Country Capacity Review Mission for Early Implementation of AMR Surveillance in Pakistan

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Contents

Acknowledgements:

Introduction

The problem of antimicrobial resistance (AMR) is now recognized as a major threat to the health and development of communities in all countries. As a part of the response to this global problem, WHO has developed a Global Action Plan on AMR (AMR GAP), which was endorsed by the World Health Assembly in 2015. One of the strategic objectives of the AMR GAP is for countries to strengthen the knowledge and evidence base. This includes monitoring the resistance situation through the establishment of national AMR surveillance programs. WHO is establishing a Global Antimicrobial Resistance Surveillance System (GLASS) with data contributed by the national surveillance programs.

In line with the resolution WHA68.7 and following an expression of interest by the Ministry of National Health Services, Regulations and Coordination (NHSRC) of Pakistan to join the early implementation of the GLASS, a joint WHO/NHSRC Team visited selected sites in the country to review and map available capacities for establishing an AMR Surveillance System in line with the recommendations outlined in the GLASS manual. Pakistan is the first country of the Eastern Mediterranean Region of WHO that has started the process of establishing early implementation of the GLASS.

During the mission, team members had meetings with the officials from the National Institute of Health (NIH) in Islamabad and Secretary Health of Sindh Province and the Director General (DG) Health Punjab province. The mission also visited the Provincial Health Information Systems (DHIS) Office and hospitals and laboratories in Karachi and Lahore identified as potential surveillance sites and reviewed capacities needed for early implementation of AMR surveillance. Following the site visits, the representative of the Secretary Health or DG health from Sindh and Punjab along with heads of the laboratories and epidemiological units from the sites visited were invited to the WHO Country Office in Islamabad for a consultative meeting to help develop a roadmap of actions for the implementation of national AMR surveillance.

The team presented their findings and outcome of the consultative meeting to the Director General for Health of the Ministry of NHSRC. During this meeting the Director General expressed interest and support for the early implementation of an AMR Surveillance System in Pakistan and advised on mechanisms for alignment with ongoing surveillance activities in the country.

The Context[1,2]

Pakistan gained independence in 1947 and has a land area of nearly 800,000 km^2 and an estimated population of 173.5 million (2010). It is the fifth most populous country in the world and the largest in the Eastern Mediterranean Region of WHO, with approximately two-thirds of the population residing in rural areas. The country is divided into five provinces, namely Punjab, Sindh, Baluchistan, Khyber Paktunkhwa (KP) and the relatively smaller Gilgit–Baltistan, as well as three territories, namely Federally Administered Tribal Areas (FATA), Azad Jammu and Kashmir (AJK) and the Islamabad Capital Territory (For detailed country situation see Annex I).

The unanimous adoption during April 2010 by the Parliament on 18th Amendment to the Constitution of Pakistan was a highly popular move that reverted many responsibilities from the federation to its provinces. As a result, as of end June 2011, 17 ministries or divisions were totally abolished at the federal level including the Ministry of Health.

Furthermore, certain critical health functions (including the newly created Health Services and Regulations Division) have been assigned mainly to seven divisions of the Government of Pakistan. In

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[1] Country Cooperation Strategy for WHO and Pakistan- 2011–2017Document WHO-EM/PME/001/E/04.13
[2] http://nhsrc.gov.pk/, Accessed on 15 December 2015

April 2012 the Ministry of National Regulations and Services was established. Later on the scope of work of the ministry was expanded and its nomenclature was also changed to Ministry of National Health Services, Regulations and Coordination[3] (NHSRC). The mission of the Ministry is to regulate and coordinate efficient, effective and equitable, health and population welfare services in the country. To improve governance on health issues, on May 4th, 2013, the federal subjects in health scattered in various divisions were consolidated under the newly established Ministry of National Health Services Regulation and Coordination (NHSRC).

Core functions of the NHSRC are as follows:

- National & International Coordination in the field of Public Health
- Oversight for regulatory bodies in health sector
- Population welfare coordination
- Enforcement of Drugs Laws and Regulations
- Coordination of all preventive programs, funded by GAVI/GFATM (TB, HIV/AIDS, Malaria, Hepatitis etc.)
- International commitments including attainment of MDGs
- Infectious disease quarantine at ports
- Coordination of Hajj medical mission
- Provision of medical facilities to the Federal employees in provinces

Pakistan is facing several major risks to health outcomes including antimicrobial resistance. Security challenges, governance issues in some parts of the country (such as lack of adequate regulation and supervision from health authorities at the federal and provincial/district levels and insufficient institutional capacity for procurement and purchase of equipment and supplies), low health investments, expenditures and utilization and poor social determinants of health (such as illiteracy, unemployment, gender inequality, social exclusion, rapid urbanization and environmental degradation) are among others. Low levels of education, low resources and weak detection and monitoring systems leave people exposed to threats from pandemics.

Performance of the public health system is marked by low utilization rates and inadequate institutional frameworks for outsourcing health services, as reflected by only 0.12 to 0.2 new cases per person per year utilization of public health services and only 20% to 30% of primary health care delivered by the public sector. Given the low coverage of governmental health facilities, the private sector has emerged as the principal provider of health services in the country contributing to 60%–70% of the health care in Pakistan; however, the private sector to a major extent is still unregulated.

In the current scenario, although the provincial and district levels of health management theoretically have clear roles and responsibilities, in practical terms many functions overlap. Moreover, the situation at federal level is somewhat fragmented after the dissolution of the Ministry of Health and devolution of its responsibilities to provincial departments of health. According to the rules of business under the Constitution, the major roles of the federal government related to policy formulation, provision of technical backstopping and coordination with different partners within and outside the country. However an overemphasis of the former Ministry of Health towards national programs diminished its stewardship and governance roles of policy-making, regulation and financing.

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[3] Source: http://nhsrc.gov.pk/, accessed on 15 December 2015

Provincial departments of health are responsible for translating the national policy into planning and actual implementation through generating the required human resources, providing specialized care through the tertiary care hospitals, and overseeing primary and secondary health services provided by the district. Actual service delivery takes place at the district level where the two tiers of primary and secondary health outlets are managed. Districts also implemented the federally or provincially financed health programs, resulting in dichotomy in the management due to the dual command mechanism. All preventive services are implemented at the district level where the government is virtually the sole provider, with a significant role of the private sector in the provision of curative services.

AMR Surveillance in Pakistan

As such AMR surveillance system does not exist in Pakistan except for programs of TB and malaria. AMR data available for common drug resistant bacterial pathogens is based on studies published in literature. Pakistan reported having a policy regarding the use of antibiotics in animal husbandry; however, the policy is not enforced 7.

Pakistan Antimicrobial Resistance Network (PARN) is a non-governmental organization involved in AMR surveillance and there is some sharing of information on AMR and healthcare associated infections by some labs, mostly from private sector. It is also creating awareness through meetings / seminars and providing advice and sharing protocols and educational material for antimicrobial testing and control of healthcare associated infections. Some labs also share their antibiograms on PARN website6.

Basic laboratory infrastructure exists in most hospitals, research institutes and universities. However Microbiological diagnostic facilities are available in few high level public and private laboratories8. Weaknesses / gaps in AMR Laboratory surveillance in Pakistan are as under8:

1. Lack of surveillance coordinating body at federal & provincial levels
2. Lack of National Laboratory Policy (under development)
3. Coordination mechanisms between laboratories are not well defined (except for TB, Malaria and HIV, polio, dengue)
4. Lack of tiered laboratory networks in public sector
5. Lack of standardization of lab services across the country
6. Lack of integration of the laboratory component of vertical programs in the general laboratory system
7. Lack of referral mechanisms
8. Sample transportation system is weak due to lack of funding and transport infrastructure
9. Lack of integrated diseases surveillance program backed with a network of Public Health Laboratories
10. Lack of integrated disease surveillance program for emerging infections
11. Lack of coordination between human and veterinary public health sectors
12. Lack of linking research labs with routine labs for use of research data for evidence based routine testing

The Mission

The World Health Assembly (WHA) in its 68th session adopted the resolution WHA68.7 in May 2015. Based on the resolution, WHO Member States were urged to implement proposed actions for the identified in the AMR GAP on antimicrobial resistance, adapted to national priorities. In this context and in line with the second strategic objective of the AMR GAP, and with the concurrence of the Government of Pakistan, WHO conducted a Country Capacity Review Mission to determine the status of AMR surveillance in the country and to map the national capacities of Pakistan to implement Antimicrobial Resistance Surveillance system. The primary objective was to establish the AMR Surveillance System in the country context and enable its integration with the GLASS.

The Terms of Reference for the mission were to:

1. Review the AMR national systems within the country to collect, collate, analyze and use the data from surveillance units, hospitals and laboratories participating in the national AMR surveillance scheme and make recommendations on strengthening and expanding the AMR surveillance scheme in a sustainable manner.

2. Conduct on-site visits to selected health and animal sector laboratories participating in the national AMR surveillance scheme and make recommendations on how to ensure the consistent quality of results provided to the scheme.

3. Define major challenges and gaps at national level in implementation of AMR surveillance.

4. Discuss additional support that WHO may be able to provide to promote national AMR surveillance and make recommendations on ways to optimize the interactions between AMR Surveillance stakeholders to strengthen surveillance and laboratory capacities.

The mission team was composed of experts from three levels of WHO paired up with the national counterparts (for names of the mission members see Annex IV). The mission team in consultation with the national counterparts decided to review the capacities of selected health centers from Lahore (province of Punjab) and Karachi (province of Sindh), where access to public and private health care systems are higher than other areas. The tem had meetings with the officials from NIH and NHSRC and provincial health authorities. The team also visited the NIH laboratory and FELTP in Islamabad. The centers visited were as follows:

1. In Islamabad:
   a. Public Health Laboratories Division, NIH
   b. Field Epidemiology and Diseases Surveillance Division, NIH
   c. FELTP
2. In Karachi:
   a. Civil hospital (public sector, teaching hospital)
   b. Jinnah Postgraduate Medical Center (JPMC) (public sector, teaching hospital)
   c. Agha Khan University Hospital (Private sector, teaching hospital)
3. In Lahore:
   a. Mayo hospital (public sector, teaching hospital)
   b. Sheikh Zayed Hospital (public sector, Autonomous, teaching hospital)

Due to time constraints the team was not able to visit the laboratories in animal health sector. The list of the people met and interviewed are in Annex II.

Observations

The following the observations were made during the mission.

Karachi:

1) Offices of the Secretary Health:

The team met with Dr Saeed Ahmed Mangnejo, Secretary for Health, Sindh Province in his offices in Karachi. Disease surveillance data are reported to the DG office located in Hyderabad which has the potential to act as the Provincial Coordinating Center (PCC). The District Health Information System (DHIS) receives all health data from public health sector in Sindh on a monthly basis. The data are analyzed and collated in periodic reports that are shared with provincial authorities. Private sector is not contributing data to the system. The Secretary Health was positive about sharing the data and cooperating with the national authorities. Health authorities of Sindh Province are developing legislation for regulation of public and private health care providers. It was understood that authorities of Sindh Province are developing legislation for regulation of public and private health care providers, which will then go through the Assembly. When the legislation is enacted, laboratories will be bound to report the data. The Secretary was positive about sharing the data and cooperating with the national authorities.

From the discussion during the meeting, it was unclear which laboratory, either in Hyderabad or Karachi, can be designated as Provincial Reference Laboratory (PRL) for Sindh Province.

2) Karachi Civil Hospital Laboratory

The team met with and interviewed Dr. Ghulam Fatima, Head Laboratory and Senior Consultant Pathologist. It is a public laboratory located in and being part of the teaching hospital. The laboratory accepts referred samples. Scope of microbiology-related operation includes bacteriology, parasitology and mycology. Work of microbiology section is supervised by the consultant microbiologist (head of lab herself) and is performed by 4 technical staff, 2 of which are hired on a "private" basis meaning that their salary comes from private donations rather than government sources.

The laboratory performs isolation and identification of bacterial cultures and Antibacterial Susceptibility Testing (AST). Large spectrum of specimens and pathogens is investigated. Tests are controlled by ATCC strains whenever the latter are available. Regular purchase of the control strains is not possible due to financial constraints. The laboratory performs about 1,000 blood cultures per month.

No External Quality Assessment (EQA) is currently available for microbiology due to financial constraints. In the past, the laboratory received 2-3 occasional EQA panels from AFIP, which was discontinued for financial reasons.

AST results are interpreted based on the current CLSI standards. AST results are reported as "resistant"/"intermediate"/"sensitive". Results are reported to requesting clinicians only. Reporting of AST results to the provincial is possible but shortage of manpower may be a limitation.

General LIS is used to store AST results. Results apparently are not collated or analyzed.

The laboratory has trained (may be certified – to be confirmed) infectious substances shippers, is procured with proper shipping materials and has experience shipping samples to NIH/Islamabad for influenza and CCHF.

3) *Jinnah Post Graduate Medical Centre (JPMC) laboratory*

The Mission met with and interviewed Dr. Naila Tariq, Head of Pathology Department and Assistant Professor, Basic Medical Sciences Institute.

Laboratory is a part of a public tertiary teaching hospital, serves hospital patients only. Scope of operation of the microbiology section includes bacteriology, virology, and parasitology. The microbiology section is run by one consultant microbiologist (head of section), 2 lab technologists and 3 lab assistants.

The laboratory performs isolation and identification of bacterial cultures and AST. Large spectrum of specimens and pathogens is investigated. Tests are controlled by ATCC strains whenever the latter are available. Regular purchase of the control strains is not possible due to financial constraints.

The laboratory performs about 3,000 bacterial cultures per month, out of which about 900 blood cultures and 1,200 urine cultures. All samples received in the laboratory are accompanied with information on patient's name, sex, age, address, hospital ward (for in-patients). Relevant clinical data are provided rarely.

No EQA is available for microbiology due to financial constraints.

AST results are interpreted based on the current CLSI standards (provided by AKUH lab). AST results are reported as "resistant"/"intermediate"/"sensitive", sometimes as MICs based on clinicians' request. Results are reported to requesting clinicians only. Reporting of AST results to the provincial level is possible provided official channels are strictly followed.

General LIS is used to store AST results. Results apparently are not collated or analyzed.

The laboratory never ships biological materials and therefore has no trained and certified shippers.

4) *Aga Khan University Hospital laboratory*

The team met and interviewed Dr. Rumina Hasan, Head Department of Pathology and Microbiology, Dr. Erum Khan, Section Head Microbiology, and Dr. Afia Zafar, a Professor in Agha Khan University.

AKUH laboratory is part of AKUH, a private entity. It has about 210 collection sites in Pakistan, but also receives referred samples from other facilities from all around country. The laboratory is accredited under JCI since 2008 and is currently preparing for CAP accreditation.

Staff of the laboratory includes 9 consultant medical laboratory scientists, including microbiologists and a mycologist, and 42 laboratory technologists and technicians.

The laboratory isolates and identifies bacterial cultures and does AST. The Pathology and Microbiology Department performs tests in bacteriology, mycobacteriology, parasitology and mycology. ATCC control strains are used. The laboratory uses only commercial media. Each month, the laboratory sets up about 3,500 cultures from blood; 4,500 from urine; 150 from urethral swabs; and 500 from cervical swabs. Culture and AST are done upon clinician's requests. All samples received in the laboratory are accompanied with information on patient's name, sex, age, telephone number, address /location. Requests complete with clinical data are only received in about 60% of cases.

The laboratory participates in a CAP-provided EQA scheme that covers all major activities, including bacterial culture and AST. CLSI system (2015 version) is used for interpretation of AST results. AST

results are reported as "resistant"/"intermediate"/"sensitive". Reports go to requesting clinicians only.

MS Excel-based sheets are used for storing and analyzing AST results. WHONET was used in the past but then was abandoned. Annual analysis of AST is published on AKU website and also publishes a hard-copy annual susceptibility report in a form of a flyer/leaflet, which is distributed among hospital clinicians.

The laboratory has trained (but not necessarily certified or with current certification) shippers.

AKHU laboratory is currently establishing a small AMR network, comprising 4 public and 3 private labs. The primary focus of the network is on capacity building and standardization of Laboratory techniques for identification and AST. Key personnel were well aware of GLASS, seemed very cooperative and suggested that AKUH lab can play much bigger role than just a surveillance site. The laboratory is well equipped and well-staffed, has a well-developed documentation system. It seems that procurement is not an issue, even though from time to time shortage of some supplies may occur. The laboratory currently reports dengue and malaria results to city authorities on a daily basis, other notifiable diseases on a monthly basis. Apparently, it can and was willing to report AST data to the provincial level if selected as a surveillance site.

5) *Meeting with representatives of potential surveillance sites in Sindh (AKUH, JPMC and Civil Hospital)*

Using the opportunity of having representation from the three WHO levels (HQ, EMRO, Karachi sub-office) and national counterparts from the central (NIH) and provincial level (Civil Hospital and JPMC) as well as from the private sector (AKUH), a meeting organized and discussed issues related to establishment of AMR surveillance system in Pakistan, in particular, in Sindh Province and from laboratory perspective. During this meeting several suggestions were made for improving the AMR surveillance in the province. Civil Hospital and AKUH expressed their willingness to join the early implementation of the GLASS.

At the end of the visit to Karachi, the team seized the opportunity of having representation from 3 WHO levels (HQ, EMRO, Karachi sub-office) and national counterparts from the central (NIH) and provincial levels (Civil Hospital and JPMC) as well as from the private sector (AKUH), and discusses in a meeting issues related to establishment of AMR surveillance system in Pakistan and in particular, in Sindh Province and from laboratory perspective. The salient points are summarized here:

- The network structure should definitely include a provincial level coordinating center and reference lab.
- Upon high-level discussions and agreement between WHO and national/provincial authorities, participating laboratories should be involved observing all necessary formalities.
- Bacterial isolation, identification and AST within the surveillance network should be standardized and unified protocols developed and followed.
- To ensure quality of microbiological work and quality of data received, an EQA scheme (national or regional) should be established. The Armed Forces Institute of Pathology may serve as a possible EQA provider as it has necessary capacities and experience. AKUH may also potentially be an EQA provider but their experience is limited to TB slides rechecking. Funding for NEQAS participation may be required.

- Laboratories in the network will need regular supportive supervision based on their EQA results and other M&E data. PRL is naturally positioned to provide this kind of supervision; if PRL does not have required capacity, AKUH may play this role through MOU with PRL.
- Referral system should be developed, with ISST training and certification and provision of packing materials where necessary.
- Public facilities may need support with procurement of key reagents.
- Other challenges for establishment and successful functioning of the AMR surveillance network include:
  o Funding constraints
  o Chronic shortage of trained staff due to high staff attrition/turnover. Continuous training/re-training of staff may be a feasible solution.
  o Access to equipment procurement/maintenance may be limited in some regions due to security issues (e.g. in Baluchistan).
- Opportunities for public-private collaboration between representatives of Sindh Province labs were discussed and may play positive role in successful functioning of AMR surveillance network.

Lahore:

1) Offices of DG Health:

The mission met with Dr. Amjad Shehzad, Director General Health Services Punjab and in an open discussion received information on the roles and responsibilities of the Offices of DG Health and provided briefing on the concepts of GLASS. The following summarizes the discussions:

The roles and responsibilities of the Offices of DG Health are as follows:

- Technical supervision of all field formations
- Establishment functions of non-gazette (1-15 excluding tertiary care and nursing cadre) employees of Health department
- Coordination with all Districts , Development partners, line Departments, Media and Civil Society
- Dissemination of policy guidelines devised by the international and National levels.

The Directorate performs a number of interrelated functions including preventive, administrative (M&E), regulatory functions, epidemic control and several vertical health programs.

The District Health Information System (DHIS) receives all health data from public health sector in Punjab on a monthly basis. The data are analyzed and collated in periodic reports that are shared with provincial authorities. This data reflects the situation of 50 days back and will not provide a real-time portrait; nevertheless the EPI data is accessible on a real-time basis. The data is for information only and not used for planning purposes. Private sector is not feeding into the system, nor are they shared with the central level. There is no legislation on mandatory reporting available at the provincial level.

The Office of the DG health services HQ receives information from the District Surveillance Coordinator and is used for implementation of IHR (2005) after validation and verification.

2) Mayo Hospital Laboratory

The Mayo Hospital, a tertiary care facility attached to the King Edward Medical University is one of the biggest hospitals in South Asia with around 2,400 beds and receives patients from all over the

province of Punjab and some other provinces. The range of services offered covers 46 disciplines and includes 16 operating theatres.

The Microbiology Laboratory receives around 50 specimens a day which are processed by a staff of three technicians. The number of specimens processed in the laboratory has been rising sharply in the past year with three times as many specimens processed in October 2015 as in the same month last year. Space is becoming a significant issue at the laboratory is very cramped. Specimens processed include respiratory tract, wounds and pus and blood cultures. Media are prepared in-house and plates are poured by hand. Identification of isolates was mostly done with conventional tube tests. Human blood is used in blood containing media. Blood borne viruses pose a potential occupational health and safety issue. Media are produced in fairly small batches and are used within a day or two of pouring which means it is difficult to do sterility checking.

Antibacterial susceptibility testing follows the CLSI method but it was not clear if the latest zone size tables were used to determine susceptibility. Control strains for quality control were not available. Currently the laboratory does not participate in any external quality assessment program that covers antibacterial susceptibility testing.

The test requests are lacking sufficient patient information necessary for AMR surveillance. The test results are shared for treatment purposes. No data is shared with the provincial or national levels.

3) Shaikh Zayed Federal Postgraduate Medical Institute & Hospital
Shaikh Zayed hospital is a tertiary care teaching hospital affiliated with the Health Sciences University. It is a public hospital with some autonomy to provide medical services on private basis.

The microbiology laboratory is a spacious facility with plenty of room to cope with an increasing numbers of specimens. Culture media are prepared in-house. The Microbiology laboratory receives around 100 urine isolates and around 30 blood cultures each day. The laboratory has a bactec automated blood culture instrument but it is not currently in use owing to the high cost of the culture bottles. Urine isolates from the family *Enterobacteriaceae* are only reported as coliforms and are not identified further. Such isolates from blood cultures are fully identified using API identification strips. The laboratory also has a MicroScan instrument for bacterial identification and susceptibility testing but it is currently not in use owing to the high cost of panels.

The laboratory uses the CLSI method for susceptibility testing but is considering switching to EUCAST for reasons of economy. The laboratory has some of the control strains used for quality control of antibacterial susceptibility testing. The laboratory does not currently participate in any EQA scheme covering AST but would be keen to do so if one was available at an affordable price.

The laboratory would have to modify some procedures to meet GLASS requirements such as further identification of enterobacteria from urine isolates. The information of a syndromic surveillance provides data on a limited number of conditions to the Deputy Health Office of the hospital on a daily basis. The data is collated and shared with the offices of the DG Health daily. The hospital benefits from presence of an academic staff member in epidemiology; however, the data is not analyzed and used for planning purposes.

Islamabad:

National Institute of Health (NIH)

The team had the opportunity to meet with the Executive Director of NIH and review the capacities of the NIH Laboratories. Summary of findings are provided below.

NIH is one of the autonomous departments under NHSRC. The NIH is involved in a number of public health activities at the national level including diagnostic services, research and production of biologicals.

NIH hosts the national Focal Point for IHR (2005) (IHR NFP) and collaborates closely with the Field Epidemiology and Laboratory Training Program (FELTP) to strengthen the disease surveillance and response capacities in the country. NIH manages the rapid response to outbreaks at the national level.

NIH laboratory is a government-run facility serving as the national reference public health laboratory. The microbiology section of the laboratory performs bacteriology and parasitology, and also has capacity (facilities and equipment) for virology (PCR). The section is supervised by a microbiologist and operated by two trained and competent technologists, along with auxiliary staff. Based on the interview of staff, the laboratory currently operates at about 50% of its capacity and can easily handle increase in workload.

The laboratory receives and processes all major types of specimens, including blood, urine, stool, respiratory samples, and swabs. Most samples received in the laboratory are for surveillance, outbreak investigation, or research purposes, but the laboratory also performs small number of clinical tests. Examination requests are sent in a variety of different formats – no standardized format exists; inspection of several randomly picked request forms revealed incomplete information, such as lack of date/time of sample collection, patient identified by the first name only, lack of information on patient location, scanty or no clinical information, etc. Examination report forms are standardized. The laboratory's information management system is completely paper-based.

The laboratory uses consumption-based method for supply quantification; minimum stock levels are not formally set. Ordering is done once a year, with receipt of supplies throughout the year based on need. Emergency orders are not unusual. Inventory management system is paper-based.

The laboratory does not separate and properly label expired reagents. Random check revealed some reagents expired in April 2015 that was kept in the fridge.

Equipment maintenance is less than adequate. Biosafety cabinets are not covered by maintenance/certification contracts; it was unclear when the last maintenance was done as no records were available. Some refrigerators lacked temperature charts.

The laboratory separates infectious waste from regular trash; infectious waste is put in biohazard bags, autoclaved and then incinerated; autoclave temperature is monitored with thermo-sensitive indicator strips. Disposition of sharps is inadequate as they are collected in regular biohazard bags. No sharps containers were available, posing a high risk of contaminated needle-pricks, cuts and other sharps-related injuries.

Bacterial strains are isolated and identified using commercial media. Manual methods are used. SOPs for analytical methods were available. ATCC control strains are used for internal quality control. The laboratory participates in the regional EQA scheme funded by WHO. The latest EQA panel results demonstrated problems with isolation and identification of microorganisms from stool and cerebrospinal fluid. The laboratory claimed to have investigated the issue and taken corrective action but the corresponding records were not available.

AST is performed using the disc diffusion method. The latest version CLSI criteria are used for result interpretation. Results are reported as "resistant", "intermediate", or "sensitive". The data of the Laboratory is compiled on yearly basis using WHONET.

The Public Health Laboratories Division at NIH is in process of installing Laboratory Information System. Through Global Health Security Agenda, the Department of Microbiology, being the focal point for AMR also intends to establish the National Reference Laboratory for AMR. The Department of Microbiology has also submitted a proposal to WHO for launching External Quality Assurance Program for selected laboratories in Microbiology. The platform may be used to run a quality assurance program for the sentinel laboratories participating laboratories.

Consultation

Following the site visits, the representative of NIH, representatives from the Secretary/DG Health from Karachi and Lahore along with heads of the laboratories and epidemiological units from those cities were invited to the WHO Country Office in Islamabad for a consultative meeting to help develop a roadmap of actions for the early implementation of the GLASS. During this consultation, participants discussed a number of critical topics. The best format of early implementation of AMR surveillance for Pakistan, use of available structures and resources to ensure sustainability of the system, working modalities at each level, technical/supporting supervisions, data sharing channels and use of data at the provincial and central levels were among others. During the discussions, participants outlined the surveillance objectives, development of standard protocols and Laboratory Information System to use and strategy for gradual expansion.

In summary, the following constraints to early implementation have been identified:

1. There is no AMR surveillance at the provincial or national level;
2. Infections with resistant pathogens are not included in any notifiable disease lists;
3. There is no effective coordination for AMR surveillance between Laboratory, epidemiology and clinical medicine;
4. AMR data are not used for planning purposes;
5. AMR data are not shared in a timely manner to those who need to know for different reasons;
6. Quality of AMR testing is unknown owing to non-participation of laboratories in EQA;
7. Quality management systems in the laboratories are lacking or fragmented;
8. Non-performance QC (disks and media) regularly; and
9. Lack of LIS that permits efficient and reliable transfer of data to the national AMR surveillance system.

The functional model of early implementation of AMR surveillance was concurred as follows:

- The goal of AMR surveillance system in Pakistan is to minimize the spread and reduce the impact of AMR on the health of the population of the country through provision of quality-assured and timely data.
- The objectives are to:
   o Detect outbreaks of infection with resistant pathogens and monitor effectiveness of the response;
   o Determine resistance patterns in different provinces of the country and provide an evidence base for development of policies and clinical practice guidelines as well as strategic and operational planning;
   o Develop local antibiograms to facilitate knowledge-based selection of antibiotics for treatment of patients to improve clinical outcomes;
   o Provide evidence for selecting antibiotics for inclusion in the national Essential Medicines List (national drug formulary); and

o Provide knowledge base for AMR advocacy and awareness campaigns in various groups.

Structure and working modalities of the AMR surveillance network during the early implementation needs to be as follows:

- Sentinel sites (in early implementation stage: three for Sindh Province and two for Punjab Province) will generate and report data to the Provincial Coordinating Centers (PCC), which will collate and analyze the data and report collated data to the National Coordinating Centre (NCC), while the National Reference Laboratory (NRL) will provide technical supportive supervision and (possibly) organize an external quality assessment program (EQA) for the participating laboratories.
- Sentinel sites include: in Lahore, Punjab Province – Shaikh Zayed Hospital and Mayo Hospital, In Karachi, Sindh Province – Aga Khan University Hospital, Civil Hospital and JPMC.
- Provincial Coordination Centers (PCCs) – considering the size of the populations of the provinces and as the Diseases surveillance and response units in the DG Offices in Lahore and Karachi are functioning, the said office will act as the PCC;
- Considering the roles and functions of the NIH, and as the national focal point for AMR it should carry out the role of the National Coordination center (NCC);
- NIH is in the best position to act as the National reference laboratory (NRL);
- While NIH would monitor the performance of laboratories in the early implementation phase, as the number of surveillance sites increased, having a provincial reference laboratory (PRL) for overseeing the testing in each province becomes necessary. It was discussed and agreed that no laboratory in either province currently has the capacity to serve as a PRL; therefore, NIH will identify candidate PRLs and target them for strengthening and capacity building activities.
- The WHONET software package is the most likely system to be used for data storage, analysis and sharing. The software is currently undergoing modifications by the developers to make it compatible with GLASS requirements. Training for users in laboratories and coordinating centers can be organized as necessary. It is highly desirable to avoid the need for double data entry and increasing the workload for laboratory workers.

The next steps were outlined as the following:

- AMR surveillance protocols to be developed;
- Inclusion of infections with resistant pathogens in the notifiable disease lists;
- Detailed assessment of participating laboratories ;
- Training of laboratories in Laboratory Quality Management System (LQMS);
- Training of PCC and NCC staff on data management by FELTP;
- Specialized training on WHONET;
- AMR surveillance protocols to be developed;
- Centers participating in early implementation could serve as hubs for gradual expansion; and
- Develop a plan for rolling out the AMR surveillance to include other provinces/areas.

Debriefing

The mission found the opportunity to have a short but productive debriefing meeting with Dr. Assad Hafeez, Director General Health, Ministry of National Health Services Regulation and Coordination. During this meeting, the concept and principles of early implementation of the GLASS, overview of findings and recommendations of the mission were presented. DG expressed the willingness and commitment of the Ministry of NHSRC, for implementation of the GLASS in selected sites and requested continued WHO technical support in this filed.

Conclusions

Based on the interviews, field reviews and expert opinions during the consultative meeting the mission concluded that there is a high level of commitment and willingness at the national and provincial levels for establishing a national AMR surveillance system. Despite the fact that many of the components needed for AMR surveillance exist, additional work is required for development of the national AMR surveillance system capable of generating quality data for evidence informed national policies, strategies and plans and contributing to the GLASS.

Meanwhile, there is a need to strengthen the culture of quality, data sharing and evidence informed planning at all levels.

Decentralization is an opportunity for a bottom up planning that takes into consideration local priorities. At the same time it emphasizes the critical importance of the national coordination mechanisms. Commitment to contribute to the international health, implementation of WHA resolution, implementation of the IHR (2005), availability of trained HR and presence of major partners in the country are treasurable opportunities. In addition, the reform of disease surveillance under way will provide an excellent opportunity for early implementation of national AMR surveillance.

Recommendations

The capacity review mission team recommends that the National and provincial health authorities:

- Provide sustained support and coordination for AMR surveillance ensuring enabling environments for generation and reporting of good quality national data on AMR in a timely manner;
- Join the WHO invitation to participate in GLASS upon the open call on the WHO website. The announcement is expected early 2016. WHO EMRO will communicate the link as soon as available;
- Develop a National Plan for early implementation of the GLASS in Pakistan. The plan needs to be built upon the available capacities in the provinces and contain strategies for monitoring the progress and gradual expansion of the GLASS to other provinces. It is crucial that the local context in provinces and the recommended road-map by participating sites are taken into consideration; and

Develop an evidence-informed national action plan on AMR through a participatory consultative process. Current activities for developing a national AMR strategy should be harmonized with the relevant WHA resolutions and WHO Guidelines.

Annex I: Country Situation
Part I. Country Health Profile

General	Value	References/ Source
Total population	184.5 Million	PDHS 2013
Population living in urban areas (%)	37.9	PDHS 2013
Gross national income per capita (PPP international $)	5,110	World Bank

Mortality and burden of diseases	Value	References/ Source
Life expectancy at birth m/f (years)	Y=2012-13 M=64.6 F=66.5	PDHS 2013
Adult mortality rate (per 1 000 adults 15-59 yrs)	204	World Health Statistics 2007
Under-5 mortality rate (per 1 000 live births)	89 deaths	PDHS 2013
Maternal mortality ratio (per 100 000 liver births)	170	WHO
Prevalence of HIV (per 1000 adults 15-49 yrs)	0.1	WB
Prevalence of tuberculosis (per 100 000 population)	275	WB
Distribution of years of life lost by communicable diseases (%)	55	WHO
Distribution of causes of deaths in children under-5 (%)		
1. Prematurity	9.2	PDHS 2006-07
2. Congenital abnormalities	4.0	PDHS 2006-07
3. Birth asphyxia	22.1	PDHS 2006-07
4. Neonatal sepsis	14.2	PDHS 2006-07
5. Pneumonia	13.3	PDHS 2006-07
6. Diarrhea	10.8	PDHS 2006-07
7. Malaria	<1	WHO
8. Measles	1.7	PDHS 2006-07
9. Injuries	2.4	PDHS 2006-07

Health Expenditure	Value	References/ Source
Total expenditure on health per capita (Intl $, 2009)	64	WHO
Total expenditure on health as % of GDP (2009)		
Total health expenditure (THE) % Gross Domestic Product (GDP)	2.9	NHA
External resources on health as % of THE		
General government expenditure on health (GGHE) as % of THE	30.0	WHO
Private expenditure on health (PvtHE) as % of THE	70.3	NHA
GGHE as % of General government expenditure		
Out of pocket expenditure as % of PvtHE	82.4	NHA
Private insurance as % of PvtHE	Not Available	
Prevention and public health services as % of THE	Not Available	
General government expenditure on health / cap x-rate	Not	

	Available	
Hospital beds (per 10 000 population)	**20**	**WHO**
Median availability of selected generic medicines (%) - Public	**3.3**	**UN data**
Median availability of selected generic medicines (%) - Private	**31.3**	**UN data**

Utilization of health services	Value	References/ Source
Contraceptive prevalence	**35**	**UNICEF**
Antenatal care (4+ visits)	**37**	**UNICEF**
Births attended by skilled health personnel	**52.1**	**UNICEF**
Measles immunization in 1-year-plds	**61**	**WHO**
Smear-positive TB treatment success	**91**	**WHO**

Health workforce	Value	References/ Source
Physicians per 10 000 population	**7.8**	**WHO**
Nurses & midwives per 10 000 population	**3.8**	**WHO**
Licensed pharmacists (all sectors) per 10 000 population	**0.61**	**WHS**
Pharmacists in the public sector per 10 000 population	**0.092**	**WHS**
Pharmaceutical technicians and assistants (all sectors) per 10 000 population	**1.22**	**WHS**
Hospitals per 10 000 population	**0.058**	**WHS**
Primary health care units and centers	**0.33**	**WHS**
Licensed pharmacies	**0.43**	**World Health Statistics**

Part II. IHR National Capacity Monitoring Tool

Program	Value	References/ Source
Has a monitoring system for antimicrobial resistance been implemented, with data on the magnitude and trends available?	**No**	
Has a national Programme for protecting health care workers been implemented?	**No**	

Part III. Pharmaceutical Sector Country Profile

National Pharmaceutical Policy (KNPP)	Covered (Yes/No)	References/ Source
KNPP has been developed	**Yes**	**Pakistan, Pharmaceutical Country Profile**
Areas of policy covered by National Pharmaceutical Policy (KNPP)	**Yes**	**PPCP**
• Selection of essential medicines	**Yes**	**PPCP**
• Medicines financing	**No**	**PPCP**
• Medicines pricing	**Yes**	**PPCP**
• Medicines procurement	**Yes**	**PPCP**
• Medicines distribution	**Yes**	**PPCP**
• Medicines regulation	**Yes**	**PPCP**
• Pharmacovigilance	**Yes**	**PPCP**
• Rational use of medicines	**Yes**	**PPCP**

	Covered (Yes/No)	References/ Source
• Human resource development	**Yes**	**PPCP**
• Research	**Yes**	**PPCP**
• Monitoring and evaluation	**Yes**	**PPCP**
• Traditional Medicine	**Yes**	**PPCP**

Regulations	**Covered (Yes/No)**	**References/ Source**
Medicines Regulatory Authority (MRA)	**Yes**	**PPCP**
Legal provisions require that all pharmaceutical products on the market receive marketing authorization (registration).	**Yes**	**PPCP**
Legal provisions exist allowing for the appointment of government pharmaceutical inspectors	**Yes**	**PPCP**
Legal provisions requiring authorization to import medicines	**Yes**	**PPCP**
Legal provisions requiring that manufacturers are licensed	**Yes**	**PPCP**
Guidelines on Good Manufacturing Practices		
Legal provisions for controlling the pharmaceutical market	**Yes**	**PPCP**
A national laboratory for Quality Control testing	**Yes**	**PPCP**
Legal provisions to control the promotion and/or advertising of prescription medicines	**Yes**	**PPCP**
Legal provisions requiring authorization for conducting Clinical Trials by the MRA	**Yes**	**PPCP**
Legal provisions in the Medicines Act that provide for pharmacovigilance activities as part of the MRA mandate	**Unknown**	

Medicines Financing	**Covered (Yes/No)**	**References/ Source**
A public programme exists providing free medicines for:		
• All diseases in the EML	**Yes**	**PPCP**
• Any non-communicable diseases	**Yes**	**PPCP**
• Malaria	**Yes**	**PPCP**
• Tuberculosis	**Yes**	**PPCP**
• Sexually transmitted diseases	**Yes**	**PPCP**
• HIV/AIDS	**Yes**	**PPCP**
• Expanded Program on Immunization (EPI) vaccines for children	**Yes**	**PPCP**

Selection and rational use of medicines	**Covered (Yes/No)**	**References/ Source**
National Standard Treatment Guidelines (STGs) for the most common illnesses exists	**Yes**	**PPCP**
• STGs has been updated in last two years	**Yes**	**PPCP**
• A National Essential Medicines List (EML) exists	**Yes**	**PPCP**
• EML has been updated in the last two years	**Yes**	**PPCP**
• Number of medicines listed in the EML	**345**	**PPCP**
• Number of antibiotics listed in the EML		
• A written process for selecting the medicines on the EML	**Unknown**	
• A public national medicines information centre exists	**No**	**PPCP**
• A public education campaign on rational medicine use topics has been conducted by the country in the last two years	**No**	**PPCP**
• A national medicines and therapeutics committee, involving	**No**	**PPCP**

government, civil society, and professional bodies, to monitor and promote rational use of medicines exist		

Prescribing	Covered (Yes/No)	References/ Source
Legal provisions that govern the licensing of prescribers exist	**Yes**	**PPCP**
Legal provisions that govern the prescribing practices of prescribers exist	**Yes**	**PPCP**
Legislation exists to restrict dispensing by prescribers	**No**	**PPCP**
Regulations require hospitals to establish Drug and Therapeutics Committees (DTCs)	**No**	**PPCP**
An average of number of medicines prescribed per patient in public health facilities	**2.85**	**PPCP**
Proportion of patients treated in public health care facilities received antibiotics (%)		

Dispensing	Covered (Yes/No)	References/ Source
Legislation governing the dispensing practices of pharmaceutical personnel exist	**Yes**	**PPCP**

Governance of Antimicrobial Resistance	Covered (Yes/No)	References/ Source
Does the country have a National AMR Focal Point?	Yes	Ministry of NHSRC
Is the Focal Point appointed by the HM (or equivalent)?	Yes	
Is there a written TOR for the AMR NFP?	No	
Is there a national multi-sectorial coordination mechanism established? (if yes please attach list of the members and their affiliations)	Yes	
Has the National coordination mechanism met? (if yes please attach the MoM)	No	
Are there AMR activities included in the WHO Program of Collaboration with the country for 2016-17? (if yes, please attach the plan).	Yes	WHO may provide details

Part IV. Other information

Review on existing survey or study of other international organizations.

N/A

References:

1. Pakistan Demographic Health Survey 2012_13
2. World Bank Data, (data.worldbank.org)
3. World Health Statistics 2007
4. World Health Organization
5. Pakistan Demographic Health Survey 2006_07
6. National Health Accounts for Pakistan 2009_10, www.pbs.gov.pk/content/national-health-accounts-pakistan-2009-10
7. United Nation Data, http://data.un.org/
8. UNICEF, www.unicef.org/pakistan
9. Pakistan, Pharmaceutical Country Profile, http://www.who.int/medicines/areas/coordination/pakistan.pdf

Annex II: People met (in alphabetic order)

Dr. Aamir Nazir, Additional Director, TB, DG Health offices, Lahore

Dr. Afia Afzal, Professor, AKUH, Karachi

Dr. Amjad Shehzad, Director General Health Services Punjab

Dr. Bilal Munir Ahmad, Sr. Biochemist, Mayo Hospital, Lahore

Dr. Erum Khan, Section Head, Microbiology, AKHU, Karachi

Dr. Farnaz Niaz Rathore, Executive Director, National Institute of Health, Chak Shahzad, Islamabad

Prof. Farrukh Iqbal, Professor of medicine and Deputy Dean, Shaikh Zayed Hospital, Lahore

Dr. Ghulam Fatima, Head Laboratory and Senior Consultant Pathologist, Civil Hospital Karachi

Dr. Hassan Orooj, Chief/Director, Public Health, Islamabad

Dr. Ijaz Khan, Infectious Disease specialist, Shifa Hospital, Islamabad

Dr. Jalis Khalid Khan, AP. King Edward Medical University, Mayo Hospital, Lahore

Dr. Jamil Tahir, Deputy Administrator, Shaikh Zayed Hospital, Lahore

Dr. M Usman, Consultant Microbiologist, Shifa hospital, Islamabad

Dr. Masood Anwar, Director, DHIS Lahore

Prof. Mateen Izhar, Head of Division of Pathology, Shaikh Zayed Hospital, Lahore

Dr. Naeem Lone, APMO Mayo Hospital, Lahore

Dr. Naila Tariq, Head of Pathology Department and Assistant Professor, Basic Medical Sciences Institute, JPMC Karachi

Dr. Rana Jawad Asghar, Director, FELTP/CDC Resident Advisor, Islamabad

Dr. Rumina Hassan, Clinical Microbiology, AKUH, Karachi

Dr. Sabeen Afzal, Deputy Director Programs, Ministry of National Health Services Regulation and Coordination

Dr. Saeed Ahmed Mangnejo, Secretary Health Sindh

Dr. Tayyaba Ijaz, Sr. Microbiologist, Mayo Hospital, Lahore

Annex III: Program of the visit.

Timing	Activity	By
22 November 2015		
14:00-16:00	• Introductions and Internal meeting • Discuss the program of the visit • Preliminary information on the arrangements	*Mission members, WHO staff and AMR NFP*
23 November 2015		
08:30-09:00	• Briefing with the WHO Representative (Internal)	*Mission members[4]*
09:00-09:30	• Security brief	•

09:00-11:00	• Briefing by the national team on:
	   o Current National Disease surveillance system: capacities
	   o AMR Surveillance
	   o NIH (potential NCC)
	• Laboratory setup in the country
		• *Mission members*
		
		• *National counterparts*

11:00-12:00	• Meeting with DG Health, officials of MO NHSR&C, FELTP and briefing on:
	   o AMR Resolutions,
	   o National Action Plans,
	   o Global AMR Surveillance System (GLASS)
	• Expectations from the mission
		Mission Members

12:00-13:00	Break	
13:00-15:00	Visiting Potential NCC (NIH Islamabad) and Potential NRL (NIH)	*Assessment tea 1[5]*
15:00-15:30	Internal Meeting of the Mission members	*Mission members*
15:30	Travel to Karachi, and Lahore (subject clearance of UNDSS) ***Lahore team by Road leave latest by 15:30*** ***Karachi team by air 19:00***	
24 November 2015 (team divides into two: program for visiting Lahore and Karachi)		
08:30-09:30	• Meeting with Provincial Health Authorities at the provincial DG / Secretary Health Offices: - Disease surveillance system at the provincial level - AMR Surveillance at the provincial level - Laboratories systems at the provincial level • Mission objectives and methods	*Assessment team*
09:30-10:30	• Meeting with representatives of potential surveillance site in provinces ***(Civil, JPMC, AKUH in Karachi)***	*Assessment team1*

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[4] Mission members are the WHO staff and International consultants
[5] Assessment team is a team composed of internationals and national counterparts. The team will divide into two while assessing NIH capacities for GLASS

Timing	Activity	By
10:30-12:30	• Visiting potential Provincial reference laboratory **(AKUH in Karachi, Mayo Lahore???)**	*Assessment team*
12:30-13:30	• Break	
13:30-15:00	• Visiting potential Surveillance Site #1**(JPMC hospital Karachi, Jinnah Lahore)**	*Assessment team*
15:00-16:30	• Visiting Surveillance Site #2 **(civil hospital Karachi, Shaikh Zaid Lahore)**	*Assessment team*
25 November 2015		
07:00-12:00	• Return to Islamabad (Lahore team by road and Karachi team by air)	*Assessment team*
12:30-13:30	• Meeting of the mission members to discuss the findings at the filed	*Mission members*
13:30-15:00	• Visiting Surveillance Site #1 and #2 in Islamabad	*Assessment team*
15:30-16:30	• Consolidation of the findings: - Available Capacities - Gap analysis	*Assessment team*
26 November 2015		
08:30-12:30	• Drafting the outline of a roadmap for establishing the AMR Surveillance System in Pakistan based on the findings	*Assessment team*
12:30-13:30	• Break	
13:30-17:30	• Continue with drafting the outline of the Roadmap Preparing the debriefing materials for next day	*Assessment team*
27 November 2015		
09:00-11:00	• Debriefing with the WR (internal)	*Mission members*
11:00-12:30	• Debriefing meeting with the National authorities at NIH (DG Health, ED- NIH, MO NHSR&C and FELTP Officials, NCC officials)	*WR and the Mission members*
12:30-13:30	• Break	
13:30-16:30	• Developing the draft mission report	*Assessment team*
28 November 2015		
09:00-12:00	Developing the draft mission report	*Mission members*
12:00-13:00	Present the report to the WR for approval	*Mission members*

Annex IV: Names of the mission members

- NIH Pakistan:
  - Dr Muhammad Salman, AMR National Focal Point for Human Health
  - Dr Jameel Ansari, Scientific Officer, Field Epidemiology and Disease Surveillance National Institute of Health, Chak Shahzad Islamabad
- WHO:
  - Regional Office:
    - Dr Alireza Mafi (AMR Regional Focal Point, PED/DCD/EMRO/WHO)
    - Dr Karen Nahapetyan (Scientist, PHL/DCD/EMRO/WHO)
  - HQ:
    - Dr Christopher Oxenford (Technical Officer, CAD /GCR/HSE/HQ/WHO)
    - Dr Kenth Peter Ulleryd (AIP/PED/HSE/HQ/WHO)
  - Country Office:
    - Dr Musa Rahim (Medical Officer, WRO Pakistan)
    - Dr Sara Salman, Operations Officer (acting) WHO Sub Office, Karachi
    - Dr Jamshaid Ahmed, National Program Officer Surveillance, Head of Office (de-interim), Punjab

Participants to the Stakeholders Meeting for Developing a Road-map for Early Implementation of the Global Antimicrobial Resistance Surveillance System in Pakistan

26 November 2015