



# Critical Quality Control Issues of Antibiotic Susceptibility Tests for Developing Countries

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## Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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## ABSTRACT

Antibiotic therapy has been the mainstay of treatment of bacterial infections and the initial successes of the earlier generations of antibiotics for treatment and prevention of bacterial infections spurred further efforts to discover newer antibiotics. Antibiotic Susceptibility Test (AST) is a standardized procedure usually carried out on cultivable bacterial pathogens to determine their sensitivity to specific antibiotics, and to guide physicians on the best antibiotic treatment regimens for specific infections. The quality assurance and control for antibiotic susceptibility tests should be prioritized in deliberate efforts to reduce the burden of antibiotic resistant bacterial infections in developing countries.

**Keywords:** Antibiotic therapy; antibiotic susceptibility test; bacterial infections; diarrhea.

## 1. INTRODUCTION

Infectious diseases have continued to pose significant public health problem globally with

fears that it could be aggravated by the current COVID-19 pandemic [1,2]. The infectious disease burden both in economic terms and in terms of morbidity and mortality has continued to

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increase, especially in developing countries [3]. Specifically, bacterial infections have been reported to account for sizable portion of infectious diseases globally [4]. Diarrhea still constitutes a leading cause of deaths among children under five years in Africa and Asia [5,6]. Despite improvement in treatment regimes for tuberculosis, the disease is still a serious threat in Africa and Asia with 90% of cases reported in developing countries [7,8]. Neonatal sepsis is a leading cause of neonatal mortality in developing countries [9] while salmonellosis is common in developing countries despite the gradual reduction in the prevalence of the diseases over the years across the globe [10,11].

Antibiotic therapy has been the mainstay of treatment of bacterial infections and the initial successes of the earlier generations of antibiotics for treatment and prevention of bacterial infections spurred further efforts to discover newer antibiotics [12]. Furthermore, antibiotics are used to support various life saving procedures in hospitals to prevent life threatening infections and enhance the success of such procedures [13]. However, the overdependence on antibiotics has created a crisis of antibiotic resistance and developing countries have continued to suffer their share of antibiotic resistant infections [14]. For instance, the extensively resistant tuberculosis is a serious problem in developing countries [15,16]. Multi drug resistant diarrheagenic bacteria have been increasingly implicated among children in developing countries [17,18]. Overall, the implication of the increasing prevalence of multidrug resistant bacteria is evident in the overall increase in cost of healthcare, hospital stays and increase in morbidity and mortality [19].

## **2. STANDARDS FOR ANTIBIOTIC SUSCEPTIBILITY TESTS**

Antibiotic susceptibility test (AST) is a standardized procedure usually carried out on cultivable bacterial pathogens to determine their sensitivity to specific antibiotics and to guide the physician on the best antibiotic treatment regimens for specific infections [20]. This procedure is routine in most medical microbiology laboratories in Africa and across the world [21]. In view of the importance of ASTs in their potential to reduce prevalence of antibiotic resistant bacterial infections, this procedure is standardized to ensure quality, reliability and reproducibility of test results obtained [22]. The Clinical Laboratory Science Institute (CLSI) in the

United States and the European committee on Antimicrobial Susceptibility Testing (EUCAST) release and update the standard procedures for ASTs for different bacterial pathogens [23]. The strict adherence to these standards is expected to ensure that results obtained from such tests are uniform across different laboratories. The most common methods used for antibiotic susceptibility tests are the disk diffusion methods and dilution methods and the interpretative criteria for the different methods and different bacterial pathogens are available in their respective documents [24].

Urgent attention needs to be given to the quality aspects of ASTs as part of measures to address the growing prevalence of bacterial infectious diseases caused by antibiotic resistant bacteria in developing countries. The key aspects of quality of ASTs fall into quality assurance and quality control [20]. Quality assurance places emphasis on the overall routine of ASTs in laboratories as a means to ensure that AST results are accurate, dependable and reproducible. This actually encompasses pre-analytical, analytical and post-analytical processes of ASTs [20]. Quality control on the other hand focuses mostly on the analytical processes involved in ASTs to ensure that results obtained can be relied on for proper diagnosis and prescription.

In addition to the drawbacks of phenotypic ASTs, most ASTs carried out in clinical microbiological laboratories in developing countries do not comply with the precincts of expected quality [25]. This is due to the peculiarities of developing countries like lack of technical equipment, poor funding and poor regulatory processes that should have enhanced the capacity of most clinical microbiology laboratories in developing countries. This has been responsible for the high rate of empirical treatments with antibiotics is high [22].

## **3. COMMON PROBLEMS OF QUALITY IN ASTS**

The following problems commonly compromise the quality of ASTs in developing countries and resource limited settings:

Firstly, there are no well defined regulatory regimes for supervision of clinical microbiology laboratories in many developing countries to ensure reliable and qualitative results are produced. Normally, there should be regulatory agency or protocols to supervise such medical

and diagnostic laboratories to ensure that they produce quality results [26]. The COVID-19 pandemic has exposed this necessity and relevant agencies in some countries have established molecular biology laboratories for diagnosis of the viral infection. The same approach should be applied to microbiology laboratories that perform ASTs. The specific activities of such regulations should be to conduct routine inspections of physical and technical facilities available in the laboratory, use of clinical QC bacterial strains, storage of pathogens for surveillance purposes, etc. The cumulative of these activities is expected to enhance the confidence that infectious disease physicians will have in the laboratory result obtained.

Secondly, many clinical microbiology laboratories in developing countries do not adhere to strict quality control recommendations as contained in the CLSI used in many laboratories in developing countries. This is partly due to the lack of technical requirement to comply with the recommended standards while performing ASTs. However, there is noticeable improvement in meeting such standards in medical microbiology research and infectious disease surveillance [27]. But compliance to such standards is lacking in routine ASTs and clinical diagnosis of antibiotic resistant bacterial infections. Furthermore, the AST of fastidious bacterial pathogens like *Mycobacterium tuberculosis* are only carried out in standard reference laboratories and this extends the turnaround time to produce diagnostic results. This is because most medical microbiology laboratories do not have capacity to carry such tests for fastidious organisms.

Thirdly, another crucial aspect of quality control for ASTs in clinical microbiology laboratories is the use of quality control strain during ASTs. It is strongly recommended that ASTs should also be carried out on quality control strains along with the test pathogens [28]. In the absence of use of quality control strains, there are usually no comparative standards for the results obtained. This is because most clinical microbiology laboratories in developing countries lack the capacity to maintain such cultures at recommended and acceptable conditions for a prolonged period of time. It should be noted that if quality control strains cannot be used in daily during routine ASTs, they can be used on a weekly basis to enhance the quality and improve confidence in AST results.

#### 4. CONCLUSION

In conclusion, the quality assurance and control for antibiotic susceptibility tests should be prioritized in deliberate efforts to reduce the burden of antibiotic resistant bacterial infections in developing countries. The centers for disease control in respective countries should enforce protocols that will streamline quality assurance into AST protocols in medical microbiology laboratories.

#### COMPETING INTERESTS

Authors have declared that no competing interests exist.

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