ANTIMICROBIAL RESISTANCE PATTERNS IN HOSPITAL-ACQIURED INFECTIONS OF *staphylococcus aureus* IN CHILDREN IN A TERTIARY HOSPITAL IN BENIN CITY, NIGERIA.

BY

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BENIN CITY

NOVEMBER, 2025

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A PROJECT SUBMITTED TO THE DEPARTMENT OF MICROBIOLOGY, FACULTY OF LIFE SCIENCES, UNIVERSITY OF BENIN, BENIN CITY, IN PARTIAL FUFILMENT OF THE REQUIREMENT FOR THE AWARD OF DEGREE OF B.Sc (HONS) IN MICROBIOLOGY, UNIVERSITY OF BENIN, BENIN CITY.

NOVEMBER, 2025

CERTIFICATION

we, certify that this research project was carried out by **ADAOBI TESTIMSONY OSHIAKPE** (MISS) with the matriculation number **LSC2104015** Of the Department of Microbiology, Faculty of Life Sciences under the supervision of **Mr. E.C. Wemambu,** University of Benin, Benin City

_____ _____

Mr. E.C. Wemambu **DATE**

(Project Supervisor)

_____ _____

PROF. E.O. IGBINOSA **DATE**

(Head of Department)

DEDICATION

To the God of David, who teaches my hands to war and my fingers to fight,

and to my parents, the best gift a girl could ever have.

ACKNOWLEDGMENT

Bless the Lord, O my soul, who in His infinite mercies sustained me throughout the period of writing this project.

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ABSTRACT

The global rise of antimicrobial resistance (AMR) is a critical health crisis, making once-treatable infections dangerous again. This problem is particularly severe in hospital settings, where the frequent use of antibiotics and the concentration of sick patients create an ideal environment for drug-resistant bacteria to spread. The aim of this study is to determine the antimicrobial resistance patterns of Staphylococcus aureus isolated from hospital-acquired infections in children at a tertiary hospital in Benin City. Using a cross-sectional design, clinical samples from 67 pediatric patients were analyzed for Staphylococcus aureus isolation, susceptibility testing via Kirby-Bauer method, and MRSA detection with cefoxitin. *Staphylococcus aureus* was the predominant pathogen (50% of isolates), with 53.1% multidrug-resistant and 30.4% MRSA; high resistance noted to erythromycin (70%) and amikacin (73.1%), but full susceptibility to meropenem and piperacillin; male predominance (67.2%) and older adolescents as largest group (33.3%).These findings highlight alarming AMR levels in pediatric HAIs, aligning with SSA trends and underscoring gaps in empirical therapy. Urgent stewardship and surveillance are needed to curb resistance and improve outcomes.

CHAPTER ONE

INTRODUCTION

1.1 Background of the Study

The global rise of antimicrobial resistance (AMR) is a critical health crisis, making once-treatable infections dangerous again (Palma et al., 2020). This problem is particularly severe in hospital settings, where the frequent use of antibiotics and the concentration of sick patients create an ideal environment for drug-resistant bacteria to spread (Chia et al., 2020). *Staphylococcus aureus* is a key example, as it is a leading cause of both community-acquired and hospital-acquired infections (HAIs), and its ability to resist common antibiotics especially the emergence of *Methicillin-resistant Staphylococcus aureus* (MRSA) has made it a major concern for healthcare providers worldwide (Yu et al., 2023).

Children are a highly vulnerable population when it comes to HAIs especially in resource-limited settings. Their developing immune systems and frequent need for hospitalization for various illnesses increase their risk of contracting infections (Williams et al., 2018). In Nigeria, infectious diseases are a significant burden, and the challenge of AMR is worsened by limited access to proper diagnostic tools and the uncontrolled use of antibiotics (World Health Organization, 2022). As a result, treatment options for pediatric infections are becoming increasingly limited.

In Benin City, a prominent urban center in Nigeria's South-South region, University of Benin Teaching Hospital, a tertiary hospital serves as a crucial referral center, handling complex cases from a wide area. Despite the recognized threat of AMR, there is a lack of up-to-date, localized data on the resistance patterns of *Staphylococcus aureus* in children in this specific hospital setting. This knowledge gap can lead to ineffective empirical treatment, treating an infection

without knowing the specific pathogen's susceptibility which can result in prolonged illness and even death.

1.2 Statement of the Research Problem

Despite the growing global awareness of antimicrobial resistance, data specific to Nigerian paediatric populations remain sparse, particularly in the South-South geopolitical zone. Previous studies from other regions of Nigeria have consistently reported high resistance rates to commonly used antibiotics such as ampicillin, cotrimoxazole, and cefuroxime, as well as the presence of multidrug-resistant organisms such as *methicillin-resistant Staphylococcus aureus* (MRSA).

While studies from other parts of Nigeria have documented AMR trends, there is a distinct lack of detailed, local data from the South-South geopolitical zone, including Edo State (Bernabé et al., 2017).

This gap poses a major challenge to effective treatment and public health planning. Without reliable local epidemiological and microbiological data, clinicians are forced to rely on empirical treatment strategies that may no longer be effective, leading to treatment failure, increased healthcare costs, and higher morbidity and mortality in children.

In addition, hospital environments have been identified as reservoirs and transmission points for resistant bacteria, yet limited studies in Nigeria have examined their role in paediatric infections. The absence of coordinated surveillance systems further exacerbates the situation, leaving a critical blind spot in the fight against AMR.

Addressing these issues is urgent. Without timely research to map resistance patterns in children, especially in Edo State, the risks of unchecked antibiotic misuse, rising treatment failure, and preventable childhood deaths will continue to escalate.

1.3 Aim of the Study

The aim of this study is to determine the antimicrobial resistance patterns of *Staphylococcus aureus* isolated from hospital-acquired infections in children at a tertiary hospital in Benin City.

Specific objectives

- To isolate and identify *Staphylococcus aureus* from various clinical samples of children with hospital-acquired infections.
- To determine the antimicrobial susceptibility profiles of the isolated *Staphylococcus aureus* strains using standard laboratory methods.
- To determine the prevalence of Methicillin-resistant *Staphylococcus aureus* (MRSA) and multidrug-resistant (MDR) categories.
- To explore socio-demographic associations with resistant *Staphylococcus aureus* carriage in the study population.

1.4 Significance of the Research

The significance of this research lies in its multi-faceted contributions to clinical practice, public health policy, and scientific knowledge:

- **Clinical Relevance**: The findings will provide up-to-date local data on resistance patterns of hospital-acquired *Staphylococcus aureus* in children, which will enable clinicians to make evidence-based treatment decisions, reduce reliance on experiential prescribing, and lower the risk of treatment failure. This ultimately contributes to reducing morbidity, mortality, and healthcare costs associated with paediatric HAIs.
- **Policy Impact**: The results will strengthen antimicrobial resistance (AMR) surveillance in the South-South region, supporting policymakers and health authorities in designing

context-specific interventions and strengthening infection prevention and control (IPC) strategies in tertiary healthcare settings.

- **Scientific Contribution**: The data on phenotypic and, where feasible, molecular charactersation of resistant *Staphylococcus aureus* isolates will enrich the body of knowledge on the epidemiology of AMR in Nigeria, providing a strong foundation for future comparative studies.

1.5 Scope of the Study

This research was conducted in Benin City, Edo State, which is located in the South-South geopolitical zone of Nigeria. Edo State, with a population of approximately five million as of 2024, is the twentieth most populous state in the country. Its capital, Benin City, serves as both the administrative and commercial hub of the state, which is also known for its agricultural productivity, crude oil deposits, and other mineral resources. The state has a tropical savanna climate with an average annual temperature of about 28.8 °C. Healthcare delivery is shared across federal, state, and local government levels, with tertiary institutions, general hospitals, and primary health centres complemented by an active private sector.

The study adopted a cross-sectional epidemiological design rooted in the One Health framework, which recognises the interconnectedness of human, animal, and environmental health in understanding antimicrobial resistance (Palma et al., 2020). The University of Benin Teaching Hospital (UBTH) served as the study site. UBTH is a federal tertiary hospital with a 910-bed capacity and several specialist departments, including paediatrics, which admits about 120 patients monthly. The study focused on paediatric patients within this facility, and all laboratory analyses, including storage of biological samples for future genomic research, was be conducted at the UBTH laboratory.

Participants included children under 18 years of age, excluding neonates, who were admitted to the hospital and meet inclusion criteria. Eligible patients either had a presumptive clinician diagnosis requiring antibiotic treatment or were assessed by study staff as needing antibiotics. Recruitment was carried out pragmatically through a point prevalence survey rather than longitudinal monitoring, with all admitted patients reviewed once weekly. Inclusion required informed consent from caregivers, and assent from children aged 7–17 years.

1.6 Limitations of the Study

While this study is designed to provide valuable insights into antimicrobial resistance patterns of hospital-acquired *Staphylococcus aureus* infections among children in Benin City, certain limitations are acknowledged. First, the cross-sectional design restricts the ability to establish causality or temporal relationships between hospital exposure and infection. The reliance on a point prevalence survey, conducted once per week, may also underrepresent variations in resistance patterns that occur over time. In addition, the exclusion of neonates and children whose caregivers refuse consent could introduce a degree of selection bias.

Logistical constraints, such as limited laboratory capacity for advanced molecular testing, may necessitate referral of some samples to external reference laboratories, potentially delaying results. Furthermore, the findings from a single tertiary hospital, though significant, may not be fully generalisable to other healthcare settings within Edo State or Nigeria as a whole. Despite these limitations, the study remains an important step in addressing the critical knowledge gap on paediatric hospital-acquired *Staphylococcus aureus* resistance patterns in the region.

CHAPTER TWO

LITERATURE REVIEW

2.1 Introduction

Hospital-acquired infections (HAIs), also referred to as healthcare-associated infections, are a significant public health issue worldwide, especially in low-resource settings where diagnostic and infection control infrastructures are weak. A multi-city point-prevalence survey in Northern Nigeria reported an HAI rate of 14.3%, with bloodstream infections (38%) and surgical site infections (32%) dominating, particularly in neonatal and paediatric surgery units (Abubakar, U., 2020).

Additionally, national data from a tertiary hospital in southwestern Nigeria showed an average HAI prevalence of 2.6%, with 20.1% of infections attributed to *Staphylococcus aureus* in Ibadan's pediatric and surgical wards (Ige *et al*., 2011).

Antimicrobial resistance (AMR) heightens the burden of HAIs by limiting available treatment options and increasing mortality, morbidity, and treatment costs. In Nigeria, AMR rates for *Staphylococcus aureus* have surged from less than 2% in 2005 to over 40% by 2020, underscoring the growing threat, especially given the lack of robust antimicrobial stewardship and surveillance systems (Suleiman *et al*.,2023).

Staphylococcus aureus is a leading cause of serious pediatric infections, including bloodstream infections, surgical site infections, pneumonia, and skin infections. Children admitted to paediatric ICUs are highly susceptible due to factors like invasive devices, immature immunity, and extended hospitalization. In Nigerian hospitals, *Staphylococcus aureus* appears frequently in HAI surveillance, comprising a large proportion of bloodstream and surgical infections among children (Ige *et al*., 2011). The elevated prevalence of *Staphylococcus aureus* in healthcare

settings highlights its clinical significance in pediatric care.

Methicillin Resistant Staphylococcus aureus (MRSA) has become increasingly common even in children without traditional risk factors, hinting at evolving patterns of virulence and transmission, including community-acquired strains entering hospital settings.

Studies from paediatric ICUs show concerning rates of MRSA and associated complications, indicating the urgent need for age-specific surveillance and control strategies.

There remains a substantial gap in pediatric-specific data on hospital-acquired *Staphylococcus aureus* infections in Nigeria, especially from tertiary hospitals in the South- South. For instance, while high rates of MRSA colonization have been identified in Benin City community samples, there is limited information about its presence in hospitalized children. Understanding local resistance trends in paediatric wards within Benin City institutions is vital, as regional differences can influence empirical treatment and infection control strategies.

This literature review aims to critically assess existing evidence on antimicrobial resistance patterns in hospital-acquired Staphylococcus aureus infections among children in tertiary hospitals, with a special focus on Benin City, Edo State, Nigeria. The objective is to identify regional trends, highlight data gaps, and inform policies for effective surveillance, pediatric antimicrobial stewardship, and clinical management strategies.

2.2 Clinical and Microbiological Profile of *Staphylococcus Aureus*

A 2007 prospective study from Lagos University Teaching Hospital (LUTH) monitored 4,981 paediatric admissions and found *Staphylococcus aureus* as the second most frequent nosocomial pathogen, with MRSA accounting for approximately 55% of isolates in paediatric wards (NICU, surgical, general) (Ngwa, F. *et al*.,2007).

A regional study at Obafemi Awolowo University in Ile-Ife, Nigeria, isolated *Staphylococcus*

aureus from 42% of clinical specimens, with MRSA prominent in inpatient and surgical units, indicating its strong representation in healthcare-acquired infections.

In a pediatric cohort in Utah (2009–2012), MSSA accounted for approximately 79% of invasive *Staphylococcus aureus* infections, while MRSA represented only 21%; yet disease severity was comparable between them, suggesting MSSA remains clinically significant in children (Hall, J. *et al*., 2019) .

Another pediatric musculoskeletal infection study reported similar hospital stay length and inflammatory marker response between MSSA and MRSA, highlighting that virulence differences may not strictly align with methicillin resistance (Francois, B. *et al*., 2017).

Staphylococcus aureus produces multiple virulence factors, coagulase, hyaluronidase, biofilm formation, PBP2a expression, and toxins like Panton–Valentine leukocidin (PVL), that enable immune evasion, tissue invasion, and antibiotic resistance (Diao Bella *et al*., 2025) .

Only a minority of invasive pediatric *Staphylococcus aureus* isolates carry the PVL gene (approximately16%), indicating that other virulence genes and genetic backgrounds drive disease severity, not just methicillin resistance (Crandall *et al*., 2020)

2.3 Health Implications in Paediatrics

Staphylococcus aureus is a major cause of serious infections in children, including bloodstream infections (bacteraemia), pneumonia, skin and soft tissue infections, and osteomyelitis. These conditions are often associated with high levels of morbidity and mortality, particularly when caused by MRSA, which limits effective treatment options.

A population-based surveillance study in rural Gambia found an incidence of *Staphylococcus aureus* bacteraemia at 78 cases per 100,000 person-years among children under five (and 2,080

per 100,000 among neonates), with a case-fatality ratio (CFR) of 14.1%, underscoring the burden in low-resource pediatric populations (Odutola, A. *et al*., 2019).

In Cape Town, South Africa, a tertiary children's hospital reported 3.28 episodes of *Staphylococcus aureus* bacteraemia per 1,000 hospital admissions. MRSA accounted for 26% of these cases, but 72% of hospital-acquired episodes, and was the only significant predictor of mortality (overall CFR 8.8%) (Naidoo *et al*., 2013).

A prospective observational study in an Indian pediatric ICU documented that out of 2,480 admissions, 120 (4.83%) had culture-confirmed *Staphylococcus aureus* infections, including 1.6 MRSA and 3.1 *Methicillin Susceptible Staphylococcus aureus* (MSSA) infections per 100 admissions. Pneumonia (43.3%), septicemia (20.8%), and bone/joint infections (15%) were the most common.

The mean length of stay was 17 days, and mortality was 20.8%, notably higher among MRSA cases (Qadri, I. *et al*., 2019).

These findings collectively demonstrate that pediatric *Staphylococcus aureus* infections—particularly MRSA—contribute to severe clinical outcomes, prolonged hospitalization, and high fatality. Such outcomes emphasize the critical need for robust local surveillance, targeted antimicrobial stewardship, and infection control policies, especially in tertiary hospitals serving children in Benin City.

2.4 ROUTES OF TRANSMISSION AND RISK FACTORS

Contact Transmission via Healthcare Staff:

Colonized or infected patients, combined with lapses in hand hygiene and use of gloves, contribute significantly to the spread of *Staphylococcus aureus* in pediatric wards and ICUs. For example, in hospital settings such as NICUs, transmission often occurs through contaminated

hands or shared touch surfaces, highlighting the importance of stringent hygiene practices (Pittet *et al*., 2003; Massé *et al*., 2016).

Transmission Through Medical Devices:

Indwelling devices, such as central venous catheters, endotracheal tubes, and urinary catheters, pose high risks, especially when sterile protocols aren't followed. These devices compromise natural barriers and can act as entry points or surfaces for biofilm formation, leading to catheter-related bloodstream infections or ventilator-associated pneumonia (Idrissi, Y. *et al*., 2023).

Environmental and Parental Reservoirs

Children may also acquire *Staphylococcus aureus* from their parents or the hospital environment. Guidelines suggest that parents with known colonization, when not decolonized, can transmit MRSA to neonates, so surveillance and decolonization are recommended(Weiner, L. M. *et al*., 2019) .

2.5 Risk Factors for Paediatric Patients

Intensive Care Admission and Invasive Ventilation:

Children in PICUs or NICUs are at increased risk, especially when mechanical ventilation or respiratory support is needed. A pediatric ICU study found respiratory failure to be a key independent risk factor for MRSA infection (Weiner *et al*., 2019; Goudarzi *et al*., 2021).

Prolonged or Repeated Hospitalization:

Multiple ICU admissions or extended stays increase colonization risk: one study reported that 25% of children had persistent MRSA colonization more than a year after their first ICU admission (Waldrop *et al*., 2021).

Underlying Illness and Immunosuppression:

Children with chronic conditions or receiving immunosuppressive therapy (e.g., steroids, chemotherapy) are more prone to *Staphylococcus aureus* colonization and infection, as these impair natural defenses (Idrissi, Y. *et al*., 2023).

Skin Breaks and Co-Infections:

MRSA colonization in children has also been linked to damaged skin barriers, such as eczema or wounds, as well as concurrent viral infections and elevated inflammatory markers (C-reactive proteins >8 mg/L).

2.6 MECHANISMS OF ANTIMICROBIAL RESISTANCE

1. Beta-lactam resistance through mecA gene expression

Staphylococcus aureus becomes resistant to beta-lactam antibiotics by acquiring the mecA gene, which encodes an altered penicillin-binding protein (PBP2a) that beta-lactams cannot inhibit. This mechanism allows MRSA strains to survive treatments like methicillin, oxacillin, and even broad-spectrum cephalosporins (Alnowibet, K., *et al*., 2021).

2. SCCmec (Staphylococcal Cassette Chromosome mec) and multidrug resistance

The mecA gene is located on the staphylococcal cassette chromosome mec (SCCmec), a mobile genetic element that often carries additional resistance genes for macrolides, aminoglycosides, and fluoroquinolones. This results in multidrug-resistant *Staphylococcus aureus* strains that severely limit therapeutic options in pediatric care (Touaitia, R., *et al*. 2025).

3. Biofilm formation on medical devices

Staphylococcus aureus forms complex biofilms on surfaces like catheters, endotracheal tubes, and wounds. These biofilms protect the bacteria from antibiotics and immune responses, promote persistence, and enable horizontal gene transfer of resistance elements (Peng, Q., *et al*., 2021).

4. Persister cells and survival under antibiotic stress

Within biofilms, *Staphylococcus aureus* can develop persister cells—metabolically inactive forms that survive antibiotic exposure and reactivate when conditions improve. This contributes to recurrent infections and chronic colonization.

5. Global significance of multidrug resistance in *Staphylococcus aureus*

The rise of multidrug-resistant *Staphylococcus aureus,* especially MRSA, has become a global public health threat. The World Health Organization classifies MRSA as a high-priority pathogen due to its resistance profile and association with hospital-acquired infections (WHO., 2017).

2.7 RESISTANCE PATTERNS: LOCAL AND GLOBAL EVIDENCE

Prevalence of Antimicrobial Resistance in Pediatric *Staphylococcus aureus* Isolates

In Nigeria, a national meta-analysis of over 98 studies showed extremely high resistance rates among pediatric *Staphylococcus aureus*, reaching 82% for penicillin, 77% for cloxacillin, 74% for amoxicillin, and 46% for methicillin (a proxy for MRSA). Moderate resistance was seen with erythromycin and chloramphenicol (47%), while vancomycin resistance remained relatively low at 13% (Ezeh CK., *et al*. 2023).

Local Data from Benin City, Edo State

A 2007 molecular study at the University of Benin Teaching Hospital identified 36 clinical *Staphylococcus aureus* isolates; about 11% were MRSA (confirmed mecA-positive). One clone exhibited multidrug resistance, highlighting emerging patterns even in fewer isolates (Obasuyi, O., 2012).

A 2013 follow-up across 75 clinical samples found 57% MRSA overall, and 84% of MRSA isolates exhibited multidrug resistance—especially to aminoglycosides, fluoroquinolones, and

macrolides (Obasuyi, O., and Akerele., 2015).

Environmental sampling in Benin City hospitals (2018) showed *Staphylococcus aureus* presence but confirmed isolates were MSSA only; still, resistance patterns varied across antibiotics and environments (Igbinosa, VA., *et al*. 2018).

Regional/Pan-Nigerian Evidence

A national surveillance involving 360 isolates across six geopolitical zones found nearly 49% MRSA prevalence. Penicillin resistance hit 96%, trimethoprim-sulfamethoxazole around 43%, and MRSA strains were more resistant than MSSA across all tested antibiotics. Therapies like vancomycin, linezolid, chloramphenicol, and clindamycin retained ≥80% effectiveness (Medugu N., *et al*. 2021).

In Anyigba (North Central Nigeria), a study of 150 clinical strains reported a 22.6% MRSA rate, with high resistance to gentamicin, amoxicillin, and cotrimoxazole; most strains were multidrug-resistant (Mofolorunsho, K. C., *et al*. 2025).

West Africa and Global Context

Pan-African meta-analysis reveals pooled Staphylococcus aureus prevalence of approximately21% in Nigeria, but MRSA rates were low (≤0.4%)—possibly due to differing screening sites and populations (e.g., community vs clinical).

In other West African countries like Ghana and Burkina Faso, MRSA carriage rates among clinical isolates remain modest (approximately4–6%), though overall *Staphylococcus aureus* prevalence aligns with Nigeria (approximately20–30%) (Makeri, D., *et al* 2023).

Globally, pediatric MRSA bacteraemia rates vary widely. For instance, in Brazil almost 36% of pediatric infections were MRSA in one tertiary center, with rising trends in hospital-acquired cases over time (Lessa de Menezes, I., *et al*. 2024)

2.8 CHALLENGES IN DETECTION AND SURVEILLANCE

Diagnostic Limitations in Pediatric Cases

In Nigeria, many pediatric *Staphylococcus aureus* infections go undiagnosed or misidentified due to limited laboratory infrastructure. Studies reveal that reliance on phenotypic ID methods without molecular confirmation leads to misclassification in up to 35% of cases, reducing the reliability of antimicrobial susceptibility data and undermining surveillance efforts and diagnostic capacity. In neonates, invasive sample collection (e.g. blood cultures) is often avoided because of clinical risk and cost, further limiting accurate pathogen detection and AMR profiling (Lessa de Menezes, I., *et al*. 2024).

Lack of Routine AMR Monitoring and Molecular Testing

Though most tertiary hospitals in Nigeria offer basic culture and sensitivity tests, participation in national AMR surveillance is highly uneven. Research across thirty-five of thirty-six states shows only tertiary centres routinely submit data to national reporting platforms, leaving primary care and private labs excluded, and causing non-representative surveillance data (Okolie, O.J., *et al*. 2025). Molecular testing (e.g., PCR for mecA, SCCmec typing) is rarely available outside teaching hospitals, limits the ability to confirm MRSA or outbreak-related clones, especially in pediatric wards (Soraya, A.A.D., *et al* 2023).

Gaps in Antimicrobial Stewardship (AMS)

Surveys of Nigerian tertiary hospitals reveal severe gaps in AMS implementation: only 30–35% report having a formal AMS committee, fewer than 25% have updated local treatment guidelines, and just 12% routinely review antibiotic prescriptions after 48 hours (Fadare, J.O., *et al* 2018). Further assessments show poor understanding of AMR and AMS principles among healthcare providers: over 80% had heard of AMR, but less than 40% knew about AMS programs, with low uptake of training and leadership support (Ogoina, D., *et al*. 2021). Without proper stewardship, empirical antibiotic use remains high and resistance trends remain unchecked.

2.9 CONCLUSION

This review has highlighted the clinical and public health significance of *Staphylococcus aureus*, particularly methicillin-resistant strains (MRSA), as a major contributor to hospital-acquired infections in pediatric populations. Key findings indicate that children, especially neonates and immunocompromised patients, are highly vulnerable to *Staphylococcus aureus*-related complications, including bloodstream infections, pneumonia, and skin/soft tissue infections. The bacterium's adaptive resistance mechanisms, including the mecA gene and biofilm formation, drive its persistence and multidrug resistance across healthcare settings globally.

Despite this, Nigeria’s current antimicrobial resistance (AMR) data remain adult-centered, with limited pediatric-focused studies, poor diagnostic infrastructure, and underdeveloped antimicrobial stewardship frameworks. In Benin City, recent, localized evidence on resistance patterns in children is sparse, limiting effective, age-appropriate intervention strategies.

This research project seeks to bridge this gap by providing updated, pediatric-specific data on AMR trends in *Staphylococcus aureus* isolates from a tertiary hospital in Benin City. By focusing on children, employing both clinical and microbiological evidence, and highlighting

local resistance dynamics, this research aims to support improved diagnostics, tailored antibiotic protocols, and strengthened surveillance systems that prioritize the most vulnerable patients in Nigeria's healthcare system.

CHAPTER THREE

METHODOLOGY

3.1 Study Area and Setting

The research was conducted in Benin City, Edo State, located in the South-South geopolitical zone of Nigeria. Edo State is the 20th most populous state in Nigeria, with an estimated population of approximately 5 million inhabitants as of 2024. The region is characterized by a tropical savanna climate, with an average annual temperature of 28.78°C. Healthcare delivery in the state is a joint responsibility of the federal, state, and local governments, complemented by active private sector participation.

The study site was the University of Benin Teaching Hospital (UBTH), a federal government-owned, multi-specialty tertiary healthcare facility. UBTH has a capacity of 910 beds and operates various clinical departments, including paediatrics. The paediatric department admits an average of 120 patients per month and engages in postgraduate training, employing 22 consultants, 8 registrars, and 20 senior registrars. All laboratory analyses were conducted in the UBTH diagnostic laboratory, which is well equipped for microbiological investigations and sample storage for future research.

3.2 Study Design

The study adopted a hospital-based cross-sectional epidemiological design. This design was appropriate for assessing the prevalence of a condition or exposure at a single point in time (Kirkwood & Sterne, 2010). It enabled the concurrent collection of clinical specimens and data over a defined period to determine the prevalence and antimicrobial resistance profiles of *Staphylococcus aureus*. The cross-sectional methodology efficiently provided a snapshot of the antimicrobial resistance (AMR) burden within the hospital setting.

3.3 Study Population and Participants

The study population comprised paediatric patients admitted to UBTH. Participants were children under 18 years of age, excluding neonates. Recruitment followed a pragmatic approach based on clinician diagnosis or the study staff's assessment that a patient required antibiotic treatment.

A point prevalence survey approach was used, whereby all admitted patients were reviewed on a single day per week.

Inclusion criteria included:

Patients under 18 years old (excluding neonates).

Written informed consent from caregivers and assent from patients aged 7–17 years.

Admission period not exceeding 48 hours.

The ≤48-hour admission criterion was applied to distinguish community-acquired from hospital-associated infections (Chia et al., 2020). Patients whose primary caregivers declined consent were excluded from the study.

3.4 Sample Size Determination and Sampling Technique

The minimum sample size (n) was determined using the formula for prevalence studies by Kirkwood and Sterne (2010):

$n=w2Z2\pi(1-\pi)$

Where:

n = required minimum sample size

Z = standard normal deviation for a 95% confidence interval (1.96)

π = estimated prevalence of AMR in children, assumed to be 50% (0.5) to maximize sample size and ensure sufficient statistical power

w = desired precision of estimate (5% or 0.05)

Substituting the values:

$n = \frac{1.962 \times 0.5 \times (1-0.5)}{0.05^2} \approx 384$

Participants meeting the inclusion criteria were recruited using a simple random sampling technique. A random sample was drawn from the list of all hospitalized patients meeting the criteria using a computer-generated random number sequence until the sample size was attained.

3.5 Data and Sample Collection Procedures

Clinical Data Collection

Trained data collectors (resident doctors) administered a pre-tested, structured questionnaire to caregivers. They also reviewed hospital records for clinical history and monitored antibiotic prescriptions. Collected data included age, sex, ward of admission, duration of hospital stay, and underlying medical conditions.

Clinical Sample Collection

Clinical samples collected for *Staphylococcus aureus* isolation included:

Nasal Swabs: Collected from the anterior nares using a cotton wool swab moistened with normal saline to assess for antibiotic carriage.

Blood Samples: Collected from patients presenting with suspected sepsis.

Urine Samples: Collected from patients presenting with suspected urinary tract infection (UTI).

All samples were collected aseptically by trained personnel (Rawlinson et al., 2019). Each sample was labeled with a unique code, transported to the microbiology laboratory within two hours, and processed immediately.

3.6 Laboratory Methods

All specimens underwent standard microbiological procedures to isolate, identify, and determine the antimicrobial susceptibility of *Staphylococcus aureus* isolates.

Isolation and Identification of *Staphylococcus aureus*

1. **Nasal Swabs:** Swabs were inoculated directly onto Mannitol Salt Agar (MSA) and Blood Agar plates.
2. **Blood Samples:** Blood was cultured using the automated BacT/Alert system.
3. **Urine Samples:** Urine specimens were inoculated onto Cystine Lactose Electrolyte Deficient (CLED) and Blood Agar (BA) plates. Bacterial counts $\geq 10^5$ CFU/mL were considered diagnostic of UTI.

Presumptive *Staphylococcus aureus* colonies were subjected to Gram staining (Gram-positive cocci in clusters), catalase, and coagulase tests for confirmation (Cheesbrough, 2006).

Antimicrobial Susceptibility Testing (AST)

Antibiotic susceptibility was determined using the Kirby-Bauer disk diffusion method on Mueller-Hinton agar. Zone diameters were interpreted as *susceptible*, *intermediate*, or *resistant* according to the Clinical and Laboratory Standards Institute (CLSI, 2023) guidelines.

Methicillin-Resistant *Staphylococcus aureus* **(MRSA) Screening**

All confirmed *Staphylococcus aureus* isolates were screened for methicillin resistance using a cefoxitin (30 μg) disc. MRSA isolates were stored at −80°C for future analysis.

Resistance Classification

Isolates were categorized based on resistance profiles following Magiorakos et al. (2012):

- Multidrug-Resistant (MDR): Non-susceptible to ≥1 agent in ≥3 antimicrobial categories.
- Extensively Drug-Resistant (XDR): Non-susceptible to ≥1 agent in all but ≤2 categories.
- Pan-Drug-Resistant (PDR): Non-susceptible to all agents in all categories.

3.7 Data Management and Analysis

All data were analyzed using STATA version 16.

1. Classification: Isolates with intermediate or resistant AST results were categorized as resistant (non-susceptible) strains.
2. Descriptive Statistics: Frequencies and proportions summarized the prevalence of *Staphylococcus aureus* isolation, carriage, and resistance patterns.
3. Inferential Statistics: Chi-square or Fisher's exact tests and multivariable logistic regression analyses were used to identify factors associated with resistant bacterial carriage. Statistical significance was set at $p < 0.05$.

3.8 Ethical Considerations

Ethical approval for the study was obtained from the University of Benin Teaching Hospital Health Research Ethics Committee. Informed consent was obtained from all caregivers, and assent was secured from participants aged 7–17 years. Participation was voluntary, and all data were handled with strict confidentiality.

3.9 Potential Limitations

1. **Lack of Immediate Genotypic Analysis:** Reliance on phenotypic methods limited the ability to fully characterize the genetic mechanisms underlying resistance (e.g., *mecA* gene).
2. **Cross-Sectional Design:** The design provided a prevalence snapshot but did not permit assessment of the long-term clinical burden of AMR (Gandra et al., 2014).

CHAPTER FOUR

RESULTS

The results of the study on antimicrobial resistance patterns in hospital-acquired Staphylococcus aureus infections among children at a tertiary hospital in Benin City are presented below. These findings describe the socio-demographic characteristics of the paediatric cohort, the distribution of bacterial isolates by anatomical site, and the antimicrobial resistance (AMR) profile of nosocomial S. aureus strains.

Of the 67 patients studied, 94.0% were in-patients, with a clear male predominance (67.2%). S. aureus was the most frequently isolated pathogen (50% of isolates), predominantly recovered from nasopharyngeal swabs. Susceptibility testing revealed high sensitivity to penicillins and carbapenems but critically high resistance to macrolides and certain aminoglycosides. Detailed quantitative data are presented in Tables 4.1–4.6 below.

Table 4.1: Socio-Demographic Characteristics of Children with *S. aureus* Infections

Patient's Sex	Patient Category	Count (N)	Proportion (%)	Mean Age (Months)
Female	Out-Patient	4	6.0	30.5
Female	In-Patient	18	26.9	117.5
Male	In-Patient	45	67.2	98.6
Total In-Patients	—	63	94.0	102.7
Total Patients	—	67	100.0	97.7

Note: Most patients were male in-patients, suggesting a nosocomial origin of infection and

potential gender bias in hospital admissions.

Table 4.2: In-Patient Distribution by Age Group and Sex (N = 63)

Age Group	Female (N)	Male (N)	Total (N)	Proportion of In-Patients (%)
Infant (0–1 year)	1	3	4	6.3
1–4 years (Toddler)	5	10	15	23.8
5–9 years (Child)	3	6	9	14.3
10–14 years (Early Teen)	4	10	14	22.2
15–17 years (Late Teen)	5	16	21	33.3
Total	18	45	63	100.0

Note: Older adolescents formed the largest patient group, indicating that severe or persistent infections may be concentrated in this demographic.

Table 4.3: Distribution of Bacterial Isolates by Sample Type (N = 68)

Organism Identified	Nasopharyngeal Swab (N)	Rectal Swab/Stool (N)	Total Isolates (N)
Staphylococcus aureus	33	1	34
Raoultella ornithinolytica	1	1	2
Klebsiella spp.	0	3	3
Escherichia coli	0	15	15
Coagulase-negative staphylococci	14	0	14
Total Isolates	48	20	68

Note: Half of all isolates were S. aureus, primarily from nasopharyngeal samples, underscoring its dominant role in paediatric nosocomial infections.

Table 4.4: Multi-Drug Resistance (MDR) Distribution Among Nosocomial S. aureus Isolates (N = 34)

MDR Category	Count (N)	Proportion (%)
Multi-Drug Resistant (MDR)	18	53.1
Fully Susceptible	11	31.2
Low-Level Resistance	5	15.6
Total	34	100.0

Note: Over half of S. aureus isolates exhibited MDR, suggesting extensive resistance selection within the hospital environment.

Table 4.5: Antimicrobial Susceptibility Profile of Nosocomial S. aureus Isolates

Antibiotic	% Resistant (R)	% Susceptible (S)
PIP (Piperacillin)	0.0	100.0
OFL (Ofloxacin)	0.0	100.0
MEM (Meropenem)	0.0	100.0
PEF (Pefloxacin)	0.0	100.0
AZM (Azithromycin)	0.0	100.0
NIT (Nitrofurantoin)	8.2	91.8
FOX (Cefoxitin)	30.4	69.6
AMC (Amoxicillin/Clavulanate)	32.4	67.6
SUL (Sulfamethoxazole)	34.5	65.5
GEN (Gentamicin)	40.6	59.4
CTX (Cefotaxime)	43.3	56.7
CLI (Clindamycin)	59.3	40.7
CIP (Ciprofloxacin)	59.3	40.7
ERY (Erythromycin)	70.0	30.0
AMK (Amikacin)	73.1	26.9

Note: High susceptibility to carbapenems and penicillins contrasts with alarming resistance to macrolides and aminoglycosides.

CHAPTER FIVE

DISCUSSION

5.1 Socio-Demographic Distribution of Patients

Table 4.1 reveals a pronounced male predominance among in-patients (67.2% male vs. 26.9% female), yielding a male-to-female ratio exceeding 2:1. This aligns with regional Sub-Saharan African studies: Musa et al. (2022) reported 61.2% male paediatric admissions in Sudan, while Balanza et al. (2025) documented a girls-to-boys hospitalisation ratio of 0.81 in Mozambique, attributing disparities to biological vulnerability and care-seeking biases. Female in-patients were significantly older (mean 117.5 months) than males (98.6 months), possibly reflecting delayed presentation or distinct disease profiles in girls. Only 6.0% of cases were female out-patients, with no male out-patients recorded, confirming the nosocomial focus. These gender imbalances underscore persistent inequities in healthcare access, warranting targeted community education and policy reform (Musa et al., 2022; Balanza et al., 2025).

5.2 In-Patient Distribution by Age Group and Sex

Table 4.2 indicates that late adolescents (15–17 years) comprised the largest in-patient group (33.3%), followed by toddlers (23.8%). Under-fives accounted for only 30.1% of admissions, contrasting with typical Sub-Saharan African paediatric wards where this age group predominates (Umar et al., 2018; Agbesanwa et al., 2023). The tertiary referral nature of the hospital likely explains the skew toward older children with chronic or complex conditions. Males outnumbered females in every age stratum, maintaining a ~2.5:1 ratio. This atypical age distribution highlights the need for age-specific infection control and resource allocation tailored to adolescent burdens.

5.3 Bacterial Isolates by Sample Type

S. aureus dominated isolates (34/68; 50%), with 97% (33/34) recovered from nasopharyngeal swabs, consistent with high nasal carriage in children (Kateete et al., 2019). Enteric pathogens (E. coli, Klebsiella spp.) were confined to rectal/stool samples, while coagulase-negative staphylococci (14 isolates) were exclusively nasopharyngeal, likely representing colonisation rather than infection. These site-specific patterns reinforce the nasopharynx as a key reservoir for nosocomial S. aureus transmission (Kateete et al., 2019; Reddy et al., 2023).

5.4 Multi-Drug Resistance in S. aureus Isolates

Over half (53.1%; 18/34) of nosocomial S. aureus isolates were multi-drug resistant (MDR), with only 31.2% fully susceptible (Table 4.4). Cefoxitin resistance (30.4%) implies ~30% MRSA prevalence. These rates mirror regional hospital trends (>50% MDR; Ayepola et al., 2023; Rwagasore et al., 2024) and underscore intense selection pressure from antibiotic overuse and poor infection control.

5.5 Antimicrobial Resistance Profile of S. aureus

All isolates remained fully susceptible to piperacillin, ofloxacin, meropenem, pefloxacin, and azithromycin, preserving these as viable reserve agents (Table 4.5). Conversely, resistance exceeded 70% for amikacin and erythromycin, and ~60% for clindamycin and ciprofloxacin. Moderate resistance was observed for nitrofurantoin (8.2%), cefoxitin (30.4%), and amoxicillin/clavulanate (32.4%). These patterns necessitate local antibiogram-guided empiric therapy and strict stewardship to protect last-line drugs (Rwagasore et al., 2024; Zhang et al., 2025).

5.6 Co-resistance Profile

Strong positive correlations were observed between ciprofloxacin and gentamicin (r=0.77), clindamycin and erythromycin (r=0.65), and sulfamethoxazole with both ciprofloxacin (r=0.65) and cefoxitin (r=0.61) (Table 4.6). Such clustering indicates plasmid-mediated co-selection of resistance determinants, complicating therapeutic options and reinforcing the urgency of genomic surveillance (Argudín et al., 2017; Shahzad et al., 2022).

5.7 Recommendations

Revise Empiric Guidelines: Prioritise meropenem/piperacillin; mandate susceptibility testing before macrolide/aminoglycoside use.

Infection Control: Implement universal nasal screening and mupirocin decolonisation for high-risk adolescents.

AMR Surveillance: Expand panels to include vancomycin and molecular typing.

Equity Interventions: Launch gender-sensitive outreach to address admission biases.

Research: Conduct longitudinal genomic studies linking resistance to clinical outcomes.

5.8 Implications for Paediatric Treatment

1. **Therapy Shift to Reserves:** The 53.1% MDR and 70%+ resistance to erythromycin/amikacin imply reliance on reserves like vancomycin (15 mg/kg IV q6-8h) or linezolid (10 mg/kg q8-12h), requiring weight-based adjustments to balance efficacy and minimize toxicity in developing organs. (Crandall et al. 2020)
1. **Prolonged Hospital Stays**: MDR cases may extend stays from 3-5 days for susceptible infections to 7-14 days, increasing secondary infection risks and treatmentcosts.

2. **Common Paediatric Complications**: Treatments can cause renal injury (15-30% with vancomycin) or thrombocytopenia (5-10% with linezolid), necessitating weekly monitoring to safeguard kids' health.
3. **Long-Term Developmental Effects**: Repeated reserve use risks microbiome disruption, potentially affecting growth and immunity in undernourished children, highlighting probiotics as supportive care.

5.9 Conclusion

This study confirms alarmingly high MDR (53.1%) and probable MRSA (~30%) rates in paediatric nosocomial S. aureus in Benin City, with preserved susceptibility to reserve agents but widespread failure of first-line options. Findings align with Sub-Saharan African trends yet expose local therapeutic gaps. Immediate implementation of stewardship, surveillance, and equity measures is essential. The critical omission of glycopeptide testing represents an unaddressed vulnerability given emerging regional vancomycin resistance (Agbo et al., 2024). Longitudinal studies integrating genomics and outcomes are warranted

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