

MOLECULAR EPIDEMIOLOGY AND CHARACTERIZATION OF ANTIBIOTIC
RESISTANCE GENES IN STAPHYLOCOCCUS AUREUS BLOODSTREAM ISOLATES
IN AFRICA: A SYSTEMATIC REVIEWAhmed Mohamed Mohamoud^{1*}, G. R. Neel¹, Chinyere Nkemjika Anyanwu¹, Yahye Ahmed Abdi²¹Faculty of Biomedical Sciences, Department of Microbiology, Kampala International University. Uganda.²Faculty of Allied Health Sciences, Department of Medical Laboratory Sciences. Uganda.***Corresponding Author: Ahmed Mohamed Mohamoud**

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ABSTRACT

Background: *Staphylococcus aureus* is a major cause of bloodstream infections (BSIs) globally, with increasing rates of multidrug resistance posing a significant threat to public health, especially in Africa. The molecular mechanisms underlying antibiotic resistance in *Staphylococcus aureus* are diverse and poorly characterized in many African regions. **Objective:** This systematic review aimed to evaluate the molecular characterization of antibiotic resistance genes in *Staphylococcus aureus* isolates from bloodstream infections in Africa. **Methods:** A comprehensive literature search was conducted in PubMed, Scopus, and Web of Science databases for studies published between 2010 and 2024. Eligible studies were those reporting molecular detection of resistance genes in *Staphylococcus aureus* isolated from bloodstream infection in African countries. Data were extracted on study design, country, sample size, resistance genes detected, and resistance profiles. The review followed PRISMA guidelines, and risk of bias was assessed using a modified JBI checklist for molecular studies. **Results:** Out of 267 identified articles, 12 studies met the inclusion criteria. Most were cross-sectional and hospital-based, covering countries such as Egypt, Uganda, Ghana, Nigeria, Ethiopia, South Africa, and Tunisia. The most commonly identified resistance genes included *mecA*, *ermA*, *ermB*, *ermC*, *blaZ*, *tetK*, and *tetM*. A high prevalence of multidrug-resistant *Staphylococcus aureus* strains was reported, with methicillin resistance (MRSA) being predominant at many sites. **Conclusion:** The molecular evidence demonstrates a high burden of antibiotic resistance genes in *Staphylococcus aureus* bloodstream infections in African hospitals. This underscores the urgent need for molecular surveillance, antimicrobial stewardship, and policy interventions to combat the spread of multidrug-resistant *Staphylococcus aureus* in the region.

KEYWORDS: *Staphylococcus aureus*, bloodstream infection, antibiotic resistance, resistance genes, MRSA, Africa, molecular characterization, multidrug resistance.

1.0 INTRODUCTION

Bloodstream infection (BSI) is a serious medical condition characterized by the presence of viable microorganisms in the bloodstream, leading to systemic inflammatory response, sepsis, organ failure, and potentially death if not promptly treated. (Weiner-Lastinger et al. 2020).

Globally, approximately 30 million people develop BSIs each year, accounting for nearly 6 million deaths. Pediatric and neonatal sepsis alone affects millions

annually. In Eastern Africa, BSI prevalence has been reported between 11% and 28%, reflecting a substantial regional burden.(Kern and Rieg 2020). Reported mortality associated with *Staphylococcus aureus* bacteremia ranges between 15% and 60%, highlighting its severe clinical impact(Jamalludeen 2021). Each year, sepsis affects around 1.2 million children and 3 million newborns (Fleischmann-Struzek et al. 2018).

In Eastern Africa, the prevalence of bloodstream infections has been reported to range between 11% and

28% (Deku et al. 2019). BSIs are defined by the presence of viable bacterial or fungal organisms in the bloodstream that trigger an inflammatory response, often accompanied by changes in clinical, biochemical, and hemodynamic parameters (Viscoli 2016).

Bloodstream infections are caused by a wide spectrum of pathogens, including Gram-negative bacteria such as *Escherichia coli*, *Klebsiella* species, *Pseudomonas aeruginosa*, and *Neisseria meningitidis*, as well as Gram-positive organisms including *Staphylococcus aureus*, coagulase-negative staphylococci, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, and *Enterococcus faecium* (Ambachew, Gebrecherkos, and Ayalew 2022).

Host-related factors such as extremes of age, immune suppression, and acquisition of microbial virulence determinants significantly contribute to BSI occurrence (Papadimitriou-Oliveri et al. 2016). Based on host characteristics, BSIs may occur in individuals at the extremes of age, immunocompetent hosts, and patients with underlying conditions that increase susceptibility (Viscoli 2016).

Staphylococcus aureus is one of the leading causes of BSIs globally. This Gram-positive, coagulase-positive bacterium is associated with severe outcomes including sepsis, prolonged hospitalization, and high healthcare costs (Tong et al. 2015). It is also responsible for numerous infections in both community and healthcare settings (Haque et al. 2018). *Staphylococcus aureus* is a Gram-positive, facultative anaerobic coccus with distinct virulence factors. Adhesins enable the organism to enter the bloodstream and bind to biotic and abiotic surfaces, after which coagulase facilitates biofilm formation through fibrinogen interaction, enhancing drug resistance (Jenkins et al. 2015).

Following *Escherichia coli*, *Staphylococcus aureus* is the second leading cause of bloodstream infections

globally (Laupland et al. 2013). Its estimated incidence ranges from 10 to 30 cases per 100,000 person-years, with hospital mortality reaching up to 40% (Nambiar et al. 2018). Approximately one-third of the human population is colonized with *S. aureus*, providing a continuous reservoir for invasive infections (Jamalludeen 2021). The organism's ability to form biofilms on intravascular devices further increases its persistence and resistance to antimicrobial agents (Watkins and Unnikrishnan 2020).

1.2 OBJECTIVES

1.2.1 GENERAL OBJECTIVE

To systematically review and analyze published data on the molecular characterization of antibiotic resistance genes in *Staphylococcus aureus* isolated from bloodstream infections in Africa.

1.2.2 Specific Objectives

1. To evaluate the molecular diagnostic techniques used for detecting resistance genes.
2. To determine and summarize the types of antibiotic resistance genes reported in *Staphylococcus aureus* bloodstream infection in Africa.
3. To assess the prevalence of key resistance genes, such as *mecA*, *blaZ*, *erm* variants, and *tet* genes, in the included studies.

2.0 METHODOLOGY

2.1 Search Strategy

The molecular characterization of antibiotic resistance genes of *Staphylococcus aureus* in bloodstream infection in Africa was examined using a structured and search strategy (Scopus, PubMed, and Web of Science). We formulated our search query by combining key concepts including ("Molecular characterization" AND "antibiotic resistance genes" AND "*Staphylococcus aureus*" AND "bloodstream" AND "Africa") with their variations using the Boolean operators (AND, OR).

2.2 Search Query

Database	Search query	Date
PubMed	"Molecular characterization" AND "antibiotic resistance genes" AND " <i>Staphylococcus aureus</i> " AND "bloodstream" AND "Africa" OR "Algeria" OR "Angola" OR "Benin" OR "Botswana" OR "Burkina Faso" OR "Burundi" OR "Cabo Verde" OR "Cameroon" OR "Central African Republic" OR "Chad" OR "Comoros" OR "Congo, Democratic Republic of the" OR "Congo, Republic of the" OR "Cote d'Ivoire" OR "Djibouti" OR "Egypt" OR "Equatorial Guinea" OR "Eritrea" OR "Eswatini" OR "Ethiopia" OR "Gabon" OR "Gambia" OR "Ghana" OR "Guinea" OR "Guinea-Bissau" OR "Kenya" OR "Lesotho" OR "Liberia" OR "Libya" OR "Madagascar" OR "Malawi" OR "Mali" OR "Mauritania" OR "Mauritius" OR "Morocco" OR "Mozambique" OR "Namibia" OR "Niger" OR "Nigeria" OR "Rwanda" OR "Sao Tome and Principe" OR "Senegal" OR "Seychelles" OR "Sierra Leone" OR "Somalia" OR "South Africa" OR "South Sudan" OR "Sudan" OR "Tanzania" OR "Togo" OR "Tunisia" OR "Uganda" OR "Zambia" OR "Zimbabwe"	
Scopus	"Molecular characterization" AND "antibiotic resistance genes" AND " <i>Staphylococcus aureus</i> " AND "bloodstream" AND "Africa" OR "Algeria" OR "Angola" OR "Benin" OR "Botswana" OR "Burkina Faso" OR "Burundi" OR "Cabo Verde" OR "Cameroon" OR "Central African Republic" OR "Chad" OR "Comoros" OR "Congo, Democratic Republic of the" OR "Congo, Republic of the" OR "Cote d'Ivoire" OR "Djibouti" OR "Egypt" OR "Equatorial Guinea" OR "Eritrea" OR "Eswatini" OR "Ethiopia" OR "Gabon" OR "Gambia" OR "Ghana" OR "Guinea" OR "Guinea-Bissau"	

	Bissau" OR "Kenya" OR "Lesotho" OR "Liberia" OR "Libya" OR "Madagascar" OR "Malawi" OR "Mali" OR "Mauritania" OR "Mauritius" OR "Morocco" OR "Mozambique" OR "Namibia" OR "Niger" OR "Nigeria" OR "Rwanda" OR "Sao Tome and Principe" OR "Senegal" OR "Seychelles" OR "Sierra Leone" OR "Somalia" OR "South Africa" OR "South Sudan" OR "Sudan" OR "Tanzania" OR "Togo" OR "Tunisia" OR "Uganda" OR "Zambia" OR "Zimbabwe"	
Web of science	"Molecular characterization" AND "antibiotic resistance genes" AND "Staphylococcus aureus" AND "bloodstream" AND "Africa" OR "Algeria" OR "Angola" OR "Benin" OR "Botswana" OR "Burkina Faso" OR "Burundi" OR "Cabo Verde" OR "Cameroon" OR "Central African Republic" OR "Chad" OR "Comoros" OR "Congo, Democratic Republic of the" OR "Congo, Republic of the" OR "Cote d'Ivoire" OR "Djibouti" OR "Egypt" OR "Equatorial Guinea" OR "Eritrea" OR "Eswatini" OR "Ethiopia" OR "Gabon" OR "Gambia" OR "Ghana" OR "Guinea" OR "Guinea-Bissau" OR "Kenya" OR "Lesotho" OR "Liberia" OR "Libya" OR "Madagascar" OR "Malawi" OR "Mali" OR "Mauritania" OR "Mauritius" OR "Morocco" OR "Mozambique" OR "Namibia" OR "Niger" OR "Nigeria" OR "Rwanda" OR "Sao Tome and Principe" OR "Senegal" OR "Seychelles" OR "Sierra Leone" OR "Somalia" OR "South Africa" OR "South Sudan" OR "Sudan" OR "Tanzania" OR "Togo" OR "Tunisia" OR "Uganda" OR "Zambia" OR "Zimbabwe"	

2.3 Criteria of study

2.3.1 Inclusion Criteria

Only peer-review articles on the molecular characterization of antibiotic resistance genes in *Staphylococcus aureus* of bloodstream infection published in the English language were included in the present review.

2.3.2 Exclusion Criteria

The studies were excluded if they were not related to *Staphylococcus aureus*, not focused bloodstream infection, did not address molecular characterization, were not conducted Human, or lack of abstract, also outside Africa, and not specific country.

2.4 Study of Selection

The database (Scopus, PubMed, and Web of Science) search yielded and was extracted as comma-separated

value (CSV) files, saved, and combined. Duplicates were arranged and removed.

2.5 Data Extraction

The data was extracted and grouped into the following information: Author, Country, Study Design, sample size, setting design, antibiotics test, resistance profile, identified resistance genes, prevalence of resistance genes (see tables 1&2).

2.6 Risk of Bias

The Joanna Briggs Institute (JBI) critical assessment checklist for observational studies was used to evaluate the methodological quality of the included research. Study design, sample selection, outcome assessment, and data analysis were taken into consideration when rating the studies. The methodological quality of the majority of the included research was moderate to excellent.

		Risk of bias										Overall
		D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	
Study	Zaki et al, 2020	+	+	+	+	+	✗	+	+	+	+	-
	El sherif et al, 2022	+	+	+	+	+	+	+	+	+	+	+
	Elbargis et al , 2022	+	+	+	+	+	+	+	+	+	+	+
	Desta et al, 2022	+	+	+	+	+	✗	+	+	+	+	-
	Hamd et al, 2024	+	+	-	+	+	+	+	+	+	+	+
	Ackers-Joh et al, 2021	+	+	+	+	+	+	+	+	+	+	+
	Kpeli et al, 2016	+	+	+	+	+	+	+	+	+	+	+
	Zmatar et al, 2012	+	+	+	+	+	+	+	+	+	+	+
	Hetsa et al, 2024	+	+	+	+	+	+	+	+	+	+	+
	Balasopoulou et al, 2017	+	+	-	+	+	+	+	+	+	+	+
	Zmatar et al, 2008	+	+	+	+	+	+	+	+	+	+	+
	Shittu et al, 2011	+	+	-	+	+	-	+	+	+	+	✗

D1: Was the study design appropriate to address the research question?
 D2: Were study participants sampled properly?
 D3: Were the criteria for inclusion/exclusion clearly defined?
 D4: Was the sample size adequate?
 D5: Were the study subjects and setting described in detail?
 D6: Was there a control group (if applicable)?
 D7: Were there clear definitions for the variables under investigation?
 D8: Were the outcome measures appropriate?
 D9: Was the statistical analysis appropriate for the type of study?
 D10: Were the findings presented with adequate precision

Judgement
 ✗ High
 - Unclear
 + Low

3.0 RESULTS

3.1 Study Selection Outcome

The systematic search of PubMed, Scopus, and Web of Science databases identified a total of 267 records. After removing 123 duplicate articles, 144 studies remained for title and abstract screening. Of these, 124 articles were excluded for not meeting the eligibility criteria. Consequently, 20 full-text articles were assessed for eligibility. Among them, 8 studies were excluded (five were conducted outside Africa, and three lacked country-specific data). Finally, 12 studies fulfilled all inclusion criteria and were included in the qualitative synthesis. The study selection process is presented in the PRISMA flow diagram (Figure 1).

3.2 Study Characteristics

Out of the 12 included studies, 7 studies (58.33%) were published between 2020 and 2024. Egypt contributed the highest number of studies, 4/12 (33.3%), followed by Tunisia and Nigeria, 2/12 (16.6% each). Ghana, South Africa, Ethiopia, and Uganda each contributed 1 study (8.33%).

Most of the investigations were hospital-based 10/12(83.3%), while only 2 studies (16.6%) were community-based. Regarding molecular detection methods, the majority of studies employed PCR-based techniques, while three studies utilized whole-genome sequencing (WGS). Sample sizes varied widely, ranging from 22 to 1056 isolates, all obtained from blood specimens.

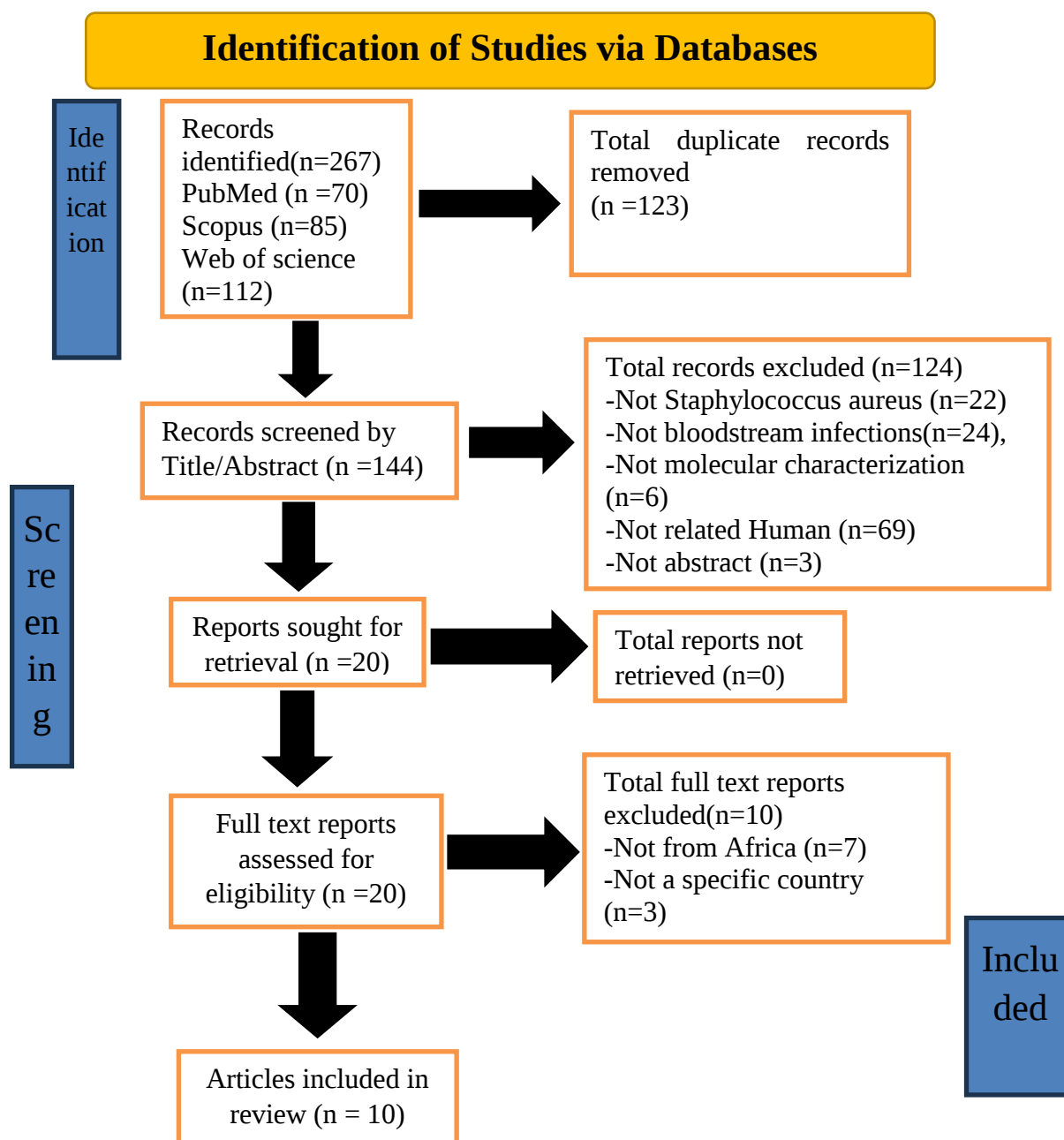


Figure 1: PRISMA flowchart.

Table 1: Study Characteristics.

S/N	Authors	Year	Country	Study Setting	Study Design	Sample Size	Specimen Type	Detection Method
1	Zaki et al., 2020	2020	Egypt	Hospital-based	Retrospective cross-sectional	250	Blood	PCR-detection
2	El Sherif et al., 2022	2021	Egypt	Hospital-based	Cross-sectional study	104	Blood	PCR-detection
3	Perovic et al., 2015	2015	South Africa	Community-based	Cross-sectional study	2709	Blood	Real PCR
4	Desta et al., 2022	2019	Ethiopia	Community-based	Cross-sectional study	1056	Blood	PCR-detection
5	Hamd et al., 2024	2024	Egypt	Hospital-based	Cross-sectional study	196	Blood	PCR-detection
6	Worku et al., 2025	2025	Ethiopia	Hospital-based	Cross-sectional study	111	Blood	Culture and Antimicrobial Test
7	Hetsa et al., 2024	2024	South Africa	Hospital-based	Cross-sectional study	45	Blood	Whole genome sequencing
8	Shittu et al., 2011	2011	Nigeria	Hospital-based	Cross-sectional study	68	Blood	PCR-detection
9	(Kajumbula et al. 2018)	2018	Uganda	Hospital	Cross-sectional study	3197	Blood	PCR detection
10	(Vandendriessche et al. 2017)	2017	DR Congo	Healthcare facilities	Cross-sectional study	108	Blood	PCR detection

Table 2: summarized data on antibiotics tested, resistance profile, identified genes, and prevalence of genes from the included studies.

S/N	Authors	Antibiotics test	Resistance profile	Identified genes	Prevalence of genes
1	Zaki et al.,2020	cefoxitin, ciprofloxacin, clindamycin, erythromycin, gentamicin, amikacin, oxacillin, rifampin, tetracycline, sulfamethoxazole	MDR	mecA, vacA, B, C	70%, 0%, 0%, 0%
2	El Sherif et al., 2022	cefoxitin, ciprofloxacin, clindamycin, erythromycin, gentamicin, amikacin, oxacillin, rifampin,	MDR	mecA/C, blaCTX-M	N/A
3	Perovic et al., 2015	Gentamicin, Tobramycin, Oxacillin, Erythromycin, Azithromycin, Clindamycin, Ciprofloxacin, Tetracycline, Rifampicin, Linezolid, TMP-SMX, Mupirocin, Vancomycin, Teicoplanin, Fosfomycin, Fusidic acid, Daptomycin	MDR	mecA, MRSA	43%, 0%
4	Desta et al, 2022	Penicillin, cefoxitin, erythromycin, clindamycin, tetracycline, trimethoprim-sulfamethoxazole, rifampin	MDR	mecA, vanA, vanB	4.8%, 25% ,0%
5	Hamd et al., 2024)	Azithromycin, doxycycline, gentamicin, cefoxitin, moxifloxacin, vancomycin, clindamycin, erythromycin, tetracycline	MDR	ermA, ermB, ermC, ermT, msrA	79.41%, 38.24%, 58.33%,14%
6	Worku et al., 2025	Penicillin, Cefoxitin, Gentamicin, Tobramycin	MDR	N/A	N/A
7	Hetsa et al., 2024	penicillin G, tetracycline, doxycycline, clindamycin, moxifloxacin, rifampicin, and erythromycin	MDR	mecA, erm(C), erm(A), blaZ, tetK, tetM	N/A
8	Shittu et al., 2011	Penicillin, Minocycline, Tetracycline, Kanamycin, Erythromycin, Cotrimoxazole, Oxacillin, Rifampicin, Gentamicin	MDR	mecA, ermA, msrA, tetK, tetM	16.2%, 8.8%, 2.9%, 39.7%, 16.2%

9	(Kajumbula et al. 2018)	Ceftriaxone, ciprofloxacin, chloramphenicol, piperacillin/tazobactam, imipenem, clindamycin, gentamicin, trimethoprim/sulfamethoxazole, methicillin	MDR	MRSA	32%
10	(Vandendriessche et al. 2017)	Penicillin, Cefoxitin, Gentamicin, Kanamycin, Tobramycin, Erythromycin, Tetracycline, Ciprofloxacin, Clindamycin, TMP-SMX, Chloramphenicol, Linezolid, Mupirocin, Vancomycin	MDR	mecA, dfrG, dfrK, ermA/B/C/T, tetM/K, aac(6')-aph(2''), aph(3'), ant(4'');	dfrG: 66.7% (72/108); mecA (MRSA): 25.0% (27/108); aac(6')-aph(2''): 92.6% of MRSA; tet(K): 85.2% of MRSA; erm(C): 74.1% of MRSA.

4.0 DISCUSSION

Bloodstream infections remain a leading cause of illness and death among people of all ages, especially those with weakened immune systems. (Weiner-Lastinger et al. 2020). In hospital environments, these infections are frequent and often result in severe or fatal outcomes. (Kern and Rieg 2020). *Staphylococcus aureus* bacteremiae, in particular, has reported mortality rates ranging from 15% to 60% (Jamalludeen 2021).

This systematic review demonstrates a concerning level of antibiotic resistance genes in *Staphylococcus aureus* associated with bloodstream infections (BSIs) across Africa. Most of the studies included were hospital-based (83.3%), emphasizing the substantial role of healthcare facilities as reservoirs of multidrug-resistant *Staphylococcus aureus*. (Tong et al. 2015).

The high detection rates of resistance genes such as *mecA*, *ermA*, *ermB*, *ermC*, *blaZ*, *tetK*, and *tetM* highlight the growing challenge posed by multidrug-resistant strains across the continent. These findings are aligned with international data showing that *Staphylococcus aureus* continues to be a major cause of BSIs with significant morbidity and mortality. (Tong et al. 2015).

The dominance of hospital-based studies (10 out of 12) suggests that clinical settings are central hubs for the proliferation of multidrug-resistant *Staphylococcus aureus*. Factors contributing to this include invasive procedures, prolonged hospitalization, and frequent use of devices such as intravascular catheters, which support biofilm formation, a key virulence feature of *Staphylococcus aureus*. (Peng et al. 2023).

In the Ghanaian study, 58 (63%) of 91 isolates were methicillin- or oxacillin-resistant phenotypically, and 43 (74%) were confirmed as MRSA by *mecA* detection. This proportion is much higher than the previously reported MRSA prevalence of 5.7% (B. et al. 2013). Comparable results have been documented in Ethiopia, Egypt, and Algeria, reporting MRSA prevalences of 55%, 52%, and 45%, respectively. (M.E. et al. 2013).

Among phenotypically methicillin-resistant isolates lacking *mecA*, alternative resistance mechanisms may be involved, such as altered penicillin-binding protein affinity (Clinical and Laboratory Standards Institute 2021). Other chromosomal factors, including *FemA* and *FemB*, influence methicillin resistance expression (Anon 2011), while genes such as *mecC* or *mecB* may also confer methicillin resistance (Becker et al. 2018).

For example, Zaki et al. (Zaki et al. 2020) identified a 71% *mecA* prevalence in Egypt, indicating significant methicillin resistance among clinical isolates. High levels of *mecA* and tetracycline-related genes, such as *tetK* and *tetM*, in several countries point toward variations in antibiotic use across regions. (Kotey et al. 2022). For instant (Khoramrooz et al. 2017) reported *tetK* in 98% of isolates in Ghana, likely related to widespread tetracycline use in both healthcare and agricultural settings. Similar trends have been described in other Ghanaian studies. (Monecke et al. 2023). Genes like *tetK* and *tetM* mediate efflux or ribosomal protection mechanisms, reducing tetracycline effectiveness. (Monecke et al. 2023).

Whole genome sequencing (WGS) has been instrumental in identifying diverse resistance genes. For example, (Kpeli et al. 2016) detected *ermA*, *ermC*, *mecA*, *blaZ*, *tetK*, and *tetM* in Uganda. Although PCR and WGS are powerful diagnostic tools, limited laboratory capacity, high costs, and infrastructure constraints remain major barriers in many African settings. (Kirkliauskienė et al. 2024). Expanding access to molecular diagnostics is critical for timely resistance detection and improved management outcomes.

Presence of *erm(A)* and *erm(C)* in macrolide, lincosamide, and streptogramin B resistant isolates aligns with expected resistance patterns, since erythromycin exposure can select for MLSB resistance. (Warsa et al. 1996). The *ermC* gene, which modifies the 23S rRNA and prevents drug binding, is commonly found in clinical *Staphylococcus aureus* isolates, including those from South Africa. (Kirkliauskienė et al. 2024).

5.0 CONCLUSION

The findings of this systematic review confirm a high prevalence of antibiotic resistance genes, including *mecA*, *erm*, *blaZ*, and *tet* variants in *Staphylococcus aureus* bloodstream isolates across Africa. The predominance of multidrug resistance, especially in hospital-acquired infections, underscores the urgent need for improved infection control, molecular surveillance, and antimicrobial stewardship programs.

The detection of resistance genes in community settings further highlights the expanding public health threat posed by *Staphylococcus aureus* beyond clinical environments. Combating this challenge will require coordinated, cross-sectoral interventions, including enhanced laboratory capacity, access to molecular diagnostics, regulatory enforcement on antibiotic use, and education of healthcare providers and the public.

Ultimately, robust policy frameworks, regional collaboration, and evidence-based practices are essential to slowing the spread of multidrug-resistant *Staphylococcus aureus* and improving patient outcomes in Africa's healthcare systems.

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Disclosure

The author declares that there are no conflicts of interest regarding the publication of this paper.

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