

Knowledge and perceptions regarding Antimicrobial Resistance and Antimicrobial potential of metal-based agents: Systematic Review of available Evidence

Fajar¹, Zunaira Rahim¹, Washam Awan², Ayesha Khawar³, Momina Saleem³, Aaiza Irfan Butt³, Jaweria Waris³, Momina Yasir⁴

Abstract

Background: Antimicrobial resistance (AMR) is a major global public health concern that threatens the successful treatment of infectious diseases. The increasing prevalence of multidrug-resistant (MDR) bacteria has led to the exploration of alternative antimicrobial strategies, including metal-based antimicrobial agents such as silver, copper, and zinc.

Objectives: To assess knowledge and perceptions regarding antimicrobial resistance among various human populations, and to investigate the antimicrobial potential of silver-, copper-, and zinc-based materials against multidrug-resistant bacteria.

Methods: A systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Literature published between January 2017 and June 2025 was searched using PubMed, Google Scholar, Science Direct, and Scopus. We included 17 sources, including original research, systematic reviews, observational studies, cross-sectional studies, and relevant national or international surveillance reports and authoritative reports. The included human population studies comprised residents of Wah aged ≥ 16 years, adults in Punjab, Pakistan aged ≥ 18 to < 80 years, and university students in Brunei Darussalam aged 18–29 years, while laboratory and surveillance studies were included according to their respective study designs and eligibility criteria.

Results: The reviewed studies reported increasing antimicrobial resistance due to unsuitable antibiotic use, self-medication, and insufficient awareness. Studies among students reported varying levels of AMR knowledge, with important knowledge gaps and misconceptions remaining. Experimental evidence further indicated that silver-, copper-, and zinc-based antimicrobial agents possess important antibacterial activity against multidrug-resistant pathogens through multiple mechanisms of action.

Conclusion: The available evidence suggests that improving awareness of AMR is essential for promoting responsible antibiotic use. However, none of the included studies directly assess students' knowledge or perceptions regarding metal-based antimicrobial agents, highlighting a major research gap.

Keywords: Antimicrobial resistance; Multidrug-resistant bacteria; Metal-based antimicrobial agents; Silver nanoparticles; Copper nanoparticles; Zinc nanoparticles

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¹ BS Microbiology and Molecular Genetics, Department of Microbiology and Molecular Genetics, University of the Punjab, Lahore, Pakistan

² BS Social and Cultural Studies, Department of Social and Cultural Studies, University of the Punjab, Lahore, Pakistan

³ BS Zoology, Department of Zoology, Government College University (GCU), Lahore, Pakistan.

⁴ A Levels, ISL International School, Lahore, Pakistan.

Introduction:

Antimicrobial resistance (AMR) is recognized as one of the most serious public health challenges of the twenty-first century. It occurs when tiny organisms, including bacteria, viruses, fungi, and parasites, develop the ability to fight against antimicrobial agents that were previously effective in treating the infections they cause. Consequently, infections become more difficult to manage, leading to long-term illness, extended hospital stays, increased healthcare costs, and a higher death rate. Recognizing the scale of this problem, the World Health Organization (WHO) has identified AMR as one of the leading global health threats requiring urgent and coordinated action ¹

The increasing spread of antimicrobial resistance (AMR) is driven by the inappropriate and excessive use of antibiotics across human healthcare, veterinary medicine, agriculture, and the environment. Practices such as self-medication, inappropriate prescribing, failure to complete prescribed antibiotic courses, and inadequate infection prevention and control measures have accelerated the emergence and spread of multidrug-resistant (MDR) microorganisms ² The global impact of AMR is substantial. According to Murray et al. (2022), bacterial AMR was directly responsible for an estimated 1.27 million deaths worldwide in 2019 and contributed to 5 million deaths, underscoring its serious threat to public health ³

Among antimicrobial-resistant pathogens, *Escherichia coli* is one of the most commonly reported multidrug-resistant bacteria and is a common cause of urinary tract infections, bloodstream infections, wound infections, and gastrointestinal diseases. Recent studies from Pakistan have reported increasing resistance of *E. coli* to several commonly prescribed antibiotics, highlighting the urgent need for responsible antimicrobial management treatment strategies ⁴

Pakistan is among the countries that are facing a rapidly growing burden of antimicrobial resistance. Several factors contribute to this challenge, such as easy availability of antibiotics without a prescription, limited public awareness, fewer infection control measures, and inappropriate antibiotic use ⁵ Although previous studies conducted in Pakistan suggest that awareness of AMR is gradually improving, misconceptions about the proper use of antibiotics remain common, particularly among university students. These findings highlight the need for continued educational initiatives and stronger antimicrobial efforts to promote the responsible use of antibiotics ^{6,7}

To address this growing challenge, researchers have investigated alternative antimicrobial strategies that may support traditional antibiotics. Metal-based antimicrobial agents, particularly silver, copper, and zinc, have attracted significant scientific interest due to their broad-spectrum antimicrobial activity. Unlike common antibiotics, these metals act through multiple mechanisms, including disruption of bacterial cell membranes, generation of reactive oxygen species, inhibition of essential enzymes, protein denaturation, and damage to bacterial DNA ^{8,9} Their multiple mechanisms of action may reduce the likelihood of resistance arising through a single bacterial target; however, bacterial adaptation and resistance to metal-based agents have also been reported. ¹⁰

Recent laboratory studies have shown that silver, copper, and zinc nanoparticles possess strong antibacterial activity against several multidrug-resistant pathogens, including resistant *Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa* [11]. In addition, growing evidence suggests that combining metal-based antimicrobial agents with standard antibiotics may produce combined effects, thereby improving their antibacterial performance.

The selected human population studies evaluated AMR awareness, knowledge, and perceptions across diverse age groups and social settings. Specifically, Shan et al. evaluated community residents aged 16 years in Wah, while Gillani et al. investigated adults aged 18 to 80 years in Punjab. Additionally, Shahpawee et al. targeted university students aged 18–29 years. Investigating cohorts aged 16 years is critical, as these individuals directly influence antibiotic use patterns through self-medication practices, over-the-counter procurement, and family healthcare decisions. Including people who are 16 or older is important because people in these age groups might affect how antibiotics are used through how they take medicine themselves, how they get medicine without a doctor, how they decide to see a doctor, and how they talk about health with family and friends. Younger groups are also important for learning about resistance because the ideas and wrong beliefs formed during being a teenager and early adult might affect how they use antibiotics later. So, looking at information from people who were 16 years old or older helps get a better idea of how people in communities and at university understand antimicrobial resistance^{6,7,13}. In addition, advances in nanotechnology have increased interest in metal-based nanoparticles as alternative antimicrobial agents. Their multiple mechanisms of action may reduce the likelihood of resistance arising through a single bacterial target; however, bacterial adaptation and resistance to metal-based agents have also been reported and warrant further investigation^{14,15}.

Global and national surveillance systems play an important role in monitoring antimicrobial resistance trends and guiding public health improvement. The World Health Organization's Global Antimicrobial Resistance and Use Surveillance System (GLASS) has reported increasing resistance among important bacterial pathogens worldwide, highlighting the need for standardized surveillance and international

collaboration¹⁶. Similarly, the National Institute of Health (NIH) Pakistan has documented rising antimicrobial resistance among clinically important bacterial isolates, underscoring the need to strengthen national surveillance programs, promote responsible antimicrobial use, and strengthen infection prevention strategies¹⁷.

Despite extensive research on antimicrobial resistance and the antimicrobial properties of metal-based agents, none of the included studies directly assessed university students' knowledge or perceptions of these agents. University students, particularly those enrolled in healthcare-related disciplines, are future healthcare professionals whose knowledge and attitudes will play an important role in antibiotic prescribing, antimicrobial management, and public health education. Assessing their understanding of AMR and emerging antimicrobial approaches is therefore essential for identifying knowledge gaps and guiding the development of effective educational and awareness programs.

This systematic review was conducted to synthesize the available evidence on antimicrobial resistance, evaluate university students' perceptions of AMR, and examine the antimicrobial potential of silver-, copper-, and zinc-based agents against multidrug-resistant bacteria.

Methodology

Study Design

This study was conducted as a systematic review to summarize and analyze published evidence on antimicrobial resistance (AMR), knowledge and perceptions of AMR, and the antimicrobial potential of metal-based antimicrobial agents. The review was performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure a clear, systematic, and reliable research process.

Search Strategy

A complete literature search was conducted using four electronic databases: PubMed, Google Scholar, Scopus, and ScienceDirect. Articles published between January 2017 and June 2025 were searched. The search strategy included terms related to antimicrobial resistance, antibiotic resistance, multidrug-resistant bacteria, students, adults, community populations, general population, knowledge, awareness, perceptions, and metal-based antimicrobial agents, including silver, copper, and zinc. Boolean operators (AND, OR) were used to improve the search strategy.

Eligibility Criteria

Inclusion criteria.

Studies were chosen if they were written in English and published between January 2017 and June 2025. These studies had to be about what people know or think about antimicrobial resistance; the efficacy of metal-based agents (silver, copper, and zinc) against bacterial pathogens. Eligible human-subject studies were restricted to populations aged 16 years, focusing on AMR knowledge, awareness, and attitudes, alongside laboratory studies demonstrating the in vitro antibacterial efficacy of metal-based agents. We included various study designs, including original research, systematic reviews, observational cohorts, cross-sectional surveys, and laboratory assays.

Exclusion criteria.

Studies were excluded if they were conference abstracts, editorials, letters, or opinion articles; included insufficient or incomplete data; or were published in languages other than English.

Study Selection

The titles and abstracts of retrieved records were screened by eight members of the review team independently according to the predefined

eligibility criteria. No disagreements occurred among the reviewers during study selection or data extraction. Potentially relevant articles were subsequently assessed through full-text review. Studies that met all inclusion criteria were selected for the final systematic review.

Data Extraction

Data were extracted using a predefined data-extraction form by the eight members of the review team independently. The information extracted included author(s), year of publication, country, study design, key findings, experimental laboratory findings, and conclusion from each included study. The findings from the included sources were then summarized and compared according to their relevance to the objectives of the review. Due to substantial heterogeneity among the included studies in terms of study design, study populations, antimicrobial agents, bacterial species, experimental conditions, and outcome measures, a quantitative meta-analysis was not considered appropriate. Therefore, the findings were synthesized narratively and organized according to the major themes and characteristics of the included studies. No disagreements occurred among the reviewers during data extraction.

Quality Assessment and Risk of Bias

The methodological quality and risk of bias of the 17 included sources were assessed according to their study designs. Cross-sectional studies were assessed for sampling, measurement methods, response rates, and potential sources of bias; retrospective and experimental studies were assessed for study design, controls, replication, and analytical methods; and review and surveillance sources were assessed for methodological transparency, data sources, and reporting quality.

Results

Study Selection

A literature search was conducted using PubMed, Google Scholar, Scopus, and ScienceDirect. A total of 55 records were identified through database searching. After removing duplicate articles, 37 records remained for title and abstract screening. Following screening, 25 full-text articles were assessed for eligibility. After applying the predefined inclusion and exclusion criteria, 17 studies/sources were included in the final systematic review. The study selection process is illustrated in the PRISMA flow diagram (Figure 1).

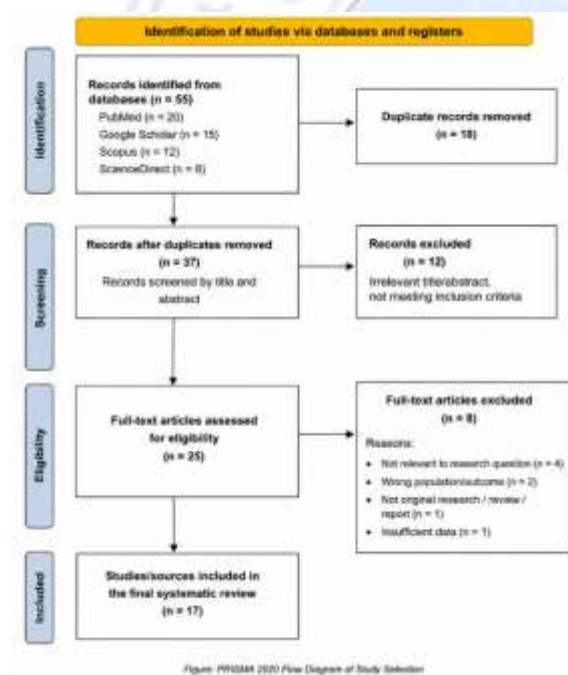


Figure 1: PRISMA Flow Diagram

Characteristics of Included Studies

The 17 included studies/sources were published between Jan 2017 and June 2025 and represented evidence from Pakistan, India, the United Kingdom, Mexico, China, South Africa, and global organizations such as the World Health Organization. The studies consisted of systematic reviews, cross-sectional surveys, retrospective

analyses, observational studies, surveillance reports, and laboratory-based experimental research. Human population studies assessing AMR knowledge and perceptions included residents aged ≥ 16 years, adults aged ≥ 18 years to < 80 years, and university students aged 18–29 years. Their primary focus included antimicrobial resistance, knowledge, perception, and awareness regarding AMR, responsible antimicrobial use, and the antibacterial activity of silver-, copper-, and zinc-based antimicrobial agents against multidrug-resistant bacteria.

Table 1. Characteristics of Included Studies

R ef .	Auth or	Y ea r	Coun try	Study Design	Main Findin gs
[1]	World Health Organization (WHO)	2024	Global	Fact sheet	AMR is one of the most serious global public health threats, leading to prolonged illness, treatment failure, increased healthcare costs, and higher

					mortality. The WHO emphasizes coordinated global action and responsible antimicrobial use.
[2]	Samajdar et al.	2024	India	Comprehensive review	Inappropriate antibiotic use in humans, animals, and agriculture is a major driver of AMR. The study highlights the importance of the One Health approach

					ch for preventing and controlling antimicrobial resistance.
[3]	Murray et al.	2022	Global	Systematic analysis	Bacterial AMR directly caused approximately 1.27 million deaths and contributed to 5 million deaths worldwide in 2019, suggesting a huge global health burden.
[4]	Fayyaz et al.	2025	Pakistan	Retrospective study	A 10-year analysis showed increases

					ing multidrug resistance in Escherichia coli, with high resistance to several commonly prescribed antibiotics, emphasizing the need for continuous surveillance.						antibiotic use, self-medication, over-the-counter availability of antibiotics, and inadequate antimicrobial stewardship.
[5]	Bilal et al.	2021	Pakistan	Systematic review	Antibiotic resistance has increased in Pakistan because of irrational	[6]	Gillani et al.	2021	Pakistan	Cross-sectional study	Public knowledge regarding appropriate antibiotic use was inadequate. Misconceptions about antibiotic use and self-medication were

					common, indicating the need for educational interventions.
[7]	Shan et al.	2018	Pakistan	Cross-sectional study	Participants demonstrated moderate awareness of AMR; however, misconceptions regarding antibiotic use and resistance remained common. Increased public education was

					recommended.
[8]	Raja et al.	2023	United Kingdom	Experimental study	Silver, copper, zinc, and cobalt nanoparticles demonstrated strong antibacterial activity against multidrug-resistant bacteria. Combining different metals enhances antimicrobial effectiveness.
[9]	Prabhu et al.	2025	India	Review	Heavy metals and nanoparticles inhibit

					bacteria through membrane disruption, oxidative stress, protein denaturation, and DNA damage. The review also discussed mechanisms of bacterial resistance to metals.						against resistant pathogens but highlighted concerns regarding toxicity, environmental impact, and resistance development.
[10]	Ngope et al.	2025	South Africa	Review	Metal oxide nanoparticles showed promising antimicrobial activity	[11]	Garza-Cervantes et al.	2017	Mexico	Experimental study	Silver combined with transition metals produced synergistic antibacterial effects, improving antimicrobial activity against

					resistant microorganisms compared with individual treatments.
[12]	Guo et al.	2024	China	Experimental study	Metal nanocomposites demonstrated rapid and effective antibacterial activity against multidrug-resistant bacteria, including biofilm-forming organisms, support

					ing their therapeutic potential.
[13]	Shahpawee et al.	2020	Brunel Darussalam	Cross-sectional study	University students demonstrated moderate knowledge of antimicrobial resistance; however, misconceptions regarding antibiotic use and self-medication persisted, highlighting the need for

					educational programs.
[14]	Mondal et al.	2024	Global	Review	Antimicrobial nanoparticles possess broad-spectrum antibacterial activity and multiple mechanisms of action, making them promising alternatives to conventional antibiotics against resistant pathogens.
[1]	Gupta et al.	2020	United	Review	Nanomaterials demon

5]		19	States		strated significant potential to combat multidrug-resistant bacteria through multiple antibacterial mechanisms and may enhance the effectiveness of existing antimicrobial therapies.
[16]	World Health Organization (WH	2022	Global	Surveillance report	Global surveillance identified increasing

	O GLA SS)				antimicrobial resistance among priority bacterial pathogens and emphasized the importance of standardized surveillance systems and international collaboration.		Pakistan				antimicrobial resistance among clinically important bacterial pathogens in Pakistan and highlighted the need to strengthen antimicrobial stewardship and infection prevention measures.
[1 7]	National Institute of Health (NIH)	2 0 2 2	Pakistan	Surveillance report	National surveillance confirmed increasing						

Quality Assessment and Risk of Bias

Overall, the methodological quality of the included evidence ranged from moderate to high. Cross-sectional, retrospective, and experimental studies generally demonstrated adequate methodological characteristics, although self-

reported measures, retrospective data, and laboratory-based designs introduced potential limitations. Systematic reviews and surveillance reports provided comparatively stronger evidence, whereas narrative reviews showed greater methodological limitations. These

differences were considered when interpreting the findings and conducting the narrative synthesis.

Summary of Findings

The included studies showed that antimicrobial resistance (AMR) is a growing global health problem. WHO reported that AMR causes treatment failure, longer illness, increased healthcare costs, and higher mortality, requiring responsible antimicrobial use¹. Inappropriate antibiotic use in humans, animals, and agriculture was identified as a major cause of AMR, highlighting the need for a One Health approach². Global analysis also showed a high burden of bacterial AMR, causing millions of deaths worldwide³.

Studies from Pakistan reported increasing antimicrobial resistance, particularly among *Escherichia coli*, with the need for continuous surveillance⁴. Irrational antibiotic use, self-medication, and easy access to antibiotics were identified as important factors contributing to resistance in Pakistan⁵.

Awareness studies showed that knowledge about AMR was still insufficient, with common misconceptions regarding antibiotic use and self-medication among the students^{6,7}. Studies on metal-based antimicrobial agents found that silver, copper, zinc, and other nanoparticles showed antibacterial activity against resistant bacteria⁸. These agents work through mechanisms such as membrane damage, oxidative stress, and DNA disruption⁹. However, their use requires further evaluation due to concerns about toxicity, environmental effects, and resistance development¹⁰.

A combination of metal-based agents showed improved antibacterial effects against resistant microorganisms^{11,12}. Human population studies demonstrated variation in AMR knowledge and perceptions across different age groups. Shan et

al. assessed residents of Wah aged ≥ 16 years, while Gillani et al. investigated adults aged ≥ 18 to < 80 years in Punjab, Pakistan. Shahpawee et al. assessed university students aged 18–29 years in Brunei. Across these populations, misconceptions regarding antibiotic use, self-medication, and antimicrobial resistance were identified, indicating that AMR knowledge gaps are not restricted to a single age or population group^{7,7,13}. Reviews highlighted that antimicrobial nanoparticles have potential as alternative approaches against multidrug-resistant bacteria^{14,15}. Global and national surveillance reports confirmed increasing AMR trends and emphasized the importance of monitoring, antimicrobial stewardship, and infection prevention strategies^{16,17}.

Discussion

The findings of this systematic review indicate that antimicrobial resistance (AMR) is becoming an increasingly serious global health concern. The included studies showed that the rise in resistant bacteria is associated with inappropriate antibiotic use, self-medication, misuse of antimicrobial agents, poor infection prevention practices, and inadequate antimicrobial stewardship^{1,2}. Global evidence has further demonstrated that AMR threatens healthcare systems by reducing the effectiveness of commonly used antibiotics and increasing the difficulty of treating bacterial infections. The global burden of bacterial AMR highlights the urgent need for effective strategies to control the emergence and spread of resistant microorganisms³.

The situation is particularly concerning in developing countries, including Pakistan, where antibiotic resistance among clinically important pathogens has continued to increase. Studies from Pakistan have reported rising resistance trends, especially among *Escherichia coli*, which is a major cause of community- and healthcare-

associated infections ⁴. A systematic review of antibiotic resistance in Pakistan further identified factors such as inappropriate antibiotic use, limited awareness, and weak infection control practices as important contributors to the development of AMR ⁵.

The human population studies included in this review demonstrate that AMR knowledge and perceptions should be considered across different population groups and age ranges. Shan et al. assessed residents aged ≥ 16 years, Gillani et al. examined adults aged ≥ 18 to <80 years, and Shahpawee et al. investigated university students aged 18–29 years. Although these populations differed in age, setting, and educational background, misconceptions regarding antibiotic use and antimicrobial resistance were identified across the studies. These findings suggest that AMR education should not be restricted to university students or healthcare-related populations but should also address adolescents, adults, and community populations. Age-appropriate educational interventions may therefore be important for improving understanding of antibiotic use and reducing behaviors that contribute to antimicrobial resistance ^{6,7}.

In addition to improving awareness, the development of alternative antimicrobial strategies has become an important area of research. Recent laboratory-based studies have demonstrated that metal-based antimicrobial agents, including silver, copper, zinc, and other metal nanoparticles, possess strong antibacterial activity against resistant bacterial strains ⁸. These antimicrobial effects are associated with multiple mechanisms, including disruption of bacterial cell membranes, generation of oxidative stress, interference with cellular functions, and damage to essential bacterial components ⁹. However, the use of metal-based nanoparticles also presents challenges, including possible bacterial adaptation, toxicity concerns, and environmental

impacts, which require careful evaluation before wider application ¹⁰.

Several experimental studies have suggested that metal-based antimicrobial agents may enhance the activity of conventional antibiotics when used together. Silver and transition-metal combinations have shown synergistic antibacterial effects, while other metal nanocomposites have demonstrated activity against multidrug-resistant bacteria ^{11,12}. These findings suggest that metal-based materials may serve as supportive approaches for managing infections caused by antibiotic-resistant microorganisms; however, further investigations are required to determine their safety, effectiveness, and clinical suitability. Although the included experimental studies demonstrated promising antibacterial activity of metal-based agents against resistant bacteria, clinical evidence is needed to determine their effectiveness, safety, and feasibility in human healthcare settings. Studies among university students, aged 18 to 29, have also highlighted that misconceptions regarding antibiotic use and AMR remain a concern despite increasing awareness levels ¹³. At the same time, research on antimicrobial nanoparticles has demonstrated their potential role in combating resistant bacteria, while also emphasizing the need to address limitations related to safety, resistance development, and practical applications ^{14,15}.

The findings of this review are consistent with global and national surveillance reports, which continue to emphasize the growing burden of AMR and the importance of strengthening monitoring systems, antimicrobial stewardship programs, and coordinated interventions ^{16,17}. These efforts are essential for understanding resistance patterns and developing effective strategies to reduce the spread of resistant bacteria.

A notable gap identified in this review is that none of the included studies directly evaluated students' perceptions or awareness specifically regarding metal-based antimicrobial agents. Existing student-focused studies examined knowledge and attitudes related to AMR and antibiotic use in general, whereas evidence regarding metal-based antimicrobial materials has primarily been generated through laboratory investigations^{8,12,14,15}. Future studies should therefore explore awareness, acceptance, and understanding of emerging antimicrobial technologies among students, healthcare professionals, and the general population.

The evidence from the included studies indicates that misconceptions can occur in both younger and older populations. Therefore, populations aged ≥ 16 years allow the review to capture evidence from community residents and young adults while also incorporating university student populations. However, because the included studies used different age ranges and sampling approaches, the findings should not be interpreted as representing a uniform age-specific population.

Overall, this systematic review highlights that controlling AMR requires a multidisciplinary approach involving responsible antibiotic use, improved awareness, effective surveillance, and continued research into alternative antimicrobial strategies. Metal-based antimicrobial agents represent a promising area for combating multidrug-resistant bacteria; however, further research is needed to establish their safety, effectiveness, and potential role in future clinical applications.

Limitations

This systematic review has several limitations. No included study directly evaluated students' perceptions of metal-based antimicrobial agents;

therefore, conclusions regarding student awareness of these agents remain limited and require further investigation. In addition, most evidence related to metal-based antimicrobial agents was obtained from laboratory-based studies, and further clinical research is needed to confirm their safety and effectiveness in healthcare settings^{10,12}.

The human population studies also differed in age range and population characteristics, including community residents aged ≥ 16 years, adults aged ≥ 18 years, and university students aged 18–29 years. This heterogeneity limits direct comparison of knowledge and perceptions across age groups and prevents age-specific conclusions from being generalized to all populations¹³.

The review included only studies published in English between 2017 and 2025, which may have excluded relevant studies from other languages or earlier years. Furthermore, the review was based on published literature from selected electronic databases; therefore, unpublished studies and additional grey literature outside the selected authoritative reports were not systematically searched. Variations in study design, sample size, and methodology among the included studies may have affected the comparability of findings. Some metal-based antimicrobial studies review articles rather than primary research, which may limit the strength of the conclusions^{14,15}.

Conclusion

This systematic review underscores that antimicrobial resistance remains a critical global public health threat, compounded by persistent knowledge gaps and misconceptions among community populations and university students. These findings highlight the need for tailored, age-appropriate educational interventions to address self-medication and inappropriate antibiotic use. Concurrently, metal-based antimicrobial agents (silver, copper, and zinc) represent a promising area of research against

multidrug-resistant pathogens. However, current evidence is predominantly limited to in vitro laboratory findings, highlighting a distinct lack of clinical or in vivo validation. None of the included studies directly assessed students' knowledge or perceptions regarding metal-based antimicrobial agents. Future research should therefore evaluate awareness of these emerging antimicrobial approaches and establish their safety, effectiveness, and clinical applicability.

Future Recommendations

1. Future studies should investigate whether prolonged exposure to silver-, copper-, and zinc-based antimicrobial agents can lead to microbial adaptation or the emergence of metal tolerance under clinical conditions.
2. The influence of different nanoparticle characteristics (size, shape, surface charge, and coating materials) on antimicrobial efficacy and toxicity should be systematically compared.
3. Artificial intelligence and machine learning models should be explored to predict the antimicrobial activity and safety of newly developed metal-based nanomaterials before clinical testing.
4. Future investigations should determine how metal-based antimicrobial agents interact with the human microbiome and whether they selectively eliminate pathogenic bacteria while preserving beneficial microorganisms.
5. Research should focus on developing standardized international guidelines for evaluating the antimicrobial performance, cytotoxicity, and clinical safety of metal-based antimicrobial

agents to improve comparability between studies.

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