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Original Article

Microbiology Section

Latest Trends and Modern Technology in the Diagnostics of Antimicrobial Resistance: A Scoping Review

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ABSTRACT

Introduction: Antimicrobial Resistance (AMR) is emerging as a global threat, claiming millions of lives due to therapeutic failures. For a long time, the detection of AMR has been confined to conventional culture methods, which are tedious and resource-demanding. This results in delays, inaccuracies, or misdiagnoses, worsening the burden of AMR worldwide. Thus, the need of the hour is for rapid, feasible and accurate diagnostic methods that use novel technologies for the precise detection of resistant strains and degrees of resistance among different microbes. This will aid healthcare providers in combating this hidden pandemic.

Aim: To extensively analyse and report on the evidence and gaps in the current trends in diagnosing AMR.

Materials and Methods: The present scoping review obtained information on newer diagnostic approaches for AMR by reviewing 491 articles retrieved from scientific databases like Google Scholar and PubMed. Based on the eligibility criteria for this review, 13 scientific research articles were included. The filtration process involved three levels: title screening, abstract screening and full-text screening. The articles selected after full-text screening were independently analysed by the authors and the collected data were scrutinised by other authors of this study. The extracted data were categorised and represented using tables, charts, figures and graphs. The entire manuscript was written in adherence to the reporting guidelines of the PRISMA-2020 extension for scoping reviews.

Results: The selection process yielded 13 articles that met the eligibility criteria. The predominant method for diagnosing AMR is the Polymerase Chain Reaction (PCR) technique. Most diagnoses were conducted using samples from urinary tract infections and sexually transmitted infections. Automated amplification tools have proven to diagnose AMR rapidly and cost-effectively compared to conventional culture methods.

Conclusion: Given the rapidly spreading AMR, newer, faster and more accurate modes of diagnosis should be developed to combat this hidden pandemic. Compared to traditional culture methods, genome amplification and Point-Of-Care (POC) techniques have proven to be beneficial and superior. Therefore, measures should be taken to advance these molecular techniques to broaden the scope of newer AMR diagnostics.

Keywords: Multidrug resistance, Pan resistance, Point of care test, Rapid methods, Resistant strains

INTRODUCTION

The World Health Organisation (WHO) defines AMR as the resistance that occurs in bacteria, viruses, fungi and parasites over time, causing non responsiveness to treatment. This can lead to ineffective therapy, severe illness and the rapid spread of disease [1]. This global threat claimed around 1.27 million deaths in 2019, and it is estimated that by 2050, we could lose 10 million lives every year as a result of AMR [2]. Consequently, AMR has emerged as the leading cause of death worldwide, exerting its greatest influence in low-resource settings [3,4].

AMR can be attributed to three major factors: i) AMR traits are becoming more prevalent in microorganisms as an adaptive response to the extensive use of antimicrobials; ii) pathogens in any environment can spread throughout the entire human population due to global connectivity; iii) the needless use of antimicrobials creates intense selective pressure that fuels the development of resistance in microbes [5,6]. Resistance to antimicrobials can be either intrinsically present or acquired through natural and external mechanisms. Regardless of the mode of resistance acquisition, the primary action is to prevent access to the target, cause mutations in the antimicrobial target, or modify the target to inhibit the effect of therapeutics on microbes [7,8].

The overuse and misuse of antimicrobials have drastically affected humans, livestock, food quality, hospitals and community health, making AMR a major public health concern [9]. With the growing resistance to therapeutic regimens, simply prescribing regular antibiotics is no longer sufficient. When caused by organisms resistant to antimicrobials, common diseases such as pneumonia, skin infections and urinary infections become increasingly difficult to cure [10]. Individuals with infections resistant to antimicrobials are harder to treat, exhibit a greater risk of spreading disease to others, may experience prolonged illness, require more costly medical care and medications, necessitate different antimicrobials that may have more severe side-effects and can even die without effective treatment [11-13].

To combat the overlooked AMR pandemic, it is crucial to accelerate the development of rapid and accurate diagnostic tests to effectively manage resistant infections and prevent adverse outcomes [14]. Traditional methods for identifying AMR, such as broth dilution and disk diffusion techniques, are time-consuming, costly and do not cover a wide spectrum of microorganisms. In contrast, novel molecular diagnostics like PCR and hybridisation tests are much faster and more effective, even when the microbial load in the sample is very low. However, affordability, accessibility and availability are critical components in determining the successful implementation of these high-tech solutions [15,16]. BioFire and VITEK 2 are advanced diagnostic tools used to rapidly identify pathogens and determine AMR. BioFire utilises multiplex PCR technology for quick detection of a broad range of pathogens, while VITEK 2 automates microbial identification and susceptibility testing, providing precise results to guide effective treatment decisions [12,14].

Although several methods for diagnosing AMR have been proposed, the condition still challenges infectious disease specialists in treating patients with AMR, particularly in high-risk settings such as Intensive Care Units (ICUs). Additionally, while several POC setups and techniques have already been developed, they have not been implemented effectively. It is essential not only to develop accurate, user-friendly and broad-spectrum techniques for identifying resistant organisms and their degrees of resistance for effective treatment planning, but also to ensure effective implementation to combat antimicrobial-resistant diseases. In this context, the present scoping review was conducted to exhaustively analyse and report on the current trends and future possibilities in the diagnostics of AMR.

MATERIALS AND METHODS

This scoping review was methodologically conducted, encompassing the search for relevant publications, as well as the analysis and reporting of the study's findings. The five-stage methodological framework recommended by Arksey and O'Malley [17] was employed to conduct this review. The content was structured in accordance with the requirements of the PRISMA-ScR Checklist, which expands upon the PRISMA reporting items for systematic reviews and meta-analyses (PRISMA-2020) [18].

Research question: The following research question was the focus of this study's investigation:

- What are the latest trends in the diagnostics of AMR, and how are they advantageous over conventional methods?

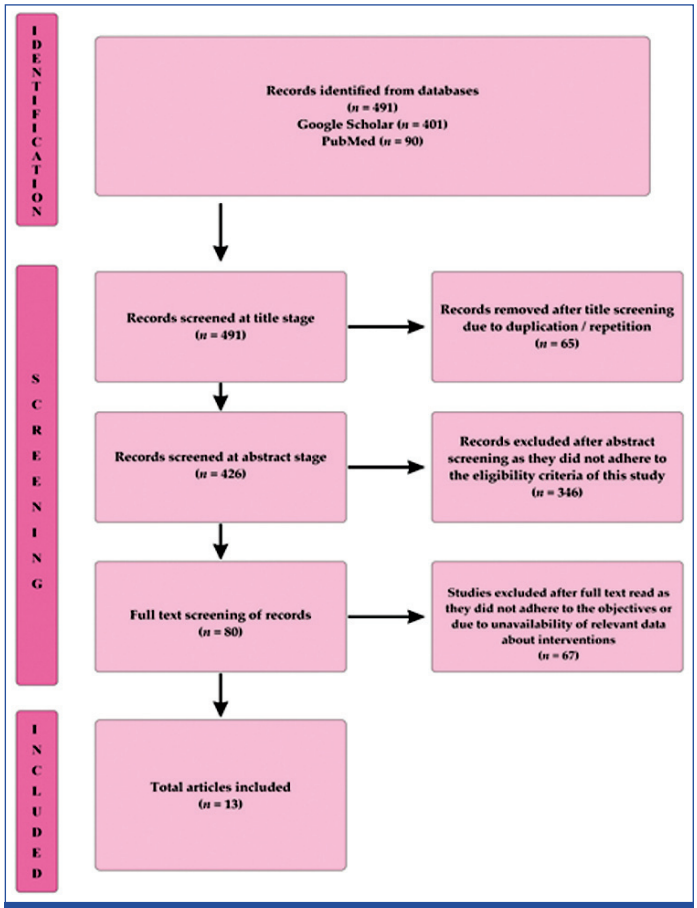
Identification of relevant studies: The pertinent publications for this study were identified to obtain evidence-based information. Online databases such as PubMed (n=90) and Google Scholar (n=401) were utilised to discover relevant studies. The literature search was conducted using a combination of primary keywords and Medical Subject Headings (MeSH) from November 2022 to January 2023 to obtain all relevant publications on the topic. The key terms used included "multi-drug resistance," "pan resistance," "point-of-care test," "diagnostics," "artificial intelligence," "resistant strains" and "rapid methods." Boolean operators such as AND and OR were employed to refine the search strategy. For example, the term "multi-drug resistance" was combined with related concepts like "pan resistance" or its abbreviation "MDR" using OR to capture all possible variations. These terms were then linked with "point-of-care test," "rapid methods," or "diagnostics" using AND to ensure that relevant diagnostic methods were included. Similarly, keywords like "artificial intelligence" and "machine learning" were searched using AND to focus on AI's role in addressing multi-drug-resistant strains.

Selection of studies: The inclusion criteria indicated in [Table/Fig-1] were used to select the applicable papers for this review. The exclusion criteria listed in [Table/Fig-1] were used to screen out publications and papers that did not align with the objectives of present study.

Criteria	Inclusion criteria	Exclusion criteria
Publication type	Clinical trials and randomised controlled trials mentioned in the heading of the paper or abstract	Reviews, cross-sectional, meta-analysis, editorials, correspondence, books
Language	English	Any other
Year	From 2013	Before 2013

[Table/Fig-1]: Inclusion and exclusion criteria.

The original search for "Diagnosis of AMR" yielded 491 full-text papers from clinical trials and Randomised Controlled Trials (RCTs), excluding meta-analyses, systematic reviews and scoping reviews. There were 401 articles from Google Scholar and 90 articles from PubMed Central published after 2013. Cross-sectional studies, reviews, meta-analyses and brief abstracts were excluded. A total of 491 articles were eligible for the title screening procedure. A total of 65 publications were rejected due to duplication, repetition and irrelevant content regarding the study's objectives. Subsequently, 426 documents were included for abstract screening, with 346 being excluded because they did not fit the inclusion criteria. The final 13 research articles included in the review were selected from the set of 80 papers that had been included for full-text screening. The selection process is illustrated in [Table/Fig-2].



[Table/Fig-2]: Flowchart for identification and selection of articles.

Charting the data: The data were plotted for further analysis after the authors thoroughly reviewed the selected papers. One author initially examined the titles and abstracts of each paper subjected to screening, followed by a cross-checking process involving the work of the other authors. The first round of analysis consisted of the authors independently reviewing the entire content of each article. In the second round of the study, additional authors corroborated the findings. To address any disagreements in data extraction or graphing, the other authors were consulted.

Collating, reporting and summarising the findings: The initial screening of papers involved one author reviewing the titles and abstracts to filter relevant studies before a cross-check by the other authors. This process meant that the first step was conducted individually by a single author and then the remaining authors verified this work to ensure accuracy. Following this, all authors individually reviewed the full text of each manuscript in the first round of analysis. During the second round of analysis, the results from the first round were confirmed by the other authors to ensure consistency. Any discrepancies that arose during data extraction or graphing were addressed through discussions among the authors, ensuring that the final analysis was collaboratively agreed upon. This process involved multiple steps, starting with individual efforts followed by collaborative review and resolution of differences. [Table/Fig-3] represents the extracted data, which underwent two rounds of validation [19-31]. The data is organised under the following categories: author name, year of publication, country of origin, study design, name of the test, method, organisms detected, resistant drugs, disease/health condition, sample collected, time

for detection and accuracy of results (as reported in each study). Extracted data is presented using graphs, charts and figures as applicable for easy comprehension by the reader. All articles have a Study ID, which will be used to identify the studies in the results.

RESULTS

Data extraction and graphing: The results of the rigorous data extraction and graphing process are presented in [Table/Fig-3] [19-31].

Study ID	Name of author, year, place of the study	Study design	Name of test	Method	Organism detected	Resistant drug	Diseases/ health condition	Sample collected	Time for detection	Accuracy of results
1	Chen Y et al., [19] 2022 China	Clinical trial	RAPID- Rapid label-free Pathogen Identification	ATR-FTIR (Fourier-transformed Infrared Spectroscopy with Attenuated Total Reflection modality)	6 different species belonging to ESKAPE group	Not mentioned	Wound	Wound sample	<10 mins for identification	>95%
2	Madden DE et al., [20] 2021 Australia	Clinical trial	SYBR Green-based mismatch amplification mutation assays (SYBR-MAMAs)	Real Time Polymerase Chain Reaction (PCR)	*Pseudomonas aeruginosa*	Fluroquinolones	CF, Chronic *P. aeruginosa* infection, urinary tract infection, non CF bronchiectasis,	Sputum, Blood, Ulcer isolate, Ear infection isolate	24 hours	100%
3	Harrison OB et al., [21] 2016 UK	Clinical trial	*N. gonorrhoeae* Whole-genome multilocus sequence typing (wgMLST)	Whole genome analysis	*Neisseria gonorrhoea*	Beta lactams, fluroquinolones, aminoglycosides, macrolides	Sexually transmitted infection	Bacterial isolates	The time duration for detection was not specified in the original studies and could not be determined from other available sources	>95%
4	Tuite N et al., [22] 2014 Ireland	Clinical trial	Gram-Negative Blood Culture Test (Nanosphere)	PCR amplification	9 bacterial species	Beta lactam	Not mentioned	Blood samples	2 hours	Not mentioned
5	Tenover FC et al., [23] 2013 USA	Clinical trial	GeneXpert MDRO Assay (Cepheid)	Multiplex PCR	3 carbapenemases species	Carbapenems	Not mentioned	Rectal swab	<1 hour	100%
6	Ferreyra C et al., [24] 2020 Switzerland	Clinical trial	TPP2 (target product profiles) AMR test	Genome analysis	*Neisseria gonorrhoeae*	Cephalosporins, beta lactam	Sexually transmitted infection	Urethral or vaginal discharge	<30 minutes	>95%
7	Sadiq ST et al., [25] 2017 UK	Clinical trial	Point-Of-Care (POC)-Antimicrobial Resistance (AMR)	Nucleic acid amplification technique	*Neisseria gonorrhoeae* and *Mycoplasma genitalium*	Not mentioned	Sexually transmitted infection	Bacterial isolate	The time duration for detection was not specified in the original studies and could not be determined from other available sources	>95%
8	Manore C et al., [26] 2019 USA	Clinical trial	POC-AMR	Antibody-based tests (predominantly serology based), bacterial culture, and Polymerase Chain Reaction (PCR)	Non-typhoidal *Salmonella* Bacteria	Not mentioned	Invasive Salmonellosis	Not mentioned	Antibody Based test : 15 minutes Bacterial Culture: 24 hours PCR: 24 hours	Antibody Based test : 78-100% Bacterial Culture: 40-80% PCR: 90%
9	Kandavalli V et al., [27] 2022 Sweden	Clinical trial	FISH	Fluorescence in situ hybridisation	*Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Proteus mirabilis, Acinetobacter baumannii, Enterococcus faecalis, Staphylococcus aureus*	Vancomycin , ciprofloxacin, gentamicin, nitrofurantoin	Infections caused by gram positive and gram negative bacteria mentioned	Urine, blood sample	The time duration for detection was not specified in the original studies and could not be determined from other available sources	Not mentioned

10	Jackson N et al., [28] 2021 USA	Clinical trial	DETECT assay	Dual-Enzyme Trigger-Enabled Cascade Technology – Biochemical method	*Escherichia coli* and *Klebsiella pneumoniae*	Beta lactam, ciprofloxacin, trimethoprim/ sulfamethoxazole, nitrofurantoin	Urinary tract infections	Blood, urine, cerebrospinal fluid, urethral swab, rectal swab, ocular swab	3 hours	>95%
11	Deatherage BL Kaiser et al., [29] 2022 USA	Clinical trial	AMR Protein Expression Pattern	Proteiomics	*Yersinia pestis* and *Francisella tularensis*	Sulfonamides, kanamycin, streptomycin, spectinomycin, ampicillin, chloramphenicol, tetracycline, and minocycline	Plague and tularemia	Bacterial isolates	The time duration for detection was not specified in the original studies and could not be determined from other available sources	Not mentioned
12	Monshat H et al., [30] 2022 USA	Clinical trial	(TIR)-coupled DNA microarray	Genotypic testing	*Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Escherichia coli*, *Campylobacter coli*, and *Campylobacter jejuni*	Quinolone	Urinary tract infections, GIT infections and pulmonary infections	Bacterial isolates	The time duration for detection was not specified in the original studies and could not be determined from other available sources	>95%
13	Tchesnokova V et al., [31] 2016 USA	Clinical trial	7- Single Nucleotide Polymorphism Based Test	PCR or Multiplex PCR	*Escherichia coli*	Amoxicillin/ clavulanate, trimethoprim/ sulfamethoxazole, cefazolin, ciprofloxacin, nitrofurantoin, and ceftriaxone	Extraintestinal *E.coli* infection	Urine samples	45 minutes	100%

[Table/Fig-3]: Extracted data from the selected articles [19-31].

Summary of the characteristics of extracted data: Authors systematically analysed and reported on various diagnostic methods for detecting AMR across a wide range of clinically significant pathogens. This analysis was based on data extracted from 13 carefully selected articles that met stringent eligibility criteria. Each of these articles was assigned a unique Study Identification ID to ensure clear and structured data presentation. The data were categorised into several key parameters, including the specific organisms detected, the resistant drugs, the associated diseases or health conditions, the types of clinical samples collected, the time required for detection, and the accuracy of the results.

The diagnostic methods reviewed encompassed a diverse array of molecular and automated technologies, each tailored to the detection of AMR in specific pathogens. Real-time PCR emerged as a frequently utilised method due to its ability to rapidly and accurately detect resistance genes, making it a crucial tool for timely clinical decision-making. Infrared spectroscopy was employed in some studies for its capability to identify molecular signatures associated with resistance, offering a non invasive approach to resistance detection. Whole-genome analysis provided a comprehensive overview of the genetic basis of resistance, enabling the identification of novel resistance genes and offering deep insights into the evolutionary pathways of resistant strains. PCR amplification and multiplex PCR were highlighted for their efficiency in detecting multiple resistance genes simultaneously, which is particularly useful in complex clinical cases where multiple pathogens may be present.

Fluorescence In Situ Hybridisation (FISH) was another important method, used to localise and visualise specific genetic markers associated with resistance within cells, thereby allowing for a more detailed examination of microbial resistance mechanisms. Biochemical methods, although more traditional, remained relevant in several studies, especially in resource-limited settings where advanced molecular techniques might not be readily available.

Proteomics was employed to study the expression of resistance-related proteins, providing insights into the functional aspects of resistance, while genotypic testing, which focuses on identifying specific genetic mutations or resistance genes, was a common approach for directly detecting resistance mechanisms. Automated systems were also reviewed for their ability to standardise and streamline the detection process, ensuring consistency and reliability in results across different clinical settings.

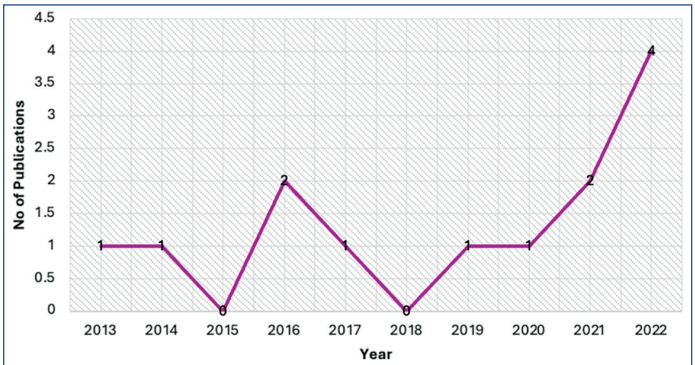
The review covered a broad spectrum of pathogens, including *Pseudomonas aeruginosa, Neisseria gonorrhoeae, Escherichia coli, Klebsiella pneumoniae, Yersinia pestis, Francisella tularensis, Acinetobacter baumannii, Campylobacter coli, Campylobacter jejuni, Staphylococcus aureus*, and the ESKAPEE group of bacteria. These pathogens were associated with resistance to a wide range of antimicrobial drugs, including aminoglycosides, macrolides, beta-lactams, fluoroquinolones, vancomycin, ciprofloxacin, gentamicin, nitrofurantoin, sulfonamides, kanamycin, streptomycin, spectinomycin, ampicillin, chloramphenicol, tetracycline, minocycline and fluoroquinolones.

The review provided detailed accounts of how these resistant organisms were isolated from various clinical samples, such as wound infections, chronic *P. aeruginosa* infections, urinary tract infections, non cystic fibrosis bronchiectasis, sexually transmitted infections, invasive *Salmonella* infections, and extraintestinal *E. coli* infections.

The types of clinical samples analysed varied widely, including wound swabs, sputum, blood, isolates from ulcers, ear infections, rectal swabs, urethral or vaginal discharges, urine, cerebrospinal fluid and ocular swabs. Each of these samples was examined using the described methods, providing a comprehensive understanding of the detection capabilities and limitations of each technique.

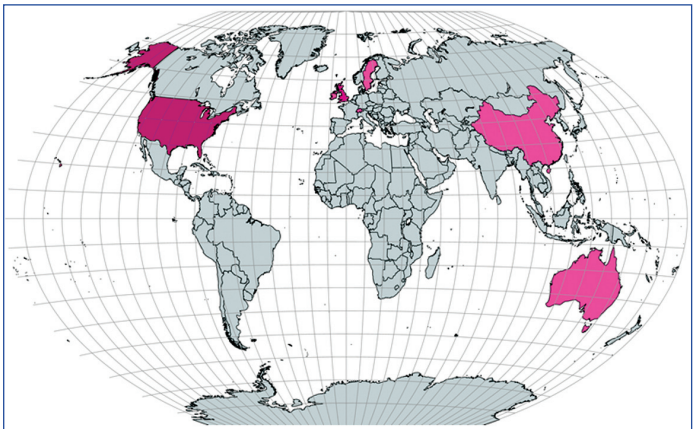
Timeline of articles included: For this study, a total of 13 articles were selected that describe the diagnostics of AMR. The majority

of the studies were conducted in 2022 (n=4), followed by two in both 2021 and 2016, and one each in 2020, 2019, 2017, 2014, and 2013. [Table/Fig-4] shows the number of articles and the year in which each one was published.



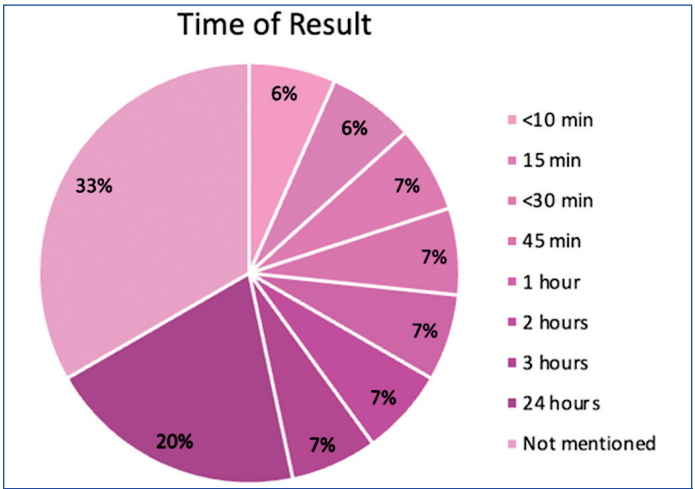
[Table/Fig-4]: Timeline of articles included.

Global mapping of planetary health interventions: Out of the 13 studies chosen, six were carried out in the United States, two in the United Kingdom and one each in Australia, China, Ireland, Sweden, and Switzerland. [Table/Fig-5] presents a globe with the locations of the included research marked on it. Darker shades represent a higher number of studies, while lighter shades indicate a fewer number of studies.



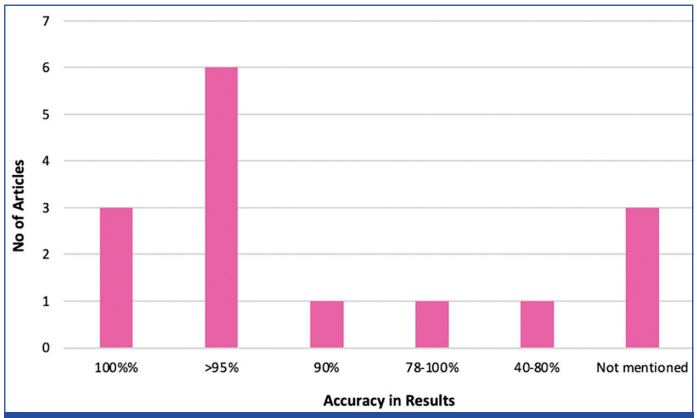
[Table/Fig-5]: Global mapping of AMR diagnostics studies.

Time of result in the diagnostic method: The time required for diagnosing AMR in the samples tested by various methods is illustrated in [Table/Fig-6]. Three of the studies we included provided results within 24 hours (STUDY IDs 2). Other studies provided results in 10 minutes (STUDY ID 1), 15 minutes (STUDY ID 8), 30 minutes (STUDY ID 6), 45 minutes (STUDY ID 13), 1 hour (STUDY ID 5), 2 hours (STUDY ID 4), and 3 hours (STUDY ID 10). Five studies did not mention the time required for results (STUDY IDs 3, 7, 9, 11, 12).



[Table/Fig-6]: Time of result in the diagnostic method.

Accuracy of result in the diagnostic method: The accuracy of the results of the tests that detect AMR in the studies included in this review is shown in [Table/Fig-7]. Most of the studies included reported results with >95% accuracy (STUDY IDs 1, 3, 6, 7, 10, 12), followed by three studies with 100% accuracy (STUDY IDs 2, 5, 13), and one each at 90% (STUDY ID 8), 78-100% (STUDY ID 8) and 40-80% (STUDY ID 8). Three studies did not mention the accuracy of the results (STUDY IDs 4, 9, 11).



[Table/Fig-7]: Accuracy of results of tests.

DISCUSSION

The results of present review indicate that newer methods for diagnosing AMR offer a wide range of benefits in terms of time and accuracy. Compared to conventional methods, which take a long time and can lead to delays in treatment, these automated, amplification, or genome sequencing methods produce results typically within 2-3 hours [19,22,24,25,28,30]. Some techniques may even yield results in less than an hour. They are not narrow in scope regarding detecting resistance; rather, they can effectively sensitise a wide range of genetic and molecular changes that produce resistance or predispose a microbe to acquiring AMR. Their specificity is high, and they produce results of high accuracy. Most of the studies included reported results with 95-100% accuracy, which can be difficult to achieve with traditional culture-based or dilution tests, whose results are interpreted manually.

AMR is a growing public health concern that leads to increased morbidity, mortality, prolonged hospital stays, a higher risk of nosocomial infections, increased costs and therapeutic failure [32, 33]. It poses one of the biggest threats to achieving the Sustainable Development Goals by 2030 [34]. Although AMR presents a complex and challenging issue, quicker diagnostic methods can assist in identifying resistant microbes sooner, allowing for the detection of resistance and the alteration of treatment plans with appropriate drugs to combat infections [35]. While conventional methods have been the mainstream technique, they have significant disadvantages due to the time required for laboratory results and delays in the initiation of treatment [36]. Therefore, rapid and newer methods for diagnosing AMR should be implemented so that resistance and resistant variants can be detected as quickly as possible, leading to better health outcomes and contributing to the achievement of the Sustainable Development Goal of good health and wellbeing [37-39].

One of the promising tools for rapid diagnosis is Matrix-Assisted Laser Desorption/Ionisation Time-Of-Flight Mass Spectrometry (MALDI-TOF MS). This automated system is capable of detecting microbes and their mechanisms of resistance against various classes of drugs, such as beta-lactams, carbapenems, aminoglycosides, macrolides, sulfonamides and others, which is highly advantageous due to its rapidity, cost-effectiveness, and accuracy [40,41]. Another method is Next Generation Sequencing (NGS), which rapidly and comprehensively analyses the bacterial genome, providing a wide range of genotypic and phenotypic data [42,43]. However, this method is expensive and requires specialised instruments to carry out the testing.

Along with rapidly emerging technologies, POC testing has also gained significant attention. These are technology-integrated systems that combine cultivation, lysis, purification and signal reading using microfluidics, enabling the examination of polymicrobial samples without the prior need to purify them [44]. Authors previously mentioned two studies that used POC-AMR systems to detect resistant genes in several organisms, including *Neisseria gonorrhoeae*, *Mycoplasma genitalium* and non typhoidal *Salmonella* bacteria associated with sexually transmitted infections and infective salmonellosis, where quick results were provided with 95-100% accuracy [25,26]. These POC tests have also been implemented to address challenges associated with locally created rapid POC diagnostics in India to control antibiotic resistance [45].

Several newer methods of AMR diagnosis have been developed, including one that utilises human indigenous microbiota as a reservoir pool to identify resistant genes and AMR among different gut pathogens [46]. The application of nanotechnology has also been explored in this regard. Biosensors designed with incorporated nanoparticles are being studied to detect AMR in a timely manner with high specificity [47,48]. Apart from MALDI-TOF MS, various other molecular approaches have proven advantageous in detecting AMR, such as PCR, Whole Genome Sequencing (WGS), Xpert MTB/RIF, Genotype MTBDRplus, MTBDRs, DNA microarray, including Verigene and FilmArray systems, with PCR being the most commonly employed molecular detection technique [49,50].

Finally, with Artificial Intelligence (AI) becoming increasingly prevalent, AMR is one area that stands to benefit significantly from AI advancements. AI has the potential to be a game-changer in assisting the diagnosis of AMR and reducing the workload on healthcare professionals [51]. The effectiveness of AI in the detection of AMR has already been suggested. It can provide rapid and accurate information within minutes to seconds, which can be utilised in developing newer therapeutics and improving treatment options for paediatric infectious diseases [52]. Thus, AI would be an excellent approach for developing drugs to combat resistant bacteria and could represent one of humanity's greatest strides in combating infectious diseases and resistant organisms, especially in ICU settings and common ailments like urinary tract infections [53-55]. However, for the successful implementation of AI, ethical and legal challenges must be addressed and a well-designed ethical framework is necessary.

GAPS IN LITERATURE

The current literature review has demonstrated the use of novel and automated tools as evolving methods for diagnosing AMR, but an integrated panomic system consisting of molecular details of AMR strains is not well established. Additionally, there is a gap in the literature regarding the application and practice of using nascent and emerging diagnostics involving nanotechnology and AI. There is scarce substantial evidence on the successful implementation of these newer diagnostic methods and a complete replacement of the time-consuming, labour-intensive conventional detection processes.

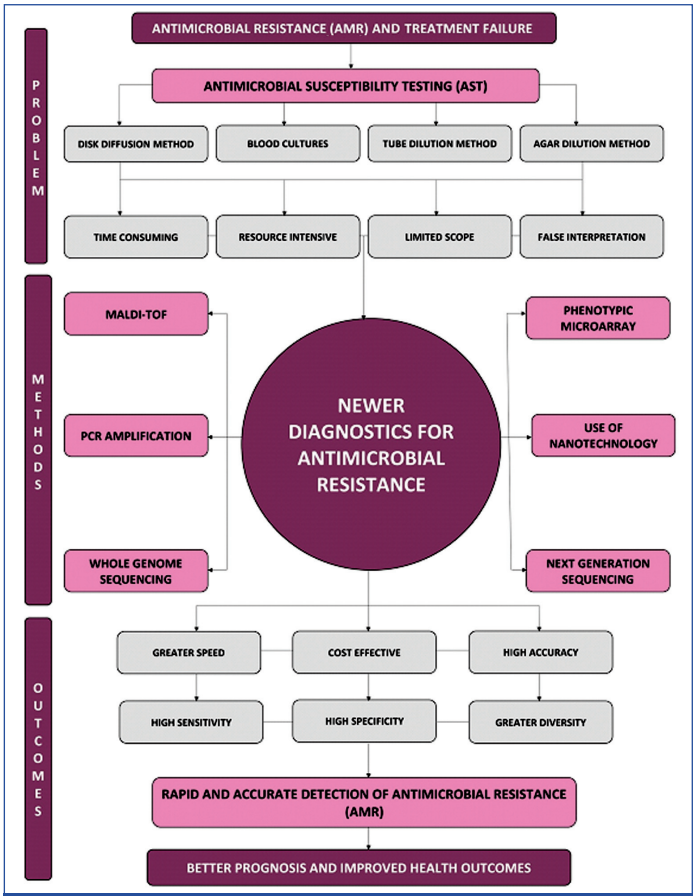
DIRECTIONS OF FUTURE RESEARCH

In the coming years, there should be a greater focus on digital and automated methods as the preferred diagnostic approach to reduce the errors and delayed results associated with manual and traditional methods. Evidence-based information on AMR mechanisms and an integrated, multi-omic database for genotype-phenotype data of potential microorganisms should be developed to assist microbiologists, laboratory technicians and healthcare professionals in making precise diagnoses. Regarding the implementation of AI, ethical issues concerning privacy, security, accuracy, data handling and interoperability should be meticulously addressed. As digital health sets the stage for future healthcare delivery, a robust laboratory networking system that manages specimen collection, testing, laboratory personnel skills, result synthesis and the transfer of information across AMR diagnostics centres will help combat the challenges in analysing and interpreting results.

This review elaborates on newer diagnostic approaches for AMR and presents a conceptual framework emphasising the importance of these methods in managing increasing AMR. This scoping review provides a comprehensive update on the use of AI in AMR diagnosis and the potential implications of employing machine learning approaches as reliable diagnostic tools for AMR.

Selection bias is relevant, as only articles published in the English language were included in this review. Manuscripts focusing on the diagnostics of AMR were selected exclusively, while articles published on antimicrobial stewardship that may contain diagnostic information were not reviewed.

Conceptual framework: The conceptual framework emphasising the need for newer diagnostics for AMR detection and their advantages over conventional methods is illustrated in [Table/Fig-8].



[Table/Fig-8]: Conceptual framework emphasising the need for newer diagnostics for AMR detection and their advantage over conventional methods.

Limitation(s)

Present study made efforts to reduce bias in the literature search by carefully selecting two comprehensive databases and employing a systematic search strategy. However, potential biases that may impact the comprehensiveness of the review remain. The reliance on only two databases may still limit the scope of the search, leading to the exclusion of relevant studies from other sources and potentially introducing selection bias. Although, present study aimed to mitigate publication bias by considering both positive and negative study outcomes, it is possible that studies with significant results are more commonly published and included. Furthermore, as the search was primarily conducted in English, there was a risk of language bias, with relevant studies in other languages potentially being overlooked. Additionally, the timeframe of the search, was limited which, may have led to the exclusion of important earlier or more recent studies, which could introduce time period bias. These potential biases

should be acknowledged to ensure a transparent interpretation of the findings.

CONCLUSION(S)

Diagnosing AMR is crucial for the effective management of infections caused by bacteria that develop resistance and fail to respond to therapeutics. While AMR can be diagnosed using conventional culture methods, these methods require considerable time and resources, which may delay appropriate treatment. More recent diagnostic methods, such as whole genome processing and rapid molecular tests made possible by PCR, can provide results within hours and assist healthcare providers in selecting the most effective course of treatment. The effectiveness of therapeutic interventions is greatly influenced by the appropriate use of antibiotics and the interpretation of results. To improve patient outcomes and prevent the spread of AMR, healthcare providers must be educated on how to properly utilise a variety of diagnostic methods while also understanding the drawbacks and advantages of each. Antibiotic-resistant infections pose a global threat; therefore, accurate and rapid diagnostics for antimicrobial resistance must be developed and implemented.

Authors' contribution: Conceptualisation: KMS; Methodology: JNB, SP, and KMS; Software: KMS; Validation: JNB, SP, NDP, and KMS; Formal Analysis: JNB, SP, and KMS; Investigation: JNB, SP, NDP, and KMS; Resources: KMS; Data curation: JNB, SP, NDP, and KMS; Writing-original draft preparation: JNB, SP, and KMS; Writing-review and editing: JNB, SP, NDP, and KMS; Visualisation: JNB, SP, and KMS; Supervision: KMS; Project administration: KMS; Funding acquisition: KMS All authors have read and agreed to the published version of the manuscript.

Data availability statement: The data that supports this study are available upon request from the corresponding author.

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