

The Utility, Development and Interpretation of Antibiograms: A Review On Their Role in Empirical Antibacterial Selection Amidst Escalating Antimicrobial Resistance

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ABSTRACT

With the global rise of antimicrobial resistance, antimicrobial stewardship efforts have been on the rise significantly. Antibiograms have become vital tools in enabling clinical decision making, guiding empirical therapy and mapping epidemiological resistance patterns. The antibiograms have now developed from the traditional antibiogram to the rolling antibiograms that changes with time to the electronic versions of the tool. Additionally, antibiograms are now bridging the gap in precision medicine with personalized antibiograms and machine learning approaches. In this review, we understand from existing literature that although antibiogram is being widely used, adherence to the standard guidelines is relatively lower in rates. Standardising antibiograms by sticking to the CLSI consensus M39 guidelines can be constitutive in making antibiograms more versatile. It has also been identified that many physicians are not used to utilizing antibiograms in their day-to-day practice. As resistance tracking tools, antibiotics can help understand local patterns of resistance in a community that can help public health policies or clinical choices. Enhancing ease of use and continuum education on their utility as part of Antimicrobial Stewardship programmes is fundamental in bridging this gap.

Keywords: antimicrobial resistance, CLSI M39 guidelines, precision antibiograms, resistance mapping, empirical therapy

1. INTRODUCTION

Antimicrobial resistance has been described as an imminent pandemic by many health experts all around the world. Without urgent actions, this slow burning crisis is likely to turn into a pandemic with serious implications. The WHO 2022 Global Antimicrobial Resistance and Use Surveillance System (GLASS) report highlights alarming resistance rates among prevalent disease-causing bacteria ¹. One in 5 cases of UTIs caused by E. coli showed less susceptibility towards standard antibacterial agents like Ampicillin, co – trimoxazole and fluoroquinolones in the year 2020. The report also notes Tuberculosis as a key contributor towards antimicrobial resistance.

GBD 2021 Antimicrobial Resistance Collaborators studied the global burden of bacterial antimicrobial resistance (AMR) from 1990 to 2021, forecasting to 2050. The researchers collected and analysed data for the study using a comprehensive and systematic approach that involved multiple data sources and methodologies. The study estimated that in 2019, there were approximately 4.95 million deaths associated with bacterial AMR, with 1.27 million deaths directly attributable to it. This highlights the significant impact of AMR on global health. The study also included forecasts of AMR burden until 2050 under different scenarios, emphasizing the need for urgent action to combat the rise of AMR. The findings from the study were used to recommend global targets, including a goal for a 10% reduction in AMR mortality from the 2019 baseline by 2030. The study also studied geographical disparities. The burden of AMR is unevenly distributed across different regions and populations. The study included detailed estimates for 204 countries and territories, indicating that certain regions, particularly in low- and middle-income countries, face a higher burden of AMR-related deaths and disability-adjusted life-

years (DALYs)²

Antimicrobial resistance (AMR) poses a significant threat to global public health, driven by multiple factors across human, animal, and environmental domains. In humans, misuse and overuse of antibiotics in healthcare settings contribute significantly to AMR development ^{3,4}. In addition to that, evolution of bacteria, mutation of bacteria and passing the resistance via genes are the other known contributors for antimicrobial resistance ³. The agricultural sector plays a major role, with widespread use of antimicrobials in food animal production leading to subtherapeutic exposures and environmental contamination ^{5,6}. Environmental factors, including improper disposal of unused antimicrobials and contamination from various sources, further exacerbate the problem ⁶. In developing countries, additional challenges such as inadequate patient education, limited diagnostic facilities, and unauthorized antimicrobial sales contribute to AMR spread ⁴.

Antibiograms are indispensable tools in the fight against rising antimicrobial resistance, enabling clinicians to make informed decisions, guide antimicrobial stewardship efforts, and contribute to the broader epidemiological surveillance of resistance patterns. Laboratory-based antibiograms may underestimate the frequency of resistant organisms compared to clinically validated data, highlighting the need for clinical validation of susceptibility reports ⁷. However, variations in antibiogram development methodologies persist despite consensus guidelines. Institutions should adhere to standardized approaches, ensure easy accessibility, and provide education on antibiogram use. Multidisciplinary antimicrobial stewardship programs are crucial for accomplishing these goals and improving the accuracy, reliability, and clinical application of antibiograms ⁸.

This review on the utility of antibiograms highlights their central role in the development, interpretation, and empirical selection of antimicrobial therapy for combating antimicrobial resistance and tracking epidemiological patterns of resistance.

ANTIBIOGRAM

Antibiograms, which are snapshots of antimicrobial susceptibility patterns at any point in time, has become increasingly crucial in the face of the global challenge posed by rising antimicrobial resistance. They are also called as Cumulative Susceptibility Reports. They summarize the susceptibility rates of bacteria to routinely used antibiotics in a hospital or nursing clinic. They have become an important component of antimicrobial stewardship efforts, by providing timely and accurate data on resistance patterns, enabling healthcare providers to tailor antimicrobial prescriptions, promoting the rational use of these essential medications.

Antibiograms are beneficial tools that aid in the development, interpretation, and empirical selection of antimicrobial therapy. They provide important information on the local prevalence and patterns of resistant microorganisms ⁹. This data is necessary to make an informed decision on what antimicrobial agents to use. In general, it is especially beneficial in the initial treatment of infections when the specific microorganisms and their susceptibility are not yet identified. Moreover, as part of combatting antimicrobial resistance, it can inform the empiric selection of antimicrobial therapy. By analysing the resistance pattern within the local area, the most potent ones may be selected, which would ensure the efficacy of treatment and decrease the risk of its failure, as well as reduce the local spread of resistant strains ¹⁰.

SURPASSING CONVENTIONAL ANTIBIORAM APPROACHES

A traditional antibiogram is the most easily utilized. The percentage of microorganisms that are susceptible to an institution's formulary antibiotics during a particular duration of time, usually a year, is profiled routinely in a typical antibiogram. Although traditional antibiograms have shown an improved selection of appropriate antibiotic therapy ¹¹, they do not provide viable information on cross resistance amongst various antibiotics. On the other hand, combination antibiograms can provide information regarding the combination of agents that would be pertinent to treat a specific organism¹².

A combination antibiogram is a graphical representation of the susceptibility of an organism to multiple antibiotics or a combination of antibiotics. It is an improvised version of a conventional antibiogram which can be a very useful laboratory tool that helps identify the most effective combination of antibiotics to treat an infection ¹³. Alice J Hsu et al¹⁴ studied the use of a combination antibiogram to assist with the selection of appropriate antimicrobial therapy for carbapenemase - producing Enterobacteriaceae infections. According to the study's findings, combination antibiograms can be used to assess organism cross-resistance to several antibiotics and can offer significant information into the antibiotic combinations that have the highest probability of providing sufficient coverage against CPE¹⁴. Laura Puzniak ¹³ (2019) evaluated Combination Antibiogram for Pseudomonas aeruginosa in Respiratory and Blood Sources from Intensive Care Unit (ICU) and Non-ICU Settings in U.S. Hospitals. In the study, it was found that Local institutional use of combination antibiograms has the scope to optimize empirical therapy of infections caused by hard-to-treat pathogens like P. aeruginosa¹³.

For hospital-acquired infections, unit-specific antibiograms offer more specific indications for empirical antibiotic use than hospital-wide antibiograms. Antimicrobial susceptibility rates in various hospital units have been found to vary significantly; in general, intensive care units had lower susceptibility rates than non-ICU units^{15,16,11}. For common infections like Escherichia coli, Pseudomonas aeruginosa, and Staphylococcus aureus, these variations can be very noticeable ^{15,16}. Furthermore, the length of hospital stay and the anatomical site of infection may have an impact on susceptibility rates ¹⁶. Remarkably, one study revealed that, in comparison to hospital-wide data, surgical/trauma intensive care unit patients showed higher susceptibility rates for particular antibiotics against crucial respiratory pathogens¹⁷. Unit-specific combination

antibiograms can help select appropriate empiric antibiotic therapy for gram-negative pneumonia. 12

The personalized antibiogram report is gaining significance in ameliorating the prescribing of antibiotics and the problem of anti-microbial resistance. The machine learning models help in predicting the patterns of antibiotic susceptibility which may improve the safety of patients as well as the stewardship of antibiotics by minimizing the use of broad-spectrum antibiotics without necessity ¹⁸.

Reflecting the rapid evolution of resistance, especially in Gram negatives¹⁹, the need to adopt more sophisticated and detailed antibiograms is increasing. Electronic antibiograms (e-antibiograms) provide a solution in that they facilitate real-time generation of patient-specific susceptibility data that is compliant with national standard²⁰. These e-antibiograms can be embedded in electronic health record systems, whereby they can be more frequently updated and more readily accessed by clinicians ²⁰. Antibiograms are more widely available now, but there are studies revealing discrepancies between susceptibility reports and prescribing trends that emphasize the importance and necessity of improving the use of antibiogram data in clinical practice ²¹.

A 2022 study by Daniel Teitelbaum et al, introduced a new approach called an escalation antibiograms which was designed to assess the likelihood of susceptibility to different antibiotics in cases where resistance to one antibiotic has already been observed. The researchers believed that an escalation antibiogram, could be a promising aid for escalating therapy in patients non responsive to empirical therapy. The study found that escalation antibiograms can be created to guide changes in empiric treatment for patients who are not responding. These tools provide valuable insights, such as helping to avoid the typical practice of switching from ceftriaxone to piperacillin-tazobactam in cases of suspected gram-negative bacteraemia. ²²

DEVELOPMENT

An antibiogram is generally developed using a specific guideline like the CLSI or EUCAST or FDA guidelines. All the guidelines are majorly similar except for differences in their clinical breakpoints standards which can result in slight differences in susceptibility patterns of antibiotics. The CLSI guidelines is a consensus – based guidelines that is widely accepted by laboratories, accreditors and government organisation wites is h predominance in North America whereas the EUCAST guidelines has been the major standard in Europe. The CLSI guidelines are used largely by researchers, hence it will be focused more in this review.

The contents of the antibiogram includes the name of the organisms, number of isolates, antimicrobial drugs which have been tested and the susceptible percentage of each organism is interpreted according to CLSI guidelines breakpoints ⁸.

ANTIMICROBIAL SUSCEPTIBILITY TESTING

Antimicrobial susceptibility testing has been made even easier with emerging strides in the area. Recent research presents an innovative digital microfluidic antimicrobial susceptibility test (AST) that incorporates a chip-integrated optical oxygen sensor. This device allows for real-time monitoring of bacterial growth through dissolved oxygen measurement, facilitating automated and miniaturized testing. The study emphasizes the effective integration of an oxygen-sensitive probe within the microfluidic platform, which does not negatively impact droplet manipulation or cell growth. This advancement has significant implications for microbial testing and addressing antibiotic resistance ²³.

CLSI GUIDELINES

The Clinical and Laboratory Standards Institute (CLSI) provides consensus guidelines and standards for creating antibiograms, which are essential tools for monitoring antimicrobial resistance and selecting antibiotics for therapy ²⁴. Key CLSI recommendations include annual data analysis, removal of duplicate isolates, exclusion of surveillance isolates, and reporting only species with at least 30 isolates.

For all the guidelines proposed by the Clinical and Laboratory Standards Institute (CLSI), there was a considerable lapse in following them. However, compliance rates to CLSI guidelines can vary significantly based on various factors like geographical location, regional differences, infrastructure and resource limitations. A study of University Health System Consortium hospitals in 2012 found compliance rates ranging from 64% to 98% for key CLSI recommendations in 47 hospitals that participated in the study. The compliance rates in the study to the four key CLSI recommendations were found to be: 98% reported data at least annually, 89% eliminated duplicate isolates, 83% did not include surveillance isolates, and 64% required at least 30 isolates for each reported species. 16 out of 47 hospitals, there were consequential formulary changes after the antibiogram results²⁵. A study on Challenges in Preparation of Cumulative Antibiogram Reports for Community Hospitals revealed only 3 (9%) antibiograms out of the 32-hospital provided antibiograms from 2012, adhered fully to the guidelines ²⁶. Common issues include reporting inappropriate pathogen-drug combinations and failing to exclude duplicate isolates.

Newer updates in the CLSI Guidelines

The Clinical and Laboratory Standards Institute updates the guidelines for antimicrobial susceptibility testing, such as M39 and M100. The most recent changes to M39 have been caused by the alterations in AST reporting recommendations and by

the role of the antibiogram in the antimicrobial stewardship ²⁷. The M100 31 edition has introduced a number of new breakpoints for different antibiotics and has amended testing recommendations ²⁸. The 2023 CLSI guidelines have implemented both selective and cascade reporting methods for antibacterial agents and has revised breakpoints for aminoglycosides and piperacillin ²⁹. The main difficulty for laboratories to implement these changes is the necessity of the FDA clearance and the conduct of validation studies ²⁸. The new versions of these documents are likely to improve the analysis and presentation of cumulative AST data ^{27,29}.

OTHER GUIDELINES

The updated guidelines are revised for newer trends in antimicrobial stewardship, public health initiatives, rapid diagnostics, and informatics. These changes aim to enhance the utility of cumulative AST data and antibiograms in various healthcare settings²⁷.

CLINICAL BREAKPOINTS: EUCAST, CLSI & FDA

Breakpoints are discriminatory concentrations that help to distinguish microbes as susceptible, intermediate, or resistant to antimicrobial drugs, making them essential for directing treatment choices. The FDA plays a crucial role in setting antimicrobial susceptibility test interpretive criteria (STIC) breakpoints, which are essential for interpreting antimicrobial susceptibility testing results ³⁰. The process of determining STIC involves integrating clinical, microbiological, and pharmacokinetic-pharmacodynamic (PK-PD) data³¹. Variations in PK-PD target values can impact STIC determination, with factors such as the number and MICs of bacterial isolates used in animal studies contributing to these variations ³¹. The Clinical and Laboratory Standards Institute (CLSI) and the European Committee on Antimicrobial Susceptibility Testing (EUCAST) use clinical efficacy studies, Monte Carlo simulations, and pharmacokinetic or pharmacodynamic data to establish these breakpoints ^{32,30}. Collaboration between the FDA and organizations like the Clinical and Laboratory Standards Institute (CLSI) is important for establishing consistent breakpoints³³. Regular updates to breakpoints are necessary to address emerging bacterial resistance and ensure patient safety³³. Tulkens (2005) highlights the difference between clinical and microbiological breakpoints, stating that the former is associated with clinical efficacy and the latter is used to identify resistant subpopulations³⁴.

Comparative analyses have shown varying levels of agreement between CLSI and EUCAST breakpoints for different antimicrobials, ranging from slight to almost perfect^{35,36}. Studies comparing these guidelines for various microorganisms, including Enterobacteriaceae and Candida species, generally show high agreement in susceptibility categorizations^{37,38}. However, some differences exist, particularly for certain antibiotics and organisms ^{37,39}. EUCAST guidelines may be more efficient in screening antibiotic-resistant bacteria and ESBL producers³⁹. EUCAST guidelines, being freely available, may be more accessible for laboratories in resource-poor settings ³⁹. Both EUCAST and CLSI methods demonstrate high ability to distinguish wild-type strains from those with fks mutations in Candida species³⁸. The choice of guidelines can influence therapeutic decisions, highlighting the importance of standardization in antimicrobial susceptibility testing³⁹. Studies have shown that differences in breakpoints can significantly impact the reporting of susceptibility or resistance, particularly for meropenem-non-susceptible isolates ⁴⁰. The choice of breakpoint guidelines can affect clinical decision-making, especially for carbapenem-resistant Gram-negative infections where treatment options are limited ⁴⁰. While CLSI and EUCAST breakpoints often show high concordance for many antibiotics, some discrepancies exist, especially in intermediate categories³⁶.

Monte Carlo simulations and CART analysis are two recent developments in breakpoint determination³⁴ (Tulkens, 2005). For echinocandins and Candida species, Pfaller et al highlights the significance of species-specific breakpoints, demonstrating that updated breakpoints more accurately forecast clinical outcomes and identify new resistance linked to fks mutations.³⁸ These advancements demonstrate how breakpoint determination is always being improved to enhance patient care and antimicrobial susceptibility testing.

RECENT UPDATES IN BREAKPOINTS

Both CLSI and EUCAST guidelines undergo annual revisions, with recent updates focusing on selective reporting methods, changes in breakpoints for specific antibiotics and bacterial species, and refined criteria reflecting clinical situations and administration methods²⁹. These ongoing updates underscore the importance of staying informed about the latest guidelines for accurate antimicrobial susceptibility testing interpretation.

Recently, the United States Committee on Antimicrobial Susceptibility Testing (USCAST) reviewed piperacillin/tazobactam STIC for Enterobacterales, recommending different breakpoints than those set by the FDA and other organizations ⁴¹.

UTILITY

CONTRIBUTION OF ANTIBIOGRAM IN AUGMENTING EMPIRICAL ANTIBIOTIC SELECTION AND MAPPING RESISTANCE PATTERNS.

In skilled nursing facilities, where empirical prescribing is common, antibiogram implementation may increase appropriate

antibiotic use, although more research is needed to confirm statistical significance⁴² (Furuno et al., 2014). Simple, inexpensive measures can improve physicians' comfort with, access to, and utilization of antibiograms ⁴³ (Cooper et al., 2022). Krishnamoorthy et al studied effects of antibiogram on empiric antibiotic therapy using an antibiogram toolkit in a South Indian tertiary care hospital from December, 2019 to January, 2021⁴⁴. The toolkit was designed on the basis of statistics obtained from drug utilization evaluation studies and antimicrobial susceptibility tests. The study highlighted the importance of evidence-based approaches in antimicrobial stewardship and utility of local susceptibility data to guide antibiotic selection in clinical settings. The implementation of the antibiogram indirectly led to improved usage of narrow-spectrum antibiotics, reducing usage of broad-spectrum agents for known seasonal and regional infections ⁴⁴ (Krishnamoorthy et al., 2021). Manoj Dikkatwar et al evaluated resistance patterns using an antibiogram in a tertiary care hospital. The study revealed antibiograms helped track increasing resistance rates, particularly to Ceftriaxone, a causality of the drug's high use to treat infections ⁴⁵.

Antibiograms are valuable tools for guiding empirical antibiotic selection, but research indicates gaps in their development and utilization. Many medical residents lack comfort in using antibiograms, with only 12% identifying them as a resource for empiric therapy selection ⁴⁶.

Multidisciplinary antimicrobial stewardship programs play a vital role in implementing these improvements and ensuring appropriate interpretation of antibiogram data ⁸.

ANTIBIOGRAM AS AN TOOL FOR EPIDEMIOLOGICAL SURVEILLANCE

The utility of antibiograms extends beyond their role in antimicrobial therapy selection. They also serve as valuable tools for epidemiological surveillance, allowing healthcare institutions to monitor the evolution of resistance patterns over time and across different geographic regions. This information is crucial for informing local, national, and global strategies to combat antimicrobial resistance ^{9,10,47}.

The integration of cumulative AST data into surveillance systems can improve the detection of outbreaks and the response to public health threats posed by resistant pathogens. Public health agencies can use aggregated data to allocate resources more effectively, targeting interventions and educational efforts in areas with high rates of resistance or specific outbreaks of resistant infections ²⁷.

2. CONSTRAINTS IN CLINICAL APPLICATION OF ANTIBIOGRAMS

Traditional cumulative antibiograms have certain limitations that may reduce their overall applicability. One key issue is that it does not account for the timing of isolate collection in relation to a patient's hospital admission, making it difficult to differentiate between community- and hospital-acquired infections. To address this, institutions should consider creating an antibiogram based on the timing of culture collection relative to admission. A common approach is to use a 48-hour threshold, where cultures collected before 48 hours are classified as community-onset, and those collected after 48 hours are considered hospital-onset. This stratification could provide a more accurate comparison of susceptibility rates between community and hospital settings, improving the representation of organism ecology and potentially leading to better empirical therapy choices. However, this method presents several challenges. Cultures collected more than 48 h after admission could reflect a community-onset infection that is mistakenly classified as hospital-onset. Similarly, colonizing organisms present before admission but causing infection afterward may be incorrectly categorized as hospital-acquired. Additionally, gathering the necessary data to determine infection onset can be labour intensive, possibly requiring manual chart reviews if advanced technological systems are unavailable. Another limitation is that traditional antibiograms do not distinguish between organisms isolated as pathogens and those identified as colonizers. Including colonizers in susceptibility analysis can skew the results. Antibiograms typically provide binary susceptibility data, indicating whether a pathogen is susceptible or nonsusceptible, but they do not offer quantitative information, such as minimum inhibitory concentration (MIC) values, or further break down non-susceptibility into intermediate or resistant categories. Important details, such as MIC distributions near clinical breakpoints, are not reflected in the standard antibiograms. Although antibiograms are valuable tools, they should not be the only resource used to guide empirical antimicrobial therapy. Static antibiograms may be less helpful in selecting therapy for patients with recurrent or recent infections, as a patient's specific microbiological history and prior antibiotic use may provide more relevant information. Other factors, including the site of infection, pharmacokinetics and pharmacodynamics of the antimicrobial, contraindications, selective pressures, risk of Clostridioides difficile infection, and efficacy and safety data, must also be considered alongside antibiogram results.

More advanced antibiograms are emerging, such as those utilizing machine learning to analyse individual patient data from electronic health records (EHRs) and create personalized antibiograms. While this approach shows promise, it requires further validation and the inclusion of variables not currently captured in EHRs, such as the antimicrobial history of infectious contacts ⁸.

3. DISCUSSION

Antibiograms are invaluable tools for guiding empirical antibiotic selection and supporting antimicrobial stewardship

programs, particularly as antimicrobial resistance (AMR) continues to rise. By providing localized susceptibility data, they enable clinicians to make informed decisions when choosing antibiotics. However, despite their significance, their utilization in clinical practice is often suboptimal due to several challenges.

One major issue is the limited familiarity among healthcare providers, especially junior physicians, with interpreting antibiogram data effectively. Many prescribers either underuse or misinterpret antibiograms, leading to inappropriate antibiotic choices. Studies have highlighted that only a small percentage of medical residents actively refer to antibiograms when selecting empiric therapy⁴⁶. This underscores the need for structured training programs and better integration of antibiograms into clinical workflows, such as embedding them within electronic health records (EHRs) for easier access.

Another limitation of traditional antibiograms is that they do not differentiate between community- and hospital-acquired infections, nor do they account for evolving resistance patterns in real time. This has led to the development of more advanced approaches, such as unit-specific, combination, and personalized antibiograms. For example, combination antibiograms offer insights into cross-resistance patterns, improving the precision of antibiotic selection ¹³. Personalized antibiograms, powered by machine learning, are also emerging as a promising tool, allowing patient-specific susceptibility predictions that can reduce unnecessary broad-spectrum antibiotic use ¹⁸.

Beyond guiding individual patient care, antibiograms play a crucial role in epidemiological surveillance. They help track resistance trends across different hospital units, regions, and even globally. Public health agencies rely on cumulative antibiogram data to shape antibiotic policies, optimize formularies, and design targeted interventions against resistant pathogens ²⁷. However, discrepancies in guideline adherence—such as inconsistent compliance with Clinical and Laboratory Standards Institute (CLSI) or European Committee on Antimicrobial Susceptibility Testing (EUCAST) recommendations—can affect the reliability of these data across institutions.

To maximize their impact, future efforts should focus on improving the accessibility and accuracy of antibiograms. Ensuring compliance with standardized methodologies, expanding clinician education, and leveraging real-time digital antibiograms could significantly enhance their clinical utility. As AMR continues to challenge global healthcare, the role of antibiograms in improving antibiotic stewardship and optimizing patient outcomes cannot be overstated.

4. CONCLUSION

Antibiograms are essential tools for guiding empirical antibiotic prescribing and monitoring resistance patterns. Recent advancements, including molecular profiling and automated susceptibility testing, have significantly improved the ability to rapidly and accurately identify bacterial resistance trends. The effective use of antibiograms by physicians is critical for ensuring targeted, evidence-based treatment, minimizing the misuse of broad-spectrum antibiotics, and ultimately improving patient outcomes. However, several challenges—such as delayed updates, lack of standardization, and limited awareness among healthcare providers—can limit their full potential. To enhance their utilization, antibiograms should be more accessible, integrated into clinical decision support systems, and accompanied by targeted physician training. Additionally, advancements in data analytics, machine learning, and real-time surveillance can further refine their accuracy and clinical relevance, making them even more effective in antimicrobial stewardship efforts.

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