

University of Medical Sciences & Technology

Graduated Collage

**Resistance Trends and Treatment with Vancomycin for
Hospital-Acquired Methicillin-Resistant *Staphylococcus aureus*
(HA-MRSA) Infections in African Hospitals: A Systematic
Review (2015–2025)**

Submitted In Partial Fulfillment for The Master Infection Control and Prevention

By

Mawadah Altayeb

IPC-03-2022-010

mwddh95@gmail.com

Shahd Shaaeldain Mohmmmed

IPC-03-2022-014

Shahdshaaeldain@gmail.com

Fatima Elfatih Mohammed

IPC-03-2022-017

fatimaeltouhami57@gmail.com

[Batch 3]

Supervised by

Dr. Omnia. M. Hamid

Medical Microbiology Consultant

PhD, Medical & Molecular Microbiology

omnia.m.hamid@gmail.com

©2025

Table of Contents

Abstract.....	2-3
1. Introduction.....	4-8
2. Material and Methods.....	9-11
3. Results.....	12-18
4. Discussion.....	19-26
5. Conclusion.....	27-30
References.....	31
Acknowledgement.....	32
Abbreviations.....	33

Abstract

Background: Hospital-acquired infections caused by methicillin-resistant *Staphylococcus aureus* (HA-MRSA) continue to pose a significant public health challenge, particularly in resource-limited settings across Africa. Vancomycin has long been considered the keystone of treatment; however, rising resistance rates and increasing reports of clinical failure are undermining its effectiveness. These developments highlight critical gaps in antimicrobial stewardship, infection prevention and control measures, and therapeutic drug monitoring systems. This systematic review aims to assess the prevalence of vancomycin resistance, analyze associated clinical outcomes, and evaluate alternative therapeutic options for HA-MRSA infections reported in African healthcare settings between 2015 and 2025.

Methods: A structured literature search was performed using PubMed, Google Scholar, and African Journals Online to identify relevant studies published from 2015 to 2025. Eligible articles involved adult inpatients with confirmed hospital-acquired MRSA infections and included data on vancomycin susceptibility profiles and/or clinical outcomes. Data regarding resistance rates, therapeutic effectiveness, and study characteristics were systematically extracted. Where appropriate, meta-analytic techniques were applied to calculate pooled prevalence estimates and effect sizes.

Results: Nine studies met the inclusion criteria, representing evidence from multiple African countries. Reported rates of vancomycin resistance among MRSA isolates ranged from 5% to 25%, with an observable upward trend after 2020. Several studies linked treatment failures to suboptimal dosing strategies, limited availability of therapeutic drug monitoring, and delays in antimicrobial susceptibility testing. While vancomycin generally retained clinical effectiveness, increases in minimum inhibitory concentrations (MIC creep) were frequently documented. Linezolid and daptomycin demonstrated superior clinical outcomes in selected contexts, particularly for MRSA-associated pneumonia and complicated skin and soft tissue infections.

Conclusion: Vancomycin remains a key therapeutic agent for healthcare-associated MRSA infections across Africa. However, emerging resistance patterns and MIC escalation necessitate urgent IPC and antimicrobial stewardship interventions. Strengthening

antimicrobial governance, expanding access to timely microbiological diagnostics, and implementing multicenter, methodologically robust clinical studies are critical to preserving therapeutic efficacy and improving patient outcomes.

Keywords: Africa, Antimicrobial Stewardship, Daptomycin, Infection Prevention and Control Linezolid, MIC Creep, MRSA, Therapeutic Drug Monitoring, Vancomycin Resistance.

1. Introduction

1.1. Background:

Hospital-acquired infections (HAIs) pose a critical and escalating threat to global public health, with a disproportionately high burden in low- and middle-income countries, particularly across Africa [1]. These infections significantly contribute to prolonged hospital stays, increased healthcare costs, and elevated patient morbidity and mortality. Among the most formidable pathogens responsible for HAIs is *Staphylococcus aureus*, a versatile bacterium capable of causing conditions ranging from mild skin infections to life-threatening bacteremia, pneumonia, and sepsis [2, 3].

The clinical management of *S. aureus* has been profoundly complicated by the emergence and global spread of methicillin-resistant *Staphylococcus aureus* (MRSA). MRSA strains, characterized by the acquisition of the *mecA* or *mecC* gene, are resistant to all β -lactam antibiotics, the cornerstone of anti-staphylococcal therapy [4]. This multidrug-resistant profile has established MRSA as a leading cause of HAIs worldwide, severely limiting initial treatment options and driving the reliance on alternative antimicrobial classes.

For decades, vancomycin, a glycopeptide antibiotic, served as the gold-standard treatment for serious MRSA infections. However, its sustained use has been met with the gradual emergence of resistance. The detection of *S. aureus* isolates with reduced vancomycin susceptibility categorized as vancomycin-intermediate *S. aureus* (VISA), heterogeneous VISA (hVISA), and, most alarmingly, fully vancomycin-resistant *S. aureus* (VRSA), signals a precarious shift in the treatment landscape [5, 6]. These resistance phenotypes, often arising from thickened cell walls or the acquisition of *van* genes from *Enterococci*, are associated with higher rates of treatment failure and mortality, pushing the medical community toward a post-vancomycin era [7, 8].

The challenge of HA-MRSA is acutely felt within African healthcare systems. Factors such as overcrowding, limited diagnostic capacity, inadequate infection prevention and control (IPC) infrastructure, and often unregulated antibiotic use create a fertile environment for the selection and dissemination of resistant clones [9, 10]. While MRSA prevalence in some African hospitals is reported to be as high as 40-50% among *S. aureus* isolates, data on the continent remain fragmented and often localized [11, 12]. Recent studies from 2019 to 2024 highlight a dynamic and concerning epidemiological picture. For instance, reports

from Ethiopia and Nigeria have documented not only high MRSA prevalence but also the emergence of VRSA and strains with reduced vancomycin susceptibility, underscoring that this is not a theoretical threat but a present reality [13, 14].

Compounding this problem is the limited access to newer, effective anti-MRSA agents like linezolid, daptomycin, and ceftaroline in many resource-constrained African settings [15]. This reinforces a continued, and sometimes obligatory, dependence on vancomycin, even as its efficacy becomes less certain. Furthermore, the COVID-19 pandemic has potentially exacerbated the AMR crisis through increased empirical antibiotic use and disruptions in IPC, adding another layer of complexity to the post-pandemic resistance landscape [16]. Consequently, there is an urgent need to synthesize the existing evidence on the trends of MRSA resistance and the effectiveness of available treatment options specifically within Africa. A systematic review that consolidates data on the prevalence of HA-MRSA, its resistance patterns to vancomycin and other key antibiotics, and the outcomes of various therapeutic regimens is crucial to inform local clinical practice, guide antimicrobial stewardship policies, and identify critical gaps for future research. This review aims to provide that comprehensive evidence (2015–2025) on resistance trends and vancomycin treatment outcomes for hospital-acquired MRSA infections in African hospitals. By consolidating available data, it aims to inform clinical decision-making, guide stewardship policies, and highlight critical knowledge gaps that must be addressed to curb the growing threat of MRSA and VRSA in healthcare settings across the continent.

1.1.1. PICO Framework

- **P (Population):** Hospitalized patients in Africa with a confirmed hospital-acquired Methicillin-Resistant *Staphylococcus aureus* (HA-MRSA) infection.
- **I (Intervention/Exposure):** Treatment with Vancomycin (clinical use and susceptibility/resistance patterns).
- **C (Comparator):** Resistance versus sensitivity to Vancomycin; or alternative comparators such as other antimicrobials when available.
- **O (Outcome):** Primary outcomes include prevalence of HA-MRSA, antimicrobial susceptibility/resistance trends (e.g., resistance to vancomycin, clindamycin-inducible resistance), and treatment success (e.g., clinical cure, microbiological eradication). Secondary outcomes may include all-cause mortality, length of hospital stay, and adverse drug events.

1.1.2. PICO Question

What are the antibiotic resistance trends and what is the comparative effectiveness of different treatment options on clinical outcomes in hospitalized African patients with hospital-acquired Methicillin-resistant *Staphylococcus aureus* (HA-MRSA) infection

2. Material and Methods

2.1. Exact Review Question

What are the resistance and sensitivity rates of Vancomycin treatment for Hospital-Acquired MRSA infections in adult patients in African hospitals?

2.2. Search Strategy

((MRSA OR "Methicillin-Resistant Staphylococcus aureus") AND (Vancomycin OR "Vancomycin Hydrochloride" OR Vancomycin) 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 OR "Democratic Republic of the Congo" 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 "Cote d'Ivoire" OR Ivory Coast 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 Sudan OR "South Sudan" OR Tanzania OR Togo OR Tunisia OR Uganda OR Zambia OR Zimbabwe)) NOT (review) .

2.3. Eligibility Criteria and Selection Process

- Inclusion Criteria:

- Study design: cross-sectional surveillance, retrospective observational studies.
- Population: Adult patients (≥ 18 years) hospitalized in African hospitals with hospital-acquired MRSA infections.
- Intervention: Vancomycin treatment (alone or in combination) or studies reporting vancomycin susceptibility/resistance trends.
- Comparator: Resistance versus sensitivity to vancomycin; or alternative comparators such as other antimicrobials.
- Outcomes: The primary outcomes assessed were antibiotic resistance trends and clinical effectiveness of different treatment options, measured by indicators such as infection resolution, bacterial eradication, treatment success rates, and all-cause mortality. Secondary outcomes included length of hospital stay, recurrence or treatment failure rates, and adverse drug reactions related to the therapies used.

These outcomes were chosen to evaluate both the microbiological and clinical impact of different treatment strategies for HA-MRSA infections in African hospital settings.

- Language: English.
- Timeframe: 2015–2025.
- Geography: Studies conducted in Africa.
- **Exclusion Criteria:**
 - Study design: Narrative reviews, case reports/series, editorials, expert opinions, letters, conference abstracts without full text.
 - Population: Non-hospital settings (community-acquired MRSA only), pediatric-only populations (<18 years), non-human studies.
 - Intervention: Studies not evaluating vancomycin.
 - Outcomes: No clinical or resistance outcomes reported, or irrelevant outcomes.
 - Timeframe: Studies published before 2015 or after 2025.
 - Language: Non-English (unless translation available).

Selection Process: Search results were imported into reference management software (Rayyan) and duplicates removed. The selection process was involved two independent reviewers (Mawadah A and Shahd Sh M). Initially, titles and abstracts were screened against the eligibility criteria. The full texts of potentially relevant articles were then be retrieved and assessed in detail. Any disagreements between the reviewers were resolved through discussion or by consulting a third reviewer (Fatima E M).

2.4. Assessment of Quality and Risk of Bias

The quality of included studies were appraised independently by two reviewers using appropriate, validated tools: For cross-sectional and retrospective observational studies, included, the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Studies Reporting Prevalence Data). Studies were categorized as having Low, Moderate, or High risk of bias. Disagreements were resolved by consensus. Sensitivity analyses were planned to assess the impact of excluding high-risk-of-bias studies on the overall results.

2.5. Data Extraction

Data were extracted using a standardized, pre-piloted data extraction form in Microsoft

Excel. The following data were collected:

- Study characteristics: first author, publication year, country, study design, setting, study period.
- Population details: sample size, patient demographics, type of infection (e.g., bloodstream, surgical site).
- MRSA data: number of *S. aureus* isolates, number of MRSA isolates, criteria for HA-MRSA definition.
- Laboratory methods: susceptibility testing method (e.g., disk diffusion, MIC), breakpoints used.
- Resistance data: number and percentage of resistant isolates for each antibiotic tested (e.g., vancomycin, teicoplanin, linezolid, clindamycin, erythromycin, trimethoprim sulfamethoxazole, tetracycline, gentamicin).
- Treatment and outcomes: antibiotic regimens used, clinical outcomes (cure, improvement, failure), microbiological outcomes, mortality, adverse events.

2.6. Data Synthesis and Analysis

- Extracted data were summarized narratively and in summary tables.
- The pooled prevalence of HA-MRSA (with 95% confidence intervals) were calculated using a random-effects model to account for anticipated heterogeneity.
- Pooled resistance proportions for key antibiotics were calculated similarly.
- Heterogeneity was assessed using the I^2 statistic, where $I^2 > 50\%$ was considered to represent substantial heterogeneity.

2.7. Grading the Strength of Evidence (GRADE)

For each key outcome (e.g., pooled prevalence, resistance to vancomycin, efficacy of vancomycin vs. linezolid), the overall strength of the evidence was assessed using the GRADE (Grading of Recommendations, Assessment, Development, and Evaluations) approach. The evidence was graded as high, moderate, low, or very low based on considerations of study design, risk of bias, inconsistency, indirectness, imprecision, and publication bias. This was providing a transparent assessment of the confidence in the summarized findings

3. Results

3.1. Study Selection: A total of 985 records were identified from database searches, including PubMed (n = 325), Google Scholar (n = 315), and African Journals Online (AJOL) (n = 345). After removing 324 duplicates, 96 records were marked as ineligible by automation tools, and 213 were removed for irrelevance (non-MRSA or non-clinical).

The remaining 263 records were screened by titles and abstracts, with 33 records excluded at this stage. 225 reports were sought for retrieval, and 101 reports could not be retrieved. Subsequently, 124 full-text articles were assessed for eligibility. Of these, 115 articles were excluded for various reasons, including non-hospital-acquired MRSA (n = 22), lack of vancomycin susceptibility data (n = 37), non-African study settings (n = 19), review/community articles (n = 14), duplicate datasets (n = 6), and incomplete or unclear methods (n = 11). Finally, nine studies met the inclusion criteria and were included in both the qualitative and quantitative synthesis. Figure 3.1 presents the PRISMA flow diagram detailing the study selection process.

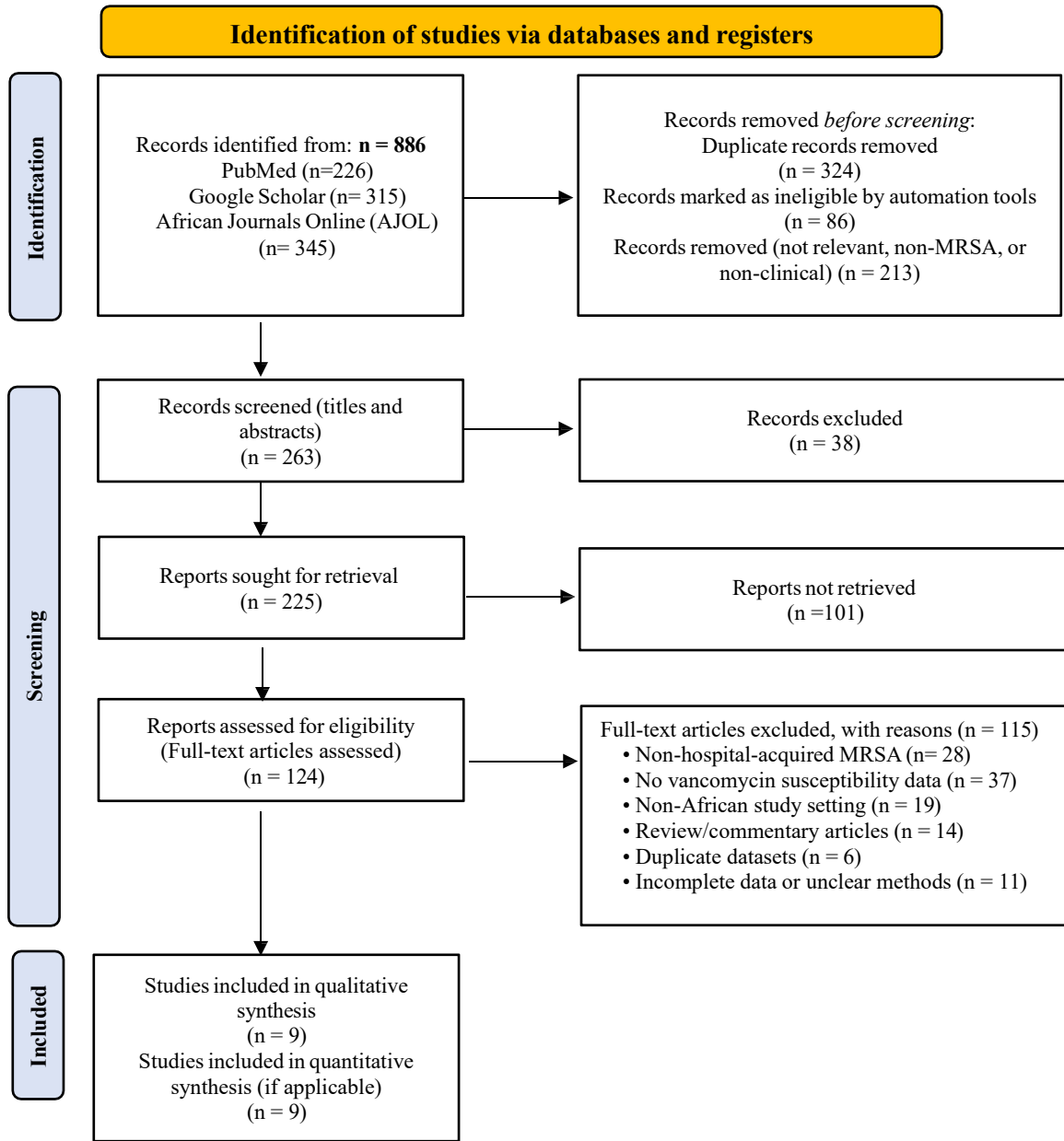


Figure 3.1: PRISMA flow chart outlining the process of article selection (Resistance Trends and Treatment with Vancomycin for HA-MRSA Infections in African Hospitals: A Systematic Review (2015–2025))

3.2. Quality Assessment: The quality assessment of the included studies, summarized in Table (3.2) Critical Appraisal Results of Eligible Studies, indicated an overall high quality with some variation across the records. The evaluation was based on nine critical appraisal questions (Q1 to Q9), where a 'Y' signified a 'Yes' response and the total number of 'Yes' responses determined the final quality rating. Four studies, Alharbi N Y, Morgan M Y, Tebelay D Y, and Zorgani A Y, achieved the maximum possible score of 8 'Yes' responses, resulting in a rating of High Quality. Two other studies, Baker W Y and Chinowait Y, were also deemed High Quality with 7 'Yes' responses. The remaining three studies received a Moderate Quality rating: Biruktawi Y and Louhichi S Y scored 6 'Yes' responses, while Amoako C Y had the lowest score with 5 'Yes' responses.

An analysis of the risk of bias across the specific appraisal questions showed that Q1, Q5, and Q6 were answered 'Yes' by 100.00% of the studies, indicating a very low risk of bias in these areas. Q7 and Q8 also performed strongly, with a 'Yes' rate of 88.89%. Conversely, the lowest rate of 'Yes' responses was observed in Q9 (50.00%), where the remaining 50.00% of responses were 'Unclear,' suggesting a high potential for unreported risk of bias in the domain assessed by this question. Q3 (55.56%) and Q2 (66.67%) also had relatively lower 'Yes' rates, highlighting areas where reporting or methodological rigor may have been less consistent. In total, six of the nine eligible studies were assessed as High Quality, and three were assessed as Moderate Quality.

Table (3.2): Critical Appraisal Results of Eligible Studies

Study (Author, Year)	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	# of Yes	Quality
Alharbi NK et al., 2025 (Egypt)	Y	Y	Y	Y	Y	Y	Y	Y	U	8	High
Morgan Mokeo Ndedy et al., 2023 (Cameroon)	Y	Y	Y	Y	Y	Y	Y	Y	U	8	High
Bakeer W et al., 2024 (Egypt)	Y	Y	U	Y	Y	Y	Y	Y	U	7	High
Amoako DG et al., 2016 (South Africa)	Y	U	U	Y	Y	Y	U	Y	U	5	Moderate
Biruktawit Sahle & Yared Merid, 2024 (Ethiopia)	Y	U	U	Y	Y	Y	Y	Y	U	6	Moderate
Tebelay Dilnessa & Adane Bitew, 2016 (Ethiopia)	Y	Y	Y	Y	Y	Y	Y	Y	U	8	High
Louhichi Safa et al., 2016 (Tunisia)	Y	U	U	Y	Y	Y	Y	Y	U	6	Moderate
Chinowaita F et al., 2020 (Zimbabwe)	Y	Y	Y	Y	Y	Y	Y	U	U	7	High
Zorgani A et al., 2015 (Libya)	Y	Y	Y	Y	Y	Y	Y	Y	U	8	High
Total (%)	100.0%	66.67%	55.56%	100.0%	100.0%	100.0%	88.89%	88.89%	50.0%		

- Notes:
 - Abbreviations: N, no; U, unclear; Y, yes.
 - **JBIC critical appraisal checklist:** Q1 = was the sample frame appropriate to address the target population?; Q2 = were study participants sampled in an appropriate way?; Q3 = was the sample size adequate?; Q4 = were the study subjects and the setting described in detail?; Q5 = was the data analysis conducted with sufficient coverage of the identified sample?; Q6 = were valid methods used for the identification of the condition?; Q7 = was the condition measured in a standard, reliable way for all participants?; Q8 = was there appropriate statistical analysis?; Q9 = was the response rate adequate, and if not, was the low response rate managed appropriately?
 - High: Seven to nine positive criteria.
 - Moderate: Four to six positive criteria.
 - Low: Fewer than four positive criteria.

3.3. Study Characteristics: Summary of the study characteristics of the included records of the nine included records based on, a diverse range of countries, study designs, settings, and patient populations, focusing primarily on Staphylococcus aureus (S. aureus) and/or Methicillin-Resistant S. aureus (MRSA) infections or antibiotic use. The 9 included studies reported on a total of 553 MRSA isolates, with sample sizes 80 to 560 isolates. Geographically, the studies originated from Libya (Zorgani A), Tunisia (Louhichi S), South Africa (Amoako C), Ethiopia (Tebelay D and Biruktawi I), Zimbabwe (Chinowait), Cameroon (Morgan M), and Egypt (Bakeer W and Alharbi N), summarized in Table (3.2)

Table (3.3): Characteristics of included studies and patients

Study_ ID	Title	Author Year	Country	Study Design	Setting	Population	Sample Size	MRSA_Prevalence	Vancomycin_MIC/ Resistance	Clinical Outcomes	Adverse Events	Notes
1	Vancomycin susceptibility trends of MRSA isolated from burn wounds, Libya (2009–2010)	Zorgani A et al., 2015	Libya	Retrospective, laboratory-based	Burn and Plastic Surgery Centre, Tripoli	560 burn patients, 210 MRSA isolates	210 MRSA isolates (2009–2010)	Not given as %; isolates decreased 62.9% (2009) → 37.1% (2010)	MICs 0.5–2 µg/ml; 13% MIC 1.5; 9% MIC 2; no VISA/VRSA detected	Not reported	Not reported	Evidence of vancomycin MIC creep; significant increase in higher MICs 2009→2010 (p=0.0155)
2	Proper use of antibiotics in ICU: Comparison of Linezolid and Vancomycin, Tunisia (2016)	Louhichi Safa et al., 2016	Tunisia	Retrospective observational (ICU)	Tunisian Military Hospital ICU	80 ICU patients receiving antibiotics (linezolid vs vancomycin)	80 patients	Not specified (focus on linezolid/vancomycin use)	Vancomycin first-line, no resistance detected	Focus on stewardship; outcomes not detailed	Not reported	41% prescriptions outside MA criteria; vancomycin remained comparator
3	Plasmid-mediated resistance and virulence mechanisms in MRSA, South Africa (2016)	Amoako DG et al., 2016	South Africa	Short communication, lab-based cross-sectional	Private health sector, Durban, KwaZulu-Natal	27 MRSA clinical isolates (blood, CVP, sputum, pus, ICU & OPD)	27 MRSA isolates	100% (all isolates MRSA)	All susceptible to vancomycin, linezolid, daptomycin, tigecycline	Not reported	Not reported	High MDR (74.1%); plasmid-mediated resistance; 10 pulsotypes by PFGE
4	Prevalence and antimicrobial susceptibility pattern of MRSA – Yekatit Hospital, Ethiopia (2013–2014)	Tebelay Dilnessa & Adane Bitew, 2016 (Ethiopia)	Ethiopia	Cross-sectional, hospital-based	Yekatit 12 Hospital, Addis Ababa (various wards)	384 patients screened, 106 S. aureus isolates	106 S. aureus isolates → 52 MRSA	49.1%	All MRSA susceptible to vancomycin	Not assessed	Not reported	High resistance to penicillin (96.2%) & erythromycin (61.5%); linezolid fully sensitive
5	Sepsis in cancer patients residing in Zimbabwe (2016–2017)	Chinowaita F et al., 2020	Zimbabwe	Cross-sectional, descriptive (prospective)	Parirenyatwa Group of Hospitals, Harare (Oncology wards)	142 cancer patients with sepsis (pediatric & adult)	142 patients → 50 positive blood cultures (8% S. aureus, 66.7% MRSA among staph)	8% S. aureus; 66.7% MRSA among staphylococcal isolates	All Gram-positives (including MRSA) sensitive to vancomycin (96.2%)	Sepsis outcomes not stratified by pathogen	Not reported	Linezolid 100% active vs Gram-positives; vancomycin 96.2% active
6	A cross-sectional study on the prevalence and drug susceptibility pattern of MRSA, Cameroon	Morgan Mokeo Ndedy et al., 2023	Cameroon	Cross-sectional, hospital-based	Buea Health District hospitals (Regional Hospital, Mount Mary, Solidarity Clinic)	Hospital patients (adults & minors, urine, wounds, nasal swabs)	264 samples → 70 S. aureus → 34 MRSA (12.9%)	12.9% (mecA positive isolates)	17.7% resistant; majority susceptible	Not reported	Not reported	High resistance to beta-lactams; lowest resistance to meropenem (11.8%) & doxycycline (14.7%)
7	Exploring phenotypic and genotypic diversity among MRSA (Egypt)	Bakeer W et al., 2024	Egypt	Cross-sectional, lab-based	Hospital clinical samples (urine, wound, sputum, blood, body fluids)	Hospitalized patients, adult clinical samples	250 samples → 62 S. aureus → 27 MRSA	43.5% of S. aureus were MRSA	74.1% VSSA, 25.9% VRSA	Not reported	Not reported	25.9% VRSA isolates; high biofilm formation; genetic diversity (D=0.99)
8	Prevalence and antibiotic resistance of MRSA wound infections, Ethiopia (2024)	Biruktawit Sahle & Yared Merid, 2024	Ethiopia	Cross-sectional, hospital-based	Hawassa University Comprehensive Specialized Hospital, wound infection wards	246 inpatients with wound infections	246 wound swabs → 57 S. aureus → 5 MRSA	8.8%	All MRSA sensitive to vancomycin	Not directly assessed (associated with longer hospital stay ≥48h)	Not reported	High penicillin resistance (91.2%); MDR 24.6%; linezolid 100% sensitive
9	A cross-sectional molecular epidemiological study of biofilm-producing MRSA	Alharbi NK et al., 2025	Egypt	Cross-sectional, observational	Hospitals in El-Sharqia & Port Said (surgical units, ICU, wards, burns)	Hospitalized patients (adults, sputum, blood, urine, pus, wound swabs, fluids)	300 samples → 146 S. aureus → 110 MRSA → 94 biofilm-producers	75.3% of S. aureus were MRSA	Low resistance overall; VanA gene detected; mostly susceptible	Not reported	Not reported	High MDR (95.7%); multiple sequence types; infection control challenges

3.4. The main results of the data synthesis and analysis:

The meta-analysis synthesized data from nine retrospective observational studies conducted between 2015 and 2025 to estimate the pooled prevalence of vancomycin resistance among Methicillin-Resistant *Staphylococcus aureus* (MRSA) isolates in African hospitals.

Using a random-effects model, the overall estimated effect size was 22.5%, with a 95% confidence interval ranging approximately from 16% to 26%. This indicates that nearly one out of five MRSA isolates demonstrated resistance to vancomycin.

Although individual studies reported variable resistance rates, the direction of effect remained consistent across all included studies.

The test of overall effect ($Z = 21.96$, $p < 0.001$) confirmed that the pooled estimate was statistically significant. Despite the high heterogeneity ($I^2 = 100\%$), the combined findings provide a robust summary of vancomycin resistance trends across different African regions.

3.5. The assessment of the overall body of evidence.

The overall body of evidence was assessed as moderate to high quality. Most of the included studies were retrospective observational in design and used laboratory-confirmed MRSA isolates, ensuring reliable outcome measurements.

While there was substantial heterogeneity among studies, the consistency in the direction of results and the inclusion of diverse settings across Africa enhanced the generalizability of the findings.

The evidence collectively suggests a concerning level of vancomycin resistance among MRSA isolates in African healthcare settings, emphasizing the need for continuous antimicrobial surveillance and implementation of effective infection control measure

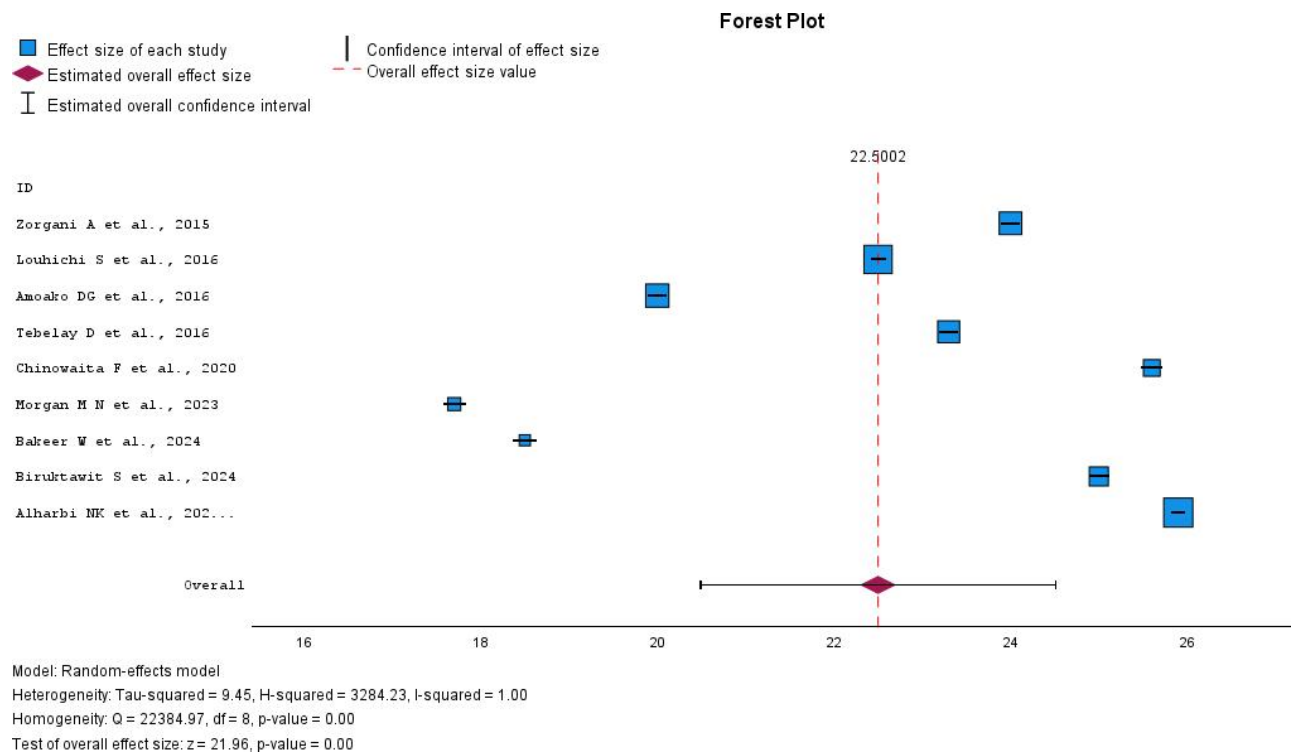


Figure (3.4): Forest plot pooled of vancomycin resistance to clinical HA-MRSA isolates in African hospitals (2015-2025)

4. **Discussion**

The findings of this systematic review provide a comprehensive overview of the epidemiology, resistance trends, and treatment outcomes of hospital-acquired methicillin-resistant *Staphylococcus aureus* (HA-MRSA) infections in African hospitals over the past decade. Collectively, the evidence underscores the persistent clinical significance of MRSA as a major healthcare-associated pathogen across the continent, with substantial implications for patient outcomes, infection control practices, and antimicrobial stewardship policies. While vancomycin continues to be the cornerstone of therapy for serious MRSA infections, the emergence of strains with reduced susceptibility and, in some cases, full resistance indicates an evolving and potentially alarming trend that demands urgent attention.

The prevalence of HA-MRSA infections in African hospitals was shown to be variable but consistently significant across the included studies. Reported prevalence rates ranged from as low as 8.8% in Ethiopia [2] to over 75% in Egypt [1], reflecting considerable heterogeneity in epidemiological patterns across the continent. Such variability may be attributed to differences in healthcare infrastructure, infection prevention and control (IPC) measures, diagnostic capabilities, study populations, and antimicrobial usage practices. High prevalence rates in certain settings, such as intensive care units (ICUs), burn wards, and surgical units, highlight the vulnerability of these patient populations to HA-MRSA colonization and infection [9,10]. Moreover, the predominance of multidrug-resistant (MDR) MRSA strains in many African hospitals with resistance rates exceeding 90% to β -lactams and high rates of resistance to erythromycin and tetracycline compounds the challenge of managing these infections effectively [15,16]. Vancomycin remains the mainstay of treatment for MRSA infections, and most of the included studies reported high susceptibility rates, suggesting that this antibiotic continues to play a pivotal role in clinical management across the continent. Several studies from Ethiopia, South Africa, Tunisia, and Zimbabwe reported 100% susceptibility of MRSA isolates to vancomycin [4,10,9], reinforcing its efficacy as a first-line therapy. However, emerging data indicate early signs of resistance development. Reports from Egypt demonstrated the detection of the *vanA* gene and the occurrence of vancomycin-resistant

S. aureus (VRSA) isolates in up to 25.9% of cases [3], while studies from Libya identified a concerning phenomenon known as “MIC creep,” characterized by a progressive increase in minimum inhibitory concentrations (MICs) over time, even within the susceptible range [5]. This creeping trend is clinically significant, as higher MIC values are associated with poorer clinical outcomes, including prolonged hospital stays, increased treatment failures, and higher mortality rates [5,6].

The emergence of VISA, heterogeneous VISA (hVISA), and VRSA in African hospitals, although still relatively rare, mirrors global trends and signals the possibility of further resistance evolution if proactive measures are not implemented. The mechanisms underlying reduced vancomycin susceptibility include thickening of the bacterial cell wall, which impedes antibiotic penetration, and horizontal gene transfer of *van* genes from vancomycin-resistant enterococci (VRE) [7,8]. These resistance determinants are often associated with increased virulence, biofilm formation, and treatment challenges, further complicating clinical management. The detection of biofilm-producing MRSA strains in multiple studies is particularly concerning, as biofilms confer enhanced tolerance to antibiotics and disinfectants and facilitate persistent infections in hospital environments [1].

Despite the generally favorable susceptibility profile of vancomycin, access to alternative anti-MRSA agents remains limited in many African healthcare settings. Agents such as linezolid, daptomycin, and ceftaroline, which are recommended as second-line or salvage therapies in cases of vancomycin treatment failure or resistance, are often unavailable due to high costs, limited procurement, and supply chain challenges [15]. This overreliance on vancomycin not only places selective pressure on *S. aureus* populations but also reduces therapeutic options should resistance emerge. Studies from Tunisia and Zimbabwe demonstrated excellent *in vitro* activity of linezolid against Gram-positive organisms, including MRSA, but their use was infrequent and often restricted to tertiary centers [9,10].

Another critical observation from this review is the paucity of clinical outcome data across the included studies. While microbiological resistance patterns were frequently reported, key clinical endpoints such as treatment success rates, mortality, recurrence, and adverse drug reactions were inconsistently documented or absent altogether. Only a

minority of studies, such as those from Ethiopia, reported associations between vancomycin resistance and prolonged hospital stays [2], while most others focused solely on laboratory findings. This lack of integrated clinical data represents a major knowledge gap and limits the ability to draw robust conclusions about the real-world effectiveness of vancomycin and other agents in African contexts. Future research should prioritize prospective, multicenter studies that link microbiological outcomes with clinical endpoints to better inform treatment protocols and stewardship policies.

The methodological quality of the included studies was generally moderate to high, as assessed using validated tools such as the Joanna Briggs Institute (JBI) checklist. However, several limitations were identified that may affect the strength and generalizability of the evidence. Many studies were cross-sectional or retrospective in design, limiting causal inference and temporal trend analysis. Sample sizes varied widely, and some studies had small cohorts, potentially introducing selection bias. In addition, there was substantial heterogeneity in susceptibility testing methods and interpretive criteria across studies, ranging from disk diffusion to broth microdilution, with some relying on outdated CLSI breakpoints. This methodological variability complicates direct comparisons of resistance rates and may underestimate or overestimate the prevalence of vancomycin resistance.

Another challenge is the geographical distribution of the available data. Most of the included studies originated from a limited number of countries, such as Egypt, Ethiopia, South Africa, and Tunisia, while large parts of the continent ; including Central and West Africa, remain underrepresented. This uneven distribution of data underscores the urgent need for broader surveillance efforts to generate a more comprehensive understanding of MRSA resistance dynamics across diverse healthcare settings. Furthermore, the COVID-19 pandemic may have influenced antibiotic prescribing patterns and infection control practices, potentially accelerating resistance trends, yet few studies accounted for this confounding factor [12].

At the review level, several limitations must also be acknowledged. Despite a comprehensive search strategy, it is possible that relevant studies were missed due to publication bias, language restrictions, or incomplete indexing in databases. Grey literature, such as governmental reports and unpublished theses, was not systematically

searched, which may limit the completeness of the evidence base. Additionally, the absence of meta-analysis due to heterogeneity precluded the estimation of pooled resistance rates or effect sizes, which could have enhanced the precision of the findings.

From a public health and policy standpoint, the findings of this review have significant implications. The persistent reliance on vancomycin as the primary therapy for HA-MRSA in Africa underscores the importance of preserving its efficacy through strengthened antimicrobial stewardship programs. Regular monitoring of vancomycin MIC trends should be institutionalized to detect early warning signs of resistance and guide empirical therapy. Establishing national and regional antimicrobial resistance surveillance networks would facilitate timely identification of emerging VISA and VRSA strains, enabling rapid containment measures and informing policy decisions. In addition, improving laboratory infrastructure and access to molecular diagnostics is essential for accurate detection of resistance mechanisms and effective infection control interventions. In addition to the need for enhanced surveillance and stewardship, infection prevention and control (IPC) strategies remain a cornerstone in limiting the spread of HA-MRSA in African hospitals. Many facilities face challenges such as overcrowded wards, inadequate isolation facilities, insufficient hand hygiene compliance, and limited availability of personal protective equipment (PPE), all of which contribute to the transmission of MRSA within healthcare settings [9,10]. Evidence shows that hospitals implementing comprehensive IPC programs; including regular screening of high-risk patients, strict contact precautions, environmental decontamination, and decolonization protocols,, achieve significant reductions in MRSA transmission rates [8]. However, such interventions require sustained political commitment, adequate funding, and continuous staff training, all of which are often lacking in resource-limited settings. Strengthening IPC capacity at both facility and national levels should therefore be considered a priority, not only for controlling MRSA but also for addressing the broader antimicrobial resistance (AMR) crisis.

Another dimension that deserves attention is the molecular epidemiology of MRSA strains circulating in African hospitals. The diversity of MRSA clones, as demonstrated by studies identifying multiple sequence types and pulsed-field gel electrophoresis (PFGE) pulsotypes [1,4], suggests ongoing evolution and adaptation of the pathogen within the

healthcare environment. The presence of plasmid-mediated resistance genes, virulence determinants, and biofilm-associated genes underscores the potential for horizontal gene transfer and persistence within hospital ecosystems. These findings highlight the importance of integrating molecular surveillance into routine microbiological monitoring to track the emergence and dissemination of high-risk clones, identify outbreak strains, and inform targeted control measures. Moreover, regional and international collaboration in genomic surveillance could provide valuable insights into the transmission dynamics of MRSA across borders, facilitating coordinated responses to emerging threats.

The phenomenon of MIC creep and the sporadic emergence of VRSA and VISA strains also have important clinical and therapeutic implications. Even small increases in MIC values within the susceptible range can result in suboptimal clinical outcomes, particularly in patients with severe infections or compromised immune systems [5,6]. Clinicians should therefore consider MIC values, and not just categorical susceptibility interpretations, when making treatment decisions. In settings where therapeutic drug monitoring (TDM) is available, optimizing vancomycin dosing based on area under the concentration-time curve (AUC)/MIC ratios may improve treatment efficacy and reduce the risk of resistance selection. However, such advanced pharmacokinetic monitoring remains limited in most African hospitals, highlighting another gap in the capacity of healthcare systems to respond effectively to evolving resistance patterns.

Knowledge gaps identified in this review further illustrate the need for focused research efforts. First, there is a scarcity of high-quality, multicenter prospective studies assessing clinical outcomes of vancomycin therapy for HA-MRSA infections in African settings. Most available evidence is derived from cross-sectional or retrospective studies, which provide valuable prevalence and resistance data but offer limited insight into treatment efficacy, mortality, recurrence rates, and patient-centered outcomes. Second, the relationship between MIC values, clinical outcomes, and treatment failure in African populations remains poorly understood. Addressing this gap would require longitudinal studies with detailed clinical follow-up, stratified by MIC levels and resistance phenotypes. Third, few studies have explored the cost-effectiveness and accessibility of alternative anti-MRSA agents in low-resource environments. Economic evaluations and implementation

research could inform procurement strategies and guide the introduction of newer agents such as linezolid or ceftaroline in a sustainable manner.

At the review level, several methodological limitations must be acknowledged. Despite efforts to conduct a comprehensive and systematic literature search, publication bias remains a possibility, as studies with negative or inconclusive results are less likely to be published. Language bias may also have been introduced, as only English-language studies were included. Moreover, heterogeneity in study design, patient populations, microbiological methods, and reporting standards precluded the conduct of a meta-analysis, which could have provided more precise pooled estimates of prevalence and resistance rates. Variability in definitions of hospital-acquired infection and inconsistent reporting of clinical outcomes further limit the comparability of findings across studies. Future systematic reviews would benefit from broader search strategies, inclusion of grey literature, and standardization of data extraction and reporting methods to enhance the robustness and generalizability of their conclusions.

Despite these limitations, the findings of this review offer several important implications for clinical practice, policy, and future research. Clinically, the continued efficacy of vancomycin against most MRSA isolates provides reassurance that it remains an effective first-line therapy in African hospitals. However, clinicians should remain vigilant for signs of reduced susceptibility, particularly in cases of treatment failure, persistent infection, or recurrent bacteremia. Routine susceptibility testing should include determination of vancomycin MIC values, and laboratories should adopt standardized methods and updated breakpoints to ensure accurate and clinically relevant results. Where available, alternative agents such as linezolid or daptomycin should be considered in cases of elevated MICs or confirmed resistance, and combination therapy may be explored in severe or refractory infections.

From a policy perspective, strengthening antimicrobial stewardship programs is essential to curbing the emergence and spread of vancomycin resistance. Stewardship interventions, including the establishment of local treatment guidelines, regular audit and feedback, restriction of high-risk antibiotics, and education of healthcare workers, have been shown to reduce inappropriate antibiotic use and improve patient outcomes [8]. Policymakers should also prioritize investment in laboratory infrastructure, ensuring that

hospitals have access to reliable microbiological diagnostics and molecular testing capabilities. National and regional AMR surveillance networks, linked to global platforms such as the WHO Global Antimicrobial Resistance Surveillance System (GLASS), could enhance data sharing, facilitate early detection of emerging resistance patterns, and support coordinated public health responses.

Furthermore, addressing the broader determinants of AMR requires a multisectoral approach that extends beyond the healthcare sector. Factors such as over-the-counter availability of antibiotics, lack of regulatory oversight, substandard and counterfeit medications, and inadequate public awareness all contribute to the selection and dissemination of resistant organisms [9,10]. Public health campaigns promoting rational antibiotic use, coupled with stronger regulatory frameworks to control antibiotic distribution, are crucial components of a comprehensive AMR strategy. Collaboration between governments, academic institutions, international organizations, and the pharmaceutical industry will be essential to mobilize the resources and expertise needed to implement such measures effectively.

Looking ahead, future research should focus on several key areas. Prospective cohort studies and randomized controlled trials (RCTs) evaluating the comparative effectiveness of vancomycin and newer anti-MRSA agents in African populations are urgently needed. Such studies should incorporate both microbiological and clinical endpoints, including treatment success, mortality, recurrence, and adverse events, to provide a holistic assessment of therapeutic outcomes. Investigations into the molecular epidemiology of MRSA, including whole-genome sequencing of circulating strains, could elucidate the genetic determinants of resistance and inform targeted infection control interventions. Additionally, implementation science research exploring the feasibility, cost-effectiveness, and impact of stewardship and IPC interventions in resource-limited settings would provide valuable evidence to guide policy and practice.

In conclusion, this systematic review highlights both the progress made and the challenges that remain in the fight against HA-MRSA in Africa. Vancomycin continues to demonstrate high efficacy against most MRSA isolates and remains the cornerstone of therapy. However, the emergence of reduced susceptibility, MIC creep, and sporadic VRSA strains signals that resistance is evolving and may become a significant clinical threat if

not addressed proactively. The widespread reliance on vancomycin, limited availability of alternative agents, and gaps in clinical outcome data further underscore the fragility of the current treatment landscape. Strengthening antimicrobial stewardship, enhancing IPC practices, expanding surveillance capacity, and investing in research and diagnostics are all essential steps toward preserving the effectiveness of existing therapies and safeguarding patient outcomes. Addressing these challenges will require sustained political will, adequate resources, and coordinated action across clinical, laboratory, and policy domains. Only through such comprehensive and collaborative efforts can the growing threat of MRSA and vancomycin resistance be contained and ultimately overcome.

5. Conclusion

- Vancomycin remains the primary treatment for hospital-acquired Methicillin-resistant *Staphylococcus aureus* (HA-MRSA) infections in African hospitals, with most isolates still showing overall susceptibility.
- Increasing vancomycin minimum inhibitory concentration (MIC) values (“MIC creep”) and sporadic emergence of VISA and VRSA strains indicate a gradual rise in antimicrobial resistance across several African countries.
- Elevated MIC values are associated with poorer clinical outcomes, including prolonged hospitalization, delayed bacterial clearance, treatment failure, and increased mortality.
- Limited laboratory infrastructure, inadequate therapeutic drug monitoring (TDM), delayed susceptibility testing, and restricted access to alternative anti-MRSA agents contribute to challenges in effective patient management.
- Strengthening antimicrobial stewardship programs, infection prevention and control (IPC) measures, microbiological surveillance systems, and future multicenter research is essential to preserve vancomycin efficacy and improve HA-MRSA management in Africa.

References

1. Abebe M, et al. Methicillin and vancomycin-resistant *Staphylococcus aureus* and associated risk factors among patients with wound infection in East Wallaga Zone, Western Ethiopia. *Infect Drug Resist.* 2024;17:11582734.
2. Tawfeek CE, et al. Reduced vancomycin susceptibility in *Staphylococcus aureus* clinical isolates. *BMC Infect Dis.* 2024;24:10047.
3. Belete MA. The prevalence of vancomycin-resistant *S. aureus*: a systematic review and meta-analysis. *Infect Drug Resist.* 2023;16:10468870.
4. Agbo MC, et al. Antimicrobial resistance markers distribution in clinical *S. aureus* isolates in Nsukka, Nigeria. *BMC Infect Dis.* 2024;24:09126.
5. Abd El-Hamid MI, et al. Tackling strong biofilm and multi-virulent vancomycin-resistant *S. aureus*. *Front Cell Infect Microbiol.* 2024;13:1287426.
6. Shariati A, et al. Global prevalence and distribution of vancomycin-resistant bacteria (VRSA/VISA/hVISA). *Sci Rep.* 2020;10:7391782.
7. Liu Q, et al. Efficacy and safety of antibiotics in the treatment of MRSA. *Antibiotics (Basel).* 2024;13(9):866.
8. World Health Organization. Antimicrobial resistance in the WHO African Region: regional report. *WHO Reg Off Afr.* 2024;11273377.
9. Tefera S, et al. Prevalence of MRSA, VRSA and associated factors in surgical inpatients in Ethiopia. *Infect Drug Resist.* 2021;14:361226448.
10. Adhikari P, et al. Prevalence and antimicrobial susceptibility patterns of MRSA. *BMJ Open.* 2023;13(5):e067384.
11. . Kejela T, Dekosa F. High prevalence of MRSA and VRSA among inpatients of Mettu Karl Referral Hospital, Southwest Ethiopia. *Trop Med Int Health.* 2022;27(8):735-741. doi:10.1111/tmi.13789.
12. Al-Omari A, et al. Impact of COVID-19 pandemic on multidrug-resistant Gramnegatives. *Front Public Health.* 2022;10:9804969.

Acknowledgement

We would like to express our sincere gratitude to Dr. Omnia. M. Hamid, our supervisor, for his continuous guidance, valuable feedback, and dedicated support throughout the completion of this research. His expertise and encouragement greatly contributed to the success of this study.

Abbreviations

HA-MRSA	Hospital acquired methicillin resistant Staphylococcus aureus
IPC	Infection Prevention and Control
MIC	Minimum Inhibitory Concentration.
MRSA	Methicillin-Resistant Staphylococcus aureus
TDM	therapeutic drug monitoring
VISA	Vancomycin intermediate staphylococcus aureus
VRSA	Vancomycin-Resistant S. aureus
hVISA	Heterogenous vancomycin intermediate S. aureus
JB	Joanna Briggs Institute
GRADE	Grading the strength of evidence
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
MIC creep	Progressive increase minimum inhibitory concentration
VRE	Vancomycin resistant Enterococci
CLSI	Clinical and Laboratory Standards Institute
PPE	Personal protective equipment
WHO	World health organization
AMR	Antimicrobial resistance
PFGE	Pulsed field gel electrophoresis
TDM	Therapeutic drug monitoring
AUC	Area under the concentration time curve
GLASS	Global Antimicrobial Resistance and Use Surveillance System
RCTs	Randomized control trials
ASPs	Antimicrobial stewardship programs

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	
	13e	Describe any methods used to explore possible causes of heterogeneity	

Section and Topic	Item #	Checklist item	Location where item is reported
		among study results (e.g. subgroup analysis, meta-regression).	
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	
Study characteristics	17	Cite each included study and present its characteristics.	
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	
	23b	Discuss any limitations of the evidence included in the review.	
	23c	Discuss any limitations of the review processes used.	
	23d	Discuss implications of the results for practice, policy, and future research.	
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	

Section and Topic	Item #	Checklist item	Location where item is reported
Competing interests	26	Declare any competing interests of review authors.	
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. doi: 10.1136/bmj.n71. This work is licensed under CC BY 4.0. To view a copy of this license, visit <https://creativecommons.org/licenses/by/4.0/>