

Improving the Quality of Laboratory Diagnostics for bacteria causing Bloodstream Infections and Better Antimicrobial Resistance Control in Benin: A Case Study

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Abstract

The " Quality Laboratory Testing " training project was established to strengthen the diagnosis of bloodstream infections, including sepsis, by improving laboratory diagnostics in Benin. First, a gap analysis was conducted, then the Train-the-Trainer approach was utilized to train 50 laboratory staff in blood cultures, antibiotic susceptibility testing, and quality assurance in bacteriology. Furthermore, workshops were held to improve dialogue between clinicians and laboratory experts, and to share project results with the Ministry of Health. As a result we compiled a set of recommendations for improvement of the laboratory diagnostics of infections, prescription and delivery of antibiotics and optimizing the role of laboratories in the surveillance of bacterial resistance to antibiotics.

Antimicrobial resistance (AMR) is a major public health problem, particularly in low- and middle-income countries (LMICs), where significant challenges remain in improving the quality of laboratory diagnostics, monitoring AMR, and preventing infections (Zahra *et al.*, 2022). The prescription of antibiotics should be based on quality laboratory diagnostics, which include the identification of the infectious organism and determining its susceptibility to appropriate antibiotics through antibiotic susceptibility testing (AST) (Koura *et al.*, 2013). Unfortunately, in most countries in West Africa, these diagnostic options are limited due to a shortage of well-equipped laboratories and adequately trained staff (Adeyi, 2011; Legba *et al.*, 2023). Consequently, in most cases, clinicians are forced to treat patients without laboratory confirmation of the pathogen, sometimes leading to inappropriate use of antimicrobials. Moreover, even in the existing clinical diagnostic laboratories, quality standards are not guaranteed. Very few laboratories have a high-performing quality assurance system (Okeke *et al.*, 2020; Freaan *et al.*, 2012). In addition, these laboratories are generally poorly connected to clinical services, under-resourced, and therefore underutilized

(Nkengasong *et al.*, 2018; Jacobs *et al.*, 2019; Ombelet *et al.*, 2022).

Improving laboratory quality to combat AMR

The World Health Organization (WHO) Global Action Plan (GAP) for antimicrobial resistance, established in 2015, has identified five key objectives with the aim of ensuring the continued treatment and prevention of infectious diseases with the use of antibiotics. The five WHO GAP objectives are to (i) improve awareness of the resistance problem, (ii) strengthen research and surveillance, (iii) reduce incidence by improving sanitation, (iv) optimize the use of antibiotics in humans and animals, and (v) develop the economic case for alternatives. National action plans (NAP) are needed to localize the GAP. In Benin, a national plan exists to control AMR, but the national network of AMR surveillance laboratories is still in its infancy and poorly structured (Sariola *et al.*, 2022). Despite the NAP's strategic axis 2 recommendation to strengthen the capacity of laboratory professionals in AMR detection, very few initiatives have been put in place. In 2017, Benin went through the Joint Expert Evaluation (JEE) of

its core capacities for the International Health Regulations (IHR). According to the JEE, important gaps in laboratory capacities exist compared to the target level of the IHR core capacities. Benin's laboratories are thus not deemed ready to respond to the need of diagnostics in the case of a pandemic, such as Covid-19, or other major public health events (JEE Benin, 2017).

Improving laboratory quality is a crucial strategy to combat AMR. The strategy will require a multipronged approach, taking into account the science-policy-society interfaces. In the following, we present the approach of a laboratory quality enhancement project in Benin as a case study.

For this project, we first performed a survey to examine how blood cultures and AST are performed in clinical diagnostic laboratories, as well as how laboratory results are used in antibiotic prescribing. To address some of the identified gaps, we then provided training to laboratory professionals, utilizing the Train-the-Trainer approach. Finally, we organized workshops and awareness raising events involving health and laboratory professionals and stakeholders.

Gathering evidence on laboratory diagnostics in Benin

Routine monitoring and evaluation of laboratories in Africa is often lacking and thus they essentially form a "black box" in AMR control (Okolie *et al.*, 2023). Yet, the quality of data generated by laboratories is essential for effective AMR surveillance as well as in treating patients.

Our project started with a survey of practices related to conducting blood cultures and antibiotic susceptibility testing (AST) in clinical bacteriology laboratories (figure 1) (Legba *et al.*, 2023), assessed according to the recommendations of the World Health Organization. Furthermore, physicians were asked about their practice of requesting blood cultures and AST before prescribing antibiotics and about their interpretation of the test results. Pharmacists were asked about their knowledge and practices in dispensing antibiotics for the treatment of suspected sepsis.

The study revealed poor performance in conducting blood cultures and AST due to low technical expertise and limited adherence to international standard procedures among the 25 laboratories surveyed. While all laboratories included in the survey conducted AST, only six conducted blood cultures, and most lacked core resources. Half of the prescribers followed their hospital's antibiotic therapy protocol, while the other

half did not have access to one. Physicians recognized inappropriate antibiotic choice as a leading cause of therapeutic failure in bacterial infection treatment, along with antibiotics not purchased or taken by the patient, superinfections, resistant bacteria, and low efficacy of antibiotics. Pharmacists indicated the lack of cause of disease on medical prescriptions as a challenge for providing proper guidance to patients and suggested improvements in prescription accuracy, monitoring mechanisms, and antibiotic awareness raising for rural populations (Legba *et al.*, 2023).

The findings in Benin showed that laboratory practices do not meet international standards when it comes to identifying antibiotic-resistant bacteria responsible for infections. This highlighted the need to improve the quality of laboratory practices to ensure accurate and reliable results for efficient treatment of patients and probabilistic prescription, when needed, based on the knowledge of the local AMR situation.

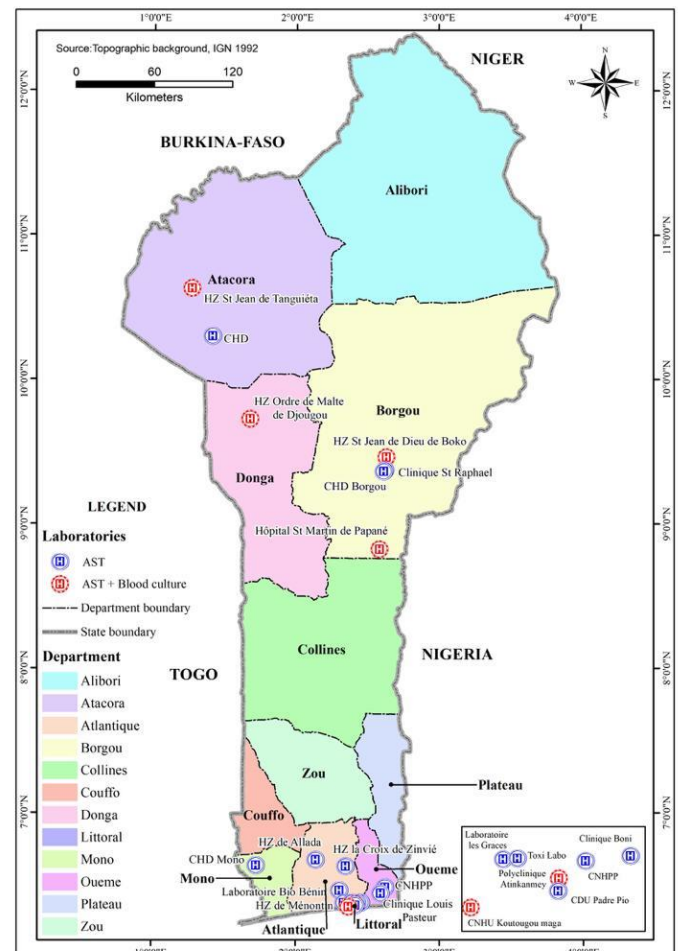


Figure 1: Distribution of the healthcare facilities with laboratories conducting blood cultures and/or antibiotic susceptibility testing (AST) in Benin. CNHPP : Centre National Hospitalier et Universitaire de Pneumo-physiologie ; CNHU : Centre National Hospitalier Universitaire ; CDU : Centre de Diagnostics et d'Urgences ; CHD : Centre Hospitalier Départemental ; HZ : Hôpital de Zone.

Source: Legba *et al.*, 2023

Training of laboratory personnel

We designed a new training course for laboratory staff using the Train-the-Trainer approach (manuscript in preparation). The topics covered were microbiological diagnostics of sepsis using blood culture, bacterial identification tests, AST and quality assurance in bacteriology. A team of qualified researchers from Benin and Finland first trained ten expert trainers, who in turn trained 3 cohorts of laboratory technicians from different health facilities across the country. Out of the 12 participants in the Training of Trainers (ToT) program, 7 (58%) were female. Among the 40 trainee technicians, 25 (62.5%) were female. To evaluate the impact on the laboratory practices of the knowledge acquired during the training, follow-up visits to the laboratories of the trained technicians were organized.

Feedback from health center directors and laboratory managers showed that most of them found the training useful, and positive changes were observed in routine practices. Trained technicians are better able to conduct tests such as AST and blood culture. For the conduct of AST, antibiotic discs are chosen more objectively and accurately, ensuring reliable results for use by the physician. As far as bacterial identification is concerned, a better ease in the choice of culture media and a more objective interpretation of the characteristics of bacterial colonies is observed. Sterility and fertility of culture media are now controlled in the laboratory. Procedures have been written and posted in most laboratories, with a view to quality assurance.

The training received a high level of satisfaction from participants. Specifically, 87.5% of the directors reported being very satisfied, while the remaining directors reported being satisfied. Among laboratory managers, 81.25% reported being very satisfied with the training, with the remaining managers reporting being satisfied.

All technicians found the training to be useful, with 81.25% reporting being very satisfied and the remaining technicians being satisfied with the training.

They suggested expanding it to cover other relevant topics in diagnostics. As positive impacts were achieved with only the limited resources available, more comprehensive initiatives at the national level could significantly improve laboratory diagnostics and control of AMR in Benin.

Catalysing change for laboratory quality

Implementation of policies and guidelines, a national network of AMR surveillance laboratories, and antimicrobial stewardship programs would amplify the impact of the training initiatives, resulting in long-lasting improvements to public health in Benin. The issues impeding the provision and improved quality of laboratory services also elsewhere in Africa, especially related to AMR, are primarily due to the lack of national policy that would provide clear guidelines for continuous monitoring of the quality of the laboratory results. A long-term strategy is needed and engagement of relevant stakeholders, for which, in our project, several workshops and awareness-raising activities were carried out. The workshops organized focused on the use of laboratory results for the prescription of antibiotics and the challenges of sustainable improvement of the quality of laboratory testing in Benin. One workshop was organized to develop a handbook to guide and facilitate the interpretation of laboratory results for the correct prescription of antibiotics by the medical doctors. Another workshop was organized to share the results of the project with the authorities of the Ministry of Health of Benin, and to discuss sustainable ways to improve the quality of laboratory testing. Also, we celebrated the World Sepsis Day in 2021 and 2022, both preceded by a week-long digital campaign to raise awareness about sepsis and the issues related to its management. The campaign material consisted of infographics, and videos on sepsis, AMR, and means of prevention, including hand hygiene, and it was distributed through several social networks.

Policy recommendations / conclusions

For improved bacteriology laboratory diagnostics in Benin

The technical platform of laboratories must be a priority to optimize the diagnosis and management of infections (Jacobs *et al.*, 2019; Diatta *and al.*, 2021). The reliability of laboratory results is dependent on the technical platform as well as the skills of the staff (Hamouda *et al.*, 2016). In the fast-developing field of laboratory diagnostics, continuous training of laboratory professionals must be promoted. Laboratories must

improve their operations, implement a program of self-assessment and equipment maintenance (Katawa *et al.*, 2011). Quality assurance must be one of the priorities in a laboratory. This requires the drafting of standard operating procedures (SOPs), documents and instructions dedicated to the microbiological controls, reference strains, culture media and hygiene of the premises (WHO, 2015).

For Improved prescribing and dispensing of antibiotics by healthcare professionals

The dialogue between clinicians and the laboratory is the starting point for implementing antimicrobial stewardship, for the improved, long-term health benefits to the population. Based on our experience, we recommend also stronger collaboration between clinicians, pharmacists, and other health care professionals. Successful collaboration requires implementation a joint plan focusing on the well-being of the patients (Mrozovski *et al.*, 2022). Additionally, there is a need for a surveillance system to monitor and detect changes in the antimicrobial resistance (AMR) properties of different bacteria in the region and to inform prescribers and other relevant parties of the effective antibiotics available. The development of a national antibiotic therapy guidelines for each infection, based on AST results and bacterial ecology, is essential to optimize antibiotic prescribing and dispensing. These guidelines would help to ensure that safe, effective, quality, responsibly used, and accessible medications are available for the treatment and prevention of infectious diseases for as long as possible.

For optimization of the role of laboratories in the surveillance of AMRs and the role of laboratories in the fight against epidemics

AMR is on the rise globally and there is an urgent need for its better containment. Therefore, it is necessary also in LMICs to organize training on AMR and its mechanisms for all health workers, to commit to the "one world, one health" approach and to organize workshops gathering together experts to define the bacterial species to be monitored. The surveillance can be based on the compilation of routine AST results, which are also used to guide the patient treatment. The regional surveillance results can guide the empirical treatment for a given indication in a given hospital. The establishment of an effective laboratory system also has a positive impact on pandemic preparedness. Indeed, it helps to strengthen the capacity of laboratories to ensure correct identification of pathogens during an epidemic, allow the monitoring of hospital epidemiology and discover new epidemics at the early

stage. In addition, improved training programs for laboratory professionals are necessary.

In essence, progress will rely on a multipronged approach which addresses the science-policy-society interfaces. In our case study, the scientific research aimed at understanding the gap between the normative quality standards and SOPs and the actual laboratory and prescription practices. But the scientific evidence will also need to translate in practice, which was done in our project through an extensive training programme. And finally, our case study also underlines the need to involve different stakeholders such as laboratory technicians, physicians or pharmacists to interact and discuss about way forward.

Acknowledgments

The study was funded by the grant from the Finnish Ministry for Foreign Affairs to the Physicians for Social Responsibility (PSR)—Finland for the Quality laboratory testing training project in Benin. We are grateful to the staff from the Ministry of Health in Benin for supporting the implementation of the activities.

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