

Regional workshop on Invasive Bacterial Disease (IBD) surveillance

New Delhi, India, 20 December 2022

Report of the meeting



REGIONAL OFFICE FOR

**World Health
Organization**

South-East Asia

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Abbreviations

AEFI	adverse events following immunization
AMR	antimicrobial resistance
CBDDR	Centre for Bacterial Disease and Drug Resistance
CDS	Communicable Diseases and Surveillance Department (of WHO)
CMC	Christian Medical College
COVID-19	SARS coronavirus disease 2019
DTP	diphtheria–tetanus–pertussis
EPI	Expanded Programme on Immunization
EQA	external quality assessment
HTP	high-threat pathogens
IBD	invasive bacterial disease
IB-VPD	invasive bacterial vaccine-preventable diseases
IEDCR	Institute of Epidemiology, Disease Control and Research
IPV	inactivated polio vaccine
ISS	immunization systems strengthening
IVB	immunization, vaccines and biologicals
JDW	Jigme Dorji Wangchuck National Referral Hospital
PCV	pneumococcal conjugate vaccine
QC	quality control
RCDC	Royal Centre for Disease Control
RRL	Regional Reference Laboratory
US CDC	United States Centers for Disease Control and Prevention
VPD	vaccine-preventable diseases
WHE	World Health Organization Health Emergencies Programme
WHO	World Health Organization
WHO-HQ	World Health Organization headquarters
WHO-SEARO	WHO Regional Office for South-East Asia

1. Background

The Invasive bacterial disease includes surveillance for *Haemophilus influenzae type b* (Hib), *Streptococcus pneumoniae* (pneumococcus), *Neisseria meningitidis* and Group B *streptococcus*.

The bacteria *Streptococcus pneumoniae* (pneumococcus) is the most frequent cause of severe pneumonia and pneumonia-related deaths worldwide. Pneumococci frequently and asymptotically colonize the human nasopharynx, particularly in children, but can spread contiguously to cause otitis media and sinusitis, be aspirated to cause pneumonia or invade normally sterile sites to cause sepsis or meningitis.

Development of pneumococcal resistance to commonly used antibiotics, such as penicillin, macrolides, cephalosporins and cotrimoxazole, is a serious problem in some parts of the world. Prior to the introduction of pneumococcal conjugate vaccines, six to 11 serotypes accounted for $\geq 70\%$ of all invasive pneumococcal diseases occurring in children worldwide.

Among the countries of the WHO South-East Asia Region, Sri Lanka and Myanmar are second to India in pneumococcal disease burden. Pneumococcal vaccines are either polysaccharide or conjugate vaccines. Polysaccharide vaccines are recommended in some developed countries to prevent pneumonia in older persons and persons with underlying medical conditions. The available pneumococcal conjugate vaccines (PCVs) are effective in preventing pneumococcal diseases in children due to vaccine serotypes. Overall rates of invasive pneumococcal disease remain reduced after conjugate vaccine introduction.

The bacteria *Haemophilus influenzae type b* (Hib) was the leading cause of non-epidemic bacterial meningitis worldwide in children prior to the introduction of Hib vaccine. *H. influenzae* can asymptotically colonize the human nasopharynx, particularly in children. The bacteria can cause pneumonia, and more rarely, it can cause invasive disease, predominantly meningitis and pneumonia, but also epiglottitis, septic arthritis and others.

Over 90% of invasive *H. influenzae* disease occurs in children < 5 years of age, the majority in infants. Children in less developed settings tend to be infected earlier in infancy. Hib vaccines are available in monovalent formulations or combined with other antigens: diphtheria–tetanus–pertussis (DTP) vaccine, hepatitis B vaccine and inactivated polio vaccine (IPV). Countries that have high coverage of Hib vaccine have observed a $> 90\%$ decline in invasive Hib disease.

Neisseria meningitidis (Nm) is a gram-negative bacterium that usually resides harmlessly in the human pharynx. Under certain conditions, asymptomatic carriage can progress to invasive meningococcal disease (IMD), resulting in meningitis, fulminant septicaemia, or both. *Neisseria meningitidis* can also rarely cause arthritis, myocarditis, pericarditis, invasive pneumonia, necrotizing fasciitis and endophthalmitis.

Most invasive infections are caused by meningococci of serogroups A, B, C, X, W or Y capsular polysaccharides. These serogroups can cause both endemic disease and outbreaks, but their relative prevalence varies considerably with time and geographical location. In Asia, serogroups A and C appear to cause most disease. Both polysaccharide and protein-polysaccharide conjugate vaccines are available against meningococci of serogroups A, C, W and Y; with protein-polysaccharide conjugate vaccines being more immunogenic.

Group B *streptococcus* has 10 serotypes, with 1a, 1b, II, III, IV and V causing most disease. Conjugate and protein vaccines designed to protect against group B streptococcal disease in mothers and babies are in clinical development.

Invasive bacterial diseases (IBD) have a higher burden in children under 5 years in low and middle-income countries such as India and other Southeast Asian countries. Maintaining case-based, active surveillance with laboratory confirmation remains a critical component of the global agenda in public health.

Since 2018, the WHO Regional Office for South-East Asia and Christian Medical College (CMC) in Vellore, India, which is the WHO regional reference microbiology laboratory for South-East Asia, have supported IBD surveillance network for countries of the South-East Asia Region to ensure high performance. This support facilitates data flow, contributes to monitoring the changing trends in distribution and replacement of serotypes/ serogroups of these pathogens, as well as to the fight against antibiotic resistance, and to decision-making over new vaccine introductions and vaccine impact assessments.

2. Objectives of the workshop

The general objective of the workshop was to strengthen the capacity of surveillance focal persons to coordinate and monitor the performance of invasive bacterial disease (IBD) surveillance at the country level.

The specific objectives were to:

- Brief surveillance focal points on the new guidelines for IBD surveillance.
- Share results from IBD surveillance from global, regional and country levels.
- Share lessons learnt (successes and challenges) from IBD surveillance.
- Identify way forwards to improve IBD surveillance in the Region.

3. Organization of the workshop

The workshop was organized virtually. It was attended by national surveillance officers involved in IBD surveillance from nine Member States (one each from Bangladesh, Bhutan, Indonesia, Maldives, Nepal, Sri Lanka, Thailand and Timor-Leste; and two from India). Accompanying them were WHO surveillance focal points from 10 Member States (one each from Bangladesh, Bhutan, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand and Timor-Leste; and two from India). Myanmar was represented by the WHO Country Office in that country.

Also attending were representatives of partner agencies: laboratory staff from Christian Medical College, Vellore, from the IBD regional reference laboratory (one participant), and the US Centers for Disease Control and Prevention (one participant). Also in attendance were three surveillance technical officers from the WHO headquarters. Secretarial support was provided by WHO-SEARO. The list of participants is provided in Annex 3.

The one-day workshop was organized around eight agenda items areas that included the following activities (see Annex 1 for the agenda of the meeting):

- Global IB-VPD surveillance: objectives, current status, COVID-19 impact. summary global results;
- Regional overview: Status of IBD surveillance in SEARO – successes and challenges;
- Defeating Meningitis by 2030 roadmap: Contribution of vaccination and IBD surveillance to the milestones;
- Overview of IBD Laboratory surveillance guidelines and support;

- IB VPD Global Reference Laboratory – Support and Resources for Moving Forward
- Country presentation of IBD surveillance;
- Data management solutions: Overview of IBD surveillance database; and
- IBD surveillance performance indicators.

All sessions of the workshop were held live through Zoom.

4. Proceedings of the workshop

Pre-meeting preparatory activities

To ensure a very successful conduct of the workshop all Member States and the representing participants were provided with key pre-meeting documents through respective WHO country offices. These included:

- (1) WHO Global Surveillance standards for VPD-Modules on Pneumococcus, *Haemophilus influenzae*, and Meningococcus. September 2018.
- (2) SEARO Surveillance Guide for Vaccine-Preventable Diseases in the WHO South-East Asia Region. Module on IBD surveillance (2017, under revision at the time).
- (3) Vaccine position papers:
 - *Haemophilus influenzae* type b (Hib) Vaccination. Position Paper – July 2013
 - Meningococcal A conjugate vaccine: updated guidance, February 2015
 - Pneumococcal conjugate vaccines in infants and children under 5 years of age: WHO position paper – February 2019.

Participants were also provided other reference documents referred to during the discussions.

Opening session

The workshop was opened by Dr Suman Rijal. Director, Department of Communicable Disease Control at the Regional Office, welcomed the participants and delivered the opening remarks. Dr Suman Rijal then requested Dr Sunil Bahl, Coordinator, Immunization and Vaccine Development, to outline the objectives of the meeting. Dr Jayantha Liyanage, Regional Adviser, Immunization Systems Strengthening at the Regional Office, coordinated the rest of the meeting.

Technical sessions

The technical sessions covered various activities following the objectives and agenda of the meeting. These included a global IB-VPD surveillance: objectives, current status and impact of COVID-19. Summary global results, regional overview: status of IBD surveillance in SEARO – successes and challenges; Defeating Meningitis by 2030 roadmap: contribution of vaccination and IBD surveillance to the milestones; Overview of IBD Laboratory surveillance guidelines and support, IB-VPD Global Reference Laboratory – support and Resources for moving forward, country presentation of IBD surveillance, data management solutions: overview of IBD surveillance database and presentation of IBD surveillance performance indicators.

Participants asked for support for typhoid surveillance and especially the laboratory manual. WHO-HQ informed that the manual is in the final drafting stages and will be

shared soon. There were also concerns about aligning the IBD surveillance with other ongoing VPD surveillance in countries, with specific support requested by Bangladesh. The IBD surveillance was conducted by Dakar Shishu Hospital, which has a separate institute called the Child Health Research Foundation (CHRF).

Initially, support was received from the WHO Regional Office through the country office and some partners. IBD surveillance has continued in CHRF. However, since it is not a government institute, the government will have to initiate the discussion to bring this under its leadership and integrate with the existing AFP and priority VPD surveillance. Discussions need to be held with the Institute of Disease Control and Research (IEDCR) on whether they can start IBD surveillance in partnership with CHFR.

Discussions were also held on the number of cases expected from sentinel sites, as well as how to select the sentinel sites if the expected number of cases is low. The best samples to collect, and the optimum conditions for collection and transportation of samples to get the best results, were also discussed.

Closing session

The participants recognised that the workshop comes at an opportune time after COVID-19 pandemic. The meeting was recognised as a point of restart of the coordination for IBD surveillance and opportunity to reconnect stakeholders and countries.

Participants made suggestions about follow-up actions to strengthen IBD surveillance. It was observed that the workshop connects partners post-pandemic. Bhutan observed that it had been part of the GBS surveillance. Interest in meningococcal is reviving, but the documentation is poor, it was observed.

Non-invasive, non-typeable Hib cases are on the rise. A virtual call every three months with countries and hands-on training for typhoid and GBS was recommended. There is a need for hands-on workshops to reskill those who were trained before as well as train new laboratory recruits. The support from CDC was recognised and information shared that new diagnostic techniques have become available now with new the TAC card that can detect all bacteria and viruses.

5. Technical sessions

The technical sessions had presentations in the following areas:

- Global IB-VPD surveillance included an overview of vaccine-preventable disease surveillance as an integral part of the Immunization Agenda 2030 and the Invasive Bacterial Vaccine-Preventable Disease (IB-VPD) Surveillance Network, its objectives, current status, use of data for public health action and measuring the impact of vaccination.
- A session on regional overview included the status of Hib vaccine and PCV introduction in the SE Asia Region, status of IBD surveillance, regional support to IBD surveillance, and challenges and perspectives for improvement.
- The session on “Defeating Meningitis by 2030 roadmap” showed the contribution of vaccination and IBD surveillance towards achieving the milestones.
- Overview of IBD laboratory surveillance guidelines, updates on IBD surveillance results, and support from the regional reference laboratory.
- IB VPD Global Reference Laboratory, including resources for moving forward.

- Country presentation of IBD surveillance outlining the main institution responsible, participating institutions (including lab), list sentinel sites, surveillance types and definitions, protocols used, surveillance enrolment data and national indicators, impact of COVID-19 on the surveillance, use of the data for action, challenges and ways forwards.
- Data management solutions with an overview of IBD surveillance database including the objectives of data management, status and challenges, ways to improve data sharing, and presentation of the regional IBD surveillance database.
- IBD surveillance performance indicators, including recommended analyses for pneumococcal, Hib and meningococcus cases, and data management performance indicators for meningococcus.

6. Key conclusions and action points

The following were the key conclusions and action points recommended:

- Follow-up with each Member State, on needs basis, to address data management challenges, including data sharing with the Regional Office.
- Continue support to countries for procurement of IBD laboratory supplies and equipment.
- Support more countries to participate in IBD quality control (QC) and external quality assessment (EQA) exercises.
- Strengthen serotyping/serogroup capacity for IBD pathogens by including testing for Group B Strep in select sites/Member States and improving documentation of *meningococcus* and non-*b* *Haemophilus* serotypes.
- Use regionally available IBD surveillance data to advocate for the introduction of pneumococcal conjugate vaccines in the remaining Member States of the Region.
- Strengthen and expand IBD surveillance in other countries to increase representation across the SE Asia Regional Office over time.
- Support Bangladesh to establish IBD surveillance and liaise with existing surveillance and other VPD in the Institute of Epidemiology, Disease Control and Research (IEDCR).
- Member States are encouraged to reach out to the Regional Office or the RRL for any support required for typhoid and Group B *streptococcus* surveillance. Refresher hands-on trainings will be organized for target countries by RRL.
- Organize regular coordination calls/meetings/reviews between RO, RRL, country focal persons and other partners (initially proposed on a quarterly basis).

Annex 1

Agenda

- (1) Opening session
- (2) Welcome and opening of the workshop
- (3) Objectives of the workshop and introduction of participants
- (4) Global IB-VPD surveillance: objectives, current status, COVID-19 impact. Summary global results
- (5) Regional overview: Status of IBD surveillance in WHO-SEARO - Success and challenges.
- (6) Defeating Meningitis by 2030 roadmap: Contribution of vaccination and IBD surveillance to the milestones
- (7) Overview of IBD Laboratory surveillance guidelines and support
- (8) IB VPD Global Reference Laboratory – Support and Resources for Moving Forward
- (9) Country presentation of IBD surveillance
- (10) Data management solutions: Overview of IBD surveillance database
- (11) IBD surveillance performance indicators
- (12) Next steps and closing

Annex 2

Message of from Dr Suman Rijal, Director for Communicable Disease Control, WHO South-East Asia Region

Welcome to the Regional Workshop on Invasive Bacterial Disease (IBD) surveillance. Invasive bacterial disease surveillance includes surveillance for *Haemophilus influenzae type b* (Hib), *Streptococcus pneumoniae* (pneumococcus), *Neisseria meningitidis* and Group B *streptococcus*. Clinically, the invasive bacterial diseases caused by these pathogens manifest as pneumonia, meningitis and sepsis.

Invasive bacterial diseases have a higher burden in children under 5 years of age in low- and middle-income countries. It is estimated that the South-East Asia Region accounts for 27% of the global bacterial meningitis cases and 19% of the global bacterial meningitis deaths.

Childhood pneumonia deaths decreased from 1.7 million in the year 2000 to 0.9 million in 2015. The diseases caused by these pathogens are preventable or potentially preventable by vaccination.

In the South-East Asia Region, all countries have introduced one or more vaccines targeted against these pathogens. The Hib vaccine has been introduced in all countries of the Region. With the completion of nationwide introduction of the pneumococcal conjugate vaccine in 2021 in India and in Indonesia in 2022, the Region now has good coverage with vaccines against these diseases.

In addition to vaccination, maintaining case-based, active surveillance with laboratory confirmation remains a critical component for controlling these diseases. Since 2011, the WHO Regional Office and the WHO Regional Reference Microbiology Laboratory for South-East Asia at the Christian Medical College in Vellore, India, have been supporting countries for IBD surveillance. This facilitates data-sharing, contributes to monitoring the changing trends in distribution and replacement of serotypes/serogroups of these pathogens, as well as supports the fight against antimicrobial resistance, the decision-making for new vaccine introduction and the vaccine impact assessments.

Invasive bacterial disease surveillance is currently conducted in seven Member States and is planned in the remaining Member states of the WHO South-East Asia Region. However, due to the COVID-19 pandemic and other factors, IBD surveillance faces some challenges and needs to be strengthened.

This workshop has been organized for surveillance focal points involved in invasive bacterial disease surveillance with the objective of strengthening IBD surveillance in countries of the South-East Asia Region.

At the end of this workshop, we expect surveillance focal persons from the countries will have updated information on various aspects of IBD surveillance, as well as have a better understanding of the coordination and support provided for this activity that will contribute to strengthening surveillance of Invasive Bacterial Diseases. I welcome you once again to this workshop and wish you all a productive and engaging workshop

Annex 3

List of participants

Ministry of Health

Bangladesh

Dr Mahbubur Rahman
Assistant Professor
Institute of Epidemiology, Disease Control &
Research (IEDCR)
Mohakhali, Dhaka
Bangladesh

Bhutan

Dr Kinley Gyem
Deputy Chief Laboratory Officer
RCDC
Thimphu, Bhutan

Dr Tshokey
Consultant Clinical Microbiologist & Head
Department of Pathology and Laboratory Medicine
JDW National Referral Hospital
Thimphu, Bhutan

India

Dr Madhumita Barua
Deputy Director
National Centre for Disease Control
Ministry of Health & Family Welfare
New Delhi
India

Dr Trupti Shende
Assistant Director, CBDDR
National Centre for Disease Control
Ministry of Health & Family Welfare
New Delhi
India

Indonesia

Dr Eka Muhiriyah
Epidemiologist
Directorate of Surveillance
Ministry of Health
Indonesia
Maldives

Dr Fathimath Nazla Rafeeq
Medical Officer
Health Protection Agency
Ministry of Health

Maldives

Dr Nazla Musthafa Luthufee
AEFI committee chair
Ministry of Health
Maldives

Nepal

Dr Anu Shakya
Disease Surveillance Research Section Chief
Epidemiology and Disease Control Division
Ministry of Health and Population
Kathmandu, Nepal

Dr Meeru Gurung
Project Coordinator
Pediatric Research Unit, Patan Hospital, Patan
Academy of Health Sciences
Kathmandu, Nepal

Sri Lanka

Dr Lilani Karunanayake
Senior Consultant Microbiologist
Medical Research Institute
Ministry of Health
Sri Lanka

Thailand

Ms Oiythip Yasopa
Public Health Technical Officer
Practitioner Level
Division of Epidemiology
Department of Disease Control
Ministry of Health
Thailand

Regional Reference Laboratory

Dr Balaji Veeraraghavan
Professor & Hilda Lazarus Research Chair
Clinical Microbiology
Christian Medical College
Vellore, India

CDC

Dr Stephanie Schwartz
Professor & Hilda Lazarus Research Chair
Clinical Microbiology
Christian Medical College
Vellore, India

WHO

WHO-HQ

Dr Heidi Soeters
Epidemiologist
Immunization Analysis & Insights Unit
Department of Immunization, Vaccines and
Biologicals
WHO-HQ

Dr Lorenzo Pezzoli
Team Lead
High Impact Epidemics
Health Emergency Interventions
Division of Emergency Response WHO-HQ

Ms Katya Fernandez
High Impact Epidemics
Health Emergency Interventions
Division of Emergency Response
WHO-HQ

WCO Bangladesh

Dr Md. Tanbirul Islam
National Professional Officer-EPI
WHO Country Office
Dhaka, Bangladesh

WCO Bhutan

Dr Sonam Wangdi
National Professional Officer
(Communicable Disease Control)
WHO Country Office
Paro, Bhutan

WCO India

Dr Arun Kumar
National Professional Officer-surveillance
WHO Country Office
New Delhi, India

Dr Preeti Nigam
Deputy Surveillance Team Leader
WHO Country Office
New Delhi, India

WCO Indonesia

Dr Mushtofa Kamal
National Professional Officer
(VPD Surveillance)
WHO Country Office
Indonesia

WCO Maldives

Mr Ikram Hameed
National Consultant-Vaccine Preventable
Diseases and COVID-19 Vaccination
WHO Country Office
Maldives

M Sana Saleem
National Consultant
Communicable Diseases
WHO Country Office
Maldives

WCO Myanmar

Dr Balwinder Chawla
Technical Officer
WHO Country Office
Yangon, Myanmar

Dr Khaing Khaing Gyi
National Professional Officer (Immunization &
Surveillance)
WHO Country Office
Yangon, Myanmar

Dr Nandar Than Aye
National Technical Officer
WHO Country Office
Yangon, Myanmar

Ms Lei Lei Mon
Data Management Associate
WHO Country Office
Yangon, Myanmar

Dr Yee Cho
National Professional Officer
WHO Country Office
Yangon, Myanmar

WCO Nepal

Dr Pawan Upadhyaya
New Vaccines & Immunization Programme
Support Officer
WHO Country Office
Kathmandu, Nepal

WCO Sri Lanka

Dr Preshila Samaraweera
WHO Country Office
Sri Lanka

WCO Thailand

Ms Aree Mounsookjarean
National Professional Officer
WHO Country Office
Bangkok, Thailand
WCO Timor-Leste

Dr Dongbao Yu
Medical Officer Epidemiologist
WHO Country Office
Timor-Leste

WHO SEARO

Dr Suman Rijal
Director
Department of Communicable Diseases (CDS)
WHO-SEARO
New Delhi, India

Dr Sunil Bahl
Coordinator
(COVAX, Immunization and Vaccine Development)
WHO-SEARO
New Delhi, India

Dr Jayantha Liyanage
Regional Adviser – Immunization Systems
Strengthening
Immunization and Vaccine Development (IVD)
WHO-SEARO
New Delhi, India

Dr Tondo Opute Emmanuel Njambe
Technical Officer
Immunization and Vaccine Development (IVD)
WHO-SEARO
New Delhi, India

Dr Lucky Sangal
Virologist/immunologist
Immunization and Vaccine Development (IVD)
WHO-SEARO
New Delhi, India

Dr Manish Kakkar
Medical Officer (High Threat Pathogens - HTP)
WHO Health Emergencies Programme (WHE)
WHO-SEARO
New Delhi, India

Ms Balreen Kaur
Executive Assistant
Immunization and Vaccine Development (IVD)
WHO-SEARO
New Delhi, India



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