Laboratory informatics capacity is a neglected component of effective antimicrobial resistance surveillance in resource-limited settings

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Summary

Antimicrobial resistance (AMR) is a major threat to human health globally. Surveillance is a key activity to determine AMR burden, impacts, and trends and to monitor effects of interventions. Surveillance systems require efficient capture and onward transmission of high-quality laboratory data. Significant investment is being made to improve laboratory capacity, particularly in high disease burden low- and middle-income countries (LMIC). However, building capacity for effective laboratory data management remains an under-resourced area which, unless addressed, will limit progress towards comprehensive AMR surveillance in LMICs. The lack of fit-for-purpose and open-source laboratory information management system (LIMS) software is of particular concern. In this Personal View we summarise the technical requirements for microbiology laboratory data management, provide a snapshot of the current state of affairs in LMIC laboratories, and describe the key steps required to improve the situation. Without action to improve microbiology laboratory IT infrastructure and data management systems, the on-going efforts to develop capacity for AMR surveillance in LMICs may not realise their full potential.

Key words

Antimicrobial resistance; surveillance; microbiology; data; informatics

Antimicrobial resistance surveillance and the under-recognised challenge of microbiology data management

Surveillance is a cornerstone of global antimicrobial resistance (AMR) containment and control activities.[1] High quality surveillance is critical for the estimation of AMR burden, trends over time, and impact of interventions. These themes are echoed in the specific objectives of the World Health Organization Global Antimicrobial Resistance Surveillance System (WHO-GLASS).[2] Importantly, in the human health sector, AMR surveillance data can be used to inform empiric treatment guidelines which is, alongside confirmation of individual patient infection, arguably the most important function of clinical microbiology data.[3] An ideal AMR surveillance system would include both clinical and laboratory data,[4] although many surveillance systems remain predominantly laboratory focused.[5] The complex flow of data through a human infection-focussed AMR surveillance system is summarised in Figure 1, which highlights the centrality of microbiology laboratory data capture, collation, and transmission.

Unfortunately, it remains challenging for many countries to generate and submit high quality, population representative data to international AMR surveillance systems.[6] These challenges are often greatest in low- and middle-income countries (LMICs) where healthcare resources are limited but the burden of AMR is estimated to be high.[7,8] Ideally, AMR surveillance data should be generated by accredited, or at least quality-assured, laboratories. In recognition of the technical, logistical, and human resource issues associated with provision of quality-assured microbiology data, there are many international initiatives currently aimed at improving the number and technical capability of diagnostic microbiology laboratories in LMICs (e.g. the UK Department of Health and Social Care / UKaid Fleming Fund[9]). However, one area of laboratory strengthening that has consistently been neglected and remains under resourced is that of data management.[10]

In this Personal View we summarise the technical requirements for microbiology laboratory data management, provide a snapshot of the current state of affairs in LMIC laboratories, and describe the urgent next steps required to improve the situation.

What is needed for microbiology laboratory data management?

A comprehensive review recently summarised the informatics requirements for diagnostic microbiology laboratories in general.[11] Several requirements are unique to microbiology and require a considerably more complex system design than is typically necessary for the blood sciences. Multiple results are generated per specimen and tests are added dynamically based on initial microscopic and culture findings. Result reporting is complex, e.g. antimicrobial susceptibility (AST) data with multiple reference ranges depending on bug-drug

combination, and both preliminary and final reports must be generated and retained (Figure 1). Bacterial nomenclature changes over time, as new species are identified and existing ones are reclassified based on newly generated sequence data. There is also the requirement for periodic generation of antibiograms, i.e. institution-level summary resistance profiles for key bacterial species to aid empiric treatment decision-making. In addition to these unique requirements for microbiology, a LIMS should support data quality management activities, including monitoring of quality control data, specimen numbers and workflow, and test turnaround times. Technical standards and functional requirements for LIMS have been developed by ASTM International.[12] For unambiguous transmission of results and onward data sharing, storage of laboratory data in standardised formats is desirable. The various terminology systems in current use include Logical Observation Identifiers Names and Codes (LOINC)[13] for laboratory tests, Systematized Nomenclature of Medicine (SNOMED)[14] for test results, and the Health Level Seven (HL7)[15] format for data transmission. Unfortunately, not all these systems and standards documents are freely available, which may limit their use.

A recent general review of laboratory medicine in LMICs commented that "examples of the successful implementation of laboratory information systems in LMICs are scarce".[16] High costs of commercial LIMS systems and lack of IT infrastructure were cited as major barriers to implementation. The authors highlighted the limitations of current open source LIMS. These limitations included lack of local IT systems capacity and human resources for implementation, inadequate support, and poor standardisation. They noted that "the creation of a free open sourced laboratory information system that is appropriate for an LMIC context would provide substantial benefits for global pathology integration". Many LMIC microbiology laboratories use WHONET, an excellent freely available and widely used system for capture, analysis, and sharing of AMR data in a standardised format.[17] Data import into WHONET can be semi-automated using the add-on BacLink software, which allows for import from other data files, e.g. text files exported from a LIMS or directly from a laboratory instrument. However, WHONET intentionally provides only a solution for basic laboratory specimen management and result reporting but does not have comprehensive LIMS functionality. For example, it is difficult to generate individual patient level data for clinical microbiology liaison work. Furthermore, WHONET has proved difficult to implement in LMICs lacking IT capacity.

AMR surveillance stakeholders in South East Asia reviewed recently the informatics requirements for collection, storage, quality assessment, and transfer of data from site to central level for analysis.[18] They reflected on the limited open-source software tool options that are available currently and emphasised the need for support and capacity building. The authors highlighted the potential difficulties in configuration of

WHONET and analysis / report generation in the LMIC context and mentioned how web-based apps may help in settings with weak IT capacity. A subsequent review of electronic infectious disease and AMR surveillance systems summarised 110 studies and noted that very few systems include regular results reporting.[19] This latter point highlights a critical failing of some surveillance at the local level: i.e. the upward transmission of data is the dominant activity and generation of locally usable results is frequently inadequate.

A snapshot of the current status of microbiology data management in LMICs

In 2018, the Surveillance and Epidemiology of Drug-resistant Infections Consortium (SEDRIC)[20] established a working group to identify priority areas for research to improve patient-centred surveillance of drug-resistant infections (DRI) in LMICs and to propose where informatics technology could accelerate progress. One activity implemented by the working group was an online survey to collect information on current laboratory data management practices. The intention was to capture one response per laboratory from 50 – 100 diagnostic microbiology laboratories in LMICs. Sampling was purposive, with links to the survey sent out via email to organisations and colleagues known to be working in, or associated with, such laboratories.

Between 5th March and 29th April 2019, 55 survey responses were received, with 49 usable responses remaining after cleaning (removal of blank responses [n=3], data from non-LMIC laboratories [n=2], and duplicates [n=1]). Responses were received from 19 countries: nine African, eight Asian, and two South American (Table 1). Almost two-thirds (30/49; 61%) of responses were from government / public laboratories. Over 90% (45/49) of laboratories provided patient diagnostic services, with 28 (57%) reporting involvement in research work, and 26 (53%) providing reference laboratory services. Two-thirds (31/49; 63%) of laboratories were located within a hospital or clinic, 22% (11/49) within a university or research institute, 12% (6/49) in a public health institute, and one laboratory was a standalone organisation. All but three laboratories reported participation in a surveillance system, most commonly a national Ministry of Health system (33/49). Overall data management features are summarised in Table 1. Amongst 15 laboratories using a dedicated LIMS, five (42%) were commercial systems, four (33%) were systems developed in-house and three (25%) were free or open-source systems (all the Basic Laboratory Information System, BLIS[21]). Fewer than half of the LIMS systems (5/12, 42%) could integrate with laboratory instruments. Around half (6/11; 55%) could be accessed directly by clinicians for result queries. LIMS were used for local data analyses in 8/13 (62%) cases. Laboratories reporting use of a LIMS were located in Argentina, Cambodia, Ghana, Kenya, Malawi, Malaysia, Mozambique, Nepal, Thailand, and Vietnam. There were 18 laboratories where WHONET was used. Manual data entry was done in 16/18 laboratories (nine completely manual; seven manual and BacLink combined), with

only two laboratories doing fully automated data capture via BacLink. Two-thirds (12/18) of laboratories used WHONET for local data analyses and half of the laboratories shared their WHONET data externally.

Following the survey, working group members commented that, in their experience, current low-cost / open source LIMS are frequently inadequate for robust management of AST data. The working group also noted difficulties managing manual data entry in high throughput laboratories, where >1,000 specimens may be received per day. These difficulties were felt to be compounded if additional data entry is required for surveillance (e.g. where automated import of data into WHONET cannot be set up).

Thus, it is clear that microbiology laboratory data management in LMICs is relatively heterogeneous, but paper-based request, report, and storage systems remain commonplace. Only around half of the laboratories surveyed used a dedicated LIMS or WHONET as the primary system for laboratory data storage. This may well be an over-estimate of the general situation given the number of research laboratories included in the survey. The LIMS systems in use often appeared to have limited functionality and/or documentation. IT infrastructure, software and hardware costs, and human resources are cited as barriers to deployment of more fit-for-purpose LIMS. A recent description of design and implementation of a new LIMS in Malawi, based on an existing free / open source LIMS software package, highlights some of these challenges.[22]

The pressing need for a fit-for-purpose microbiology LIMS for LMICs

We believe that laboratory data management solutions for LMICs require urgent attention and, more specifically, that development of a fit-for-purpose microbiology LIMS is required. Whilst WHONET is an entirely functional and useful repository for microbiology data and critically outputs standardised shareable data files, it does not provide full LIMS functionality. Unfortunately, there appear to be few alternate systems that are either affordable or functionally appropriate for microbiology laboratories in resource-limited settings. Whilst current prices for LIMS are not readily accessible via the internet, a review of 26 systems from 2008 quotes minimum initial software costs of US$1,500 to US$250,000 (median US$25,000).[23] The functionality provided by a fully-fledged LIMS will be required as the technical capacity and operational complexity of LMIC microbiology laboratories develops. For example, it is desirable to be able to manage specimen workflow from specimen request to report via the LIMS and these workflows should be customisable. Inclusion of an audit trail and electronic validation of results prior to reporting are important quality management functions. Management of interpretative criteria for AST result reporting should be built in. Although use of a LIMS does not reduce reporting bias in surveillance (or solve other issues around generating appropriately representative

surveillance data), it will improve the ready availability of relevant quality-managed data without the need for repeat data entry.

A new LIMS should be open-source and available without cost, must balance the need for comprehensiveness with LMIC IT and laboratory resources, should be provided with full user documentation, and have a clear plan for on-going development and support. A modular and scalable design will be necessary to ensure the system can be implemented in a wide range of settings. Core modules / functions include user management; patient, specimen, culture and AST data capture; result validation and reporting; data export; and quality management. Optional modules / functions include integration with laboratory instruments (e.g. automated blood culture, bacterial identification, and antimicrobial testing instruments); molecular test data management; reagent and consumable management; remote report viewing (e.g. ward / clinician level); billing; and linkage with electronic patient records and infection control / clinical surveillance systems. Versions that can be run from a single workstation, a local server, or a cloud-based server will be desirable as will the capability for tablet-based data entry. Training, support, and in-built analysis and visualisation tools must be intuitive and user friendly. Output of data must be user configurable and compatible with existing and planned global surveillance systems. In particular, compatibility with WHONET will be essential. Input and support from countries and large-scale funders will be necessary to ensure that this critical component of AMR surveillance is implemented widely. Tied to the development of the LIMS will be the requirement to build necessary local / national IT infrastructure and ensure that there are the human resources to maintain the system. Linkage to existing IT development projects, e.g. implementation of health information systems, may be an efficient way to do this.

The District Health Information Software 2 (DHIS2) provides a precedent for such an ambitious IT development project specifically targeting LMIC settings.[24] This open source modular health management information system, developed and managed by the Health Information Systems Program (HISP, University of Oslo), is widely used by Ministries of Health for capture and analysis of a range of heath data.[25] Key strengths of the system include comprehensive support and local capacity building via HISP and the extensive interoperability provided. One example of the latter is integration of AMR surveillance data from WHONET via middleware developed as part of the FIND AMR connectivity project (AMR Cx).[26] Funding for on-going development and support comes from a range of sources including the Bill and Melinda Gates Foundation, GAVI, the Global Fund, Norwegian Agency for Development Cooperation (Norad), and WHO. However,

despite the many positives of DHIS2, human resource and IT capacity can be challenges to successful implementation.[27,28]

Following a recommendation from SEDRIC and a roundtable "Data form Surveillance in Health" meeting held in October 2019,[29] it is encouraging that the Wellcome Trust have recently funded an initial 18-month LIMS development and pilot implementation project. Broad stakeholder engagement will be a major component of this project, to ensure post-pilot uptake, along with development of a plan for sustainable support and on-going development.

Conclusion

In summary, we have demonstrated the complexity of microbiology laboratory data and the tools required to manage it effectively. To ensure that the substantial on-going efforts to develop capacity for AMR surveillance in LMICs realise their full potential, urgent investment in laboratory IT infrastructure and data management systems is required.

Contributors

EAA and PT conceived the work. EAA, NAF, WJ, JAO, SJP, PR, and PT participated in working group meetings where the subject matter was discussed. PT analysed the survey data. PT and EAA prepared the first manuscript draft. All authors reviewed, revised, and approved the final manuscript.

Declaration of interest

PT and NAF are members of the steering committee for the Wellcome LIMS project. All other authors have no conflicts of interest to declare.

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Tables

Table 1. Key findings from a low- and middle-income country laboratory data management survey

Survey area	Number (%) of laboratories
Region	
Africa	Nigeria (6), Ghana (6), South Africa (2), Malawi (2), Burkina Faso (1), DR Congo (1), Kenya (1), Mozambique (1), Zimbabwe (1)
Asia	India (5), Myanmar (4), Cambodia (3), Malaysia (3), Nepal (3), Thailand (3), Lao PDR (2), Vietnam (2)
South America	Argentina (2), Brazil (1)
Test requesting capability*	49 responses
Paper-based	42 (86)
Electronic	12 (24)
Result reporting capability*	49 responses
Hand-written report	18 (37)
Computer-generated paper report	30 (61)
Electronic report	14 (3)
Data management†	47 responses
Paper-based	
All results	36 (77)
Some results	9 (19)
None	2 (4)
Electronic	
All results	22 (47)
Some results	21 (45)
None	4 (8)
Electronic data management solutions	43 laboratories
Dedicated LIMS‡	15 (35)
Microsoft Excel	10 (23)
WHONET	7 (16)
Microsoft Access	5 (12)
Other	6 (14)

*Multiple options were possible, hence totals > number of responses
†The proportion of results captured by paper and/or electronic systems
‡Laboratory information management system

Figures

Figure 1. Antimicrobial resistance surveillance data flow, from patient specimen to global situation report

The centre panel documents the laboratory workflow. In the example shown, a swab has a Gram stain and is cultured onto three solid culture media. Three potential pathogens are isolated and identified (the coloured tubes represent biochemical identification tests and the bar graphs represent identification by MALDI-ToF mass spectrometry). Finally, antimicrobial susceptibility tests are performed on the two organisms confirmed as pathogenic species. Data from all of these steps should be recorded in the laboratory information management system and reports issued at each stage.