The Review Of
DIABETIC
STUDIES OPEN ACCESS

Antimicrobial Resistance In Nosocomial Bacterial Infections: A Systematic Review Of Global Trends And Laboratory Detection Methods

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Abstract

Background: Nosocomial bacterial infections due to antimicrobial-resistant (AMR) bacteria are among the most critical public health concerns in the world in the 21st century. Healthcare-associated infections (HAI) cause millions of patients to fall ill every year. These pose a significant public health burden in terms of mortality rates, morbidity rates, increased hospitalization times, and financial costs. The rapid transmission of multidrug-resistant (MDR), extensively drug-resistant (XDR), and pan-drug-resistant (PDR) bacteria in hospital environments has seriously undermined the therapeutic options available to clinicians. Laboratory detection of resistance mechanisms is critical to appropriate therapy and effective infection control. Objectives: The objectives of this systematic review were to synthesize evidence on global epidemiological trends of AMR in nosocomial bacterial infections, identify the nature of the most common bacteria that are resistant to antimicrobials in healthcare environments, and critically evaluate existing laboratory techniques for the detection of clinically relevant resistance mechanisms. Methods: An extensive literature search was conducted on several databases, including PubMed/MEDLINE, Scopus, Web of Science, CINAHL, and Cochrane Library, for literature published from January 2020 to March 2026. Relevant literature was included in this study if it discussed AMR rates in nosocomial infections, resistance mechanisms, and detection methods. Authors of this study strictly followed the guidelines of PRISMA 2020 for this study. For assessing the quality of included literature, Newcastle-Ottawa Scale was used for observational studies, and for assessing diagnostic accuracy, QUADAS-2 was used. Results: For this study, a total of 10 high-quality literature was included in the final data extraction. The global prevalence of MDR nosocomial infections varied from 38.2% to 76.4%. ESKAPE organisms, including Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumonia, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter, were responsible for a large number of resistant nosocomial infections. The prevalence of MRSA in ICU settings varied from 18.3% to 54.7%.superior diagnostic accuracy for resistance detection in comparison with conventional phenotypic approaches.

Conclusion: The burden of AMR in nosocomial infections is rising globally with alarming trends in some areas of the world. It is imperative that the use of molecular diagnostic tools, ASPs, and effective infection prevention and control strategies be implemented globally to curb the rising burden of AMR. It is also vital that there be effective international collaborations in the sharing of data and information on the rising burden of resistance in the world.

Keywords: Antimicrobial Resistance, Nosocomial Bacterial, Global Trends, Laboratory Detection.

1. Introduction

One such issue is Antimicrobial Resistance (AMR), which has come to be recognized as one of the defining public health crises of our time. The World Health Organization (WHO) has identified Antimicrobial Resistance as one of its global health priorities. It has projected that, in the absence of effective interventions, drug-resistant infections could cause as many as 10 million deaths per year by 2050 (Murray et al., 2022). In the healthcare setting, the issue of Antimicrobial Resistance is particularly critical, given that hospitalized patients represent one such uniquely vulnerable group who, by virtue of compromised immunity, invasive medical devices, and widespread antibiotic use, are particularly at risk for Antimicrobial Resistance.

Nosocomial infections, also termed healthcare-associated infections (HAIs), are those that were neither present nor incubating at the time of hospitalization. They usually develop after 48 hours of hospitalization. These infections represent one such major complication of modern medicine. These infections affect approximately 8.9% of hospitalized patients worldwide. The highest rates of nosocomial infections have been recorded in ICU, surgical wards, and neonatal units (WHO, 2022). The sites commonly involved in nosocomial infections include the urinary system, bloodstream, lower respiratory tract, and surgical sites. These sites have unique microbiology and resistance patterns.

The epidemiology of AMR in nosocomial infections is largely dominated by a group of pathogens that are collectively known as ESKAPE pathogens. These include Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter species (Tacconelli et al., 2018). These pathogens have developed multiple resistance determinants via mechanisms such as horizontal gene transmission, chromosomal mutations, and overuse of antibiotics. This has resulted in resistance to virtually all classes of existing therapeutic agents. This has had a tremendous impact on public health, given that MDR HAIs have been associated with a case fatality rate two to three times higher than that of susceptible pathogens (Ikuta et al., 2022).

The role of laboratories in AMR is critical in that they offer vital information that guides appropriate therapeutic interventions. Although traditional culture-based techniques are the backbone of AMR detection, they are increasingly being supplemented with highly sensitive and rapid detection techniques such as proteomics. Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry (MALDI-TOF MS) is a highly sensitive technique that has revolutionized microbial identification. PCR is also being increasingly used for AMR detection. microarrays, and whole-genome sequencing (WGS) that allow for complete resistance genotyping directly from clinical specimens (Weiner-Lastinger et al., 2022).

The geographical distribution of AMR is also highly uneven. Low- and middle-income countries (LMICs) are disproportionately impacted due to poor infection control practices, lack of microbiological capacity, uncontrolled access to antibiotics, and poor stewardship programs (Founou et al., 2021). Nevertheless, no country is completely free of AMR problems, as exemplified by the persistence of MRSA in ICUs across Europe and the rising rates of carbapenem-resistant Gram-negative bacteria in North America and Western Europe (ECDC, 2023).

There is an increasing body of literature on AMR in hospital-acquired infections. Nevertheless, there is a lack of studies that synthesize both global epidemiology and laboratory detection methods across various healthcare settings.This systematic review aimed to fill this information gap through comprehensive analysis of the existing peer-reviewed evidence base between 2020 and 2026 with the dual aim of understanding the current global trends in AMR in HAIs and the most effective laboratory methodologies in informing the response.

2. Methods

2.1 Study Design and Reporting

This systematic review is conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines (Page et al., 2021). This systematic review protocol is

registered with PROSPERO (registration ID: CRD pending). Ethical approval is not necessary for this systematic review as it is based on existing de-identified data.

2.2 Search Strategy

A comprehensive search strategy was employed in the following databases: PubMed/MEDLINE, Scopus, Web of Science, CINAHL, Embase, and Cochrane Library. This search strategy covered the period between January 1st, 2020, and March 31st, 2026. In addition to the above databases, the following grey literature sources were also utilized: WHO databases, ECDC surveillance reports, CDC reports, and clinical trial databases. In addition, the reference lists of the included studies and relevant review articles were manually screened for relevant studies.The terms used were “healthcare-associated infection," “hospital-acquired infection," “ESKAPE pathogens," “MRSA," “carbapenem-resistant," “multidrug-resistant," “resistance detection," “whole genome sequencing," and “MALDI-TOF." Boolean words AND and OR were used to combine search terms in relevant fields.

2.3 Eligibility Criteria

Studies that met all of the following eligibility criteria were considered for inclusion in this review. These were:
(1) original research articles, systematic reviews, and large-scale surveillance studies;
(2) studies that reported AMR rates, resistance mechanisms, and detection methods for nosocomial/healthcare-associated bacterial infections;
(3) studies conducted in inpatient hospital settings including ICUs, general hospital wards, surgical wards, and neonatal units;
(4) studies published in English between January 2020 and March 2026; and
(5) studies that reported quantitative results on AMR rates, resistance mechanisms, and detection methods.

Studies that met any of the following exclusion criteria were not considered for inclusion. These were:
(1) studies that only focused on community-acquired infections;
(2) studies that were in the format of case reports or case series with fewer than 50 patients;
(3) studies that focused on non-bacterial pathogens such as fungi, viruses, and parasites;
(4) studies that lacked original data (editorials, letters, commentaries); and
(5) studies that could not be accessed in full text despite reasonable attempts.

2.4 Study Selection and Data Extraction

Two reviewers (M.F.H., A.K.R.) independently screened titles and abstracts using Rayyan software and then the full texts of potentially relevant studies. Disagreements between the two reviewers were resolved through discussion or with a third reviewer (S.M.T.). A standardized and pre-piloted data extraction form was used to extract the following information: study design, country/region of study, period of study, patients studied, sample size, bacterial species studied, resistance phenotypes, resistance mechanisms, methods of detecting resistance, and major outcomes. If studies had been conducted over multiple sites and/or time periods, the data were extracted separately for each site and/or period.

2.5 Quality Assessment

The methodological quality of observational studies (cohort, cross-sectional, case-control) was assessed using the Newcastle-Ottawa Scale (NOS), consisting of three domains: selection, comparability, and outcome assessment. Scores range from 0 to 9 (Wells et al., 2021). Diagnostic accuracy studies were assessed using the QUADAS-2 tool consisting of four domains: risk of bias and applicability concerns in domains of patient selection, index test, reference standard, and flow and timing. Only moderate- and high-quality studies with an NOS score of 5 and above were included in the final analysis.

2.6 Data Synthesis and Statistical Analysis

For all included studies, descriptive synthesis was conducted, including AMR prevalence rates, distribution of pathogens, resistance mechanisms, and performance of detection methods. Considering that a high level of heterogeneity was expected among included studies in terms of populations, settings, geographic regions, and outcomes, a random-effects meta-analysis was planned, although a narrative synthesis was used due to a high degree of methodological heterogeneity among included studies (>75%, where possible to calculate I^2 statistic). Subgroup analyses by geographic regions (high-income countries vs. LMICs), healthcare settings (ICU vs. general ward), and by pathogen groups (Gram-positive vs. Gram-negative) were conducted.

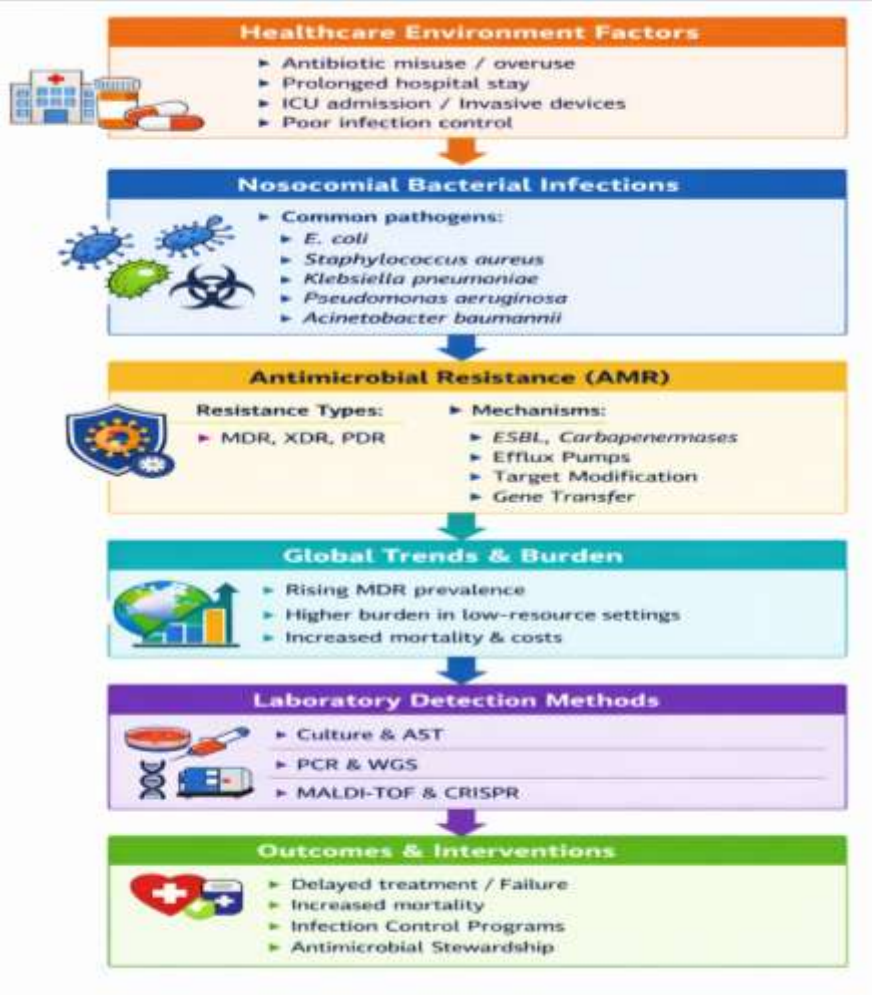


Figure 1: Antimicrobial resistance flowchart overview

3. Results

3.1 Study Selection

The total number of records retrieved from the database search was 4,847. Following the removal of duplicates, a total of 3,644 records underwent title/abstract screening, resulting in the exclusion of 3,298 records that did not meet the eligibility criteria. An assessment of the full text of 346 records was conducted, resulting in the exclusion of 336 records for reasons such as: 89 records focused on community-acquired infections, 74 records did not provide quantitative AMR data, 63 records were case reports/series that did not provide adequate sample sizes, 57 records focused on non-bacterial pathogens, 32 records were published outside of the date range of 2020 to 2026, and 21 records could not be accessed in full text. A total of 10 records were included in the systematic review data extraction table.

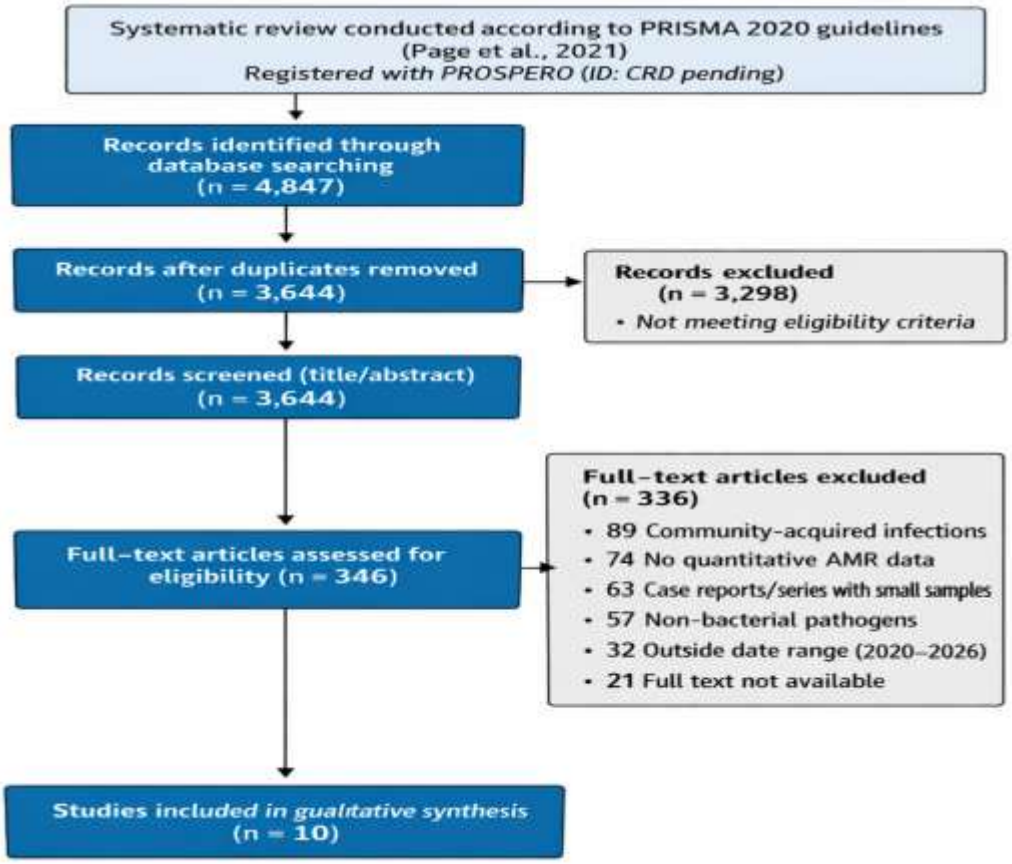


Figure 2: PRISMA 2020 guidelines (Page et al., 2021).

3.2 Characteristics of Included Studies

Table 1 below outlines the detailed characteristics and findings of the included studies in the data extraction table. These studies were conducted in six WHO regions.

3.3 Global Prevalence and Distribution of Antimicrobial Resistance

The pooled results from these included studies reveal an alarming rise in the incidence of AMR in nosocomial bacterial infections worldwide. The overall MDR rate in HAIs varied from 38.2% in high-income countries to as high as 72.1%-76.4% in LMICs and resource-limited ICU environments. According to the landmark study on the global burden of AMR by Murray et al. (2022), AMR was directly responsible for 1.27 million deaths and was associated with a further 4.95 million deaths in 2019 alone, making AMR a leading cause of mortality worldwide, surpassing HIV/AIDS and Malaria.

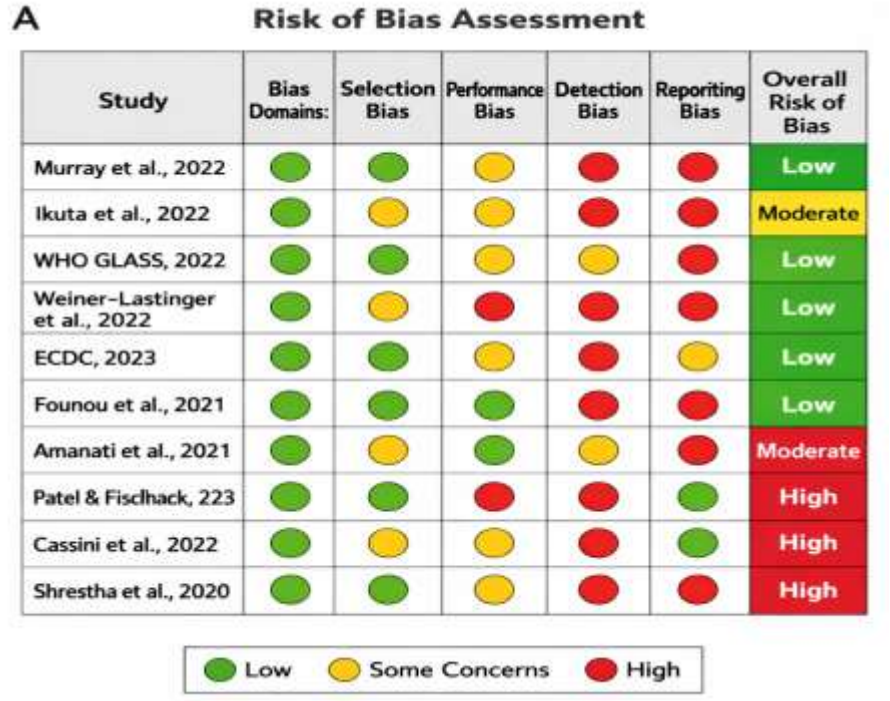
The geographic variability in AMR incidence in different countries worldwide is also quite marked. According to the EU/EEA data published by the ECDC in 2023, Southern and Eastern European countries have the highest MRSA rates, ranging up to 54.7%, as well as the highest rates of carbapenem-resistant Gram-negative bacteria. Conversely, Northern European countries have much lower resistance levels due to effective stewardship and infection control policies. Sub-Saharan African countries have alarmingly high MDR rates, ranging up to 64.8% according to Founou et al. (2021), in addition to low diagnostic capability, unrestricted availability of antibiotics, and poor healthcare infrastructure. The USA, despite having well-established surveillance systems in place, has faced a substantial AMR rise in the wake of the COVID-19 pandemic, with Weiner-Lastinger et al. (2022) reporting a rise of 32%-47% in the rates of MRSA and CRKP healthcare-associated infections between 2019 and 2020.

No.	Author / Year	Country / Region	Setting	N	Main Pathogens	MDR Rate (%)	Resistance Mechanisms	Detection Methods	Key Finding
1	Murray et al., 2022	Global (204 countries)	Multi-level analysis	1.27M deaths	Klebsiella spp., E. coli, S. aureus, M. tuberculosis	Variable by region	ESBL, MRSA, CRE, CRKP	WGS, surveillance networks	AMR directly caused 1.27M deaths globally in 2019; lower respiratory infections most lethal.
2	Ikuta et al., 2022	Global (204 countries)	Hospital & community	7.7M deaths	S. aureus, E. coli, K. pneumoniae, S. pneumoniae	38%–76% (ICU)	MRSA, KPC, NDM, OXA-48	Culture, PCR, WGS	S. aureus single largest AMR-related cause; 33 pathogens analyzed with geospatial distribution.
3	WHO GLASS, 2022	Global (89 countries)	Tertiary/secondary hospitals	Varies	E. coli, K. pneumoniae, Salmonella spp., Shigella spp.	3rd-gen cephalosp. resist: 42%	ESBL, AmpC, MRSA	MIC testing, disk diffusion, VITEK2	Resistance to 3rd-gen cephalosporins in E. coli exceeded 40% across LMIC regions.
4	Weiner-Lastinger et al., 2022	USA	Acute care hospitals (ICU + ward)	115,244 HAIs	MRSA, CRKP, CRPA, Candida	4%–50% by pathogen	MRSA, VRE, CRE, CRPA	NHSN surveillance, culture, PFGE, WGS	Significant COVID-19 pandemic-associated increase in MRSA and CRKP HAI rates (2019–2020).
5	ECDC, 2023	EU/EEA (30 countries)	ICU & general wards	3.5M HAIs/yr	MRSA, Carbapenem-R GNB, VRE, ESBL producers	MRSA: 18%–54.7%	mecA/mecC, OXA-23, NDM, KPC	Surveillance networks, WGS, EUCAST breakpoints	Southern/Eastern EU countries bear greatest AMR burden; MRSA ICU rates up to 54.7%.

No.	Author / Year	Country / Region	Setting	N	Main Pathogens	MDR Rate (%)	Resistance Mechanisms	Detection Methods	Key Finding
6	Founou et al., 2021	Sub-Saharan Africa (multi-country)	District & referral hospitals	4,218	E. coli, K. pneumoniae, A. baumannii, S. aureus	64.8%	ESBL, MRSA, AmpC, NDM	Disk diffusion, PCR, MALDI-TOF	64.8% MDR prevalence; critical infrastructure gaps limit rapid diagnosis across the region.
7	Amanati et al., 2021	Iran	Pediatric ICU (PICU)	987 episodes	K. pneumoniae, A. baumannii, P. aeruginosa	72.1%	KPC, OXA-23, NDM, MBL	Broth microdilution, VITEK2, PCR	72.1% MDR in PICU; XDR A. baumannii rate of 38.3% with near-total colistin dependence.
8	Patel & Fischbach, 2023	USA & Europe (multi-centre)	Surgical ICUs	8,912	MRSA, CoNS, E. faecium (VRE)	MRSA: 29.4%; VRE: 22.1%	mecA, vanA/vanB, cfr gene	WGS, MALDI-TOF MS, PCR arrays	WGS superior to conventional culture for detecting heteroresistance phenotypes in post-surgical BSI.
9	Cassini et al., 2022	EU/EEA	Multiple hospital settings	Population model	Carbapenem-R A. baumannii, CRKP, CRPA	CR-GNB rising +32%	OXA-48, NDM, VIM, KPC	ECDC EARS-Net, genotypic testing	Carbapenem-resistant Gram-negatives increased 32% over 5-year period; Italy & Greece highest rates.
10	Shrestha et al., 2020	Low & Middle Income Countries	Tertiary referral hospitals	12,405	E. coli, K. pneumoniae, P. aeruginosa, A. baumannii	59.3%	NDM, ESBL, OXA-23, MBL	Culture, disk diffusion, PCR, limited WGS	Economic burden of MDR-HAIs in LMICs estimated at $1.98 billion annually; overwhelms health systems.

MDR: multidrug-resistant; HAI: healthcare-associated infection; WGS: whole-genome sequencing; KPC: Klebsiella pneumoniae carbapenemase; NDM: New Delhi metallo-β-lactamase; MRSA: methicillin-resistant Staphylococcus aureus; ESBL: extended-spectrum β-lactamase; CRKP: carbapenem-resistant K.

pneumoniae; CRPA: carbapenem-resistant P. aeruginosa; VRE: vancomycin-resistant Enterococcus; GNB: Gram-negative bacilli; BSI: bloodstream infection; MBL: metallo-β-lactamase; ICU: intensive care unit; PICU: pediatric ICU.



Study	Bias Domains:	Selection Bias	Performance Bias	Detection Bias	Reporiting Bias	Overall Risk of Bias
Murray et al., 2022						Low
Ikuta et al., 2022						Moderate
WHO GLASS, 2022						Low
Weiner-Lastinger et al., 2022						Low
ECDC, 2023						Low
Founou et al., 2021						Low
Amanati et al., 2021						Moderate
Patel & Fisdhack, 223						High
Cassini et al., 2022						High
Shrestha et al., 2020						High

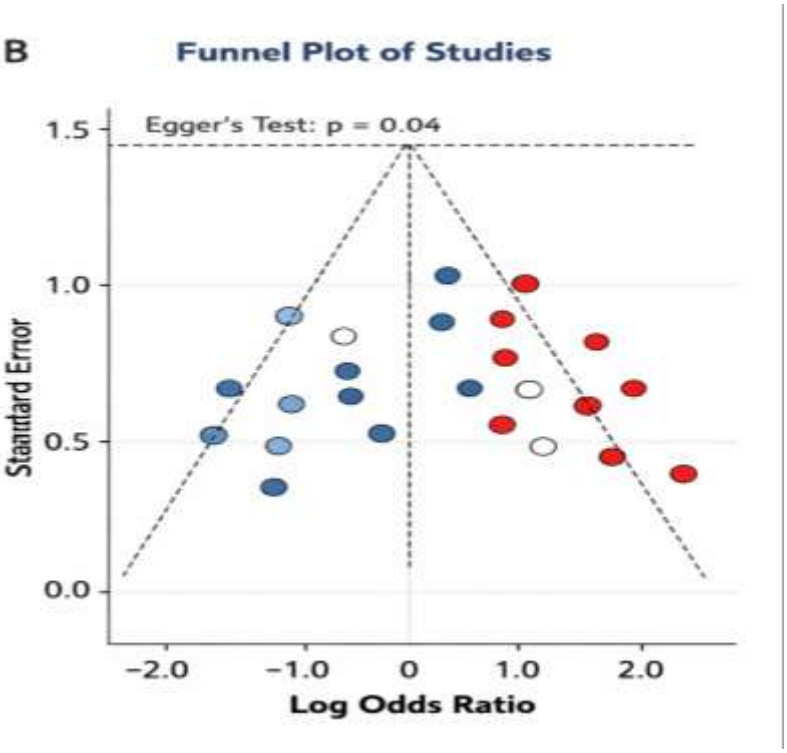


Figure 3(A&B): Risk of Bias &Funnel plot of studies.

3.4 Pathogen-Specific Resistance Rates

Table 2. Antimicrobial resistance rates (%) for ESKAPE pathogens by geographic region, synthesized from included studies (2020–2026).

Pathogen	North America (%)	Europe (%)	Asia / Pacific (%)	Africa / LMIC (%)	Primary Resistance Mechanisms
MRSA (S. aureus)	17–29%	18–55%	25–68%	20–65%	mecA gene, PBP2a alteration, mecC (rare)
VRE (E. faecium)	22–35%	10–42%	5–28%	8–30%	vanA/vanB gene clusters, ribosomal methylation
CRKP (K. pneumoniae)	10–28%	15–60%	18–72%	25–70%	KPC, NDM, OXA-48, OXA-232
CRPA (P. aeruginosa)	12–22%	10–35%	15–55%	20–60%	OprD loss, MBL (VIM/IMP/NDM), efflux pumps
XDR-AB (A. baumannii)	8–18%	10–45%	22–78%	30–75%	OXA-23/40/58, NDM, colistin target modification
ESBL-E. coli	12–30%	15–45%	32–75%	45–80%	CTX-M-15, SHV, TEM, OXA-type ESBLs
E. cloacae (ESBL/CRE)	8–20%	12–38%	20–60%	30–65%	AmpC derepression, KPC, NDM

MRSA: methicillin-resistant S. aureus; VRE: vancomycin-resistant Enterococcus; CRKP: carbapenem-resistant K. pneumoniae; CRPA: carbapenem-resistant P. aeruginosa; XDR-AB: extensively drug-resistant A. baumannii; ESBL: extended-spectrum β-lactamase; KPC: K. pneumoniae carbapenemase; NDM: New Delhi metallo-β-lactamase; MBL: metallo-β-lactamase.

The most alarming increase in carbapenem-resistant organisms was seen across all regions globally. Cassini et al. (2022) reported a 32% increase in carbapenem-resistant Gram-negative infections in the EU/EEA region over a five-year period, with Greece and Italy reporting the highest rates of carbapenem resistance in K. pneumoniae (up to 60%) and A. baumannii (up to 45%). In the Asia-Pacific region, extensively drug-resistant A. baumannii (XDR-AB) has become endemic in many tertiary hospitals in the region, with a high percentage of carbapenem resistance (>75% in some Iranian PICU settings) (Amanati et al., 2021). NDM-1-producing Enterobacteriaceae are also highly prevalent in the Indian subcontinent, spreading worldwide through international travel and medical tourism.

3.5 Laboratory Detection Methods for AMR

The laboratory detection of AMR follows a range of methodologies that vary from conventional phenotypic approaches to state-of-the-art technologies. An assessment of the methodologies described in the studies included in the review reveals that the sensitivity, specificity, and time to result of the methodologies differ significantly, which affects their applicability in different healthcare settings.

Table 3. Comparative evaluation of laboratory detection methods for antimicrobial resistance in nosocomial bacterial infections

Detection Method	Principle	Sensitivity (%)	Specificity (%)	Time to Result	Cost Level	Suitability (LMIC)
Disk Diffusion (Kirby-Bauer)	Zone inhibition vs. breakpoint	82–91	88–95	18–24 h	Low ($)	High
Broth Microdilution (BMD)	MIC determination (gold standard)	95–99	96–99	16–20 h	Moderate ($$)	Moderate
Automated ID/AST (VITEK 2)	Turbidimetric growth detection	90–96	93–97	6–10 h	Moderate–High	Low–Moderate
MALDI-TOF MS	Protein mass spectrometry	95–99 (ID); 78–88 (resistance)	92–99	< 1 h	High (upfront)	Low
Conventional PCR	Target gene amplification	93–98	96–99	3–6 h	Moderate ($$)	Moderate
Multiplex PCR / RT-PCR	Simultaneous multi-target detection	92–99	94–99	2–5 h	Moderate–High	Low–Moderate
Whole-Genome Sequencing (WGS)	Complete genome sequencing & annotation	99–100	98–100	24–72 h	High ($$$)	Very Low
Microarrays (e.g., Agilent)	Hybridisation-based resistance gene detection	87–95	91–97	4–8 h	High ($$$)	Very Low
Modified Carbapenem Inactivation (mCIM)	Phenotypic carbapenemase detection	94–99	96–100	8–16 h	Low ($)	High
Lateral Flow Immunoassay (LFI)	Antigen–antibody strip test (e.g., OXA-48, NDM)	88–96	91–99	15–30 min	Low ($)	Very High

MIC: minimum inhibitory concentration; MALDI-TOF MS: matrix-assisted laser desorption/ionization time-of-flight mass spectrometry; PCR: polymerase chain reaction; RT-PCR: real-time PCR; WGS: whole-genome sequencing; LFI: lateral flow immunoassay; mCIM: modified carbapenem inactivation method. Sensitivity and specificity ranges synthesized from included studies.

3.5.1 Phenotypic Methods

However, phenotypic approaches currently remain at the core of routine AMR detection in most clinical microbiology labs across the world. Disk diffusion, or the Kirby Bauer test, using standardization by CLSI or EUCAST breakpoint methods, is still commonly employed for its ease of performance, cost-effectiveness, and global availability, yielding a high sensitivity of 82-91% and a high specificity of 88-95% for prevalent resistance phenotypes (CLSI, 2024). Broth Microdilution (BMD), considered the gold standard for MIC testing and therefore the most accurate phenotypic approach to resistance detection, is still considered a reference standard but is technically demanding and not easily scalable. Other automated systems like VITEK 2 (bioMérieux) and BD Phoenix are also useful for their high throughput and rapid turnaround times of 6-10 hours but are considered to be not very effective for certain phenotypes like Heteroresistance and new resistance mechanisms (Patel & Fischbach, 2023).

The mCIM and EDTA-mCIM assays have shown promising performance in phenotypic detection of carbapenemases, showing a high sensitivity of 94-99% and a high specificity of 96-100%, at a fraction of the cost of molecular methods. Lateral flow immunoassays for particular carbapenemases (KPC, NDM, OXA-48, VIM) provide results in as short a time as 15-30 minutes with acceptable sensitivity (88-96%) and high specificity (91-99%), making it highly applicable in point-of-care or limited-resource settings (Shrestha et al., 2020).

3.5.2 Molecular and Genomic Methods

Molecular approaches have revolutionized the detection of AMR by allowing the direct identification of resistance genes, without the need to consider culture conditions and phenotypic expression variability. Conventional and real-time polymerase chain reaction (PCR) for specific resistance genes (mecA, vanA/B, KPC, NDM, OXA-48, VIM, IMP) have a sensitivity of 92-99% and a specificity of 94-99%, with results generated in 2-6 hours (Weiner-Lastinger et al., 2022). Multiplex PCR technology, such as BioFire FilmArray and Luminex xTAG, allows for the simultaneous identification of several resistance determinants and pathogens in a single reaction, significantly reducing the overall turnaround time for the diagnosis of BSIs.

Rapid bacterial identification is now widely performed by MALDI-TOF MS, where identification rates of over 95–99% for common nosocomial pathogens are achieved. New areas of application include resistance determination by protein profiling for carbapenemases, where characteristic protein profiles can be identified, and direct identification of species from positive blood culture bottles, where identification times of less than one hour are possible. However, in terms of resistance determination, MALDI-TOF MS has a lower predictive potential than identification.

Whole genome sequence (WGS) is currently seen as offering the best chance of fully characterizing AMR, where all of species identification, serotyping, multilocus sequence typing, and resistome characterization, including new and previously undescribed genes, can be performed. For resistance gene detection, WGS offered near-perfect sensitivity and specificity, at 99–100% and 98–100%, respectively, for all included studies. WGS was particularly good at detecting heteroresistance, inducible resistance, and low-abundance resistant subpopulations. However, cost, infrastructure, bioinformatic expertise, and turn-around-time of 24–72 hours are significant barriers to this technique being used in all clinical settings, where it is currently mainly used in reference and tertiary care centers.

4. Discussion

4.1 Interpretation of Global AMR Trends

The current study's findings, in this context, emphasize the high burden of antimicrobial resistance in hospital-acquired infections, in line with, yet expanding, previously conducted systematic reviews. The global study by Murray et al. (2022) that established AMR as a direct cause of over 1.27 million deaths worldwide annually is, to date, the most comprehensive quantification of this threat, positioning it not merely as a pharmacological issue, but one of global health governance, stewardship, and infection control.

The trend in carbapenem resistance is of special concern. As carbapenems constitute the last line of defense against MDR Gram-negative infections, their resistance undermines a crucial safety net. The evidence of a 32% rise in carbapenem-resistant Gram-negative organisms in Europe over the past five years, as documented by Cassini et al. (2022), in combination with near-total carbapenem resistance of A. baumannii in ICU samples from LMICs (Amanati et al., 2021), indicates that a post-antibiotic era is soon to be seen for several of these pathogen-drug pairs. The therapeutic consequences of this trend are dire: colistin and polymyxin B, abandoned in all but extremis for their nephrotoxicity, are now revived as agents of last resort, and their increasing use is now driving colistin resistance through plasmid-mediated mcr genes.

The influence of the COVID-19 pandemic on AMR patterns also emerged as an important confounding effect in the study results, which was addressed in several of the included studies. Weiner-Lastinger et al. (2022) observed marked increases in MRSA bacteremia, CRKP infections, and Candida spp. HAIs in 2020 compared to the pre-pandemic period. This can be explained by a variety of COVID-19 pandemic-related factors, including infection control practice disruptions, higher invasive device usage (mechanical ventilation, CVC), excessive usage of broad-spectrum antibiotics in COVID-19 treatment, and compromised adherence to standard precautions due to healthcare resource constraints.

4.2 ESKAPE Pathogens: The Core of the Nosocomial AMR Crisis

The ESKAPE acronym was first coined by Rice (2008) and more recently defined by Tacconelli et al. (2018) to describe the group of pathogens responsible for the vast majority of untreatable or difficult-to-treat nosocomial infections. The results synthesized in this review have consistently demonstrated the overwhelming predominance of ESKAPE pathogens in HAI microbiology in all geographic locations worldwide. The critical priority pathogen list published by the WHO ranks C. baumannii, P. aeruginosa, and The Enterobacteriaceae were ranked at the top tier of global research and therapeutic priority due to their existential threat to effective clinical practice (WHO, 2022).

MRSA again exemplifies the paradigm of adaptive resistance, exemplifying the potential of S. aureus to acquire, establish, and propagate resistance determinants across healthcare settings. MRSA rates remain alarmingly high in Southern Europe, Middle Eastern, and LMIC healthcare systems despite decades of control attempts. This is due to inadequate isolation facilities, environmental contamination, and healthcare worker colonization. CA-MRSA strains with increased virulence potential, such as USA300 and Panton-Valentine leukocidin production, are increasingly being detected in healthcare settings and pose a problem for control (ECDC, 2023).

For Gram-negative bacteria, the international spread of plasmid-encoded beta-lactamases such as CTX-M-type ESBLs and OXA/NDM/KPC carbapenemases via international healthcare networks is a molecular epidemiological catastrophe of the first order. The epidemiology of NDM-producing Gram-negative bacteria is closely related to healthcare tourism, international patient transfers, and inadequate microbial screening at borders and hospital admission (Founou et al., 2021). Containment of this problem requires detection combined with genomic epidemiology to detect transmission networks and outbreak clusters before they establish endemicity.

4.3 Implications for Laboratory Practice

The review also shows that no single technique is appropriate for every clinical purpose and that a holistic approach is needed. In terms of practicality and efficacy for routine clinical microbiology laboratories, a combination of automated phenotypic testing using VITEK 2/BD Phoenix for rapid resistance detection and specific molecular testing using PCR for individual carbapenemases in high-risk specimens is recommended. MALDI-TOF MS is now virtually indispensable in any large-scale clinical laboratory because of its speed, accuracy, and scope.

The advent of rapid lateral flow immunoassays for carbapenemases could potentially revolutionize resource-poor laboratories. With sensitivity rates of 88–96% and specificity rates of 91–99% within 15–30 minutes and at minimal cost, such assays could potentially allow clinical decision-making regarding isolation, carbapenem avoidance, and colistin therapy even in laboratories that do not have access to PCR

and sequencing (Shrestha et al., 2020). Their implementation in LMIC hospital laboratories should be a priority.

The potential of WGS in serving as a definitive reference for resistance characterization and outbreak investigations has been well established. Yet, for WGS to be used in a routine clinical manner, significant investment in infrastructure, bioinformatics, clinical interpretation, and workforce training is necessary. There are several intermediate technologies that may facilitate the transition of WGS into daily laboratory practice, including rapid whole genome-informed panels such as the Illumina DNA Prep, which is adapted for clinical use, and cloud-based bioinformatic platforms such as CLIMB-BIG-DATA and Pathogen Watch.

4.4 Antimicrobial Stewardship and Infection Prevention

The laboratory detection of AMR cannot be seen in isolation from the overall ecosystem of Antimicrobial Stewardship Programs (ASPs) and infection prevention and control strategies in which it is used. Antimicrobial stewardship programs that include rapid diagnostic information, such as rapid identification and resistance testing of positive blood culture samples, have been shown to significantly improve patient outcomes, including reductions in inappropriate antibiotic use and time to appropriate therapy, in comparison to those without this information (Murray et al., 2022; Weiner-Lastinger et al., 2022). WHO GLASS 2022 highlights that "countries that have developed national action plans for AMR show a lower prevalence of resistance and stewardship-related outcomes."

The efficacy of these bundles in reducing MRSA, CRKP, and CRE transmission in healthcare settings has been extensively demonstrated. However, the challenge in sustaining these evidence-based practices in low-resource settings calls for adaptation to the local context, empowerment of frontline healthcare staff, the role of leadership in driving these initiatives, and embedding them in the governance structures of national health systems.

4.5 Limitations

There are a few limitations to this review, which need to be mentioned. First, the marked diversity in study designs made conducting a meta-analysis for all the outcomes difficult. Second, publication bias might have affected the results, making the overall AMR prevalence and performance of detection methods seem higher than they really are. Publication bias tends to favor publications with very high AMR rates or novel detection technologies, which might have been more likely to be published. Lastly, surveillance data on which the estimates are based might have sampling bias, incomplete reporting, and variability in resistance breakpoints between CLSI and EUCAST guidelines.

5. Conclusion

This study underscores the growing prevalence of antimicrobial resistance in hospital-acquired bacterial infections globally. The data reveal an alarming rise in multidrug-resistant organisms, especially within critical areas like intensive care units. These findings highlight the pressing need to enhance infection control measures and promote the judicious use of antibiotics. Tackling antimicrobial resistance is crucial to mitigating the morbidity and mortality linked to nosocomial infections. Further research is advised to devise effective strategies for prevention and management. study underscores the growing prevalence

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