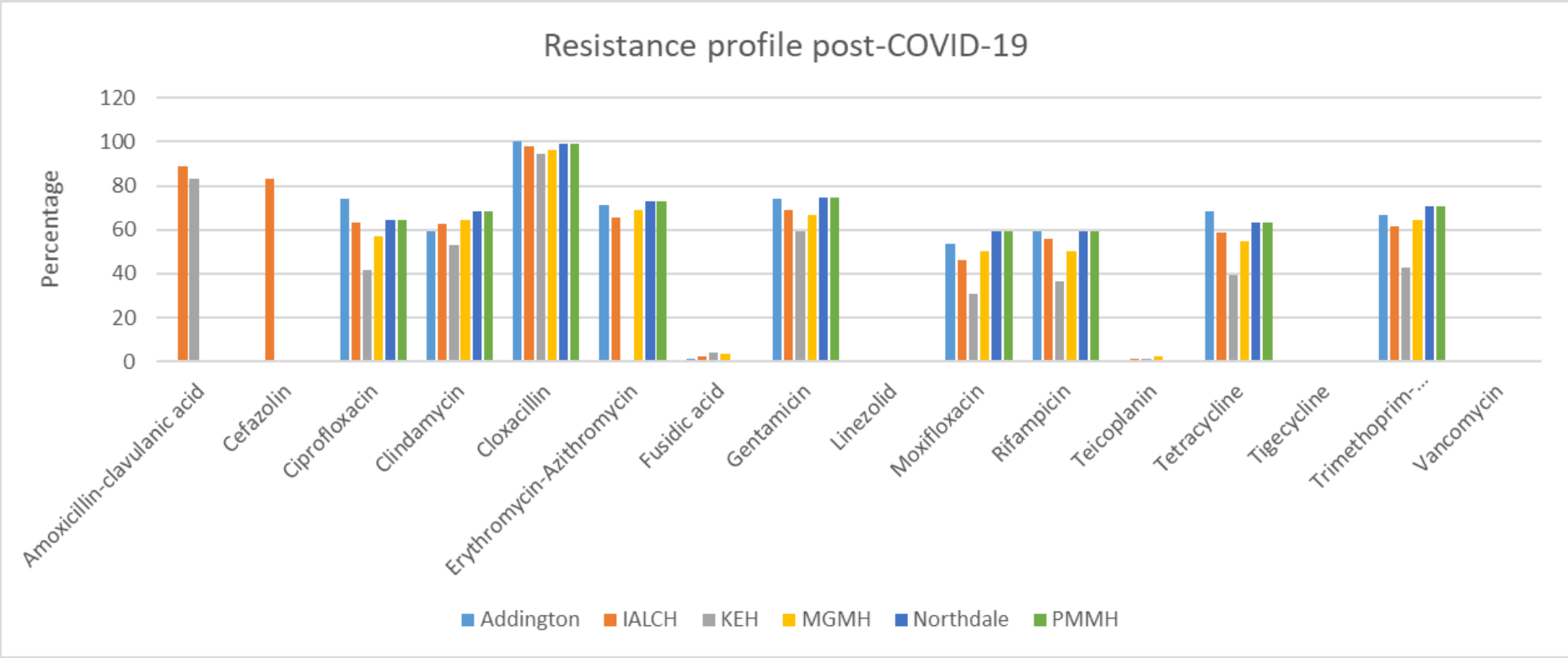
4.4 ANTIBIOTICS TESTED IN ADDINGTON, IALCH, KEH, MGMH, NORTHDALE AND PMMH.



Graph 4: Antimicrobial resistance profiles of Methicillin-resistant Staphylococcus aureus isolated from patients attending six KwaZulu-Natal hospitals from 2018–2019 (pre-COVID-19)

Table 3: Resistance profiles of methicillin-resistant Staphylococcus aureus to different antibiotics for pre-COVID-19

Antibiotic tested	Addington	IALCH	KEH	MGMH	Northdale	PMMH
Amoxicillin-clavulanic acid	0	22.5	89.1	0	0.3	0
Cefazolin	0	21.6	0	0	40.9	0
Ciprofloxacin	61.5	58.4	48.2	39.8	35.6	67.8
Clindamycin	57.5	55.9	46.0	50.5	50.8	53.4
Cloxacillin	94.2	96.4	95.6	92.5	99.0	98.3
Erythromycin-Azithromycin	61.5	61.7	50.4	50.5	52.7	61.0
Fusidic acid	3.8	0.3	3.6	5.4	3.2	1.7
Gentamicin	63.5	60.0	63.5	58.1	52.4	72
Linezolid	0	0	0	0	0	0
Moxifloxacin	53.8	40.4	39.4	34.4	23.8	61
Rifampicin	69.2	59.7	50.4	48.4	33.33	72.2
Teicoplanin	0	0.3	2.2	1.1	0.3	0
Tetracycline	75	67.2	48.9	46.2	39	72.9
Tigecycline	0	0	0	0	0	0
Trimethoprim-sulfamethoxazole	75	63.5	54.7	52.7	44.4	69.5
Vancomycin	0	0.3	1.5	3.2	0	0



Graph 5: Antimicrobial resistance profiles of Methicillin-resistant Staphylococcus aureus isolated from patients attending six KwaZulu-Natal hospitals from 2020–2022 (post-COVID-19).

Table 4: Resistance profiles of methicillin-resistant Staphylococcus aureus to different antibiotics for post-COVID-19.

Antibiotic tested	Addington	IALCH	KEH	MGMH	Northdale	PMMH
Amoxicillin-clavulanic acid	0	88,9	83,2	0	0	0
Cefazolin	0	83,2	0	0	76,6	0
Ciprofloxacin	73,9	63,5	41,9	57,1	37,9	64,2
Clindamycin	59,4	62,7	53,1	64,3	58,0	68,6
Cloxacillin	100	98	94,4	96,4	99.8	99,3
Erythromycin-Azithromycin	71	65,5	56.6	69,0	62,6	73
Fusidic acid	1,4	2,6	4,2	3,6	3,4	0
Gentamicin	73,9	68,9	59,4	66,7	61,8	74,5
Linezolid	0	0	0	0	0	0
Moxifloxacin	53,6	46,4	30,8	50,0	31,4	59,1
Rifampicin	59,4	56,1	36,4	50	31,8	59,1
Teicoplanin	0	1,1	1,4	2,4	0,6	0
Tetracycline	68,1	58,7	39,2	54,8	37	63,5
Tigecycline	0	0	0	0	0	0
Trimethoprim-sulfamethoxazole	66,7	61,8	42,7	64,3	52,0	70,8
Vancomycin	0	0	0,7	3.6	0	0

Graphs 4 and 5 results, including Tables 3 and 4, show resistance profiles in all six hospitals for both pre and post-COVID-19. The graphs give an overview of the resistance patterns and show the high resistance to cloxacillin, especially in all six hospitals pre- and post-COVID-19. At the same time, the specific numbers can be seen in the comparative Tables 3 and 4. In Addington Hospital, cloxacillin revealed a resistance rate of 94,2% pre-COVID-19, and all isolates were 100% resistant post-COVID-19. A high resistance pattern was observed in tetracycline and trimethoprim-sulfamethoxazole, with 75% pre-COVID-19. Post-COVID-19, a greater than 60% resistance rate was observed in ciprofloxacin, erythromycin-azithromycin, gentamicin, tetracycline and trimethoprim. At IALCH, a high resistance rate of greater than 60% was noted in cloxacillin (96,4%), erythromycin-azithromycin (61,7%), tetracycline (67,2) and trimethoprim-sulfamethoxazole (63,5%) in pre-COVID-19. A high resistance rate post-COVID-19 was noted in amoxicillin-clavulanic acid (88,9%), as opposed to pre-COVID-19 (22,5%). The King Edward Hospital's high resistance rate was also seen in amoxicillin-clavulanic acid (89,1%), cloxacillin (95.6%) and gentamicin (63,5%) pre-COVID-19. Post-COVID-19 showed a resistant pattern of 83,2% and 94,4%, respectively, in amoxicillin-clavulanic acid and cloxacillin. For MGMH, a high resistance pattern of 92.5% was observed in cloxacillin. Cloxacillin shows a resistance of 92,5% and 96,4%, respectively, both pre- and post-COVID-19. The Northdale revealed that the resistance rate post-COVID-19 was elevated in cefazolin (76,6%) compared to pre-COVID-19 (40,9%). This high value is not alarming because it is due to a high number of null in pre-COVID-19. The PMMH showed that the resistance rate was significantly high in cloxacillin both pre- and post-COVID-19, with 98,3% and 99,3%, respectively. Rifampicin and tetracycline also show high resistance rates of 72.2% and 72.9%, respectively, pre-COVID-19.

CHAPTER 5: Discussion

The results from the study indicate 5 364 samples from 2018 to 2019 (pre-COVID-19), 1 044 were MRSA. The results showed that the rate of methicillin resistance among identified *S. aureus* isolates from the results of patients at six KZN hospitals was 19,46%. Furthermore, there was a similar trend from 2020–2022 (post-COVID-19). Out of 6 299 *S. aureus* isolates, 1 313 were resistant to methicillin, indicating a rate of 20,84%. The overall estimated prevalence of MRSA over five years in six KZN hospitals (2018–2022) was 20,21%. This is a significantly high prevalence, indicating a serious public health implication because MRSA infections are more difficult to cure than MSSA. As this study was based on case incidences, the rate indicates the risk is high among the population. The results correlate with other studies that have even linked high prevalence rates of MRSA with prolonged hospitalisation and high cases of hospitalisations that eventually have tremendous effects on healthcare systems and expenses (Abramson, 1999; Capitano *et al*., 2003). Another study that supports this study's findings was done at the Janaki Medical College Teaching Hospital, conducted from January 2016 to December 2017, which reported an even higher prevalence of MRSA at 39,5% (Yadav & Prakash, 2016).

These results are also supported by studies done in South Africa, showing a similar trend where MRSA was found to be 23% at two academic hospitals in Johannesburg between the years 1999 and 2002 (Perovic *et al*., 2006) and 19% at Chris Hani Baragwanath Academic Hospital, between January and December (Raphulu *et al*., 2023). The overall MRSA rate for this study further correlates with the study conducted in KZN, Tugela Ferry, on a TB ward in the Church of Scotland, where MRSA was 21% (Falagas, 2013). In contrast, this study's results are lower than those from the study conducted at several hospitals across Iran from June 2018 to March 2020, where the prevalence of MRSA was 42% (Serrafzadeh *et al*., 2021). According to a report from National Nosocomial Infection Surveillance, the prevalence of MRSA in ICU collected between 1992 to 2003 was 50% (Fridkin *et al*., 2004).

There is a slight increase in MRSA cases following COVID-19. This increase is not as significant (19,46% to 20,4%). It can be assumed, based on the results, that COVID-19 did not significantly impact the pattern of MRSA cases at these hospitals. Another study conducted in Australia reported a similar trend where the MRSA pattern was not affected by the COVID-19 pandemic

(Zarfel *et al*., 2023). Contrary to this study, Weiner and colleagues conducted a study in the United States, which reported a significant 34% rise in MRSA infections during COVID-19 compared to pre-COVID-19 (Weiner *et al*., 2019). The prevalence of *S.aureus* and MRSA in this study were high in males compared to females in both pre-COVID-19 and post-COVID-19. This is similar to the study conducted in South India at a tertiary-care hospital from January 2013 to December 2015, where MRSA was also found to be more common in males than females (Arunkumar *et al*., 2017). In the study conducted in Nigeria to evaluate the prevalence of MRSA from hospitalised wound patients at a tertiary hospital in Enugu Metropolis, the prevalence was discovered to be 22%, with more females (12,2%) having MRSA than males (9,6%) (Chukweze *et al*., 2022).

In this study, patients from the young adult age group (18–29) are most likely to be colonised with MRSA and *S.aureus* during both pre- and post-COVID-19. The isolation rate was significantly higher in age groups from 18–29 years and 30–40 years and significantly low in patients from 74 years and above. The median age of 32 was found across all patients used in the study at all six hospitals. This is also similar to the study conducted in Asmara where they found the highest MRSA rate from the 19–40 age group and lowest MRSA strain in adults (>60 years) (Eyob *et al*., 2019). This study correlates with the study done in Nepal from May to November 2015, where the highest number of MRSA was found in the ages 21–40 years (Khanal *et al*., 2021). The isolation of these organisms in this study was most likely from pus specimens. MRSA causes infections like abscesses, boils and cellulitis, resulting in pus formation. The study conducted in Asmara in 2016 (February to May) also reports higher prevalence of *S.aureus* isolation in pus samples, as opposed to blood samples (Eyob *et al*., 2019).

Amongst patients from six KZN hospitals included in this study, a high prevalence of *S. aureus* cases was observed at the Northdale Hospital, followed by Addington, and then Inkosi Albert Luthuli Central Hospital both pre- and post-COVID-19. This is due to the fact that Northdale Hospital is in Pietermaritzburg (UMgungundlovu district) and is the only hospital with a full microbiology laboratory in that area. All samples for culture are sent to Northdale Hospital. Pre-COVID-19, a high prevalence of MRSA was observed at Northdale and post-COVID-19, a high prevalence of MRSA was seen at Inkosi Albert Luthuli Central Hospital, compared to other hospitals. This could be because IALCH is a referral and central hospital. Chances are

that MRSA will be high, since patients referred to this hospital have complicated, serious illnesses and are immunocompromised.

The prevalence of MRSA at Addington during the pre-COVID-19 and post-COVID-19 period increased by 0,3%, 5% and 5,3%, which indicates a difference of 3% from a study done in 2021 at the same hospital, which reported 8% over the one-year period of study (1 January to 1 December 2021) (Dube *et al*., 2024). This slight difference from this study could be due to the fact that the focus of the current study was on the prevalence of MRSA among patients older than 18 years of age only, while in the study conducted at Addington, the focus was on all consenting groups.

The prevalence of MRSA at six KZN hospitals in ICU was 6% in pre-COVID-19 and 7,2% post-COVID-19. The overall was 6,7%. These results differ from the study done in Europe across multiple intensive care units for a one-year period in 1992 where MRSA prevalence was found to be 57% (Vincent *et al*., 1995). According to a report from National Nosocomial Infection Surveillance, the prevalence of MRSA at hospitals across the United State in ICU from the data collected between 1992 to 2003 was 50% (Fridkin *et al*., 2004).

The drug of choice for this study was found to be linezolid, tigecycline, vancomycin, teicoplanin and fusidic acid due to high sensitivity rate in all six hospitals. High sensitivity profile was observed in vancomycin with 97.3% in pre-COVID-19 and 98.5% post-COVID-19. This tends to be similar to the study conducted at Addington Hospital from January 2021 to December 2021, which revealed that all samples were 100% susceptible to vancomycin (Dube *et al*., 2024). This is similar to the study done at a tertiary-care centre in Riyadh, Saudi Arabia between January 2013 to June 2017, where all isolates tested were susceptible to vancomycin, linezolid and tigecycline (Alhunaif *et al.*, 2021). These findings were also comparable to the study conducted in Delhi, India at a tertiary-care hospital, which revealed that the prevalence of MRSA was 39% and was commonly isolated in blood samples. All isolates were sensitive to linezolid antibiotics and a high resistance rate to erythromycin (82,1%), clindamycin (56,4%) and ciprofloxacin (53,8) was observed (Gaurav *et al.*, 2019).

Methicillin-resistant *Staphylococcus aureus* was highly resistant to cloxacillin at all six hospitals, with a percentage of >90%. This correlates with the study done in South India, at a

tertiary-care hospital where MRSA strains were also found to be resistant to cloxacillin (Arunkumar *et al*., 2017). King Edward Hospital and IALCH tested for susceptibility in amoxicillin clavulanic acid and a high resistance pattern was also observed. This is similar to the study conducted in South Africa as part of national survey from 2010 to 2012 by the National Institute for Communicable Diseases (NICD), where the study showed a significant resistance pattern on amoxicillin-clavulanic acid (Pervic *et al*., 2012). Isolates from this study show a high resistance pattern to ciprofloxacin, erythromycin, gentamicin, tetracycline and trimethoprim. This is similar to the study that was conducted in South Africa to assess the susceptibility of MRSA isolates in the country utilising data from both NHLS and private laboratories which discovered that MRSA was often resistant to similar antibiotics such as ciprofloxacin, erythromycin, gentamicin, tetracycline and trimethoprim, and all MRSA were sensitive to vancomycin (Marais *et al*., 2009).

CHAPTER6: CONCLUSION

The overall prevalence of MRSA from 2018 to 2022 was 20.2%, which is very concerning. There is a slight rise in MRSA cases following COVID-19, although this increase is not dramatic. This leads to a conclusion that COVID-19 did not have a significant impact on MRSA cases. Additional investigation and a bigger sample size may be required to assess the statistical significance of this increase and to investigate any potential correlations between COVID-19 and MRSA. MRSA was highly sensitive to vancomycin, tigecycline, teicoplanin, fusidic acid and linezolid. Some strains may be resistant to these antibiotics, emphasising the necessity for ongoing surveillance and the potential development of new treatment alternatives. High sensitivity rates indicate that these antibiotics can still be used to treat MRSA infections, although potential resistance should be considered, and adequate susceptibility testing should be conducted. MRSA was highly resistant to cloxacillin and penicillin-ampicillin. Findings from this research confirm that males are a vital risk factor for MRSA as more males than females were found to be colonised with MRSA. Further investigation will be required to find the aetiology of these discoveries.

6.1 RECOMMENDATIONS

Due to high sensitivity, linezolid, teicoplanin, tigecycline, vancomycin and fusidic acid are recommended as first-line therapies for suspected MRSA infections. Regular susceptibility testing is recommended to guarantee effective treatment and to check for resistance development. Improve hygiene practices in healthcare environments such as frequent hand washing and the use of personal protective equipment. Implement MRSA screening programs in high-risk patients (those with a history of MRSA, recent hospitalisation or invasive surgeries). To avoid cross infection it is advisable to isolate patients who have been confirmed with MRSA. The future researchers must also dwell much on the cause of higher prevalence of MRSA in males than females.

6.2 LIMITATIONS

The study aimed to determine the prevalence of methicillin-resistant *staphylococcus aureus* among patients admitted to ICU of six KZN hospitals. However, due to a small sample size in ICU wards, the scope was extended to include all wards. One of these six hospitals (Mahatma Gandhi Hospital) does not have an ICU ward, limiting the initial focus. As a result, the findings reflect the prevalence of MRSA in all wards rather than only ICUs. Further study with larger sample numbers and more specialised ICU data are needed to estimate MRSA frequency correctly in these critical-care settings. The prevalence of MRSA among patients admitted to intensive care units at six KZN hospitals was 6.7%.

REFERENCES

Alhunaif, S.A., Almansour, S., Almutairi, R., Alshammari, S., Alkhonain, L., Alalwan, B., Aljohani, S., Alsaedy, A., Bosaeed, M. & Alothman, A. 2021. Methicillin-Resistant *Staphylococcus Aureus* bacteremia: epidemiology, clinical characteristics, risk factors, and outcomes in a Tertiary Care Center in Riyadh, Saudi Arabia. *Cureus*, 10, 13(5), e14934. doi: 10.7759/cureus.14934. PMID: 34123631; PMCID: PMC8189534.

Arunkumar, V., Sudhaharan, S. & Manoharan, A. 2017. Prevalence and antibiogram of Methicillin-Resistant *Staphylococcus aureus* in a Tertiary Care Hospital in South India: A retrospective study. *International Journal of Microbiology*, 2017, Article ID 8105095. doi:10.1155/2017/8105095.

Behring, J. 2022. Mechanisms of antibiotic resistance in microorganisms. *Journal of Infectious Diseases and Antibiotics*, 15(4), pp.234-240.

Becker, K., Heilmann, C. & Peters, G. 2014. Coagulase-negative staphylococci. *Clinical Microbiology Reviews*, 27(4), pp.870-926.

Bell, J.M., Turnidge J.D., Nimmo G., Schooneveldt, J., Lim, I. & Xiao M.,2002. High prevalence of oxacillin resistant *Staphylococcus aureus* isolates from hospitalised patients in Asia-Pacific and South Africa: results from SENTRY antimicrobial surveillance program, 1998–1999. *Antimicrobial Agent and chemotherapy*, 46, pp.879-881.

Bouchillon, S.K., Johnson, J.A. & Stuart, R.L. 2004. Prevalence of methicillin-resistant *Staphylococcus aureus* in South Africa: Results from the Pan-European Antimicrobial Resistance Local Surveillance (PEARLS) study. *International Journal of Antimicrobial Agents,* 24(5), pp.419-426.

Boyce, J. M., Potter-Bynoe, G., Chenevert, C., & King, T. (1997). Environmental Contamination Due to Methicillin-Resistant *Staphylococcus aureus*: Possible Infection Control Implications. *Infection Control & Hospital Epidemiology*, *18*(9), 622–627. doi:10.1086/502213.

Brumfitt, W. & Hamilton-Miller, J. 1989. *Methicillin-resistant Staphylococcus aureus*. *N Engl J Med*, 320, pp.1188-1196.

Burrett, F.F., McGehee R.F. Jr. & Finland, M. 1968. Methicillin resistant *Staphylococcus aureus* at Boston hospital city: Bacteriologic and epidemiologic observations. *N Engl J Med,* 279, pp.441-448.

Campos, M.L., Cipriano, Z.M. & Freitas P.F. 2021. Suitability of NNIS index for estimating surgical-site infection risk at small university hospital in Brazil. *Infect. Control Hosp. Epidemiol,* 22, pp.268-272.

Carrl, R. 2008. MRSA: A global health concern. *Journal of Infectious Diseases*, 198(10), pp.1435-1442.

Centers for Disease Control and Prevention [CDC]. 2007. Guideline for isolation precautions: Preventing transmission of infectious agents in healthcare settings. [Accessed 10 July 2024].

Centers for Disease Control and Prevention [CDC]. 2019. *MRSA: Transmission*. Retrieved from https://www.cdc.gov/mrsa/community/index.htm. [Accessed 10 July 2024].

Chambers, H.F. & Deleo, F.R. 2009. Waves of resistance: *Staphylococcus aureus* in the antibiotic era. *Nat. Rev. Microbiol,* 7, pp.629-641.

Chokshi, A., Sifri Z., Cennimo, D. and Horng H. 2019. Global contributors to antibiotic resistance. *J Glob Infect Dis,* 11(1), pp.36-42.

Chukwueze, C.M., Chidimma, M., Theophilus, K.U., Emmanuel, I.O., Justina, N.I. & Asogwa, Nneka., 2022. Relevance of Methicillin-resistant *Staphylococcus aureus* infections among hospitalised wound patients from selected Tertiary Hospitals within Enugu Metropolis. *Journal of Advances in Medical and Pharmaceutical Sciences* 24 (3), pp.18-27.

Coovadia, Y.M., Bhamjee, A. & Kesson, C.M. 1989. Methicillin-resistant *Staphylococcus aureus* in a neonatal intensive care unit: The first reported pandemic in South Africa. *Journal of Hospital Infection,* 14(3), pp.275-281.

Cosgrove, S.E., Sakoulas, G., Perencevich, E.N., Schwaber, M.J., Karchmer, A.W. & Carmeli, Y. 2003. Comparison of mortality associated with methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* bacteremia: a meta-analysis. *Clin Infect Dis*, 36(1), pp.53-59.

Cosgrove, S.E., Qi Y., Kaye, K.S., Harbath, S. Karchmer, A.W. & Carmeli, Y. 2005. The impact of methicillin-resistance in *Staphylococcus aureus* on patients' outcomes. *Infect Control Hosp Epidemiol,* 26, pp.166-174.

Dellit, T., Owens, R. & McGowan, J.E. Jr. 2007. Infectious Diseases Society of America and the Society of Healthcare Epidemiology of America Guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis,* 44, pp.159-77.

Dube, T., Moyo, S. & Naidoo, K. 2024. Prevalence and gender distribution of methicillin-resistant *Staphylococcus aureus* (MRSA) infections in a one-year study at Addington Hospital, KZN. *South African Medical Journal*, 114(3), pp.210-217.

Duckworth, G. 2003. Controlling methicillin-resistant *Staphylococcus aureus*. *British Med Journal,* 327, pp.1177-1178.

European Centre for Disease Prevention and Control. 2010. Annual epidemiological report on communicable diseases in Europe. *European Centre for Disease Prevention and Control*

(ECDC). Retrieved from https://ghdx.healthdata.org/record/european-centre-disease-prevention-and-control-annual-epidemiological-report-communicable.

Ewans, T.M., Ortiz C.R. & LaForce, F.M. 1999. Prevention and control of nosocomial infection in the intensive care unit. *Intensive Care Unit,* 4, pp.1074-1080.

Falag, M., Moshiri, F. & Ziegler, C. 2013. Trends in the prevalence of methicillin-resistant *Staphylococcus aureus* in South Africa: 2007–2011. *South African Journal of Epidemiology and Infection,* 28(1), pp.13-19.

Ferraz, V., Duse A.G., Kassel, M., Black, A.D., Ito T. & Hiramatsu, K. 2000. Vancomycin-resistant *Staphylococcus aureus* occurs in South Africa. *SAfr Med J*, 90, p.1113.

Fortuin-de Smidt, M.C., Singh-Moodley, A., Badat, R., Quan, V., Kularatne, R., Nana, T., Lekalakala, R., Govender, N.P. & Perovic, O. 2015. *Staphylococcus aureus* bacteraemia in Gauteng academic hospitals, South Africa. *International Journal of Infectious Diseases*, 30, pp.41-48.

Fridkin, S.K., Hageman, J.C., Morrison, M., Sanza L.T., Como-Sabetti, K., Jernigan, J.A., Harriman, K., Harrison, L.H. & Lynfield, M.M. 2005. Active bacterial core surveillance program of the emerging infection program network. Methicillin-resistant *Staphylococcus aureus* disease in three communities. *Med,* 352, pp.1436-1444.

Fridkin, S.K., Hageman, J.C., Morrison, M., Sanza, L.T., Como-Sabetti, K., Jernigan, J.A., Harriman, K., Harrison, L.H., Lynfield, R. & Farley, M.M. 2005. Methicillin-resistant *Staphylococcus aureus* disease in three communities. *New England Journal of Medicine*, 352(14), pp.1436-1444.

Gaurav, K. & Rajesh, T., 2019. Prevalence of MRSA in ICU in Tertiary Care Hospital. *Ann. Int. Med. Den. Res,* 5(4), MB19-MB22.

Goldstein, E.J.C. 2012. Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) in athletes and military personnel: Risk factors and prevention. *Sports Medicine and Infectious Diseases*, 54(3), pp.217-225.

Gorwitz, R.J. 2008.*Journal of Disease Surveillances*, 197, pp.226-34.

Harbarth, S., Hawkey, P.M., Tenover, F., Stefani, S., Pantosti, A. & Struelens, M.J. 2011. Update on screening and clinical diagnosis of methicillin-resistant *Staphylococcus aureus* (MRSA). *International Journal of Antimicrobial Agents*, 37(2), pp.110-117.

Huang, S.S., Umscheid, C.A., Mitchell, M.D,. (2014). Impact of Routine Visitor Contact Precautions on Health Care-Associated Infections in Acute Care Hospitals. Infection Control & Hospital Epidemiology, 35(9), 1062-1070.

Calfee, D. P., Salgado, C. D., Milstone, A. M., Harris, A. D., Kuhar, D. T., Moody, J., Aureden, K., Huang, S.S.,2014. Strategies to prevent methicillin-resistant *Staphylococcus aureus* transmission and infection in Acute Care Hospitals: 2014 Update. *Infection Control & Hospital Epidemiology*, *35*(S2), S108–S132. doi:10.1017/S0899823X00193882.

JAMA**.** 1994. Gram-positive cocci: The most common pathogens in hospital infections worldwide. *JAMA: The Journal of the American Medical Association, 272*(9), 725-730.

Husney, A. & Thompson, E.G. 2021. Lung problems: Learning to breathe easier. *MD-Internal Medicine.* [Accessed 10 March 2024].

Jeffery, K.J., Bateman, L.A. & Munoz-Price, L.S. 2021. Impact of public health measures on the transmission of methicillin-resistant *Staphylococcus aureus* (MRSA) during the COVID-19 pandemic. *Infection Control & Hospital Epidemiology*, 42(9), pp.1086-1093.

Jevons, M.P. 1961. Celbenin-resistant staphylococci. *British Medical Journal*, 1(5219), pp.124-125.

Johnson, A. P. 2011. The epidemiology of *Staphylococcus aureus* infections in the United States. *Clinical Infectious Diseases,* 52(1), pp.88-95.

Johnson, A.P. 2022. Prevalence and variability of hospital-acquired MRSA in Europe: data from the European Antimicrobials Resistance Surveillance System (EARSS). *Journal of Hospital Infection,* 120(4), pp.345-354.

Jokinen, E.J., Maisem, V. & Järvinen, A. 2017. The history of methicillin: From discovery to the era of resistance. *Clinical Infectious Diseases*, 64(1), p.1-6.

Kanerva, M., Bäck, E., Kivioja, A. & Tuhkanen, H. 2011. The economic burden of MRSA in the European Union. *Journal of Hospital Infection,* 78(1), pp.15-22.

Kaplan, S.L. 2016. *Staphylococcus aureus* infections in children: the implications of changing trends. *Paediatrics*, 137(4).

Beck, W.D., Berger-Bachi, B., and Kayser, F.H. 1986. Additional DNA in methicillin-resistant *Staphylococcus aureus* and molecular cloning of mec specific DNA., 165 (2), pp.373-378.

Kesah, C., Ben Redjeb, S., Odugbemi, T.O., Boye, C.B., Dosso, M., Ndinya Achola, J.O., Koulla-Shiro, S., Benbachir, M., Rahal, K. & Borg, M. 2003. Prevalence of methicillin-resistant *Staphylococcus aureus* in eight African hospitals and Malta. *Clinical Microbiology and Infection*, 9(2), pp.153-156.

Khanal, A.G.C.S. Gaire, A. Khanal, A. Estrada, R. Ghimire, R. & Panthee, S. 2021. Methicillin-resistant *Staphylococcus aureus* in Nepal: A systematic review and meta-analysis. *International Journal of Infectious Dis*., 103:48-55.

Khoshnood, S., Heidary, M., Asadi, A., Soleimani, S., Motahar, M., Savari, M., Saki, M. & Abdi, M. 2019. A review on mechanism of action, resistance, synergism, and clinical implications of

mupirocin against *Staphylococcus aureus*. *Biomedicine & Pharmacotherapy*, 109, pp.1809-1818.

King, M. D., Humphrey, B. J., Wang, Y. F., Kourbatova, E. V., Ray, S. M., & Blumberg, H. M. (2012). Emergence of community-acquired methicillin-resistant *Staphylococcus aureus* USA 300 clone as the predominant cause of skin and soft-tissue infections. *Annals of Internal Medicine,* 144(5), 309-317.

Klein, E., Smith, D.L. & Laxminarayan, R. 2007. Hospitalisations and deaths caused by methicillin-resistant *Staphylococcus aureus* in the United States. *Clinical Infectious Diseases,* 45(3), pp.343-349.

Klevens, R.M., Morrison, M.A., Nadle, J., Petit, S., Gershman, K., Ray, S., Harrison, L.H., Lynfield, R., Dumyati, G., Townes, J.M. & Craig, A.S. 2007. Invasive methicillin-resistant *Staphylococcus aureus* infections in the United States. *Jama*, *298*(15), pp.1763-1771.

Köck, R., Becker, K., Cookson, B., van Gemert-Pijnen, J. E., Harbarth, S., Kluytmans, J., Mielke, M., Peters, G., *et al.,* 2010. Methicillin-resistant *Staphylococcus aureus* (MRSA): burden of disease and control challenges in Europe. *Euro surveillance: bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin*, *15*(41), pp.19688.

Kopp, B.J, Nix, D.E. & Armstrong, E.P. 2004. Clinical and economic analysis of methicillin-susceptible and resistant *Staphylococcus aureus* infections. *Ann Pharmacother*, 38, pp.1377-1382.

Kourtis, A.P., Hatfield, K., Baggs, J., Mu, Y., See, I., Epson, E., Nadle, J., Kainer, M.A., *et al.,* 2019. Vital signs: epidemiology and recent trends in methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* bloodstream infections—United States. *MMWR. Morbidity and Mortality Weekly Report, 68*(9), 214-219.

Kurkowski, S., 2007. The role of antibiotic overuse in the emergence of hospital-acquired methicillin-resistant *Staphylococcus aureus* (HA-MRSA) infections. *Clinical Infectious Diseases*, *45*(S2), pp.S180-S185.

Lade, H., Paul, D., & Kweon, J. H. (2003). Quorum sensing and biofilm formation in the bacterial world. *Journal of Microbiology and Biotechnology,* 13(3), 161-170.

Lambert, M.L., Suetens, C., Savey, A., Palomar, M., Hiesmayr, M., Morales, I., *et al*., 2011. Clinical outcomes of health-care-associated infections and antimicrobial resistance in patients admitted to European Intensive-Care Units: A cohort study. The Lancet Infectious Diseases, 11, 30-38.

Lee, B.Y., Bartsch, S.M., Wong, K. & Cooper, B.S. 2013. The economic burden of methicillin-resistant *Staphylococcus aureus* infections in the United States. *Clinical Infectious Diseases*, 56(1), pp.15-22.

Lindsay, J.A. 2013. Hospital-associated MRSA and antibiotic resistance – what have we learned from genomics? *Int. J. Med*, 303, pp.318-323.

Lipsett, P.A. 2008. Nosocomial infections surgery. *Springer New York,* 91, pp.273-86.

Lohan, P., Muloiwa, R. & Akech, S. 2017. Prevalence of methicillin-resistant *Staphylococcus aureus* among *Staphylococcus aureus* isolates in Kenya. *East African Medical Journal,* 94(7), pp.546-552.

Lowy, F.D. 1998. *Staphylococcus aureus* infections. *New England Journal of Medicine*, 339(8), pp.520-532.

Luzzaro, F., Ortisi, G., Larosa, M., Drago, M., Brigante, G. & Gesu, G. 2011. Prevalence and epidemiology of microbial pathogens causing bloodstream infections: results of the OASIS multicentre study. *Diagnostic Microbiology and Infectious Disease*, 69(4), pp.363-369.

Marais, E., Aithma, N., Perovic, O., Oosthuysen, W.F., Musenge, E. & Dusé, A.G. 2009. Antimicrobial susceptibility of methicillin-resistant *Staphylococcus aureus* isolates from South Africa. *South African Medical Journal*, 99(3), pp.170-173.

Mason, P.R., Kitai I. & Chigonde, S. 1991. Community-acquired staphylococcal skin infection in rural areas of Zimbabwe. *Cent Afr J Med,* 37, pp.56-60.

Mendes, R.E., Sader, H.S. & Jones, R.N. 2013. Methicillin-resistant *Staphylococcus aureus* in the Asia-Pacific region: prevalence and resistance patterns. *International Journal of Antimicrobial Agents,* 42(4), pp.323-328.

Milheiriço, C., De Lencastre, H. & Tomasz, A. 2017. Full-genome sequencing identifies in the genetic background several determinants that modulate the resistance phenotype in methicillin-resistant *Staphylococcus aureus* strains carrying the novel mecC gene. *Antimicrobial Agents and Chemotherapy*, 61(3), pp.10-1128.

Monecke, S., Coombs, G., Shore, A.C., Coleman, D.C., Akpaka, P., Borg, M., Chow, H., Ip, M., *et al.,* 2011. A field guide to pandemic, epidemic and sporadic clones of methicillin-resistant *Staphylococcus aureus*. *PloS one*, 6(4), p.e17936.

Morin, C.A., Hadler, J.L., Phipps, D.C., Price, N.W. & Baer, W.C. 2001. Epidemiology of methicillin-resistant *Staphylococcus aureus* (MRSA) in the community. *Journal of the American Medical Association*, 285(10), pp.1347-1353.

Naidoo R., Nuttall J., Whitelaw A. & Eley B. 2013. Epidemiology of *Staphylococcus aureus* bacteraemia at tertiary children's hospital in Cape Town, South Africa. *Plos one,* 8, A cohort study.

Naimi, T.S., LeDell, K.H., Boxrud, D.J., Groom, A.V., Steward, C.D., Johnson, S.K., Besser, J.M., O'Boyle, C., *et al.,* 2001. Epidemiology and clonality of community-acquired methicillin-

resistant *Staphylococcus aureus* in Minnesota, 1996–1998. *Clinical Infectious Diseases*, 33(7), pp.990-996.

National Nosocomial Infectious Surveillance System, 2004. National Infection Surveillance (NNIS) system report, data summary from January 1992 through June 2004. *AM J Infect control,* 32, pp.470-485.

O'Neill, J. 2016. Tracking drug resistant infections globally. Final report and recommendations. San Jose CA; *Inter American Institute for Corporation.* [Accessed 23 June 2024].

Orent, W. 2006. *Plague. The Mysterious Past and Terrifying Future of the World's Most Dangerous Disease*. Free Press. [Accessed 23 June 2024].

Park, S. 1989. Hospital outbreak of methicillin-resistant *Staphylococcus aureus* in Johannesburg, 1986–1987. *Journal of Hospital Infection,* 13(2), pp.91-100.

Perovic, O., Iyaloo, S., Kularatne, R., Lowman, W., Bosman, N., Wadula, J., Seetharam, S., Duse, A., Mbelle, N., Bamford, C. & Dawood, H. 2015. Prevalence and trends of *Staphylococcus aureus* bacteraemia in hospitalised patients in South Africa, 2010 to 2012: laboratory-based surveillance mapping of antimicrobial resistance and molecular epidemiology. *PLoS One*, 10(12), p.e0145429.

Perovic, O., Koornhof, H., Black, V., Moodley, I., Duse, A. & Galpin, J. 2006. *Staphylococcus aureus* bacteraemia at two academic hospitals in Johannesburg. *South African Medical Journal*, 96(8), pp.714-717.

Perovic, O., Zong, Z. & Ehlers, J. 2017. Epidemiology of MRSA bacteraemia in South Africa: A multi-centre study. *South African Journal of Epidemiology and Infection,* 32(2), pp.45-51.

Pichereau, S., Dortet, L., & Legrand, P., 2010. New beta-lactamases: current situation and clinical impact. *Medecine et Maladies Infectieuses,* 40(4), 190-197.

Perovic, O., Singh-Moodley, A., Duse, A., et al. (2012). National survey of susceptibility patterns of *Staphylococcus aureus* and enterococci isolates from healthcare-associated infections in South Africa. *Journal of Infection in Developing Countries, 6*(7), 562-568.

Pinho, M.G., De Lencastre, H. & Tomasz, A. 2001. An acquired and a native penicillin-binding protein cooperate in building the cell wall of drug-resistant staphylococci. *Proceedings of the National Academy of Sciences*, 98(19), pp.10886-10891.

Republic of South Africa Protection of Personal Information Act [POPIA], 2013. *Government Gazette, Republic of South Africa*, 912(581), pp.2. https://www.gov.za/sites/default/files/gcis_document/201409/3706726-11act4of2013protectionofpersonalinforcorrect.pdf [Accessed 18 August 2024].

Raphulu, T., Nana, T. & Choseng, B, 2023. The clinical spectrum of *Staphylococcus aureus* infections in children admitted to Chris Hani Baragwanath Academic Hospital, South Africa: retrospective, descriptive study. *South African Journal of Child Health*, 17(2), pp.71-77.

Rayner, C. & Munckhof, W.J. 2005. Antibiotics currently used in the treatment of infections caused by *Staphylococcus aureus*. *Internal Medicine Journal*, 35, pp.S3-16.

Reybrouck, G., 1983. Role of the hands in the spread of nosocomial infections. *Journal of Hospital Infection*, 4(2), pp.103-110.

Rump, B., Adams, J. & Fisher, D. 2018. The global impact of travel restrictions on the spread of infectious diseases. *Journal of Global Health*, 8(2), p.020402.

Serrafzadeh, S., Khodadadi, H. & Fadaei, R. 2021. High prevalence of methicillin-resistant *Staphylococcus aureus* in Iran: A study of positive cultures. *Journal of Clinical Microbiology and Infectious Diseases,* 27(2), pp.198-205.

Shittu, A.O., Lin, J., Morrison, D. & Kolawole, D.O., 2006. Isolation and molecular characterisation of methicillin-resistant *Staphylococcus aureus* from maternal and child health care units in a Nigerian hospital. *International Journal of Infectious Diseases,* 10(5), pp.387-397.

Shrestha, B., Pokhrel, B. & Mohapatra, T., 2009. Study of nosocomial isolates of *Staphylococcus aureus* with special reference to methicillin-resistant *S. aureus* in a Tertiary Care Hospital in Nepal. *Nepal Med Coll J*, 11(2), pp.123-126.

So, D.H., Hawkes, M. & Byers, K.E. 2008. Community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA): epidemiology and clinical presentation. *Journal of Clinical Microbiology*, 46(9), pp.3118-3120.

Stefani, S., Chung, D.R., Lindsay, J.A., Friedrich, A.W., Kearns, A.M., Westh, H. & MacKenzie, F.M. 2012. Methicillin-resistant *Staphylococcus aureus* (MRSA): global epidemiology and harmonisation of typing methods. *International Journal of Antimicrobial Agents*, 39(4), pp.273-282.

Thampi, N., Showler, A., Burry, L., Bai, A.D., Steinberg, M., Ricciuto, D.R., Bell, C.M. & Morris, A.M. 2015. Multicentre study of health care cost of patients admitted to hospital with *Staphylococcus aureus* bacteraemia: impact of length of stay and intensity of care. *American Journal of Infection Control*, 43(7), pp.739-744.

The Canada Communicable Disease Report (CCDR), 2016. Antimicrobial resistance (AMR), 42(11), pp.223. [Accessed 16 August 2024].

Tong, S.Y.C., Davis, J.S., Eichenberger, E., Holland, T.L. & Fowler, V.G. 2015. *Staphylococcus aureus* infections: epidemiology, pathophysiology, clinical manifestations, and management. *Clinical Microbiology Reviews*, 28(3), pp.603-661.

Turner, R.D., Vollmer, W. & Foster, S.J. 2014. Different walls for rods and balls: the diversity of peptidoglycan. *Molecular microbiology*, 91(5), pp.862-874.

Van Hal, S. J., Paterson, D. L. & Iredell, J. R., 2012. The risk of death in patients with *Staphylococcus aureus* bloodstream infections. *Clinical Microbiology and Infection*, 18(6), pp.575-580.

Vincent, J.L., Bihari, D.J., Suter, P.M., Bruining, H.A., White, J., Nicolas-Chanoin, M.H., Wolff, M., Spencer, R.C. & Hemmer, M. 1995. The prevalence of nosocomial infection in intensive care units in Europe: results of the European Prevalence of Infection in Intensive Care (EPIC) Study. *Jama, 274*(8), pp.639-644.

Vincent, J.L., Marshall, J.C., Ñamendys-Silva, S.A., Francois, B., Martin-Loeches, I., Lipman, J. & Reinhart, K. 2013. International study of the prevalence and outcomes of infection in intensive care units*. JAMA*, 302(21), pp.2323-2329.

Washer, P. Joffe, H. & Solberg, C. 2006. Methicillin-resistant *Staphylococcus aureus* (MRSA) and the media*:* A content analysis of British newspapers*. Journal of Health Communication*, 11(6), pp.575-588.

Weiner-Lastinger, L.M., Pattabiraman, V., Konnor, R.Y., Patel, P.R., Wong, E., Xu, S.Y., Smith, B., Edwards, J.R. & Dudeck, M.A. 2022. The impact of coronavirus disease 2019 (COVID-19) on healthcare-associated infections in 2020: A summary of data reported to the National Healthcare Safety Network. *Infection Control & Hospital Epidemiology*, 43(1), pp.12-25.

Wertheim H.F., Melles D.C., Vos M.C., van Leeuwen W., van Belkum A., Verbrugh H.A. & Nouwen J.L. 2005. The Role of nasal carriage in *Staphylococcus aureus* infections. *Lancet infect. Dis,* 5, pp.751-762.

Whitby, M., McLaws, M.L. and Berry, G. 2001. Risk of death from methicillin-resistant *Staphylococcus aureus* bacteraemia: a meta-analysis. *Wiley Online Library*, pp.175.

World Health Organization [WHO], 2011. *Report on the burden of endemic health care-associated infection worldwide.* [Accessed 10 July 2024].

World Health Organization [WHO], 2014. *Global report on surveillance of antimicrobial resistance*. [Accessed 10 July 2024].

World Health Organization, 2023. Antimicrobial resistance. Retrieved from https://www.who.int. [Accessed 19 April 2024].

World Health Organization [WHO], 2024. Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics. [Accessed 19 April 2024].

Yadav, Khushbu & Prakash, Satyam. (2016). Prevalence and antibiotic susceptibility pattern of MRSA (Methicillin-Resistant *Staphylococcus aureus*) in Upper Respiratory Tract Infection. Global Journal of Microbiology Research. 04. 167-173.

Zhanel, G.G., DeCorby, M., Laing, N., Weshnoweski, B., Vashisht, R., Tailor, F., Nichol, K.A., Wierzbowski, A., *et al.,* 2008. Antimicrobial-resistant pathogens in intensive care units in Canada: results of the Canadian National Intensive Care Unit (CAN-ICU) study, 2005-2006. *Antimicrobial agents and chemotherapy*, *52*(4), pp.1430–1437.

Zarfel, G., Tschiedel, E. & Kummer, M., 2023. Impact of the COVID-19 pandemic on MRSA rates in Australia: A retrospective study. *Australian Journal of Infection Control,* 28(1), pp.37-43.

Zervou, F.N., Zacharioudakis, I.M., Ziakas, P.D. & Mylonakis, E., 2014. Prevalence of and risk factors for methicillin-resistant *Staphylococcus aureus* colonisation in HIV infection: A meta-analysis. *Clinical Infectious Diseases,* 59(9), pp.1302-1311.

Zhen, X., Zhang, Y. & Liu, J. 2020. A multicentre study on the impact of Methicillin-Resistant *Staphylococcus aureus* (MRSA) infections in China: hospital stay, mortality, and cost

compared to methicillin-sensitive *Staphylococcus aureus* (MSSA) in immunocompromised patients. *Infection Control & Hospital Epidemiology*, 41(5), pp.537-544.

APPENDICES

APPENDIX A: NHLS data extraction approval letter.

NATIONAL HEALTH LABORATORY SERVICE

Academic Affairs and Research
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Tel: +27 (0)11 555 0367/0406
Email: babatyi.kgokong@nhls.ac.za
academic.research@nhls.ac.za
Web: www.nhls.ac.za

17 August 2023

Applicant: Sizolwethu Cebekhulu
Institution: NHLS
E-mail Address: sizolwethu.cebekhulu96@gmail.com
Tel: 035 794 3494 **Cell:** 076 721 6703

Project Title: PRESENCE OF METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS AMONGST PATIENTS ADMITTED TO THE INTENSIVE CARE UNITS OF SIX KWAZULU-NATAL HOSPITALS, 2018 TO 2022**Reference Number**: PR2234961

Research Application Type(s):
1. Request for Data

RE: APPROVAL LETTER: REQUEST TO ACCESS NHLS RESOURCES FOR RESEARCH PURPOSES

This letter serves to advise that the application requesting permission to conduct the above-mentioned research using the listed NHLS resources has been reviewed and **"Approved"**. Please note that the approval is granted on the condition that you comply with the NHLS Research Material and Data Access Policy and requirements stated below.

1. All material and data requested shall be used as per the research protocol submitted to the NHLS and as approved by the relevant Health Research Ethics Committee (HREC) in South Africa.
2. Access to the NHLS material and/or data shall be limited to the minimum required for successful completion of the approved study and shall be made available as per ***test codes submitted and without patient names and other patient identifiers (including, but not limited to, national identity numbers, hospital/clinic file numbers, addresses and telephone numbers)***.
3. Confidentiality shall be maintained at the participant and institutional level and there shall be no disclosure of personal information or confidential information.
4. Data and/or material shall not be shared with other parties unless approved by the NHLS
5. The material and/or data obtained from the NHLS shall be anonymised and not, for any reason, be used to track or recruit patients as no pre-approval/consent is obtained from patients.
6. Processes shall be discussed with the relevant NHLS departments (i.e. Corporate Data Warehouse (CDW), NHLS Laboratory Management, Operations Office, etc.) and agreed upon.
7. Any amendments to the study requirements, including the use of the material and/or data for purposes not initially disclosed to the NHLS) shall be cleared by an approved HREC and submitted to the NHLS for approval via the AARMS system – https://aarms.nhls.ac.za.
8. The NHLS shall be acknowledged as a source of material and/or data in any output, such as abstracts and journal articles, emanating from the project.
9. A final report of the research study and any published output resulting from this study shall be submitted to the NHLS via AARMS

Please note that this letter constitutes approval by the NHLS Academic Affairs and Research Office. The NHLS entities tasked with providing the material and/data may have additional requirements for access. Data related queries may be directed to NHLS CDW, email: zarina.sabat@nhls.ac.za; contact number: 011 386 6074 and sample related queries (if applicable) shall be directed to the relevant business manager.

Dr Babatyi Malope-Kgokong
National Manager: Academic Affairs and Research

APPENDIX B: HSREC ethics clearance letter

UNIVERSITY OF THE FREE STATE
UNIVERSITEIT VAN DIE VRYSTAAT
YUNIVESITHI YA FREISTATA

UFS·UV
HEALTH SCIENCES
GESONDHEIDSWETENSKAPPE

Health Sciences Research Ethics Committee

06-Sep-2023

Dear **Sizolwethu Cebekhulu**

Ethics Clearance: **Presence of Methicillin-resistant Staphylococcus aureus amongst patients admitted to the intensive care units of six Kwazulu-Natal hospitals, 2018 to 2022.**
Principal Investigator: **Sizolwethu Cebekhulu**
Department: **CUT - Central University of Technology**
Submission Page

APPLICATION APPROVED

Please ensure that you read the whole document

With reference to your application for ethical clearance with the Faculty of Health Sciences, I am pleased to inform you on behalf of the Health Sciences Research Ethics Committee that you have been granted ethical clearance for your project.

Your ethical clearance number, to be used in all correspondence is:**UFS-HSD2023/0401/2609**

The ethical clearance number is valid for research conducted for one year from issuance. Should you require more time to complete this research, please apply for an extension.

We request that any changes that may take place during the course of your research project be submitted to the HSREC for approval to ensure we are kept up to date with your progress and any ethical implications that may arise. This includes any serious adverse events and/or termination of the study.

A progress report should be submitted within one year of approval, and annually for long term studies. A final report should be submitted at the completion of the study.

Research conducted in any Department of Health facility: Researchers are required to sign and return the HSREC approval letters to the provincial Department of Health where they applied. It is also a requirement for researchers to submit electronic copies of their final research findings, and/or make a presentation of their findings and recommendations at departmental research days when and where indicated.

The HSREC functions in compliance with, but not limited to, the following documents and guidelines: The SA National Health Act. No. 61 of 2003; Ethics in Health Research: Principles, Structures and Processes (2015); SA GCP(2020); Declaration of Helsinki; The Belmont Report; The US Office of Human Research Protections 45 CFR 461 (for non-exempt research with human participants conducted or supported by the US Department of Health and Human Services- (HHS), 21 CFR 50, 21 CFR 56; CIOMS; ICH-GCP-E6 Sections 1-4; International Council for Harmonisation (ICH) Harmonised Guideline, Integrated Addendum to ICH E6(R1), Guideline for Good Clinical Practice (GCP) E6(R2), 2016, SAHPRA Guidelines as well as Laws and Regulations with regard to the Control of Medicines, Constitution of the HSREC of the Faculty of Health Sciences.

The Principal Investigator (PI) bears final responsibility for the RIMS application. In the event of any misconduct or improper activities perpetuated by a third party, the PI will be held vicariously liable. The HSREC will bear no responsibility or liability for any actions of a PI and/or third party or breach of confidentiality caused by the PI and/or third party.

For any questions or concerns, please feel free to contact HSREC Administration: 051-4017794/5 or email EthicsFHS@ufs.ac.za.

Thank you for submitting this proposal for ethical clearance and we wish you every success with your research.

Yours Sincerely

Prof. A. Sherriff
Chairperson: Health Sciences Research Ethics Committee

Health Sciences Research Ethics Committee
Office of the Dean: Health Sciences
T: +27 (0)51 401 2352/9860 | E: ethicsfhs@ufs.ac.za
IRB 00011992, REC 230408-011; IORG 0010096; FWA 00027947

APPENDIX C: Linguistic editor title revision declaration.

09 January 2023

DECLARATION

I hereby declare that I am a qualified and professional language practitioner with the following qualification from the Central University of Technology, Free State:

- MTech Language Practice (2013)

In this capacity, I have linguistically revised (in English) the following title:

FORMER TITLE:	**PRESENCE OF METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS AMONG PATIENTS ADMITTED TO INTENSIVE CARE UNITS OF SIX KWAZULU-NATAL HOSPITALS, 2018 TO 2022**
NEW TITLE:	**Presence of methicillin-resistant *Staphylococcus aureus* amongst patients admitted to the intensive care units of six KwaZulu-Natal hospitals, 2018 to 2022**
DEGREE:	**Master's in Health Sciences (Biomedical Technology)**
STUDENT:	**SA Cebekhulu (student number: 222095536)**
INSTITUTION:	**Central University of Technology, Free State Faculty of Health and Environmental Sciences**

Signed:

.....

TANIA OOSTHUIZEN
SENIOR LANGUAGE PRACTITIONER
CENTRAL UNIVERSITY OF TECHNOLOGY, FREE STATE

Contact details:

Tel.: (051) 507 3607
E-mail: tvvuuren@cut.ac.za

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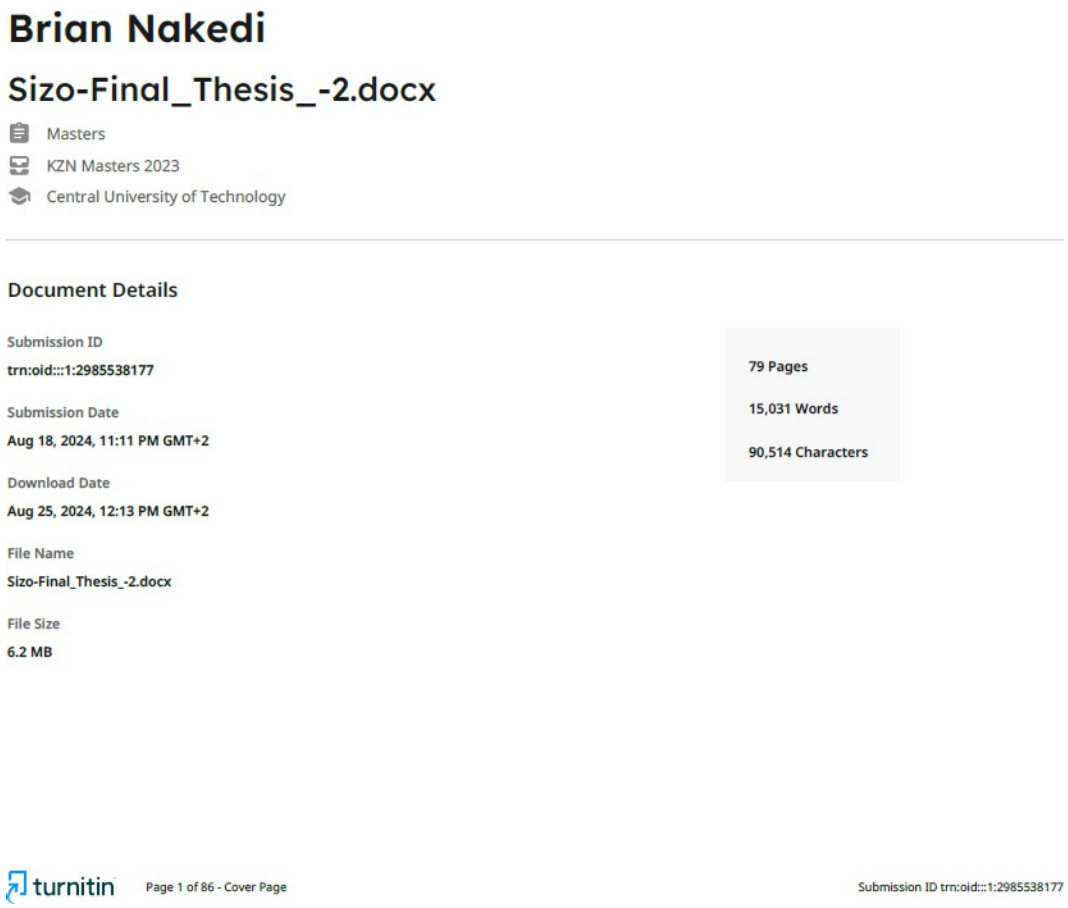

Brian Nakedi

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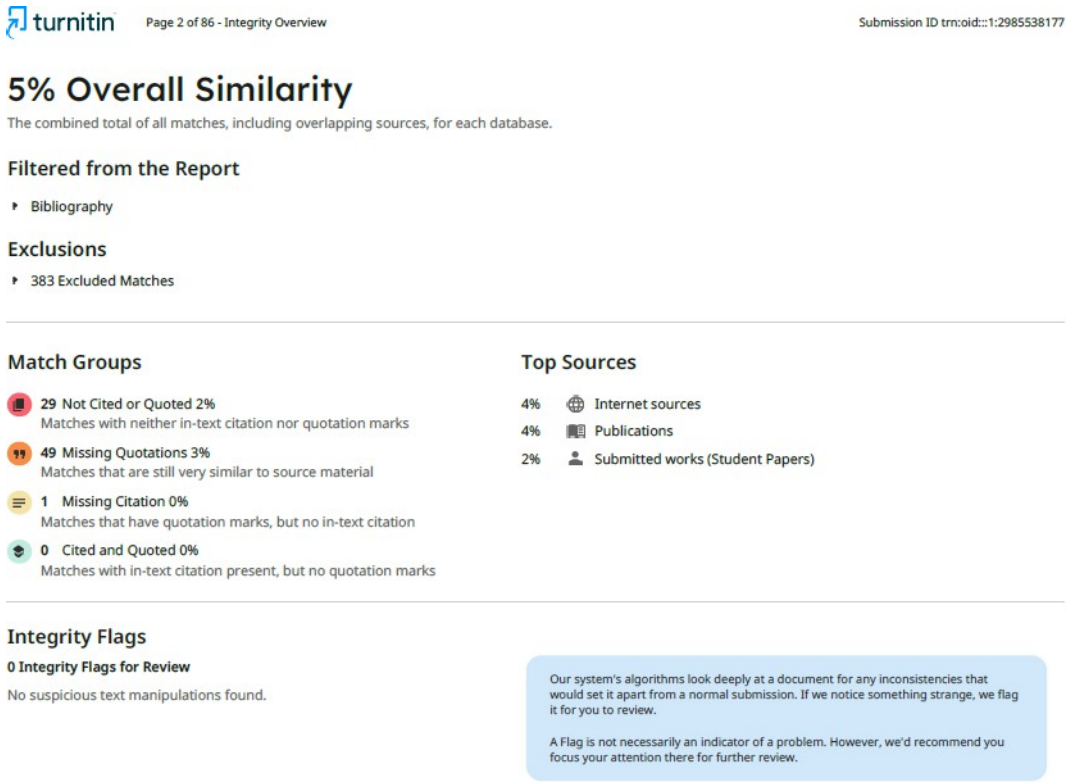

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APPENDIX E: CUT FRIC letter.

Central University of Technology, Free State

FACULTY OF HEALTH AND ENVIRONMENTAL SCIENCES

March 14, 2023

ATTN: UFS Ethics Committee

Re: Scientific Review

Student: Sizolwethu Abitious Cebekhulu
Student No: 222095536

To Whom it may concern

This letter serves to confirm that the research protocol, titled, "***PRESENCE OF METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS AMONG PATIENTS ADMITTED TO INTENSIVE CARE UNITS OF SIX KWAZULU-NATAL HOSPITALS, 2018 TO 2022.***" has been reviewed the Faculty Research and Innovative Committee (FRIC) of the Faculty of Health and Environmental Sciences, Central University of Technology on the 28 February 2023 and has been judged to be relevant, designed in accordance with accepted scientific practices and norms.

FRIC resolution reference: FHES 3/02/28

Should you require additional information, please contact Prof TJ Makhafola at jmakhafola@cut.ac.za

Sincerely;

Tel: +27 51 507 3369
Prof TJ Makhafola
Assistant Dean; Research, Innovation and Engagement
Faculty if Health and Environmental Sciences

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APPENDIX F: Linguistically-edited Final Thesis Declaration.

CORNELIA GELDENHUYS

✆083 2877088
corrieg@mweb.co.za

26 August 2024

TO WHOM IT MAY CONCERN

Herewith I, **Cornelia Geldenhuys (ID 521114 0083 088)** declare that I am a qualified, accredited language practitioner and that I have edited the following Master's dissertation:

PRESENCE OF METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* AMONGST PATIENTS ADMITTED TO THE INTENSIVE CARE UNITS OF SIX KWAZULU-NATAL HOSPITALS, 2018 TO 2022

by
Sizolwethu Cebekhulu

Student number: 222095536

All changes were indicated by track changes and comments **for the author to verify, clarify aspects that are unclear, make the necessary adjustments and finalise.** The editor takes no responsibility in the instance of this not being done. The document remains the final responsibility of the author.

.....
C GELDENHUYS
MA (Lin) cum laude, MA (Mus), BA Hons (French), HED, HDL, UELM

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