How are we responding to the COVID-19 Open Research Challenge? Experiences from South Asia

Introduction

On 23rd April, The Global Health Network (TGHN) supported the virtual open workshop, “How are we responding to the COVID-19 research challenge? Experiences from South Asia”. This workshop contributed to the workshop series on the COVID-19 response from various regions across the globe that are being organized by TGHN at the University of Oxford, UK in partnership with Shaukat Khanum Memorial Cancer Hospital and Research Centre (SKMCH&RC), Pakistan and other collaborating organisations from South Asia. The workshop featured a panel of seven experts including representation from Pakistan, India, Nepal and Bangladesh.

A total of 189 persons registered for the webinar across 24 hours. On the day of the webinar more than 70 participants joined through zoom and 1200+ viewed the session through live streaming via the Facebook page of TGHN, spanning 15 countries in North America, Europe, Middle East and North Africa, South Asia and Australia.

The aim of the webinar was to share our experiences around how South Asia is responding to the COVID-19 challenge focussing in particular on the following:

- How countries are reacting to the outbreak (surveillance, diagnostics, new interventions, prevention, government measures etc.)?
- What are the research gaps that need urgent attention?
- If there are any tools/resources, which could be useful to respond to this scenario?
Organisations Involved

- Shaukat Khanum Memorial Cancer Hospital and Research Centre (SKMCH&RC), Pakistan
- Medanta Institute of Critical Care and Anaesthesiology from Gurgaon, Haryana, India
- Initiative for Non-Communicable Disease, Health Systems and Population Studies Division at ICCRD,B in Bangladesh
- Nepal Public health foundation, Nepal

Summary of Panellist Presentations:

Sharing the experience of joining the WHO SOLIDARITY trial from Pakistan

*Dr Mariam Hassan*

Physician researcher and research administrator at the Shaukat Khanum Memorial Cancer Hospitals and Research Centre (SKMCH&RC) in Pakistan who joined from Lahore, Pakistan.

With an aim to highlight the opportunities and challenges associated with setting up international collaborative research in low and middle-income countries (LMICs), the key points covered in the presentation were:

- COVID-19 has led to massive expansion in the global collaboration for research unlike any in history. However, most of the COVID-19 research activity has been centred in the countries most affected by COVID-19, particularly China and in high-income countries across Europe and North America. Very few trials are being planned in Africa, south and southeast Asia, and Latin America and the Caribbean.
- It was highlighted that most LMICs, including Pakistan, have poor scores for the Health Research Profile indicators (i.e. National research priorities, availability of resources for conducting research, its timely production and dissemination for policy makers). The context within which research operates, such as culture, law and economy, is also not favourable for LMICs thus perpetuating the 10/90 gap in research (less than 10% of global health research expenditure is spent on the health problems of developing countries, which represent more than 90% of the world's burden of preventable mortality)
- With the above context in mind, the experience of setting up the ‘WHO SOLIDARITY trial’ in Pakistan was shared. The pressure COVID-19 places on health systems resulted in the situation whereby the WHO considered the need for speed and scale in trials. The Solidarity trial provides simplified procedures to enable even overloaded hospitals to participate. WHO is facilitating access to thousands of treatment courses for the trial through donations from a number of manufacturers. WHO is also already inviting developers and companies to collaborate, to ensure affordability and availability of the treatment options if they prove to be effective, hence ensuring post trial access which is often a neglected component. This model of ensuring wide representation in research should be pursued for all diseases with high morbidity and mortality in LMICs like Pakistan.
- In Pakistan, the public health crisis led to collaboration between clinical sites in an effort to participate in this trial. The trial set-up involved securing ethics and regulatory approvals, development of site-specific protocols and SOPs, study personnel training & arranging local finances at sites. SKMCH&RC, the national coordinating centre for the trial shared their SOPs and resources with all sites so as to help them during the trial set up. The future goal for us is to enhance the national capacity for clinical research that is relevant to health needs of the country and establishment of robust research networks.
The role of efficient ethical review of outbreak research

Dr Farah Asif  
Clinical research administrator at SKMCH&RC. Secretary to the institutional IRB

- Infectious disease outbreaks require an effective and efficient response which integrates research as part of the outbreak response. This requires careful balance of time and resources allocated to immediate management as well as for research.
- We need to find ways in which all stakeholders including political leadership, scientists, and researchers, as well as regulatory bodies and ethics review boards can act in the most synchronized way which will ensure “ethics preparedness” for research. Previous experiences during outbreaks (Ebola, Lassa fever) have also highlighted the need for ethics preparedness in the form of greater support and guidance to national research ethics committees, to develop practical and effective actions for achieving a robust but rapid research ethics review at the national level.
- With international research collaboration, the possibility for multi-country emergency ethical consultation should be explored and procedures for robust communications between (N)RECs and other key stakeholders should be established.
- Community engagement should also form part of research planning during infectious disease outbreaks.

Rapid enhancement of laboratory capacity for COVID-19 diagnostics in the face of the epidemic

Dr Romena Qazi  
Molecular biologist at SKMCH&RC

- After declaration of the COVID-19 epidemic, the Pakistan Government took several measures including implementation of rapid reliable lab testing capacity via National institute of Health (NIH).
- SKMCH&RC combined the human resource and equipment from both the molecular diagnostic lab as well as the basic science research lab and enhanced the testing capacity to 1100 tests per day in early March 2020. The centre also quickly adopted international validation protocols to validate the analysis via testing kits provided from government as well as those purchased by the hospital. After the pandemic was declared, the demand for increased capacity was met by adopting the 'pooling' strategy that enabled the testing of hundreds of samples in a single batch thus further enhancing the centre’s capacity for testing to about 20,000 tests per day. Shortage of VTM (viral transport medium) was encountered which addressed by preparing in-house VTM, tested for sterility in the microbiology lab and sent to different points for sample collection. All the new reagents and kits were validated before deployed in the lab. In essence, procuring kits, SOPS, training, safety lectures and validations are key steps in setting up a lab. All this can be achieved by keeping calm; planning and most importantly work as a team.
- Dr Romena emphasised the need for research into appropriate COVID-19 diagnostic kits validation techniques for local labs.

Prevention and treatment strategies being used for COVID-19 management in Pakistan

Dr Aun Raza  
Infectious diseases specialist at SKMCH&RC

Dr Aun emphasised the prevention strategies for COVID-19 and shared institutional practices and recommendations for health care workers and the general public. He highlighted that modes of
prevention included vaccines and public health measures including sanitization, hand hygiene and social distancing. He also provided an overview of current research for COVID-19 vaccines and the importance of other modes of prevention until the point at which a vaccine becomes available.

**Dr Salma Abbas**  
*Infectious diseases expert from SKMCH&RC, Pakistan*

- Dr Salma summarised existing evidence on the use of chloroquine and hydroxychloroquine, antivirals such as Lopinavir and Ritonavir, Remdesivir, IL 6 receptor inhibitor like Tocilizumab (TCZ) and use of convalescent plasma.
- Current evidence on use of these drugs has come from case studies, series or small studies with no comparison groups and often with conflicting results. Hence current research is hypothesis-generating but inconclusive. With the need for further studies, it is best to use these drugs in a clinical trial setting. These drugs may be considered for use in patients with moderate or severe disease where no contraindications exist but with monitoring for development of known toxicities and unexpected adverse events.
- Availability of drugs such as anti-viral medicines is also a challenge for LMICs and currently there is no role for any of the above drugs in prophylaxis.

**Indian experience around COVID-19**  
*Dr. Yatin Mehta*  
*Chairman - Medanta Institute of Critical Care and Anaesthesiology from Gurgaon, Haryana*

Dr Mehta informed that on 24th March, 2020, the country entered into locked down. According to latest available statistics, India has around 20,000 confirmed cases with 3% mortality (data accurate as of 23rd April), with an increasing trend. Government of India has started to respond by issuing guidance documents, standard operating procedures and mass awareness campaigns. In India, districts have been identified as hotspots, non-hotspots and green zones, based on number of COVID-19 cases. The hospitals within the country have also been divided strategically to treat diverse spectrum of cases. Dr Mehta shared how the treatment options are being devised in the current situation with the available drugs, absence of standard of care and evidence emerging on a daily basis. He provided details on the prophylaxis practices and the guidelines for critical care for COVID-19 affected patients.

Dr Mehta offered insight into the ongoing research projects including a randomised controlled trial on the use of convalescent plasma therapy and participation in the SOLIDARITY trial. He concluded by emphasising the pursuit of the Global research roadmap with nine core research priorities.

**Overview of COVID-19 in Bangladesh, its management, challenges in public health policymaking in LMICs.**  
*Dr Aliya Naheed*  
*Head of the Initiative for Non-Communicable Disease, Health Systems and Population Studies Division at ICCRD,B in Bangladesh*

Dr Aliya informed that, with first case identified in March, Bangladesh witnessed a steep rise in the number of cases which can be explained by the enhanced testing capability of the country.
She emphasised the need for active surveillance. With the absence of a surveillance program, identification of cases relies on self-reporting, testing, contact tracing and in turn this guides the strategic planning of the lock down.

She highlighted the challenges with imposing public health measures including difficulties in controlling group gatherings for prayers, markets and funerals. Underreporting, due to fear of stigma and isolation, was seen. Daily wage earners and those with low income faced major problems. Dhaka remained the centre, with more cases in neighbourhood cities. Providing a comparison of trends seen in Pakistan, India and Bangladesh and demonstrating that recovery rate remains low in Bangladesh.

The biggest challenge was lack of an early warning system: low preparedness, limitation of resources, and failure of public health specialists to lobby with Government, since they were not sufficiently empowered. The capacity of the healthcare system was insufficient to provide effective management of cases, control and containment of disease transmission. In conclusion this pandemic has reminded us of the value of good hygiene, healthy lifestyle, and family.

**Overview of the disease spread in Nepal since the diagnosis of the first case of COVID-19 in Jan 2020**

*Dr Mahesh Kumar Maskey*

_Prominent public health expert from Nepal and currently leads the Nepal Public health foundation._

- In Nepal, so far 9 districts have a total of 45 cases with the highest number derived in Udayapur thought to be due to a mass religious gathering in that area. The movement of labourers, including external migratory movements from bordering countries, and religious gatherings was a concern for a possible second wave of transmissions once the lockdown is relaxed in the country.
- Government has developed an active surveillance system of contacts and suspected cases in the community with volunteers and mobile apps. A total of 40,000 tests had been carried out in the country including both PCR and RDT technique. Serological survey of a sample is also being done in selected communities. Challenges associated with contact tracing and the need for research into the area is evident.
- The other area highlighted for research from a public health perspective was determining the locally applicable baseline reproduction number (R0) and actual reproduction number (Rt) for disease transmission models as current projections are using figures from Wuhan, China which may not be directly relevant for Nepal.
- Dr Maskey concluded by summarising the challenges associated with COVID-19 detection and prevention in the country which could also form the basis of priority areas for research (details given in the research priorities section)
Summary of Q&A, open discussion and comments

In the following Q&A session, the following ‘themes’ emerged during the talks and from the attendee’s questions:

Need for ensuring both speed and quality when developing research studies during an epidemic.
- importance of good science and quality of the rapid review process for infectious disease outbreak research
- adopting study designs that allow for their rapid implementation
- ensuring adaptation of the research methodology as new evidence emerges to ensure safety of participants
- rapid review (IRB) to ensure timely research response

Challenges associated with the development of scientifically sound research protocols
- The absence of clear evidence for risk: benefit assessment of proposed interventions
- Need for robust, effective, and rapid review for outbreak research to ensure timely implementation
- Sound research methodology and ethics awareness amongst researchers in the context of South Asian countries is limited leading to issues such as therapeutic misconception.

To successfully generate robust public health measures for containment of disease 2 areas where highlighted
- The role of community engagement so that these are respectful of the local culture
Importance of qualitative research for enhanced understanding of community behaviours and economic factors that impact the public’s attitude towards containment measures

Role of ‘pooling’ and rapid diagnostic tests (RDT) in mass screening
- Although antibody-based rapid tests have low sensitivity these are an acceptable alternative for population-based screening in LMICs.
- Pooling strategy to save extraction kits could be a way for lowering test costs for South Asian countries. Drugs, vaccines, and convalescent plasma as currently proposed for COVID-19 treatment.
- Safety concerns and feasibility of access.
- The importance of well-designed research to generate conclusive evidence regarding their use has conflicting results.

Role of herd immunity in control of COVID-19 in south Asia
- Separating hope from hype during public health emergencies and the importance of responsible media reporting on emerging scientific evidence.
- Planning ahead for the fair allocation of critical care resources like PPE and critical care and the importance of having national guidelines for such decision-making to ensure transparency.

All panellists agreed that South Asia faces similar challenges for COVID-19 management and collaborative research into all of the above areas is essential for effective control of the outbreak in the region.

Summary of Workshop
- Collaboration, effective communication amongst all stakeholders, ethics preparedness and enhancing research capacity rapidly are key to an effective research response during an epidemic.
- South Asian countries face similar challenges in surveillance, diagnostic capacity, availability of safe and efficacious treatment provision and supportive care in already strained health care systems while negotiating the uncertainty surrounding current evidence.
- Research into public health, community attitudes and engagement with the public would ensure that prevention and containment measures are adopted in a contextually relevant, culturally appropriate manner hence ensuring their greater success.
- Future/planned research studies: Currently most south Asian countries are planning to join the WHO SOLIDARITY trial. In addition, research into various other treatment options such as convalescent plasma use is also ongoing.
- Research/knowledge gaps identified: surveillance, diagnostics, robust ethics and regulatory review process, new interventions, prevention, public health measures and allocation of scarce resources.

List all immediate research priorities identified
Consolidating feedback from the panellists and the questions and comments made by the workshop participants has produced the following consensus on the immediate research priorities for ‘South Asian countries responding to the COVID-19 research challenge’:
• Consensus for fair and transparent allocation of critical resources for patient management and healthcare worker protection
• Optimal approaches to surveillance / case detection
• Ethics preparedness for research review processes and research conduct by investigators
• Research into low-cost and rapid diagnostics
• Qualitative research into community behaviours and economic and cultural factors that impact public attitude towards containment measures such as hand hygiene, social distancing and quarantine
• Therapeutic trials (supportive care and treatments) that measure impact of treatments and other measures in fragile healthcare systems of South Asian countries
• Community Engagement
• Greater collaboration underpinning research amongst South Asian countries as they face similar challenges and establishment of robust research networks

Call to action and next steps
‘If you are involved in COVID-19 research surveillance, diagnostics, research ethics and regulatory review, new interventions, prevention, public health measures and the allocation of scarce resources for managing this outbreak, please contact us to share any relevant protocols, associated tools and your experiences.

Over the next few days please send in your comments and feedback on the COVID-19 webinar ‘How are we responding to the COVID-19 research challenge? Experiences from South Asia’. Further virtual workshops are planned, which will be topic-specific and in response to demand. If you would like us to conduct a workshop related to a specific theme of COVID-19 research, please let us know what topics would be most helpful. You can get in touch here info@theglobalhealthnetwork.org