



STRENGTHENING KNOWLEDGE AND EVIDENCE TO COMBAT ANTIMICROBIAL RESISTANCE IN SUDAN

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ABSTRACT

The issue of antimicrobial resistance is a priority area identified by the Government of Sudan and development partners. This paper is part of a rapid assessment using the available documents covering all relevant fields pertaining to AMR. Documents were obtained from relevant websites for policies, strategies, guidelines, reports, and plans as well as relevant individuals from WHO Office Sudan, Federal Ministry of Health, Ministry of Environment, Ministry of General Education, and Sudan Medical Council in Khartoum. The review was guided by the WHO five strategic objectives of the Global Action Plan on Antimicrobial Resistance. This paper focuses on the second objective on strengthening the knowledge and evidence base through surveillance and research. The importance of improved surveillance and research in combating antimicrobial resistance has been well acknowledged in Sudan. However, a number of gaps have been identified, which include absence of a proper and functioning monitoring system on antimicrobial resistant pathogens, limited research on antibiotic usage coupled with lack of culture of research and research governance structure. There is an urgent need for a functioning surveillance system that could provide information to guide in the development of policies to tackle the problem of antimicrobial resistance in the country as well national capacity for detection and reporting of priority antimicrobial resistant pathogens. Equally important is the need to clearly define research governance in Sudan in terms of structure and processes in order to facilitate proper collaboration, coordination and harmonisation, including mechanisms to advance the quality of research.

KEYWORDS: antimicrobial resistance, surveillance, research, drug use evaluation, Sudan.

INTRODUCTION

The surveillance of antimicrobial resistance (AMR) is now one of the components of International Health Regulations (IHR). In 2012, the World Health Assembly (WHA65.23) urged State Parties to take the necessary steps to prepare and carry out appropriate national implementation plans in order to ensure the required strengthening, development and maintenance of the core public health capacities as provided in the IHR.^[1]

In 2016, a multi-sectoral international External Evaluation Team conducted a joint assessment of IHR core capacities of Sudan using the World Health Organization's (WHO) International Health Regulation (IHR) Joint External Evaluation (JEE) tool.^[2] The assessment concluded that AMR scored low. The indicators included antimicrobial resistance detection, surveillance of infections caused by resistant pathogens,

healthcare associated infection prevention and control programmes, and antimicrobial stewardship activities.^[3]

Sudan has been the focus of interest for many programmes and partners, and many capacity reviews or programmatic assessments have been conducted in different sectors relevant to AMR. A significant information gap was identified in several areas during a joint Food and Agricultural Organization-World Organization for Animal Health-World Health Organization (FAO-OIE-WHO) consultation on AMR in Sudan towards developing a national action plan on AMR.^[4] It was deemed necessary to gather information for use in developing a national action plan on AMR for Sudan, which led to undertaking a study that was guided by the five strategic objectives of WHO's Global Action Plan (GAP) on Antimicrobial Resistance.^[5]

This paper concentrates on the second objective of the study, which focuses on strengthening the knowledge and evidence base through surveillance and research in Sudan.

METHODS

The study comprised a series of methods, which involved:

- Meetings and interviews with key informants and key officials from the WHO Country Office and

- other governmental institutions in Khartoum that play a role in combating AMR, and
- Reviewing all relevant documents pertaining to the subject of AMR in Sudan that were available at the time of the study.

This study was guided by the WHO Framework for member States of the second objective, i.e. strengthening the knowledge and evidence base through surveillance and research^[5] as illustrated in Figure 1.

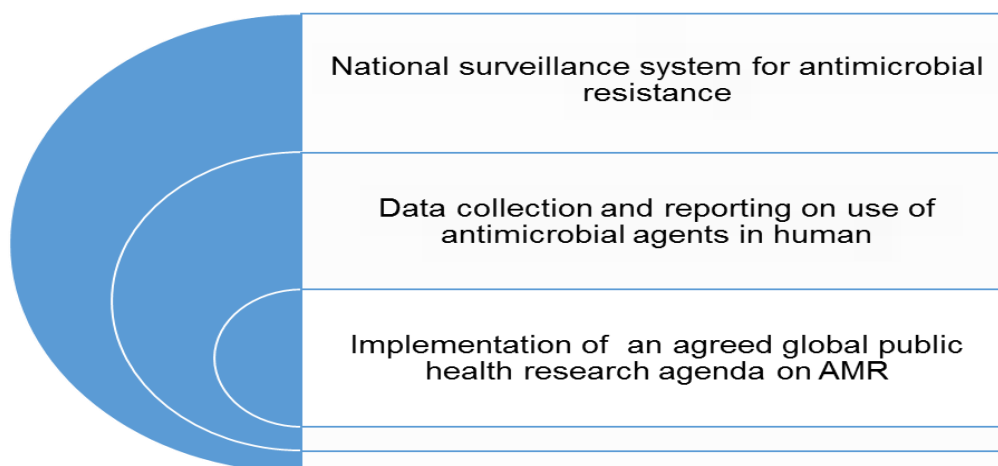


Figure 1: Objective 2 of Global Action Plan on Antimicrobial Resistance and related components.

Information from the document review and interviews was collated to identify gaps that need to be addressed in line with the objectives of the WHO Global Action Plan on Antimicrobial Resistance.

Findings

National surveillance system for antimicrobial resistance

The National Reference Centre (NRC) in Sudan should be responsible of systematically collecting and analysing data – including those on a core set of organisms and antimicrobial medicines from both health care facilities and the community – in order to inform national policies and decision-making bodies.

The Sudan National Laboratory Policy 2015 clearly states that there shall be a mechanism in place for regular analysis of laboratory information to improve planning and decision-making. However, currently there is a poor network system between laboratories at national level with regard to data collection and analysis on organisms and antimicrobial medicines. Furthermore, there is no national plan for detection and reporting of priority AMR pathogens. The capacity for detection and reporting of priority AMR pathogens outside Khartoum State is underdeveloped. Therefore, in the absence of an effective information system, decision-making and policy development becomes a challenge.

There are three human laboratories in the country, all in Khartoum State with capacity to detect (using CLSI breakpoints) and report all seven-priority AMR

pathogens listed by the World Health Organization, i.e. *E. coli*, *K. pneumonia*, *S. aureus*, *S. pneumoniae*, *Salmonella spp.*, *Shigella spp.*, *N. gonorrhoeae*) plus *Mycobacterium tuberculosis*. The Central Veterinary Research laboratory in Soba, Khartoum is also capable of detecting all relevant AMR pathogens. The NPHL and the Central Veterinary Research Lab are the designated national referral laboratories for AMR surveillance.

On the other hand, in Khartoum State there are 50 laboratories in the public hospitals of which 17 carry out Culture and Sensitivity testing, in addition to 80 laboratories in private hospitals. However, there is no system for data collection and sharing.

Participation in regional and global networks and sharing of information

Reports on AMR from Sudan are scarce. The Federal Ministry of Health (FMoH) expressed interest to join the early implementation of the WHO Global Antimicrobial Resistance Surveillance System (GLASS). A joint WHO/FMoH Team reviewed and identified the available capacities for establishing an AMR Surveillance System in line with the recommendations outlined in the GLASS manual.^[6]

A roadmap has been developed to establish a national AMR surveillance system and means to communicate data to GLASS. It is anticipated to start AMR surveillance with Khartoum state as a model, which would then be expanded to other states.

Making use of the already existing surveillance system is commendable. It has been planned that AMR surveillance sites will generate and report data through the statistician of the site to the Epidemiology Department of the FMOH as the National Coordinating Center (NCC), which will collate and analyse the data and compile the reports. Other responsibilities of the NCC will include overall development and oversight of the national AMR surveillance system, developing and/or adapting guidelines and manuals, and providing training to staff.

The National Public Health Laboratory (NPHL), which is the National Reference Laboratory (NRL), is established to provide technical support, supervision, training and capacity building in addition to monitoring laboratory competency and quality, and conduct selective validation of data from surveillance sites.

Selected surveillance sites for early implementation include Soba University Hospital and Omdurman Paediatric Emergency Hospital. Their roles and responsibilities include identification and susceptibility testing of pathogens which are prioritised based on the local context.

The current paper-based information system will be maintained, while efforts will be made to introduce an integrated computerised hospital information management system. The use of WHONET software package was discussed and considered.

The study identified major gaps in regard to the country's capacity to detect and report newly emerging resistant organisms that may constitute a public health emergency of international concern. These include:

- Lack of a national plan for detection and reporting of priority AMR pathogens.
- Poor network system between laboratories at national level with regard to data collection and analysis of organisms and antimicrobial medicines.
- Lack of capacity in terms of equipment and skills for detection and reporting of priority AMR pathogens outside Khartoum State.
- Challenge in providing good quality laboratory services and management systems due to lack of sustained provision of reagents, upgrading/maintenance of existing equipment, infrastructure, PCs, data management, reporting and training of the staff.
- Lack of the surveillance system requirements for Sudan to join GLASS.
- Challenges in making important decision on antimicrobial use due to the absence of an effective information system.

Data collection and reporting on use of antimicrobial agents in humans

There is no database or system to monitor, analyse and report antibiotic use or antibiotic consumption in Sudan.

However, there are very limited ad hoc drug use indicator studies that contribute little to the monitoring of drug use. Currently, the main source of data is the National Medicines and Poisons Board (NMPB), which is the main and sole entry port to medicines in Sudan. However, the data available at NMPB mainly reflects the amount of antibiotics entering Sudan but not the consumption. Many factors such as stock outs, financial factors and other contextual constraints may shape the figures available.

Other sources of data on antimicrobial use may be the National Health Insurance Fund (NHIF), which closely monitors the prescribing of antibiotics - value wise - as part of the drug expenditure scheme. However, data on antimicrobial agents is not analysed, reported or shared. A rough estimate of antibiotic consumption could be done using data on sales from drug suppliers (public & private), in this sense partnership with the private sector is important and mechanisms have to be sought.

In 2017, a WHO Regional Training workshop on 'Introducing WHO Methodology on Antimicrobial Consumption Monitoring' was conducted in Khartoum, Sudan. This workshop may be considered as a start for monitoring antimicrobial consumption in Sudan where participants discussed proposals that may be further developed to a functioning system. However, tracking antimicrobial use in the private sector would still remain a challenge.

A number of gaps have been identified in regard to monitoring of antimicrobials, which include, among others, the absence of proper and functioning monitoring system on antimicrobial use and limited drug use evaluations in the public sector.

Prescribing more than one antibiotic in the same prescription at the same time, when it is unnecessary is quite common in Sudan. Doctors usually use this practice as a 'backup approach', in case the first antibiotic doesn't work then the second might work. This practice necessitates finding a mechanism to monitor treatment failures by antibiotics.

Implementing an agreed global public health research agenda on antimicrobial resistance

In general, there is weak culture of research in Sudan, not just in actual conduct, but in dissemination, implementation of recommendations, and use of evidence. Other aspects of research culture that needs strengthening is the governance and accountability of research.

It is noted that there is no considerable activity in the field of health research or studies directed to the priority problems of the health system. However there are a few studies on antibiotic use and AMR that are conducted by individuals for academic purposes.

Researchers tend to focus more on clinical and biomedical issues with key findings rarely disseminated to reach decision makers in the Ministry of Health who could use the evidence for either developing new policies and/or reviewing existing ones.

There are key challenges facing the national health research system. These include lack of recent updates for research priorities, poor research dissemination and utilisation, in addition to linking research to policy making process.

Weakness of coordination of the research activity between evidence generators (research and academic

institutions) and users (Ministry of Health, National Medical Supplies Fund, National Health Insurance Fund, clinicians, etc) at the national level remains a major concern.

The health research system in Sudan has many players ranging from public and private sector, autonomous organisations, NGOs, bilateral and multi-national agencies. The National Research Policy (NRP) defines stakeholders of “research for health” as those who are governing, financing, producing and using research and those who are promoting its use. Table 1 illustrates the relevant stakeholders who have a role to play according to NRP.

Table 1: List of stakeholders and their roles in AMR research.

Organization	Role in research
Federal Ministry of Health (FMOH)	Research units in Ministry of Health act as proxies for structures of health research governance and management
States Ministries of Health (SMOH)	Research units in Ministry of Health act as proxies for structures of health research governance and management
Ministry of Science and Communications (MSC)	Located within a general research council, covering all fields of research.
Ministry of Higher Education & Scientific Research (MOHE&SR)	Involved in research as part of the academic requirements for the fulfillment of postgraduate studies or staff promotion.
Ministry of Agriculture	Involved in health related research
Ministry of Animal Resources	Involved in health related research
Ministry of Industry	Involved in health related research
National Council for Research (NCR)	Concerned with all types of research and all research institutes.
National Health Research Council (NHRC)	Its sole function was setting the national policy and guidelines concerning health research.
National Medicine and Poisons Board	Responsible for overseeing Clinical Trials (Human and Animal Experimentation) mainly for drugs/medication.
Sudan Medical Specialization Board (SMSB)	Conducts community-based research to solve the health problems of the community
Central Bureau of Statistics	Conducts research (including the national census) that includes some health indicators
Health Research Council, Army sector	Govern research within the Army Medical services affiliated to the Ministry of Defense.
Police Ribat University	Research usually conducted for academic degrees

The NRP recognises the importance of the optimum harmonisation of National Policies in a variety of areas (Education, Social Sciences, Population, Agriculture, Nutrition, Trade, Commerce, etc) to facilitate intersectoral collaboration and partnership, so that maximum developmental returns can occur from health research.

The policy also emphasises the importance of carrying out priority setting activities comprehensively, systematically, transparently and regularly. However, in the absence of a clear and well-defined governance structure, research is likely to remain poor.

According to a research priority list developed by Public Health Institute in collaboration with Research Department of the Federal Ministry of Health, Medical and Pharmaceutical Products (MPP) were included along

with Human Resources and Epidemiology. However, antimicrobial resistance was only one of the 18 research themes identified as a priority under MPP, which was limited to reviewing ‘strategies used to contain the problem AMR and how effective they are’. Nevertheless, there is no evidence if the study was ever carried out.

On the other hand, looking at the research priorities list from Khartoum State Ministry of Health (2017), there is little focus on AMR research in most of health facilities, pharmacies, and laboratories. The list mainly includes evaluation of infection control processes in nursery rooms, health centres, and labour rooms in hospitals and health centres, but not on the issues of AMR.

The majority of studies in the area of antibiotic use and antimicrobial resistance were carried out by individual researchers because of personal interest and for academic

degree awards rather than being guided by national research priorities and needs.

The research agenda in Sudan is generally not robust due to weaknesses in the overall culture to the actual conduct, dissemination and use of research as a source of evidence to make decisions. The lack of clear governance structure led to absence of national research priorities to guide research in the area of antibiotic use and AMR. There is also weakness with regard to coordination of the research activity between evidence generators (research and academic institutions) and users (Ministry of Health, National Medical Supplies Fund, National Health Insurance Fund, clinicians), coupled with limited avenues for financing research in Sudan.

DISCUSSION AND CONCLUSIONS

A well-functioning and effective information system is important for decision making and policy development in dealing with antibiotic use and abuse that could lead to AMR.^[7] This study reveals that there is an urgent need to develop and enhance the national capacity for detection and reporting of priority AMR pathogens especially outside Khartoum State. The current reference laboratories capable of susceptibility testing are few and are all located in Khartoum State. It is important to expand vertically and build laboratory capacity at the national level. In addition to the reference laboratory, a network that provides a standardised platform for resistance testing is essential. The process for setting up surveillance of antimicrobial resistance could be started in Khartoum state initially by developing criteria for assessing laboratory capacity and quality.^[8]

A functional laboratory network system; a defined package of services at all levels and effective

communication, collaboration and coordination, could be achieved by improving the quality of laboratory services through establishment/strengthening of the laboratory quality management systems including sustained provision of reagents, upgrading/maintenance of existing equipment, infrastructure, PCs, data management, reporting and training of the staffs.^[9]

Working in collaboration with the currently functioning laboratories, in both the public and private sector, may boost the surveillance capacity. However, having an accreditation system for laboratories in place or defining minimum requirements, in addition to means of validating data, is imperative.^[10]

One of the opportunities that could enhance the capacity of the surveillance system in Sudan is working towards a detailed implementation plan in order to join the WHO Global Antimicrobial Resistance Surveillance System (GLASS)^[11], which is likely to build a sustainable antibiotic consumption monitoring system at different levels (drug regulatory level, supplier level, and point of care or health facility level).

On monitoring the antimicrobial consumption at national level, it is important to decide who will undertake the monitoring, manage the data and information generated. Having a good network and an information system in place ensures the dissemination and use of evidence generated. A good start in this matter would be to use the current data available, although this may only provide a rough estimate. Meanwhile, capacity building measures need to be considered to develop a sustainable monitoring system at different levels as stated in Figure 2.

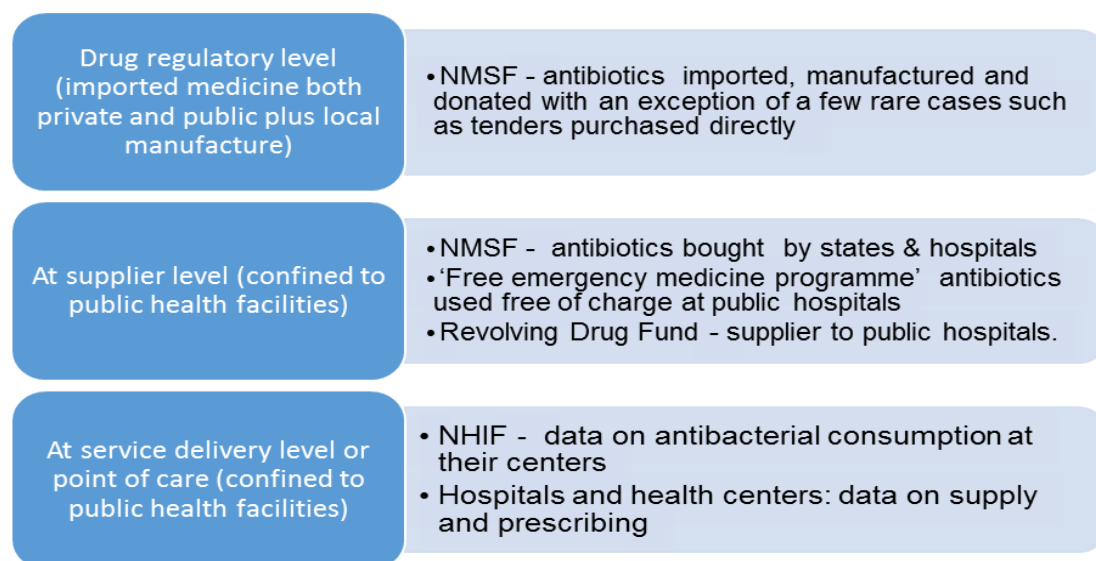


Figure 2: Sources of antibiotic data from different institutions.

Again, data on the consumption or use of antibiotics cannot be used as an indicator to show whether there is appropriate/rational or inappropriate/irrational use of

antibiotics. It needs to be coupled with another set of important data on disease burden and disease pattern, which will act as the main yardstick.^[12]

Drug use evaluation (DUE) using prescribing indicators of antibiotics could be made a requirement of the hospital's periodic reports to be analysed either at hospital level or at the FMOH to provide information that may guide in decision-making and policy development. Similarly, in order to track the consumption of antibiotics dispensed from private pharmacies, it is important to oblige the pharmacies to keep record on the sale of antibiotics and make this a requirement for the annual pharmacy licensing.

Research financing is one of the major challenges for undertaking research in Sudan. This is where international donors could play a significant role in supporting and shaping the research agenda in the country and funding priority research. Similarly, the study concluded that research governance in Sudan needs to be clearly defined in terms of structure and processes in order to plan for proper collaboration, coordination and harmonisation, including mechanisms to ensure the quality of research should be in place.^[13] These will very likely enhance research communication, not just to policy makers, but even communities and general population.

REFERENCES

1. World Health Organization. (2005). Sixty-fifth World Health Assembly Implementation of the International Health Regulations. Geneva: World Health Organization.
2. World Health Organization. Joint External Evaluation tool (JEE tool) - second edition IHR (2005) Monitoring and Evaluation framework [Online]. Geneva: WHO; 2018 [Available from: https://www.who.int/ihr/publications/WHO_HSE_GCR_2018_2/en/. [Date Accessed: 20 July 2020]
3. World Health Organization. (2016). Joint External Evaluation (JEE) of Sudan Mission Report. Khartoum: World Health Organization.
4. World Health Organization. (2017). GoS, WHO, FAO, and OIE fight antimicrobial resistance with new national plan. Cairo: WHO, Eastern Mediterranean Region.
5. World Health Organization. (2015). Global action plan on antimicrobial resistance. Geneva: World Health Organization.
6. World Health Organization. (2016). Country Capacity Review for Early Implementation of AMR Surveillance in Sudan Khartoum: World Health Organization.
7. Nicholls T, Acar J, Anthony F, Franklin A, Gupta R, Tamura Y, Thompson S, Threlfall EJ, Vose D, van Vuuren M, White DG, Wegener HC and Costarrica ML. (2001). Antimicrobial resistance: monitoring the quantities of antimicrobials used in animal husbandry. *Rev Sci Tech*, 20(3): 841-7.
8. Van Belkum A, Bachmann TT, Lüdke G, Lisby JG, Kahlmeter G, Mohess A, Becker K, Hays JP, Woodford N, Mitsakakis K, Moran-Gilad J, Vila J, Peter H, Rex JH, Dunne WM, the JAMRRDTWGoAR and Rapid Diagnostic T. (2019). Developmental roadmap for antimicrobial susceptibility testing systems. *Nature Reviews Microbiology*, 17(1): 51-62.
9. (!!! INVALID CITATION !!! [9, 10]).
10. Mosha F, Oundo J, Mukanga D, Njenga K and Nsubuga P. (2011). Public health laboratory systems development in East Africa through training in laboratory management and field epidemiology. *Pan Afr Med J*, 10 Supp 1: 14.
11. Seale AC, Gordon NC, Islam J, Peacock SJ and Scott JAG. (2017). AMR Surveillance in low and middle-income settings - A roadmap for participation in the Global Antimicrobial Surveillance System (GLASS). *Wellcome Open Res*. 2: 92.
12. Laxminarayan R and Chaudhury RR. (2016). Antibiotic Resistance in India: Drivers and Opportunities for Action. *PLoS medicine*, 13(3): e1001974-e.
13. Rani M, Bekedam H and Buckley BS. (2011). Improving health research governance and management in the Western Pacific: a WHO expert consultation. *J Evid Based Med*, 4(4): 204-13.