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Resistance gene detection database for antimicrobial resistance investigations emphasizing on genomics and metagenomics techniques

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REVIEW

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ABSTRACT: Antimicrobial resistance poses a grave threat to global health where bacteria become resistant to antimicrobials, rendering them ineffective against infections. It leads to increased illness, death, and healthcare costs. The overuse and inappropriate use of antibiotics in both human medicine and animal agriculture are the primary drivers of antimicrobial resistance. Methods for identifying antimicrobial resistance genes include culturing bacteria with antimicrobial susceptibility test, polymerase chain reaction, and whole genome sequencing for genomics and Metagenomics samples. Newer methods like whole genome sequencing are faster and more accurate. Metagenomics is a powerful tool that can be used to study antimicrobial resistance in various environments. It can study culturable and non-culturable bacteria and used to study samples from humans, animals, and the environment. Resistance gene detection databases serves as a centralized repository of knowledge about resistance genes, mechanisms, and trends of antimicrobial. Databases categorize resistance information by genetic factors, mechanisms, specific drugs, and drug families. This review focuses on powerful and updated databases for detecting resistance genes, including: CARD, ResFinder with pointFinder, ResFinderFG v2.0, MEGARes v3.0 and NDARO. This review aims to examine the significance of antimicrobial resistance databases and techniques in combating antimicrobial resistance. It compares the advantages and disadvantages of different databases for storing and techniques for identifying antimicrobial resistance genes. Additionally, it inform researchers in evaluating antimicrobial resistance study methodologies and database choices based on antimicrobial resistance factors such as microorganism type, study setting, data type, resistance gene nature, resistance focus and novelty of resistance mechanisms. The primary aim of this review is to compare different powerful databases and techniques for identifying ARGs, an issue that hasn't been thoroughly covered in other reviews. These databases provide valuable resources for researchers studying antimicrobial resistance, offering a comprehensive collection of resistance gene sequences and annotations. This knowledge is essential for developing innovative strategies to combat AMR and ensure the ongoing effectiveness of antibiotics.

KEYWORDS: Antimicrobial Resistance, Database, Metagenomics, Resistance, Resistance gène

INTRODUCTION

Antimicrobial resistance (AMR) is a significant and escalating global health challenge [1]. It leads to the lack of efficient treatment [2]. It poses danger to both human and animal health [3]. Bacteria become resistant through mutations in existing genes or acquisition of new ARGs (Antimicrobial Resistance Genes) [4]. Ways of inherit resistance are vertical and horizontal gene transfer [5, 6].

Antimicrobial resistance is primarily caused by the overuse of antimicrobial agents in both human medicine and agriculture [7]. AMR is exacerbated by inadequate antibiotic stewardship practices among healthcare professionals and the inappropriate use of antibiotics by patients [8]. Inadequate hygiene and sanitation practices can contribute to the spread of antimicrobial-resistant microorganisms [9]. Key hotspots environment niches in the spread of AMR for ARGs are aquatic water ecosystems, soil and human feces [10].

Bacterial AMR contributed directly to about 1.27 million deaths in 2019 [11]. The increasing prevalence of ARGs could lead to 10 million deaths per year by 2050 [12]. AMR will estimated to cost $100 trillion worldwide by 2050

[13]. The most significant impact of AMR will be felt in regions with limited resources to combat it, particularly due to a lack of funding and infrastructure [1]. In countries where standard treatment guidelines are not adhered to, AMR is accelerating due to the misuse and overuse of antibiotics [14]. Currently, circulating virulent and multiple drug-resistant bacteria threatens healthcare efficacy globally [15]

By studying resistance genes, researchers can uncover new ways in which pathogens develop resistance to antibiotics [16]. There is a growing need of databases for annotation, classification, and quantification of ARGs [17]. Databases are used to collect and maintain information on ARGs [18]. Bioinformatics tools identify ARGs in bacterial genomes and environmental samples (metagenomics) [19]. This review aims to examine the significance of AMR detection databases and techniques in combating AMR. It will compare the advantages and disadvantages of different databases for storing and techniques for identifying ARGs. Additionally, this framework will assist researchers in selecting appropriate AMR study methodologies and databases based on factors such as the type of microorganism (culturable or non-culturable), the study setting (clinical or non-clinical), the type of data (single genomes or metagenomics), the nature of the resistance gene (latent or established), the focus of the study (specific genes or the entire resistome), and the novelty of the resistance mechanism (known or novel). This knowledge is essential for developing innovative strategies to combat AMR and ensure the ongoing effectiveness of antibiotics.

DISCUSSION

ANTIMICROBIAL RESISTANCE

Overview

Antimicrobials are small molecules that can inhibit or kill bacteria. These molecules are commonly used to treat bacterial infections, however, certain bacteria have evolved the ability to survive and multiply in the presence of antimicrobials, a phenomenon known as antimicrobial resistance [5]. Antimicrobial drugs, biocides, and metals are commonly used to kill or inhibit the growth of microbes. However, some microbes have evolved mechanisms of AMR that allow them to survive and thrive in the presence of these compounds [20].

Antimicrobial resistance is a significant public health threat that leads to severe illnesses, prolonged hospitalizations, long-term disabilities, increased healthcare costs, overburdened healthcare systems, higher costs for second-line treatments, treatment failures, and higher mortality rates. The World Health Organization (WHO) has recognized AMR as one of the top ten global public health threats [21].

Identifying and understanding the mechanisms of AMR is essential for effective clinical management of resistant infections and for public health efforts to limit the dissemination of resistance [5]. By understanding the specific ARGs present in a pathogen and the antibiotics they confer resistance to, we can more accurately predict its phenotypic antibiotic susceptibility profile [13].

Burden of antimicrobial resistance

Statistical models suggest that AMR contributed to 4.95 million deaths globally in 2019, with 1.27 million directly linked to bacterial AMR. Death rates varied considerably across regions, ranging from 27.3 deaths per 100,000 in western sub-Saharan Africa to 6.5 deaths per 100,000 in Australasia. Lower respiratory infections were responsible for 1.5 million AMR-related deaths. ESKAPE pathogens (*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa,* and *Enterobacter* species) caused 929,000 direct deaths and contributed to an additional 3.57 million deaths. If left unchecked, AMR could significantly increase the mortality rates associated with many bacterial infections in the future [22].

Resistance to macrolides, tetracyclines, aminoglycosides, beta-lactams, and sulfonamides was most prevalent. European and North American samples primarily showed resistance to macrolides, while Asian and African samples were more resistant to sulfonamides and phenicols. Africa, Asia, and South America exhibited higher resistance to tetracycline, aminoglycosides, and sulfonamides compared to Europe, North America, and Oceania. Regional differences were more pronounced for AMR classes than specific genes. Fifteen AMR genes, especially common in Europe, North America, and Oceania, accounted for over half of the total AMR abundance [23].

Mechanisms of bacteria resistance

Commonly used antibiotics target bacterial growth by hindering peptidoglycan synthesis (a cell wall component), disrupting the cell membrane, and interfering with DNA replication, gene expression, and folate

production. In response, bacteria have evolved various resistance mechanisms to counteract these antibiotic attacks [24].

Common bacterial resistance mechanisms involve alterations in drug target sites, decreased drug uptake, activation of efflux pumps to expel drug molecules, and modifications in essential metabolic pathways. Additionally, novel mechanisms like MCR (mediated colistin resistance) due to changes in cell membrane charge or the ejection of rifamycin from its target RNA (Ribonucleic Acid) polymerase by the helicase-like protein (HelR) have been identified [26].

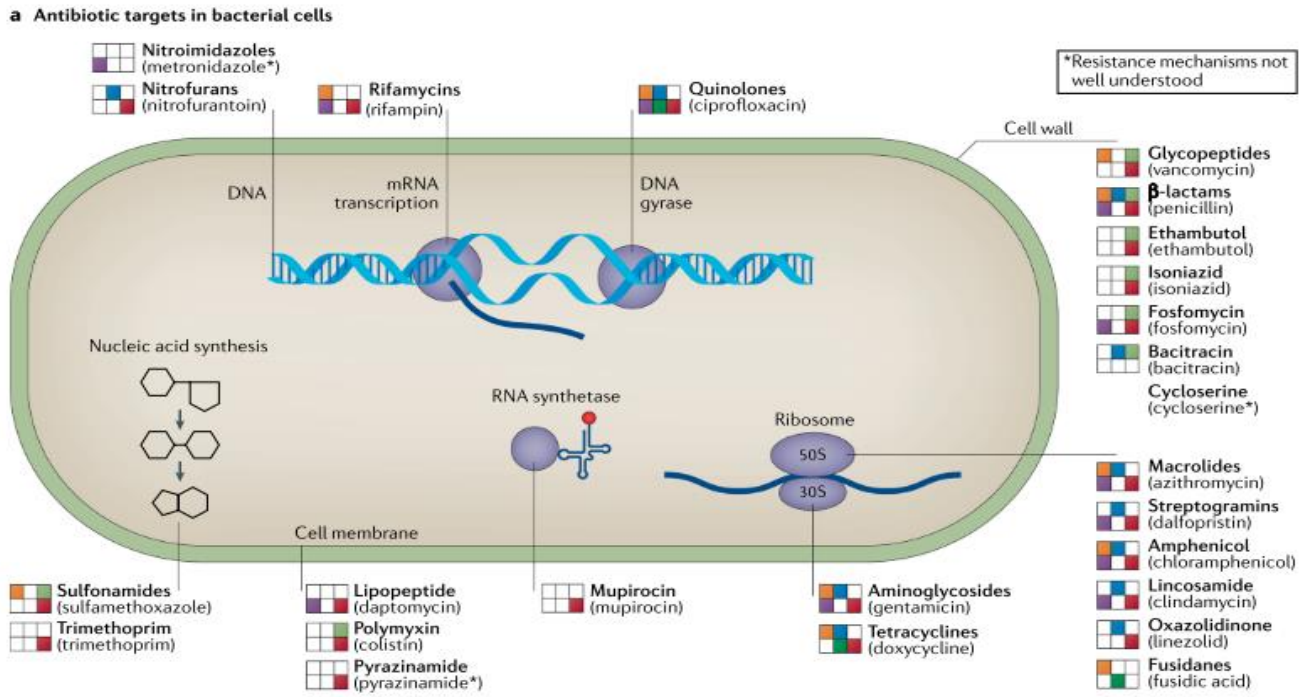

Figure. Antibiotic target in bacterial cell [25].

Common classes of antibiotics, resistance gene and resistant bacterial strains in AMR

The discovery of penicillin in 1928 was a significant breakthrough in combating infectious diseases. However, within the first five years of its use, 50% of *Staphylococcus aureus* strains had already developed resistance [27]. Antibiotics like penicillins, cephalosporins, quinolones, tetracyclines, macrolides, sulfonamides, aminoglycosides, and glycopeptides are crucial for treating severe bacterial infections. However, the increasing prevalence of antibiotic-resistant bacteria poses a significant challenge [25]. Half of ARGs detected were ESBL (extended spectrum β-lactamases) which includes TEM (Temoneira), CTX-M (Cefotaximase-Munich) and SHV (sulfhydryl variable) [28]. The ESKAPE pathogens, which are major causes of global healthcare-associated infections, have been closely monitored by the global antimicrobial resistance surveillance system since its inception in 2015 [28].

Methods for antimicrobial resistance gene identification

Various methods are used to identify antibiotic resistance genes (ARGs), including culture-based techniques, PCR (Polymerase Chain Reaction), qPCR (quantitative Polymerase Chain Reaction), genomic and metagenomic sequencing. Metagenomics allows for the sequencing of all DNA in a sample. By comparing these sequences to known ARGs using tools like BLAST (Basic Local Alignment Search Tool) or HMM (Hidden Markov Models) based tool , ARGs can be identified based on sequence similarity [2].

Traditionally, culture-based methods combined with antibiotic susceptibility testing (AST) have been used to identify antibiotic resistance. However, these methods have limitations, including long turnaround times (24-72 hours), potential errors in sample preparation or culture conditions, and limitations in testing specific antibiotic-bacteria combinations [29], [27].

Advancements in next-generation sequencing (NGS) technologies and computational methods are enabling rapid identification and characterization of antibiotic resistance genes in both genomes and metagenomes. These technologies offer the potential for quick and sensitive detection of resistance in both culturable and non-

culturable bacteria [5]. The advancement of NGS and bioinformatics has significantly improved our ability to monitor antibiotic resistance through the analysis of ARGs in both individual genomes and complex microbial communities. However, the effectiveness of this approach relies heavily on the quality and comprehensiveness of existing ARG databases and bioinformatics pipelines [19].

Public databases like CARD (Comprehensive Antibiotic Resistance Database), ResFinder (Resistance Finder), PointFinder (A tool for detecting point mutations conferring resistance), ARGANNOT (Antimicrobial Resistance Gene ANNOtation), and others serve as repositories for ARGs. Software tools based on these databases have been developed to enable whole-genome sequencing-based antibiotic susceptibility testing (WGS-AST) [29].

METAGENOMICS TECHNIQUE

Overview

Metagenomics, which involves rapidly sequencing the genetic material of microbial communities, is commonly used to study bacterial populations, including the presence of genes conferring antibiotic resistance [4]. While not all ARGs pose a direct threat to human health, these genes can spread between environments through bacterial dissemination and can be transferred to pathogenic bacteria via horizontal gene transfer [2].

No environment is entirely devoid of ARGs, making it essential to distinguish between clinically significant resistance genes. Metagenomic analysis reveals that the human and mammalian gut microbiomes harbor the greatest diversity of clinically relevant resistance genes [30].

Antimicrobial résistance gens have been found in a variety of environments, such as sediment, soil, activated sludge, and animal manure. Recently, there has been growing concern about airborne ARGs. In urban areas, adult humans may inhale around 0.1–1 µg of DNA daily (equivalent to 1014–1015 base pairs) through primary biological aerosols (PBA), with most particles capable of reaching the lungs or even penetrating deep into the alveolar regions [12].

The current focus of AMR surveillance is limited to a few specific pathogens, primarily relying on passive reporting of certain phenotypes from laboratory results. This approach restricts the scope of surveillance to a select group of pathogens, potentially overlooking a wider range of relevant ARGs. In reality, many ARGs are likely present in the commensal bacteria of healthy humans, animals, and the environment [15].

Advantages of Metagenomics in AMR

Metagenomics studies the genetic makeup of microbial communities, including genes that confer resistance to antimicrobial agents, known as the resistome. Analyzing these genes helps understand resistance prevalence, diversity, and transmission to combat this global health threat [31]. Metagenomic sequencing allows for the identification of both known and previously undiscovered genes that confer resistance to ARGs [9].

High-throughput sequencing (HTS) enables the examination of AMR across all microbial genomes within a sample, collectively known as the metagenome [32]. In recent times, metagenomic DNA (Deoxyribonucleic Acid) sequencing has been employed as a method to investigate antibiotic resistance in various environments, including the human microbiome [33].

Metagenomic techniques are commonly used to assess ARGs in the environment, as they can provide insights into the complete genetic repertoire of bacterial communities [14]. A significant benefit of shotgun metagenomics over qPCR is its capacity to examine all genetic variations, including those not detectable by PCR primers, within a single experimental analysis [33]. Metagenomics, as an AMR surveillance tool, can be directly applied to samples from healthy and sick individuals, animals, and potential reservoirs. This approach could lead to comprehensive AMR surveillance, enabling the identification of all resistance genes and their associated genetic context across various reservoirs [15].

The use of metagenomic and bioinformatic techniques to study AMR can offer rapid and accurate predictions of AMR and antibiotic usage in diverse clinical and non-clinical settings. This approach allows for the analysis of both cultivable and non-cultivable bacteria, eliminating the need for isolating and culturing microorganisms in a laboratory setting [9].

Limitation of Metagenomics in AMR

Screening for ARGs in environmental samples using metagenomic sequencing can lead to false-positive predictions of phenotypic resistance [34]. The limited sensitivity and specificity of current metagenomic methods hinder the detection of low-abundance populations and the identification of allelic variants that might impact the resulting phenotype [31].

Metagenomics is less sensitive than quantitative real-time PCR, especially when the number of sequencing reads per sample is limited [33]. Sequence homology is an unreliable indicator of resistance, and culture-independent techniques can often produce inaccurate results if the genetic context of ARGs is not taken into account. Recent advancements in long-read sequencing have enabled the generation of high-quality metagenome-assembled genomes, facilitating the analysis of the genetic context of ARGs [34].

Table 1. Comparison for Metagenomics technique and AST related to AMR factors

AMR factors	AST techniques	Metagenomics sequencing techniques	Reference
Microorganism type	Primarily for culturable organisms	Suitable for both culturable and non-culturable organisms	[9]
Study setting	Mainly used in clinical settings	Can be applied in clinical and non-clinical settings	[15], [9]
Data type	Single genomes or isolated cultures	Metagenomics	[32], [14]
Resistance gene nature	Primarily detects established resistance gene	Can detect both latent and established resistance genes	[4]
Resistance mechanism novelty	Limited to known resistance mechanisms	Can identify novel resistance mechanisms	[9]
Resistance focus	Focuses on specific antibiotic resistance genes	Can assess the entire resistome	[31]

Resistance gene detection databases

Overview

Bioinformatic tools and databases can help identify risky practices, the impact of antibiotic use, and areas with high levels of AMR. This information can be used to develop new policies to curb the spread of AMR between healthcare and non-healthcare settings. There are two main types of public databases: generalized AMR databases, which cover a broad range of ARGs and their mechanisms, and specialized databases, such as the β-lactamase database (BLAD), which provide detailed information on specific gene families [9].

A growing number of tools and databases are available to aid in the annotation process. While many are tailored to specific pathogens, drug classes, or resistance mechanisms, several databases and associated tools aim to annotate the entire collection of known ARGs for genome assemblies or metagenomic reads. Among the most notable databases for antibiotic resistance genes are CARD, ResFinder, and the NCBI Pathogen Detection Reference Gene Catalog [13].

Several databases exist for identifying ARGs in metagenomic data. Key databases include the Antibiotic Resistance Database (ARDB, established in 2009, outdated), the Comprehensive Antibiotic Resistance Database (CARD, established in 2013, regularly updated), Structured Antibiotic Resistance Genes (SARG, established in 2016, hierarchical structure), the Sequence Database of Antibiotic Resistance Genes (SDARG, large sequence database), and DeepARG-DB (enhances the DeepARG model). Limitations include outdated content, limited scope, and potential underestimation of ARGs due to database-specific biases [10].

Other bioinformatics tool for AMR analysis used were TypeWriter (2014), primarily used for *Staphylococcus aureus*. PhyResSE (2015) is primarily used for *Mycobacterium tuberculosis*. Mykrobe (2015) is primarily used for *Staphylococcus aureus* and *Mycobacterium tuberculosis*. PanPhlAn (2016) is primarily used for *Escherichia coli*. And PointFinder (2017) is primarily used for *Escherichia coli, Campylobacter jejuni, Salmonella enteric*. These models often have less potential for new biological insights into the underlying AMR mechanisms as they solely rely on already known genes and variants. Moreover, their applicability to other less studied species (especially Gram-negative bacteria with complex ARG patterns or many unknown variants) and to metagenomics samples (e.g., blood or stool samples) could be low [24].

Antimicrobial resistance genes reference sequences are available from various databases including CARD, McArthur, Wright, ResFinder, ARG-ANNOT, and MEGARes. Databases can be classified as primitive or integrated: Primitive databases (e.g., CARD) directly acquire ARG sequences from research publications. Integrated databases (e.g., ResFinder, ARG-ANNOT, MEGARes) combine data from research publications and other ARG databases. Both types of databases involve manual annotation of ARG sequences, often sourced from public repositories like NCBI.

While manual curation ensures accuracy, it is time-consuming and prone to errors such as typos or incorrect sequence extraction [7].

ABRicate software incorporates multiple ARG databases, including NCBI AMRFinderPlus, CARD, and ResFinder, each containing information on thousands of ARGs. Depending on the user's selected database, ABRicate compares all ARGs within the database to genes in the input genome to identify genetic similarities. Genes with similarity to ARGs in the database are predicted as potential ARGs, with higher similarity indicating a greater likelihood of the input genome developing antibiotic resistance [35].

Reference databases such as ARDB, SARG, CARD, and ResFinder were created for homology-based searches. However, these databases only contain a fraction of the entire resistome. Similarly, the Mykrobe predictor can only identify 12 types of antimicrobials. PATRIC (Pathosystems Resource Integration Center) is limited to identifying carbapenem, methicillin, and beta-lactam resistant ARGs [14].

SELECTED POWERFUL AND UPDATED RESISTANCE GENE DETECTION DATABASE AFTER 2020

The Comprehensive Antibiotic Resistance Database (CARD)

CARD is a valuable database for studying bacterial antibiotic resistance. It contains DNA and protein sequences, tools for identifying resistance genes, and models for predicting resistance. In 2017, CARD was significantly improved with updated sequences, a new organizational structure, hundreds of new resistance detection models, and enhanced analysis tools. A standout feature is the Resistomes & Variants module, which analyzes resistance patterns in a vast number of bacterial genomes [36].

CARD is a database that organizes and categorizes ARGs and mutations found in various bacteria from clinical, agricultural, and environmental settings. It provides tools to identify ARGs in whole genome and metagenome data, design targeted sequencing experiments, and has analyzed over 100,000 bacterial genomes and plasmids. CARD also includes a machine learning tool, CARD*Shark, that automatically scans scientific literature to identify new information on antibiotic resistance [13].

The CARD database (accessed in September 2022) categorizes antibiotic resistance genes into five groups: protein homologs (4634 genes), knockout mutations (19 genes), overexpression mutations (13 genes), variant mutations (171 genes), and rRNA gene variants (84 genes). Additionally, 1568 sequences from NCBI's (National Center for Biotechnology Information) Bacterial Antimicrobial Resistance Reference Gene Database were obtained through the AMRFinderPlus software (accessed in July 2022) [20].

The CARD web service can be accessed at https://card.mcmaster.ca. It is a bioinformatics database that provides information on resistance genes, their products, and related phenotypes. The database includes 7,170 ontology terms, 5,194 reference sequences, 2,008 SNPs, 3,279 publications, 5,242 AMR detection models, resistance predictions for 413 pathogens, 24,291 chromosomes, 2,662 genomic islands, 48,212 plasmids, 172,216 WGS assemblies, and 276,270 alleles (https://card.mcmaster.ca).

Cost-effective antibiotic resistome profiling of metagenomic samples (CARPDM) is a software tool that analyzes the antibiotic resistance genes present in metagenomic samples using the CARD database. It offers two probe sets: All CARD, targeting 4,661resistance gene and clinical CARD, focusing on 323 clinically relevant genes, enabling a comprehensive and cost-effective analysis of the resistome in metagenomic samples [1].

ResFinder and PointFinder

The ResFinder database, accessed in 2022, contains 3154 acquired antibiotic resistance genes. Recently, ResFinder was integrated with PointFinder, a tool that identifies chromosomal point mutations associated with antibiotic resistance in specific bacterial species [20].

The ResFinder tool is composed of three main parts: a database of antibiotic resistance genes, a database of point mutations, and the software itself. The antibiotic resistance genes database includes genes organized by antibiotic class, information on intrinsic bacterial resistance, and detailed descriptions of each gene, including its name, NCBI accession number, resistance mechanisms, associated publications, and any interactions with other genes [3].

The PointFinder database provides information on genetic variations, such as substitutions, deletions, and insertions that contribute to antibiotic resistance in various bacterial species, including Campylobacter, *Enterococcus faecalis, Enterococcus faecium, Escherichia coli, Helicobacter pylori, Klebsiella, Mycobacterium tuberculosis, Neisseria gonorrhoeae, Plasmodium falciparum, Salmonella,* and *Staphylococcus aureus*. This database includes details like the source publication, the specific resistance mechanism associated with the variation, and the precise mutations required for resistance [3].

Researchers with expertise in biology curate both databases, reviewing published studies to verify if newly discovered resistance genes or mutations qualify for inclusion. These biologists collaborate with bioinformaticians who update the databases with these new entries and ensure compatibility with the ResFinder software. User and researcher feedback is also critical for ongoing updates. The resources can be accessed through the following web addresses: ResFinder web service: https://cge.food.dtu.dk/services/ResFinder/, ResFinder software repository: https://bitbucket.org/genomicepidemiology/resfinder.git, ResFinder database repository: https://bitbucket.org/genomicepidemiology/resfinder_db.git, and PointFinder database repository: https://bitbucket.org/genomicepidemiology/pointfinder_db.git [3].

ResFinderFG v2.0

ResFinder and CARD databases primarily focus on ARGs from culturable and pathogenic bacteria, leaving a gap in understanding ARGs from non-culturable and non-pathogenic bacteria. Functional metagenomics, a technique that selects genes based on their function, can help identify these less-studied ARGs. ResFinderFG v2.0, accessible at ResFinderFG, incorporates 3,913 ARGs discovered through functional metagenomics from 50 curated datasets. This tool can detect ARGs not found in traditional databases, including those conferring resistance to β-lactams, cyclines, phenicols, glycopeptides/cycloserine, and trimethoprim/sulfonamides, leading to a more comprehensive characterization of the resistome [2].

MEGARes v3.0 and AMR++

MEGARes v3.0 is a database that includes a comprehensive list of antibiotic resistance genes for various antimicrobial agents, such as drugs, biocides, and metals. This updated version now contains 8,733 ARGs, an increase of 337 from the previous version. MEGARes v3.0 incorporates data from CARD, NCBI's Bacterial Antimicrobial Resistance Reference Gene Database, and ResFinder. A significant improvement in this version is the inclusion of specific genomic locations for SNPs (Single Nucleotide Polymorphisms) and indels (insertion délétion), which are crucial for the expression of resistance. This enables the updated AMR++ pipeline to identify resistance-conferring variants in metagenomic sequences. MEGARes v3.0 provides three key files: a comprehensive annotation file, a drug-specific annotation file, and a mapping file linking original headers to MEGARes headers [20].

The national database of antibiotic resistant organisms (NDARO)

NDARO is a comprehensive resource for studying antibiotic resistance in pathogenic bacteria. It curates data on clinically relevant ARGs, including genetic sequences and antibiotic susceptibility information such as minimum inhibitory concentration (MIC) values. NDARO helps track the emergence and spread of resistance, aiding public health officials and researchers in developing strategies to combat antibiotic resistance. Clinicians can use NDARO's data to make informed decisions about treatment options, while researchers benefit from its extensive information for their studies on antibiotic resistance (National Institutes of Health (NIH). https://www.ncbi.nlm.nih.gov/pathogens/antimicrobial-resistance/

Table 2. Comparison of selected powerful and updated resistance gene detection database

Database	Focus of information	Antimicrobial compounds	Scope and coverage	Choosing consideration	Reference
CARD	Comprehensive	Wide range of compounds	Broad overview of resistance mechanisms	Comprehensive understanding	[13]
ResFinder and PointFinder	Resistance genes and detailed mutation information	Wide range of compounds	Acquired resistance genes and point mutations in specific species	in-depth information on specific species	[20]
ResFinderFG v2.0	Resistance genes in bacteria & fungi	Wide range of compounds	Detects ARGs absent in conventional databases	Environmental studies	[2]
MEGARes v3.0	Resistance genes in metagenomics	Wide range of compounds (drugs,biocides, and metals)	Broad collection of ARGs with mechanisms	Large-scale analysis	[20]
NDARO	Antibiotic-resistant organisms	Limited to NDARO database compounds	Specific resistance profiles with MIC values	Clinical applications	https://www.ncbi.nlm.nih.gov/pathogens/antimicrobial-resistance

CONCLUSIONS AND FUTURE PERSPECTIVES

Antimicrobial resistance is a significant global threat that requires collaborative efforts to address. Antimicrobial resistance genes can easily transfer between bacteria, increasing their resistance to antibiotics. Advancements in technology, particularly metagenomics, enhance our ability to monitor and track AMR. Key resources include: CARD: Offers comprehensive, curated data on ARGs, including sequences, phenotypes, and ontology terms, with robust bioinformatics tools for analyzing genomes and metagenomes. It is the most complete database, covering a wide range of species and resistance mechanisms. ResFinder and PointFinder: Focus on acquired resistance genes and point mutations associated with resistance in specific bacterial species. MEGARes v3.0: Provides a broad collection of ARGs with associated mechanisms and ontology terms. The AMR++ pipeline is a tool for metagenomic analysis of these genes. NDARO: Specializes in clinically relevant ARGs in pathogenic bacteria, supporting public health surveillance. ResFinderFG: Targets environmental studies and ARGs from non-culturable bacteria. For comprehensive coverage and detailed annotations, CARD is highly recommended. NDARO is ideal for clinical applications, ResFinderFG for environmental studies, and MEGARes for large-scale analyses. CARD and NDARO offer high-quality, well-characterized ARGs, while ResFinder and MEGARes may need additional filtering to manage predicted genes and minimize false positives. Important issues for future resistance gene detection database include, enhanced data integration and interoperability, advanced computational tools and machine learning, spatiotemporal analysis and risk assessment, expanded surveillance to include environmental samples, and investigations into the linkages between humans, animals, and the environment.

DECLARATIONS

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Data availability

Data is available upon the request to the corresponding author.

Author contribution

Marew Alemnew designed and wrote the review; Aschalew Gelaw critically read and modified the review; Kindu Nibret and Addis Getu performed literature revision and took care of the editing of the review; Nega Berhane performed final revision.

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Competing interests

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