Coping with Emerging Infectious Diseases: Experience from the East Africa Public Health Laboratory Networking–Operational Research Project in Kenya

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The East Africa Public Health Laboratory Networking Project (EAPHLNP) is a regional project involving five East African countries, Namely: Burundi, Kenya, Rwanda, Uganda and Tanzania and it is supported by the World Bank.

Introduction

In the global picture according to the National Institute of Allergy and Infectious Diseases, emerging infectious diseases are commonly defined as outbreaks of previously unknown diseases or known diseases that are rapidly increasing in incidence or geographic range in the last 2 decades. These diseases include Ebola, HIV infections, SARS, Lyme disease, *Escherichia coli* E. (*coli*) O157:H7, Hantavirus, *dengue fever,* and West Nile virus to name a few.

Emerging infectious diseases are categorized into 4 categories based on the nature and characteristics of infectious agents that cause the emerging infections. These are:

(a) Known pathogens occur in new niches(i.e *chikungunya* virus)

(b) Known pathogens of new biologic phenotypes(Drug-resistant strains)

(c) Novel infectious pathogens *(Ebola virus)*

(d) Known disease of unknown etiology due to 'unrecognized' pathogens (*Helicobacter pylor*). Combinations of 6 factors provide these categories which include:

(i) changes in human demographics and behavior;

(ii) advances in technology and changes in industry practices

(iii) economic development and changes in land use patterns

(iv) dramatic increases in volume and speed of international travel and commerce

(v) microbial mutation and adaptation

vi) inadequate public health capacity.

The environmental public health and laboratory biosafety implications of these pathogens are of major concern [1, 2, 3].

Re-emerging diseases are those that appear after they have been on a significant decline. Re-emergence may happen because of a breakdown in public health measures for diseases that were once under control. It can also happen when new strains of known pathogens appear.

Human behavior affects re-emergence. For example, overuse of antibiotics has led to drug-resistant pathogens and allowed a return of diseases that once were treatable and controllable. Reemerging diseases include malaria where drug-resistant Plasmodium strains are

widespread, as are insecticide-resistant strains of the mosquitoes that carry the parasites. Others include strains of Multi-Drug Resistant tuberculosis (MDR-TB), cholera, pertussis, influenza, pneumococcal disease, and gonorrhea. Short of fast tracking these strains may hamper effective public health interventions [4, 5, 6].

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In the year 2010, the Ministry of Public Health and Sanitation identified Kenya Medical Research Institute (KEMRI) to take the leading role in the coordination of Operational Research (OR) activities in this project within Kenya and other East African member states.

KEMRI established a secretariat as a coordination body both in Kenya and regionally. The rolling-out of the actual OR activities in Kenya started in February 2013. Three thematic areas relating to the global threat of the emerging infectious diseases were addressed in this study.

References

These include:

1. Evaluation of the Impact of New Tuberculosis
2. Diagnostics on Patient Health Outcomes in Kenya;
3. surveillance of common circulating enteric pathogens and their antimicrobial susceptibility patterns in Kenya and evaluation of the efficacy of fixed artemisinin combinations therapy (ACT) [(artemether-lumefantrine) CoArtem® and (*Dihydroartemisinin-piperaquine*) Duo-cotexin®], in patients in Kenya

OR Project Broad Strategic Objectives

(i) To provide oversight and guidance in carrying out the operational research activities under the regional project.

(ii) To facilitate local and regional capacity to carry out operational research and evaluation in medical diagnostics, and involve not only the public health laboratories, but also stakeholders such as research institutions, academic institutions and civil society groups.

Methodology

Rationale for choice of research designs was in line with the project goals as outlined in the broad strategic objectives.

Three research proposals on TB, malaria and enteric were developed and adopted regionally through a carefully guided process by Operational Research (OR) Secretariat at KEMRI.

The TB and Enterics studies necessitated five satellite and five non-satellite sites per country, while for the malaria study, choice of sites depends on endemicity of the disease in each country. The TB study is a prospective quasi-experimental utilizing both qualitative and quantitative methods. This study is being conducted in two phases namely :

1. Validation phase and
2. Quasi-experimental phase.

The Validation Phase

A cross-sectional design involving determination of the diagnostic test values (sensitivity, specificity, positive and negative predictive test values) of combinations of new TB diagnostics including Gene Xpert alone; Optimized Sputum Smear Microscopy (OSSM) commonly known as Lead Emitted Diode-Fluorescent Microscopy (LED-FM) and Gene Xpert;

Gene Xpert ,OSSM, and Mycobacteria Growth Incubation Test(MGIT) vs Ziehl-Neelsen stain (ZN) as bench mark) as well as repeating all the tests that are performed at the study sites using the same samples at the KEMRI TB research laboratory and comparing results to determine reproducibility.

Quasi-Experimental Phase

Which is ongoing, satellite site form the intervention arm where new diagnostic tools including GeneXpert and LED-FM were introduced in a STEP-WISE process (still awaiting for introduction of MGIT), while the non-satellite sites continue with routine TB health care services using microscopy ZN and/or LED-FM (where available) for diagnosis.

The enterics study is cross-sectional to determine prevalence of emerging bacterial enterics pathogens. The study involves identification of emerging resistance of enteric bacterial pathogens as well as molecular phase

for characterization of virulence genes associated with *E.coli* strains.

The malaria study is a two-arm randomized clinical trial. It is a prospective evaluation of clinical and parasitological as well as molecular responses to directly observed treatment for uncomplicated P. falciparum malaria.

Project Achievements

The project has been successfully implemented for the three studies and is ongoing at national and regional level. In this issue, a supplement has been established to document some of the preliminary results from Kenya. Nine topics are included:

Performance of GeneXpert in Kenya is being documented for the first time. Findings indicate that GeneXpert has potential for use in the diagnosis of TB particularly in HIV positive persons presumed to have Tuberculosis [7].

An article on performance of clinical indicators in comparison with laboratory results indicate possibility of using clinical signs and symptoms in routine diagnosis for TB where laboratory diagnosis is not available [8].

It is now evident that sputum specimen quality assessment should be considered as an integral part of routine laboratory diagnosis of TB especially in HIV negative individuals as indicated in an article by Orina *et al* [9].

High proportion of non-adherence to follow up among HIV positive persons presumed to have TB has been shown to be a cause for concern to the national TB program [10].

In addition, there is a diminishing trend of antimicrobial agent to treat cases of enteric bacterial diseases due to resistance to all options of antibiotic available in Kenya.

More so, emergences of *E.coli* pathotype such as Entroheamorhagic *E. Coli* (EHEC) that are associated with severe diarrhea and could be fetal causative agents of Hemolytic uremic syndrome as well as hemorrhagic *colitis* are documented [11].

The malaria study on the efficacy of CoArtem® and Duo-cotexin® has only been conducted in one site and the results will be disseminated later.

Other components that complement OR activities which have been included in the supplement are:

capacity building in OR which involved development of research methodology and scientific writing curriculum and teaching manuals which have facilitated training of clinical and laboratory personnel from the project study sites in Kenya and the region.

Emphasis on the need to strengthen capacity building in operational research, especially at the established project centres of excellence in order to adequately address public health related issues [12].

To fast track OR data capture, application of bar-code technology could facilitate patients' data linkages and verification in a multi-site study leading to increased efficiency and effectiveness in maintaining patient records[13].

Finally, the importance of conducting M&E consistently and timely is emphasized in order to provide opportunities of early identification and correction of any protocol deviations [14].

Lessons Learnt and Way Forward

There were lessons learnt by the OR secretariat both at national and regional level. Overall, multidisciplinary multi-site OR studies can be implemented successfully in partnership with non-research institutions through appropriate planning, initiation, implementation, mentorship programmes and team work.

In addition, constant communication, periodic supervision coupled with efficient data management and M&E programmes will ensure success of the studies. We look forward to the completion of the entire project, both in Kenya and regionally, when findings for all the studies in all participating countries will be compared to inform policy both at national and regional level.

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