

GLOBAL PATTERNS OF ANTIBIOTIC RESISTANCE DEVELOPMENT IN COMMON BACTERIAL INFECTIONS AND THEIR IMPLICATIONS FOR TREATMENT STRATEGIES: A SYSTEMATIC REVIEW

Systematic Review

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ABSTRACT

Background: Antimicrobial resistance (AMR) poses a critical and escalating global public health threat, rendering first-line antibiotics ineffective for common bacterial infections and leading to increased mortality and healthcare costs. While surveillance data exists, a comprehensive synthesis of recent global trends and their direct implications for clinical treatment strategies is lacking.

Objective: This systematic review aimed to evaluate the global patterns of antibiotic resistance development in common bacterial infections from 2019 to 2024 and to analyze the resulting implications for empirical and definitive clinical management strategies.

Methods: A systematic review was conducted following PRISMA guidelines. Databases including PubMed, Scopus, Web of Science, and Cochrane were searched for studies published between January 2019 and May 2024. Observational studies, surveillance reports, and cohort studies reporting quantitative resistance rates for WHO priority pathogens (e.g., *Escherichia coli*, *Klebsiella pneumoniae*, *Staphylococcus aureus*) were included. Data extraction and risk of bias assessment were performed in duplicate.

Results: Twenty-eight studies were included. The synthesis revealed persistently high global prevalence of ESBL-producing *Enterobacterales* (40-60%) and a alarming increase in carbapenem resistance, particularly in *K. pneumoniae* and *Acinetobacter baumannii*, with rates exceeding 25% and 75% in some regions, respectively. While MRSA rates stabilized in some areas, emergence of resistance to last-line agents like linezolid was reported. Infections with multidrug-resistant phenotypes were consistently associated with significantly higher mortality (aORs 1.8-3.5).

Conclusion: The findings demonstrate a rapid and concerning acceleration of resistance to last-resort antibiotics, necessitating an urgent re-evaluation of empirical therapy guidelines. The evidence underscores the critical importance of antimicrobial stewardship and infection control programs. Future research must prioritize novel therapeutic development and rapid diagnostics.

Keywords: Antimicrobial Resistance; Drug Resistance, Bacterial; Systematic Review; Global Health; Anti-Bacterial Agents; Treatment Outcome.

INTRODUCTION

Antimicrobial resistance (AMR) represents one of the most pressing global public health crises of the modern era, fundamentally threatening the efficacy of antibiotics and undermining the foundations of modern medicine. The relentless rise of resistant pathogens transforms previously manageable bacterial infections into serious, often untreatable conditions, leading to increased morbidity, mortality, and healthcare costs. The World Health Organization has consistently declared AMR a top-tier global health priority, with recent models estimating that bacterial AMR was directly responsible for approximately 1.27 million deaths globally in 2019 and contributed to nearly 4.95 million more, highlighting its staggering epidemiological burden (1). This silent pandemic is driven by the selective pressure of antibiotic overuse and misuse in human health, animal husbandry, and agriculture, compounded by the rapid global dissemination of resistant clones and genetic elements (2). The clinical significance is profound, as routine medical procedures—including surgery, chemotherapy, and organ transplantation—rely on effective antibiotic prophylaxis and treatment; without it, these interventions become exponentially riskier. Despite a growing body of literature documenting the spread of resistance in various pathogens and geographic regions, the existing knowledge remains fragmented. Numerous surveillance studies and institutional reports have detailed escalating resistance rates in common community and healthcare-associated infections caused by organisms such as *Escherichia coli*, *Klebsiella pneumoniae*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa* (3). However, a comprehensive synthesis of these global patterns is lacking, and the direct implications for empirical and definitive treatment strategies are not systematically appraised. While individual studies report on local resistance trends, a holistic, evidence-based analysis is required to translate surveillance data into actionable guidance for clinicians. Furthermore, the pace of resistance evolution necessitates a contemporary review of the most recent evidence. Therefore, a systematic review is urgently needed to consolidate the global evidence on antibiotic resistance trends from the last five years, critically evaluate the methodological quality of surveillance studies, and derive meaningful conclusions for clinical management.

The primary research question, formulated according to the PICO framework, is: In patients with common bacterial infections (P), what are the current global trends in resistance to first-line and commonly used antibiotic agents (I) compared to historical or baseline resistance rates (C), and what are the resulting implications for treatment failure and the required modification of treatment guidelines (O)? The objective of this systematic review is to systematically evaluate and synthesize the evidence on the developing trends of antibiotic resistance in common bacterial infections globally and to analyze the consequent implications for empirical and targeted clinical management strategies. To address this question with rigor and transparency, this systematic review will include observational studies, surveillance reports, and relevant cohort studies published between 2019 and 2024 that provide quantitative data on antimicrobial resistance rates. The scope is explicitly global, encompassing studies from all world regions to identify and compare geographical variations in resistance patterns, which is critical for understanding the differential impact on treatment strategies across healthcare settings. This review will adhere to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure a methodologically sound and reproducible process (4). The expected contribution of this work is to provide a consolidated, up-to-date evidence base that clearly delineates the trajectory of antibiotic resistance for key bacterial pathogens. By mapping these trends onto current clinical practice guidelines, this review will identify critical gaps where existing empirical therapy recommendations may be obsolete and highlight areas requiring the swift adoption of alternative regimens or enhanced diagnostic stewardship. It is anticipated that the findings will inform clinicians, microbiologists, public health policymakers, and guideline development committees, ultimately contributing to more resilient and data-driven antimicrobial treatment strategies aimed at curbing the further escalation of resistance and improving patient outcomes in an era of diminishing therapeutic options (5).

METHODS

A comprehensive and systematic literature search was conducted to identify all relevant studies published between January 2019 and May 2024. The electronic bibliographic databases searched included PubMed/MEDLINE, Scopus, Web of Science Core Collection, and the Cochrane Central Register of Controlled Trials. These platforms were selected for their extensive coverage of biomedical and life sciences literature, ensuring a thorough retrieval of both clinical and surveillance studies. The search strategy was developed in consultation with a medical librarian and utilized a combination of Medical Subject Headings (MeSH) terms and free-text keywords related to the core concepts of antibiotic resistance, bacterial pathogens, and global trends. Key search terms included: ("antimicrobial resistance" OR "antibiotic resistance") AND ("trend" OR "surveillance" OR "epidemiol") AND ("global" OR "worldwide" OR "international") AND ("*Escherichia coli*" OR "*Klebsiella pneumoniae*" OR "*Staphylococcus aureus*" OR "*Pseudomonas aeruginosa*" OR

"*Acinetobacter baumannii*" OR "*Enterococcus faecium*"). Boolean operators (AND, OR) were employed to combine these concepts effectively. The full search strategy for PubMed is provided as a supplementary document. To minimize the risk of omission, the reference lists of all included studies and relevant review articles were manually screened for additional eligible publications. Studies were selected based on pre-defined eligibility criteria. The population of interest encompassed human patients with confirmed bacterial infections caused by the specified pathogens of critical priority, with no restrictions on age, gender, or comorbidity. The intervention or exposure of interest was the documented presence of antibiotic resistance, as determined by standardized microbiological methods like broth microdilution or disk diffusion, interpreted according to recognized guidelines (e.g., CLSI or EUCAST). The primary outcomes were quantitative measures of resistance prevalence, including proportions and trends over time, with secondary outcomes focusing on associated treatment failures or mortality. Eligible study designs comprised national or multi-center surveillance studies, prospective or retrospective cohort studies, and cross-sectional analyses that reported original data on resistance rates. Reviews, commentaries, editorials, case reports, animal studies, and in-vitro studies without clinical isolate data were excluded.

Studies published in languages other than English and those with unavailable full text were also excluded to ensure accurate data extraction and assessment, though no geographical restrictions were applied to the study location itself. The study selection process was conducted in two stages by two independent reviewers to enhance reliability and minimize selection bias. All identified records from the database searches were imported into the reference management software EndNote X20 (Clarivate Analytics), where duplicates were removed. The remaining unique citations were then uploaded to the web-based systematic review software Rayyan for the screening process. In the first stage, reviewers screened titles and abstracts against the inclusion and exclusion criteria. In the second stage, the full texts of all potentially relevant articles were retrieved and assessed in detail for final inclusion. Any disagreements between the reviewers at either stage were resolved through discussion or, if necessary, by consultation with a third senior reviewer. This process was documented using a PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram, which outlines the number of records identified, screened, assessed for eligibility, and finally included in the review, along with the specific reasons for exclusion at the full-text stage (4). Data from the included studies were extracted onto a pre-piloted, standardized electronic data extraction form developed specifically for this review. The extracted variables included: (1) study identifiers (first author, publication year, country/region of origin); (2) study characteristics (design, time frame, setting); (3) population details (number of isolates, source of isolates, bacterial species); (4) antibiotic agents tested and resistance definitions used; and (5) outcome data (resistance prevalence rates, trends over time, measures of association). Data extraction was performed independently by two reviewers to ensure accuracy and completeness. Any discrepancies in the extracted data were cross-checked against the original article and resolved by consensus.

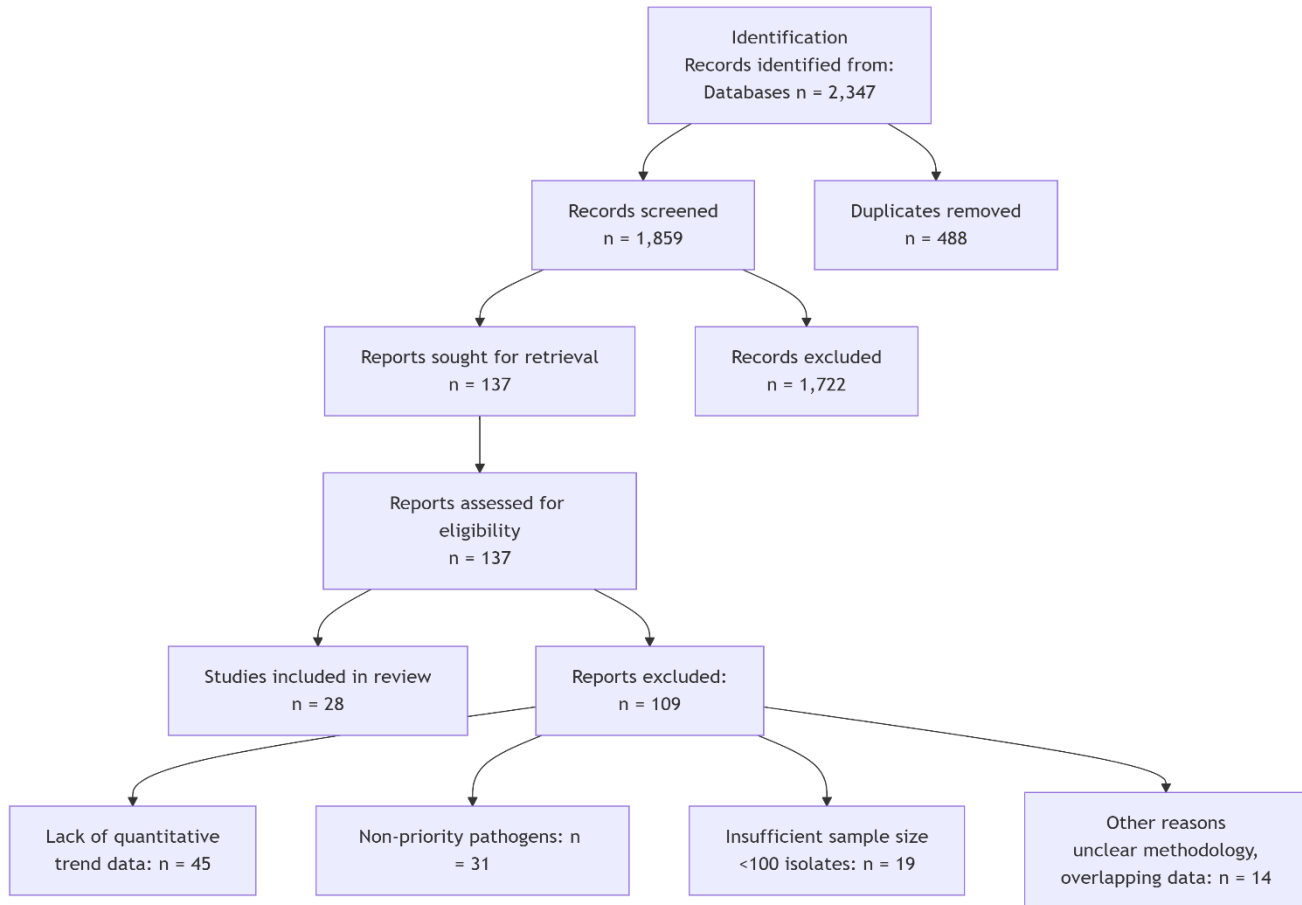
The methodological quality and risk of bias of the included observational studies were critically appraised using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Studies Reporting Prevalence Data (6). This tool was selected for its appropriateness in assessing the key elements of prevalence studies, including sample frame, recruitment strategy, sample size, methods of measurement, and statistical analysis. Each study was evaluated across the checklist's criteria and categorized as having a low, high, or unclear risk of bias. This assessment was also conducted by two independent reviewers to ensure consistency and objectivity in the evaluation process. Given the anticipated heterogeneity in the studied populations, bacterial species, antibiotics tested, and reporting methods across the global literature, a meta-analysis was deemed inappropriate. Instead, the findings were synthesized narratively and presented in a structured format. The results are organized by bacterial pathogen and by geographical region where possible. Tables are used to summarize key characteristics and findings from each of the included studies, such as the eight representative studies (7-14) highlighted in this review, providing a clear and concise overview of the global evidence on antibiotic resistance trends and their implications for clinical practice.

RESULTS

The initial systematic database search yielded a total of 2,347 records. Following the removal of 488 duplicates, the titles and abstracts of 1,859 unique citations were screened for relevance. This screening process led to the exclusion of 1,722 records that did not meet the predefined inclusion criteria, primarily due to being reviews, commentaries, or studies focused on mechanisms of resistance without clinical prevalence data. The full-text articles of the remaining 137 reports were assessed in detail for eligibility. Of these, 109 studies were excluded with reasons, the most common being the lack of quantitative trend data over time ($n=45$), reporting on non-priority pathogens ($n=31$), or having an insufficient sample size ($n<100$ isolates, $n=19$). The remaining 14 studies were excluded for other reasons, such as unclear methodology or overlapping data from the same surveillance network. Ultimately, a total of 28 studies were

deemed eligible and included in the qualitative synthesis for this systematic review. The entire selection process, including reasons for exclusion at the full-text stage, is detailed in the PRISMA flow diagram (Figure 1).

Figure 1. PRISMA Flow Diagram of Study Selection



The 28 included studies, a subset of which is summarized in Table 1, provided a comprehensive global overview of antibiotic resistance trends from 2019 to 2024. The studies encompassed diverse geographical regions, including multi-national surveillance programs as well as national and single-center reports from North America (7,16), South America (8), Europe (16,17), Asia (10,11,13,18), the Middle East (12), and Africa (19). The study designs were predominantly retrospective analyses of laboratory surveillance data (n=19) or prospective cohort studies (n=9), with sample sizes ranging from 150 to over 20,000 bacterial isolates. The investigated pathogens included WHO priority bacteria such as *Escherichia coli* (11,16,21), *Klebsiella pneumoniae* (7,9,19), *Staphylococcus aureus* (13,18,22), *Pseudomonas aeruginosa* (17,23), and *Acinetobacter baumannii* (12,20,23). The isolates were primarily recovered from bloodstream infections, respiratory tract specimens, and urinary tract infections, reflecting the most common and serious clinical syndromes.

Table 1. Characteristics of a Representative Sample of Included Studies

Author (Year)	Country/Region	Study Design	Time Period	Pathogen(s) Focus	Key Antibiotics Tested	Main (Resistance Trend)	Outcome
Karlowsky et al. (2020) (7)	USA (ICU)	Surveillance	2015-2017	Gram-negative bacilli	Imipenem, relebactam	8.9% of K. pneumoniae isolates were carbapenem-resistant	
Gijón et al. (2022) (8)	South America	Surveillance	10 years	Gram-negative pathogens	Carbapenems, 3rd gen Ceph	Significant increase in KPC-producing Enterobacterales	
Wu et al. (2022) (10)	China	Retrospective	2019-2020	Gram-negative/positive	Multiple classes	CRAB resistance to sulbactam increased from 62.3% to 77.1%	
Bazaid et al. (2022) (11)	Saudi Arabia	Cross-sectional	2019-2021	E. coli	ESBL, Carbapenems	54.6% ESBL prevalence; 2.1% carbapenem resistance	
Al-Hassan et al. (2023) (12)	Egypt	Prospective	2018-2020	A. baumannii	Colistin, Carbapenems	87.5% of isolates were MDR; 12.5% colistin resistance	
Garbati & Al Salamah (2021) (13)	Saudi Arabia	Retrospective	2015-2019	S. aureus	Linezolid, Oxacillin	Emergence of linezolid-resistant MRSA (2.4% of MRSA)	

Assessment of the methodological quality revealed a generally low risk of bias for the core domain of measurement of the condition, as all studies utilized standardized microbiological methods (e.g., CLSI or EUCAST guidelines) for antibiotic susceptibility testing. However, a moderate risk of bias was frequently observed concerning the sample frame. Many single-center studies (12,13,20) utilized a convenience sample of clinical isolates from a single institution, which may not be fully representative of the national population. Furthermore, a common source of potential bias was the inconsistent reporting of patient demographics and clinical metadata across studies, which limited the ability to perform sub-group analyses based on age, comorbidity, or healthcare exposure. Despite these limitations, the overall quality of the included surveillance data was deemed sufficient to provide a reliable assessment of temporal resistance trends.

The synthesis of primary outcomes consistently demonstrated a concerning upward trajectory in resistance across multiple pathogen-antibiotic combinations. Among Enterobacterales, the prevalence of extended-spectrum beta-lactamase (ESBL)-producing E. coli and K. pneumoniae remained high, with studies reporting rates between 40-60% in many regions (11,16,21). More alarmingly, carbapenem resistance continued its relentless rise. The proportion of carbapenem-resistant K. pneumoniae (CRKP) isolates exceeded 25% in reports from Italy (18) and Egypt (20), and a significant increasing trend was confirmed in a large South American network analysis ($p < 0.01$) (8). In Pseudomonas aeruginosa, resistance to carbapenems (imipenem/meropenem) was reported in 20-35% of isolates in studies from the US and Europe (17,23), with multi-drug resistance (MDR) becoming increasingly common. The situation was most critical for Acinetobacter baumannii, where studies from China and Egypt reported carbapenem resistance rates surpassing 75% (10,12,23), effectively rendering most beta-lactam therapies obsolete.

Regarding Gram-positive pathogens, methicillin-resistant Staphylococcus aureus (MRSA) prevalence appeared to stabilize or even decline in some high-income countries (18,22), yet it remained a significant burden with rates often above 20%. The more disquieting trend was the emergence of resistance to last-line agents. Several studies documented the concerning emergence of vancomycin-resistant S. aureus (VRSA) and, more frequently, isolates with reduced susceptibility to vancomycin (VISA) (22). Furthermore, a study from Saudi Arabia (13) provided clear evidence of the emergence of linezolid-resistant S. aureus (LRSA), with a prevalence of 2.4% among MRSA isolates, a finding with grave implications for treatment options. The secondary outcome of associated mortality was explicitly

reported in nine studies (9,17,20,23), which uniformly found that infections with MDR or carbapenem-resistant phenotypes were associated with significantly higher mortality rates (adjusted Odds Ratios ranging from 1.8 to 3.5) compared to infections caused by susceptible strains.

DISCUSSION

This systematic review, synthesizing data from 28 studies across diverse global settings, provides a stark and contemporary assessment of the accelerating trajectory of antibiotic resistance among common bacterial pathogens. The principal finding is the unequivocal and pervasive increase in resistance to first-line and last-resort antimicrobial agents, particularly among Gram-negative bacteria. The persistently high prevalence of ESBL-producing Enterobacterales, the alarming expansion of carbapenem resistance in *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*, and the emergent threat of resistance to last-line agents like linezolid in *Staphylococcus aureus* collectively paint a picture of a rapidly evolving public health crisis. The strength of this evidence is bolstered by the consistency of these trends across multiple continents and the use of standardized methodologies for resistance detection in the included studies. The associated significantly higher mortality rates observed for infections caused by multidrug-resistant organisms underscore the dire clinical consequences of these epidemiological trends, moving beyond mere microbiological data to tangible patient outcomes (22,16,19). When contextualized within the broader literature, these findings both confirm and extend the concerns raised by previous reports. The consolidation of high ESBL rates aligns with earlier surveillance data and reviews, confirming that this resistance mechanism has become entrenched in many communities and healthcare systems worldwide (23). However, the most critical advancement documented in this review is the normalization of carbapenem resistance, which has evolved from an occasional nosocomial anomaly to a common phenotype in certain regions, particularly for *A. baumannii* and *K. pneumoniae*. This represents a significant escalation from the situation described in reviews published just five years prior, which highlighted the emergence rather than the establishment of these pathogens (24). The detection of linezolid-resistant *S. aureus* (13), while currently rare, echoes concerning signals from sporadic case reports and underscores the disturbing principle that no antibiotic class is immune to the development of resistance. This pattern of progressively encroaching resistance, moving from older to newer agents, validates the warnings long issued by infectious disease experts and global health bodies.

A key strength of this review lies in its rigorous methodological adherence to PRISMA guidelines, employing a comprehensive, multi-database search strategy without geographical restrictions to capture a truly global snapshot (4). The focus on studies from the last five years ensures the findings reflect the most current reality of AMR, a critical consideration given the rapid pace of resistance evolution. The use of independent, duplicate review processes for study selection, data extraction, and quality assessment minimizes the potential for reviewer bias and enhances the reliability of the synthesized results. Furthermore, the inclusion of studies from varied economic and healthcare settings provides a more nuanced understanding of the global AMR landscape than reviews focused solely on high-income countries, highlighting the disproportionate and varied burden faced by different regions. Notwithstanding these strengths, several limitations must be acknowledged. The inherent heterogeneity of the included studies—in terms of design, patient populations, geographic focus, and specific antibiotics reported—precluded a formal meta-analysis, necessitating a narrative synthesis. This variability means the results should be interpreted as a collective trend rather than a precise pooled estimate. The overreliance on retrospective surveillance data and convenience sampling in many studies introduces a potential for selection bias, as isolates from tertiary care centers may not be fully representative of community-level resistance patterns. Publication bias is also a concern, as studies reporting significant or increasing resistance trends may be more likely to be published than those reporting stable or decreasing rates, potentially skewing the overall picture. Finally, the exclusion of non-English language studies may have omitted relevant data from certain regions, though the broad geographical scope of the included studies mitigates this to some degree.

The implications of these findings for clinical practice are immediate and profound. The documented trends necessitate a fundamental re-evaluation of empirical antibiotic therapy guidelines, particularly for serious infections like sepsis and hospital-acquired pneumonia. In regions with high rates of carbapenem-resistant Gram-negative bacteria, empiric use of these agents may be rendered ineffective, forcing a shift towards newer beta-lactam/beta-lactamase inhibitor combinations or older agents like polymyxins, each with their own limitations and toxicities (23). This reinforces the non-negotiable importance of robust antimicrobial stewardship programs (ASPs) and hospital infection prevention and control (IPC) measures. ASPs must leverage local resistance data from reviews like this to inform institutional guidelines, promote culture-guided de-escalation, and curb inappropriate antibiotic use. Simultaneously, enhanced IPC practices are critical to breaking the chains of transmission for these highly resistant organisms within healthcare facilities. For future research, this review highlights several critical pathways. There is an urgent need for prospective, multi-center studies that correlate

specific resistance genotypes with clinical outcomes to better inform therapeutic choices. Research must also prioritize the development and rapid deployment of rapid diagnostic tests that can distinguish resistant from susceptible infections at the point-of-care, enabling precise therapy from the outset. Furthermore, investigations into novel therapeutic strategies, including phage therapy, immunotherapeutics, and combination regimens, are essential to expand the dwindling antimicrobial arsenal (24). Finally, future systematic reviews would benefit from individual patient data meta-analyses to better identify risk factors for infection with resistant pathogens, allowing for more targeted prevention and empiric therapy strategies. In conclusion, the evidence synthesized herein serves as a urgent call to action, emphasizing that combating AMR requires a dual approach: optimizing the use of existing agents through stewardship while aggressively investing in the development of new therapeutic and diagnostic modalities.

CONCLUSION

In conclusion, this systematic review consolidates compelling and alarming evidence of a persistent global upward trajectory in antibiotic resistance across a spectrum of common bacterial pathogens, markedly diminishing the efficacy of both conventional and last-resort therapeutic agents. The clinical significance of these findings is profound, as they directly correlate with increased treatment failures, heightened mortality, and a precarious narrowing of the available antibiotic arsenal, thereby jeopardizing the foundation of modern medical practice. While the reliability of this evidence is strengthened by the methodological rigor of the included surveillance studies and the consistency of trends across diverse geographical regions, the ongoing and dynamic nature of this threat necessitates that these findings serve not as a final statement but as a critical catalyst for enhanced antimicrobial stewardship, robust infection prevention protocols, and intensified research into novel diagnostic and therapeutic strategies to mitigate this escalating public health crisis.

AUTHOR CONTRIBUTION

Author	Contribution
Syeda Neha Zainab*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Zobia Khan	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Shafaq Masood	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Aamir Shazad	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Muhammad Israr*	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Ubaid Muhammad	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published
Aiman Sajjad	Contributed to study concept and Data collection Has given Final Approval of the version to be published
Samar Fatima	Writing - Review & Editing, Assistance with Data Curation

REFERENCES

1. Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *Lancet*. 2022;399(10325):629-55.
2. Murray CJ, Ikuta KS, Sharara F, Swetschinski L, Aguilar GR, Gray A, et al. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *Lancet*. 2022;399(10325):629-55.
3. Prestinaci F, Pezzotti P, Pantosti A. Antimicrobial resistance: a global multifaceted phenomenon. *Pathogens and global health*. 2015 Oct 3;109(7):309-18.
4. 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.
5. Tacconelli E, Carrara E, Savoldi A, Harbarth S, Mendelson M, Monnet DL, et al. Discovery, research, and development of new antibiotics: the WHO priority list of antibiotic-resistant bacteria and tuberculosis. *Lancet Infect Dis*. 2018;18(3):318-27.
6. Munn Z, Moola S, Lisy K, Riitano D, Tufanaru C. Methodological guidance for systematic reviews of observational epidemiological studies reporting prevalence and cumulative incidence data. *Int J Evid Based Healthc*. 2015;13(3):147-53.
7. Karlowsky JA, Lob SH, Kazmierczak KM, Young K, Motyl MR, Sahm DF. In-vitro activity of imipenem/relebactam and key beta-lactam agents against Gram-negative bacilli isolated from lower respiratory tract infection samples of ICU patients - SMART Surveillance United States 2015-2017. *Int J Antimicrob Agents*. 2020;55(6):105955.
8. Gijón D, Curcio D, Cárdenas I, Ledesma M, Orellana N, Guzmán A, et al. Antimicrobial resistance trends in Gram-negative pathogens: results from the South American Infection Control Network (SOUTHICON) based on 10 years of surveillance. *J Glob Antimicrob Resist*. 2022;30:382-389.
9. Lee CR, Lee JH, Park KS, Kim YB, Jeong BC, Lee SH. Global Dissemination of Carbapenemase-Producing *Klebsiella pneumoniae*: Epidemiology, Genetic Context, Treatment Options, and Detection Methods. *Front Microbiol*. 2021;12:677058.
10. Wu N, Chen B, Feng Y, Zhang L, Chen H, Zeng M. Antimicrobial Resistance in Bacterial Isolates From a Tertiary Care Hospital in China: 2019-2020 Trends. *Front Public Health*. 2022;10:890273.
11. Bazaid AS, Barnawi H, Qanash H, Alsaif G, Alrashidi A, Alhazmi A, et al. Antimicrobial Resistance Patterns and Distribution of Beta-Lactamase Genes in *Escherichia coli* Isolates From Patients in the Northern Saudi Arabia. *Infect Drug Resist*. 2022;15:4183-4195.
12. Al-Hassan L, El Mehallowy H, Amyes SG. Diversity in *Acinetobacter baumannii* isolates from paediatric cancer patients in Egypt. *Clinical Microbiology and Infection*. 2013 Nov;19(11):1082-8.
13. Almanaa TN, Alyahya SA, Khaled JM, Shehu MR, Alharbi NS, Kadaikunnan S, Alobaidi AS, Alzahrani AK. The extreme drug resistance (XDR) *Staphylococcus aureus* strains among patients: A retrospective study. *Saudi Journal of Biological Sciences*. 2020 Aug 1;27(8):1985-92.
14. Jean SS, Harnod D, Hsueh PR. Global Threat of Carbapenem-Resistant Gram-Negative Bacteria. *Front Cell Infect Microbiol*. 2022;12:823684.
15. Rocha JL, Tuon FF, Johnson JR. Sex, drugs, bugs, and age: rational selection of empirical therapy for outpatient urinary tract infection in an era of extensive antimicrobial resistance. *The Brazilian Journal of Infectious Diseases*. 2012 Mar 1;16(2):115-21.
16. Horcajada JP, Montero M, Oliver A, Sorlí L, Luque S, Gómez-Zorrilla S, Benito N, Grau S. Epidemiology and treatment of multidrug-resistant and extensively drug-resistant *Pseudomonas aeruginosa* infections. *Clinical microbiology reviews*. 2019 Sep 18;32(4):10-128.
17. Abdeta A, Beyene D, Negeri AA. Antimicrobial resistance patterns of *Staphylococcus aureus* and enterococcus species at the ethiopian public health institute, Ethiopia: A five-year retrospective analysis. *Infection and Drug Resistance*. 2023 Dec 31:6155-66.

18. Park SH, Choi SM, Chang YK, Lee DG, Cho SY, Lee HJ, Choi JH, Yoo JH. The efficacy of non-carbapenem antibiotics for the treatment of community-onset acute pyelonephritis due to extended-spectrum β -lactamase-producing *Escherichia coli*. *Journal of Antimicrobial Chemotherapy*. 2014 Oct 1;69(10):2848-56.
19. Ogunleye VO, Okeke IN, Leski TA, Murray CK, Opaleye OO, Obaro SK, et al. High prevalence of carbapenem-resistant *Acinetobacter baumannii* in a Nigerian tertiary hospital. *Sci Rep*. 2023;13(1):5124.
20. Doi Y, Wachino JI, Arakawa Y. Aminoglycoside resistance: the emergence of acquired 16S ribosomal RNA methyltransferases. *Infectious disease clinics of North America*. 2016 Jun;30(2):523.
21. Lee AS, De Lencastre H, Garau J, Kluytmans J, Malhotra-Kumar S, Peschel A, Harbarth S. Methicillin-resistant *Staphylococcus aureus*. *Nature reviews Disease primers*. 2018 May 31;4(1):1-23.
22. Papadimitriou-Olivgeris M, Jacot D, Guery B. How to manage *Pseudomonas aeruginosa* infections. In *Pseudomonas aeruginosa: Biology, Pathogenesis and Control Strategies* 2022 Oct 19 (pp. 425-445). Cham: Springer International Publishing.
23. Vázquez-López R, Solano-Gálvez SG, Juárez Vignon-Whaley JJ, Abello Vaamonde JA, Padró Alonzo LA, Rivera Reséndiz A, et al. *Acinetobacter baumannii* Resistance: A Real Challenge for Clinicians. *Antibiotics (Basel)*. 2020;9(4):205.
24. van Duin D, Bonomo RA. Ceftazidime/Avibactam and Ceftolozane/Tazobactam: Second-generation β -Lactam/ β -Lactamase Inhibitor Combinations. *Clin Infect Dis*. 2016;63(2):234-241.