



Antimicrobial resistance in the African Region: Issues, challenges and actions proposed

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Antibiotics play a critical role in reducing the burden of communicable diseases all over the world. However, the curative power of infectious disease by drugs or drug efficacy is not infinite. Antimicrobial resistance threatens the effectiveness of successful treatment of infections and is a public health issue with national and global dimensions. In low-income countries, AMR frequently occurs in microorganisms that are likely to be transmitted in the community such as organisms causing pneumonia, diarrheal diseases, tuberculosis (TB), sexually transmitted diseases and malaria. Drug resistance has dramatically increased the costs of fighting TB and malaria, and slowed gains against childhood dysentery and pneumonia. It also threatens the push to treat people living with HIV/AIDS effectively.¹ While appearance of drug resistance is a continuous phenomenon

in microorganisms, its amplification and spread is through the improper utilization of antimicrobial agents, the use of fake and counterfeit medicines, poor prescribing habits and non-compliance to prescribed treatments.²

Detection of resistance and monitoring its spread requires appropriate laboratory-based surveillance. Thus, to maintain the useful life of antimicrobial agents in African countries there needs to be improved access to diagnostic laboratories, improved surveillance of the emergence of resistance, better regulation and better education of the public, clinicians/prescribers and veterinarians in the appropriate use of antibiotics.³

Drug resistance is a major public health problem that requires a range of interventions and multidisciplinary teams approach. The purpose of this paper is to

SUMMARY—The use of antimicrobial agents plays a critical role in reducing the morbidity and mortality due to communicable diseases. However, the emergence and spread of resistance to many of these agents are negating their effectiveness. In the African Region the understanding of issues related to antimicrobial resistance (AMR) and its magnitude are hampered by surveillance of drug resistance being limited to a few countries resulting in incomplete and inadequate data on the true extent of the problem. Despite limited laboratory capacity to monitor AMR, available data suggest that the African Region shares the worldwide trend of increasing drug resistance. This paper aims to highlight the current status and importance of this public health problem in the African Region in order to raise awareness of the need to strengthen AMR surveillance and propose actions for containing the AMR phenomenon.



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share the current status of this public health problem in the African Region, raise awareness on the need to strengthen AMR surveillance and propose key actions for monitoring this phenomenon.

Current situation of AMR in the WHO African Region

The understanding of issues related to antimicrobial resistance and its magnitude are hampered by inadequate data as surveillance of drug resistance is limited to a few countries resulting in incomplete data on the true extent of this problem.⁴ This situation leads to scarcity of accurate and reliable data on AMR in the African Region, especially for meningitis pathogens whose appropriate AMR testing methods are complex and not correctly applied in many countries.⁵ Despite limited laboratory capacity to monitor AMR, available data suggest that the African Region shares the worldwide trend of increasing drug resistance. Significant resistance has, for example, been reported for diseases such as cholera, dysentery, typhoid, meningitis, gonorrhoea, TB, malaria and AIDS.

During cholera epidemics the bacterium has the ability to develop increasing resistance, usually by acquisition of plasmids. Between 2008 and 2011 important resistance of *Vibrio cholerae* against cotrimoxazole was reported from affected countries. These pathogens remained highly sensitive to cyclines and quinolones.⁶

Between 2008 and 2009, of the 451 isolates of the *Shigella* bacterium responsible for bloody diarrhea identified by 18 countries, 78% were resistant to the primary drug used to treat this condition.⁴ This has led to the use of new medicines that are expensive.

Infection with *Neisseria meningitidis* causes large outbreaks of meningitis in sub-Saharan Africa. The antibiotic susceptibilities of a 137 isolates of *Neisseria meningitidis* recovered between 2000 and 2006 from 18 countries were susceptible to ceftriaxone and chloramphenicol. Only 2% of isolates displayed reduced susceptibility to penicillin G.⁷ Susceptibility testing for

37 invasive meningococcal disease patients under 15 years was performed in Mozambique. *N. meningitidis* remained highly susceptible to all antibiotics used for treatment in the country, although the presence of isolates presenting intermediate susceptibility to penicillin advocates for continued surveillance of this pathogen.⁸

The Group for Enteric, Respiratory and Meningitis Disease Surveillance in South Africa (GERMS-SA) has documented emerging antimicrobial resistance in several pathogens.⁹ After years of easy susceptibility of *Neisseria gonorrhoeae* to penicillin and other antibiotics, there is a worrying trend of antimicrobial resistance to the commonly prescribed antibiotics for gonococcal disease such as quinolones and emerging resistance to cephalosporin.¹⁰ Data on antiretroviral therapy (ART) resistance patterns in African countries are extremely sparse. Recent assessments show that rates of transmitted HIV drug resistance remain limited in low and middle-income countries.¹⁰ Surveys conducted at sentinel clinics providing ART in several countries in the African Region estimated that HIV resistance to all drug classes is less than 5%.^{11,12,13,14} This is likely to increase as more patients are placed on antiretrovirals.

Since 2006, the African Region has witnessed the increasing emergence of multidrug-resistant TB (MDR-TB) and

extensively drug-resistant TB (XDR-TB) which is a severer form of drug resistant TB. Between January 2004 and December 2011, a total of 53 798 MDR-TB cases were reported by 42 countries in the Region. At the same time, 3 231 XDR-TB cases were reported from eight countries.¹⁵ South Africa alone accounted for 84% of MDR-TB and 96.8% of XDR-TB cases.¹⁶ A recent survey (2007–2010) on anti-tuberculosis drug resistance found that in South Africa more than 10% of the cases of MDR-TB were extensively drug-resistant.¹⁷ Only 28 of the countries reporting MDR-TB and XDR-TB have structured drug resistant treatment programmes in place.¹⁸ Most African countries lack the laboratory capacity to confirm drug-resistant TB and so the true burden is not well known. Even where treatment programmes exist, not all confirmed cases are receiving treatment mostly due to the unavailability of adequate supplies of second-line anti-TB medicines.⁸

With regard to malaria, in the early 1990s, widespread resistance to chloroquine had been detected in the Region. This led to changes in the malaria treatment policies to new combination antimalarial medicines. The Global Plan for Artemisinin Resistance Containment developed in response to confirmation of resistance in Cambodia and Thailand defined three areas.¹⁹ The three are: tier I where there is credible evidence of resistance; tier II – significant inflow from tier I; and tier III, including Africa, with limited contact with tier I areas and no evidence of artemisinin resistance.²⁰ There are increasing reports of poor quality antimalarials in Africa.²¹ The 2011 World Health Assembly Resolution on malaria urged Member States to halt the use of oral artemisinin-based monotherapies and substandard medicines not meeting WHO prequalification standards or strict national regulatory authority standards.²²

Thus, although progress and efforts are being made by countries and WHO to address AMR issues, key issues and challenges still remain.

Issues and challenges

Although progress has been made in gathering and using AMR data in TB,



HIV/AIDS and malaria, challenges remain. Major challenges include lack of a comprehensive policy and plan to address AMR; weak medicines regulatory capacity and circulation of substandard/counterfeit antimicrobials; lack of AMR surveillance strategies; weak laboratory capacity on AMR testing and reporting; lack of essential laboratory reagents and consumables; and limited quality assurance and control protocols.

The medicines supply and distribution systems in most countries of the Region are fragmented and weak. This situation increases the opportunities for infiltration of substandard/counterfeit medicines into the supply chain. Inadequate access to basic health services coupled with shortages and frequent stock-out of essential medicines including antimicrobials in public health facilities could lead patients to look for other sources usually through illicit sources of supply, which usually deal with substandard/counterfeit medicines.

In the African Region, many countries struggle to protect their populations from unsafe and substandard/counterfeit medicines due to limited resources and the challenge of monitoring medicine supply systems within and from outside their borders. For example, several African countries have not enforced the ban on use of oral artemisinin monotherapies for treatment of uncomplicated malaria. This represents a major risk for development of resistance to artemisinin-based combination therapies (ACTs). The WHO Global Strategy for Containment of Antibiotic Resistance²³ recognized laboratory-based surveillance of antibiotic resistance as a “fundamental priority” for the development of strategies to contain antibiotic resistance and for assessment of the impact of interventions. However, laboratories are perhaps the most neglected of all health system components in developing countries and have been termed the “Achilles’ heel” of global efforts to combat infectious diseases.²⁴ Thus, a recently published article by WHO and the National Institute for Communicable Diseases (NICD) in South Africa on external quality assessment of national public health laboratories in Africa has revealed weakness in many countries for antimicrobial susceptibility testing.²⁵

Faced with the above mentioned dimensions of antibiotic resistance as a threat to public health, some countries have established national and regional surveillance collaborations, others have not. Furthermore, there is no formal framework for collaboration among surveillance programmes region-wide. This lack of a regional framework for collaborative surveillance of antibiotic resistance seriously hampers efforts to track emerging resistance challenges; to identify, characterize and contain new antibiotic threats; and to systematically compare and evaluate the value of national resistance containment activities.

Actions proposed

In order to prevent and combat AMR, comprehensive national AMR policies, strategies and plans should be developed and implemented involving policy-makers, partners and stakeholders in public health. Targeted capacity building activities in various domains including AMR surveillance, laboratory services, quality control of test reagents and protocols, effective medicines regulation and rational use of medicines are urgently needed. Furthermore, establishment of national and/or regional policy platforms for management of antibiotic resistance could play crucial role. WHO has developed a policy package to combat AMR which can be found at: <http://www.who.int/bulletin/volumes/89/5/11-088435/en/>

Develop comprehensive national policies and plans to prevent and combat AMR

Within the context of national health and medicine policies, governments should develop and implement comprehensive AMR policies and strategies that take into consideration the AMR threat to public health so as to limit the emergence and spread of resistant germs.

Establish national and/or regional policy platforms for management of antibiotic resistance in countries

Countries and health systems differ and the various barriers must be tackled in a contextualized manner. In establishing a multi-disease drug resistance surveillance network, the regional health community

can build on a range of existing efforts.²⁶ In order to initiate change, a detailed national/regional analysis of the situation on the ground by a multidisciplinary group including the agriculture and animal sectors is required.

Build clinical laboratory capacity

Understandably, the majority of surveillance programmes are laboratory based. Strategies for ensuring and maintaining the quality of laboratory test results are critical to the value of surveillance initiatives. All facilities should have procedures for ongoing assessment of the quality of test reagents and test performance by clinical laboratory technicians. In addition to internal quality control practices, laboratories should also participate in national and/or external quality assurance (EQA) programmes. Building clinical laboratory capacity will enable the generation of adequate and reliable AMR data that can guide policy actions to combat AMR.

Improve antimicrobial surveillance systems by collecting and sharing information on AMR across networks of laboratories

Surveillance is the primary strategy for tracking emerging drug resistance in the population, and thus allowing for early and appropriate action. Countries should therefore strengthen their capacity for early detection and identification of resistant germs that cause diseases of public health importance. Antimicrobial resistance surveillance data help monitor the susceptibility patterns of microorganisms to antimicrobial agents. The regular dissemination of data can be utilized by public health policy-makers to revise the national AMR policy.

Regional framework for collaborative surveillance of antibiotic resistance

The regional framework collaborative surveillance of AMR provides a standardized overview of the prevalence of AMR in many countries in a given region. The lack of this regional framework for collaborative surveillance of AMR is a key problem hindering information sharing for decision-making both at country and regional level. An efficient surveillance system for AMR, which is

part of integrated diseases surveillance and response (IDSR) implementation and health system strengthening, is necessary to reduce mortality and morbidity due to infectious diseases.²⁷ In particular, antimicrobial resistance surveillance is crucial to demonstrate efficacy when treating communities during outbreaks. It is important for detecting the emergence of novel resistance patterns and for monitoring the impact of interventions aimed at minimizing the spread and burden of AMR.²⁸

AMR surveillance could be integrated in the existing AFRO integrated disease surveillance. Making drug-resistance surveillance routine across all societies and for all significant infectious diseases offers substantial benefits. Timely information about pathogen susceptibility will enable better management of patients and infection control in clinical settings. Aggregating the data to the population level will allow for more informed policy-making and action at national, regional and global levels and in all the public health areas.

The laboratory-based surveillance system requires the following components:

- Prioritization of organisms that should be monitored taking into account the burden of disease in the country;

- Selection of antibiotics to be tested for each isolate taking into account the list of essential medicines and treatment guidelines;
- Development or updating of standard operating procedures for the isolation, identification and antimicrobial susceptibility testing for selected pathogens using standardized methods;
- Establishing or strengthening laboratory quality systems; and
- Setting up a database for collating and sharing information with stakeholders through existing mechanisms such as IDSR.


Strengthen national medicines regulatory capacities in the African Region

While the weaknesses of a single national agency create health and safety risks for people in its particular country, poor regulatory capacity becomes an even larger problem when viewed in a regional context. A country's policies and actions – or inactions – to regulate its drug supply have implications for other countries, even those well beyond its immediate borders, because of disease transmission and international trade in medicine.²⁹

Member States should establish effective national, regional and interregional

cooperation and collaboration mechanisms including reinforcing regulatory networks and exchange of information among public health, law enforcement, professional associations, NGOs and other relevant authorities to improve prevention, detection, investigation and prosecution of cases related to substandard/spurious/falsely labelled/falsified/counterfeit medical products. The quality of medicines circulating within the national pharmaceutical markets should be monitored in order to prevent smuggling and use of substandard/counterfeit antimicrobials that may contribute to increasing AMR.³⁰

Conclusion

Left unchecked, the uncontrolled rise in resistant germs threatens lives and wastes limited resources. Urgent and coordinated action is required at all levels to ensure the preservation of these life-saving drugs for future generations. Governments should develop and implement medicine policies and strategies that take into consideration the threat of drug resistance so as to limit the evolution and possible spread of resistant germs. 

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