Cholera prevention and control in Asian countries

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Abstract

Cholera remains a major public health problem in many countries. Poor sanitation and inappropriate clean water supply, insufficient health literacy and community mobilization, absence of national plans and cross-border collaborations are major factors impeding optimal control of cholera in endemic countries.

In March 2017, a group of experts from 10 Asian cholera-prone countries that belong to the Initiative against Diarrheal and Enteric Diseases in Africa and Asia (IDEA), together with representatives from the World Health Organization, the US National Institutes of Health, International Vaccine Institute, Agence de médecine préventive, NGOs (Save the Children) and UNICEF, met in Hanoi (Vietnam) to share progress in terms of prevention and control interventions on water, sanitation and hygiene (WASH), surveillance and oral cholera vaccine use.

This paper reports on the country situation, gaps identified in terms of cholera prevention and control and strategic interventions to bridge these gaps.

Keywords: Cholera, Asia, Water, Sanitation and hygiene (WASH), Cholera vaccine, IDEA

Background

Cholera represents an important public health problem in many settings. Annually, 2.8 million cases and 91,500 deaths occur in cholera endemic countries [1]. Beyond direct health concerns, cholera also presents a significant economic burden [2].

In addition to poor sanitation and inappropriate clean water supply, insufficient health literacy and community mobilization, absence of national plans and cross-border collaborations are major factors impeding optimal control of cholera in endemic countries. Poor knowledge of the real burden of cholera due to substantial under-reporting is also another obstacle [3–5]. Potential factors which will worsen the situation in the coming years are climate change, urbanization, increase in population density and, (further) rise of social inequalities [6].

Progress towards better hygiene and sanitation will be faster if a multidisciplinary and multi-sectoral approach is developed and implemented. Implementation of such strategy requires action under two key pillars: 1) increase political and financial support for cholera control and; 2) strengthen multi-sectoral cholera prevention and control programs.
| Country   | Bangladesh                                                                 | Cambodia                                                                 | India                                                                                                                                  | Indonesia                                                                                                                                  |
|-----------|----------------------------------------------------------------------------|---------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------|
| **Epidemiology** | Endemic, and seasonal outbreaks CFR 25 to 50% without treatment and 1% with treatment | Not cholera endemic, sporadic cases in 18 provinces CFR <1% but higher in hard to reach villages | Endemic with an estimated 834,000 cholera cases and 25,000 deaths every year Several states do not report any cholera cases potentially due to limited surveillance system | Low endemic. No outbreaks since 2011 Incidence of diarrheal diseases for all age population is 350/1000 population and 670/1000 children < 5 years old |
| **WASH** | Lack of water pipe                                                        | Data not available                                                        |                                                                                                                                        | Practice of healthy and hygienic behavior by only 38.7% Open defecation practiced by 94% population (2.5 millions), 109% use unsafe water, 7.3% drinks uncooked water |
| **OCV vaccination** | OCV included in national plan for at risk groups. Technology transfer for vaccine development in country Locally produced Vaccine (Cholvax) will be implemented | None                                                                       | OCV introduction study done in Odisha state OCV vaccine is not part of the EPI program                                                 | None                                                                                                                                  |
| **Surveillance/Diagnostic** | Hospital based surveillance at 2% Nationwide surveillance on-going at 21 sites | Event based surveillance, laboratory confirmed (CamEWARN) Surveillance of Acute Watery Diarrhea through CAM EWARN Reporting of laboratory confirmed cholera cases to CDC Dept Outbreak investigations | Weekly surveillance system in all regions Guidelines and SOP for early case detection Global positioning system & Google Earth in the investigation cholera outbreak Continuous laboratory surveillance of ADD in all districts Visit of collector to affected sites for monitoring quick action | |
| **Advocacy** | Advocacy meeting January 2017                                             | Communications (TV and radio spots, posters, flyers) Community mobilization | Sensitization of PRI members, local PHC staff, ASHA, AWW and community Other modes of community mobilization such as interpersonal Communication by door-to-door visit | |
| **Challenges** | Licensure and funding for locally produced vaccine (Cholvax) deployment, with WHO pre-qualification Inadequate coverage of the surveillance system | Under-reporting of surveillance systems Marginalized rural and tribal populations Poor availability of safe drinking water supply Inadequate ownership of programs Poor local health infrastructure Inadequate priority setting mechanisms Long incubation periods for research programs Introduction of OCV | Under-reporting Lack of RDT | |
| Thematic/Country | Malaysia | Nepal | Pakistan |
|------------------|----------|-------|----------|
| **Epidemiology** | Not Endemic except in Sabah region. Incidence rate < 1 per 100,000 populations and CFR < 1% in recent years. Malaysian: Foreigners incidence rate = 80:20. Cycle pick every 3 years. | Endemic, frequent outbreaks mainly during rainy season. 5042 ADD cases and 169 laboratory confirmed Cholera cases reported mainly from Kathmandu valley (150/169). No deaths occurred. | Endemic. 4-6 episodes of diarrhoea per child per year < 5 year. Under five deaths per year from Diarrhea: 13.2% |
| **WASH** | Scarce safe water supply in some areas. Unresolved environmental issues – excreta, solid waste. Poor hygiene & food sanitation with cross border crossing and illegal coastal and urban settlements. | Suboptimal WASH status. Basic Water Supply coverage: 83.59%, Sanitation: 87.17%. Hand-washing: 72.5% | 16M do not have access to clean drinking water. 27% consume tap water, 86% have access to improved water source, 73% have access to sanitation facilities. 13% no toilet facility |
| **OCV vaccination** | Vaccine and antimicrobial prophylaxis. OCV not in EPI but available in the private health facilities. Oral prophylaxis for close contacts and food handlers. | Reactive OCV Vaccination in Rautahat district in 2014. Preventive OCV vaccination campaign in Nuwakot and Dhading in 2015 and in Banke district in 2016. | OCV not registered |
| **Surveillance/diagnostic** | Mandatory web based within 24-hour notification. National guidelines and laboratory diagnostic capacity in all laboratories. Regulatory Infrastructure. | Cholera is an EWARS reportable disease. Clinical cases reported monthly from health facilities through existing HMS system. Cholera Surveillance embedded in the existing AMR sentinel surveillance system using 18 sites. Comprehensive Targeted Interventions (CTI) to Control Cholera in Kathmandu Valley in Kathmandu valley in 2016. | Facility based surveillance system in place in the province of Punjab since 2011 (which has 60% of the population of Pakistan) limited laboratory capacity. Passive case-based surveillance from large hospitals of major cities, and WHO EMRO Documents and reports of NGOs working in disaster situations. |
| **Advocacy** | Political commitment, interagency collaboration and coordination. Legal approach for child education, case notification and management; food sanitation. Subsidy for the poor (rural and urban). Ensure accessibility to affordable healthcare and education. Free treatment and quarantine leave for working parents. Restructure settlements with affordable homes. Hygiene Promotion, community engagement, Social Mobilisation campaign adapted to local culture. | Door to Door Awareness Campaign. Community Level Intervention: Booth Campaigns – Strategic Locations. -Awareness rallies: -Miking (in mobile vehicle and also during rallies) -Awareness sessions to community groups and key community actors. -Food and food outlet inspection: Food authority and Municipality. -Mass communication by various media and special programs. -Schools reached to educate and use children on Cholera and prevention. | Recurrent humanitarian emergencies. Weak surveillance system and underreporting. Limited laboratory capacity. Under resources of the public health control activities. Poor water and sanitation condition in conflict affected countries. Lack of cross border collaboration between the neighboring countries. |
| **Challenges** | Cross border crossing. Illegal coastal and urban poor settlements. Poverty, illiteracy and language barrier. Inadequate financial investment for WASH. | Identify risk groups and target mass vaccination by strengthening surveillance. Need to give high priority to improve WASH status. Enhance collaboration and coordination. Advocacy needed to introduce the OCV vaccination. | |

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Table 1  Summary of country situation update as reported by country representatives (Continued)

| Thematic/Country | Philippines | Thailand | Vietnam |
|------------------|-------------|----------|---------|
| **Epidemiology** | 14,592 diarrheal and 96 deaths cases in 2016 | Incidence significantly decreased in the past decades while outbreaks occasionally occurred: 4 outbreaks since 2017 | No Cholera since 2012 |
|                  | 124 (0.85%) were laboratory confirmed cholera | 125 cases in 2015 | |
|                  | No deaths | Main transmitters: Employees of the seafood industry, Migrant population | |
|                  | No cholera outbreaks post-flood disasters in recent years | |
| **WASH**         | Zero Open Defecation Program. Environmental Health Program: WASH, Regional Sanitary Engineers, Local Sanitary Inspectors | 100% toilets at all houses | Health education |
|                  | OCV vaccination | Sewage management | Clean water supplies and Environment sanitation |
|                  | Event-based Surveillance | Chlorinated tap water and/or bottled water | Food hygiene and safety |
|                  | Epidemiology Bureau of the DOH, Program Manager | Collection of human (rectal swab, stool) and environmental (water) samples. Laboratory testing of water samples thru the use of Colilert machine. Records review and active case finding | Local vaccine production |
|                  | Regional Epidemiology & Surveillance Units Regional Program Coordinators | Random inspection of water refilling stations Continuous surveillance of diarrhea cases Food & Water-borne Program. Regional Sanitary Engineers Local Sanitary Inspectors | NRA approved by WHO; Vaccination deployed in 16 provinces with high incidence and for high risk areas and populations |
|                  | Collection of human (rectal swab, stool) and environmental (water) samples. Laboratory testing of water samples thru the use of Colilert machine. Records review and active case finding | Hospital-based surveillance system | National guidelines for cholera diagnosis, treatment, surveillance, response, control and prevention |
|                  | Regional Laboratory Centers of department of Medical Sciences. Water and Food samples with 1% APW | - Early detection of suspected cholera cases - Laboratory confirmation - Timely and proper management of patients - Prompt investigation and control by the trained Surveillance and rapid response teams (SRRTs). Improving Sanitation and Chlorination of Water Supply | Testing in dog slaughter houses and restaurants |
|                  | Advocacy | Improving Sanitation and Chlorination of Water Supply | Mobile teams for early detection and investigation of outbreaks |
|                  | The Department of Health (DOH) recognized the distinctive link between sanitation and better health, need for a new vision in sanitation, expressed in clearer policy and action programs | Advocate for the enhancement of the Sanitation and Water Quality | Urgent reporting to higher level of health care system |
|                  | Challenges |继续 improving the sanitation and safe water | Close collaboration between treatment and preventive systems in reporting, specimen collection, and sharing specimens |
|                  | Continuing improvement of sanitation and safe water | Limited vaccination | Laboratory testing at national and regional Level |
|                  | Varying capacity in diagnosis and treatment. | Varying capacity in diagnosis and treatment. | At district level: Specimen collection, storage and transportation; Microscope examination, Gram staining, Testing of water, fresh vegetables in restaurants and markets |

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In accordance with these pillars, the Initiative against Diarrheal and Enteric Diseases in Africa and Asia (IDEA) was born in 2011. IDEA is an independent and multidisciplinary network of professionals from cholera-prone countries in Asia and Africa, in collaboration with national and international stakeholders. IDEA’s main goal is to facilitate and support the implementation of relevant prevention and control interventions on water, sanitation and hygiene (WASH), and on the use of oral cholera vaccine (OCV) by sharing information and best practices and to raise awareness on the country specific cholera situation.

Between 2015 and 2016, four IDEA workshops have been successfully achieved in Asia and Africa. The fifth IDEA meeting took place in Vietnam (Hanoi, 6–9 March 2017) and involved experts from 10 Asian cholera-prone countries (Bangladesh, Cambodia, India, Indonesia, Malaysia, Nepal, Philippines, Pakistan, Thailand, and Vietnam) together with representatives from the WHO, the US National Institutes of Health, International Vaccine Institute, Agence de médecine préventive, NGOs (Save the Children, StC), and UNICEF.

Country representatives shared their respective country situation, and progress in terms of WASH, surveillance and OCV use. Representatives from different health agencies provided an overview of available initiatives, interventions and tools in Asia. Following the plenary sessions, participants worked in subgroups to identify gaps in terms of cholera prevention and control and to discuss strategic interventions to bridge these gaps.

### Country situation

Update on cholera epidemiology, progress in the prevention and control of cholera and a mapping of country capacities were presented (Table 1). Suboptimal WASH including lack of safe water supply, appropriate sanitation facilities and persistence of open defecation were among factors that contribute to persistent cholera outbreaks. OCV has been used in Bangladesh, India, and Nepal but is not included in the National Immunization Programs. Cholera surveillance systems are in place in all participating countries but the type of surveillance and the extent of coverage differ considerably between countries. Awareness campaigns and community mobilization are regularly conducted in order to sensitize the public to simple preventive measures. Each country faces several challenges but improving WASH and increasing the coverage areas of surveillance systems were commonly reported.

### Existing interventions on cholera prevention and control in Asia

UNICEF chairs the WASH working group of the Global Task Force on Cholera Control (GTFCC). The WASH-GTFCC working group has developed technical briefs and set-up a study to estimate the effectiveness of households’ disinfection practices.

WASH is also one of the main actions of StC, an international non-governmental organization that promotes children’s rights. The StC global approach to cholera includes emergency health units, prepositioning stocks in eight countries, and a multi-sectoral approach. The objectives are to i) keep fecal matter away from drinking water, ii) inactivate cholera in contaminated water and iii) provide WASH facilities for medical teams and patients.

Another significant preventive tool available now is the global stockpile of OCV that was created in 2013 as an additional tool to help control cholera epidemics [7]. The WHO, UNICEF, and the Delivering Oral Vaccine Effectively (DOVE) project work in close collaboration.

### Table 2 The use of oral cholera vaccine stockpile in 2013–2016

| Year | Type of Campaign | Number | Country |
|------|-----------------|--------|---------|
| 2013 | Endemic         | 2      | Haiti (2) |
| 2014 | Endemic         | 10     | DRC, Guinea, Haiti (8) |
|      | Humanitarian crisis | 7    | South Sudan, Ethiopia |
| 2015 | Outbreak        | 4      | Malawi, South Soudan, Iraq, Nepal |
|      | Humanitarian crisis | 6    | South Sudan (3), Tanzania, Cameroon, Malawi |
| 2016 | Endemic         | 1      | Haiti |
|      | Humanitarian crisis | 3    | Niger, South Sudan (2) |
|      | Outbreak        | 2      | Malawi, Zambia |

### Table 3 List of oral cholera vaccine technology transfer by the International Vaccine Institute

| Company (Country) | Vaccine | Partnership | Stage of development |
|-------------------|---------|-------------|----------------------|
| Vabiotech (Vietnam) | mORCVAX | IVI re-formulated redeveloped the process to meet WHO standards | Licensed in Vietnam |
| Shanat (India) | Shancol | Technology transfer May 2008 | Licensed in India (Feb 2009) |
| Eubiologics (Korea) | Euvichol | Technology transfer May 2010–2011 | Korean export license 2014 |
| Incepta (Bangladesh) | Cholvax | Technology transfer May 2014 | WHO prequalified Dec 2015 |

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to ensure that at-risk populations will benefit from OCV in an appropriate and effective manner.

The dynamic creation by the establishment of stockpiles has played a key role in increased use of OCV [8–11] (Table 2). However, vaccine availability remains a major barrier limiting mass vaccination interventions. Two campaigns were conducted in South Sudan (2015) and in Zambia (2016) to evaluate the efficacy of a single dose strategy during outbreaks. The results showed that vaccinating twice the number of people with a single dose can prevent more cases and deaths during an outbreak by providing rapid herd protection. Similar findings have been provided by a modeling study that assessed the impact of one-dose OCV versus 2-doses in outbreak settings [12].

Other novel strategies including self-administration of the second dose (fisherman living in floating homes), out of cold chain use during distribution (Guinea 2012) and OCV delivery combined with other interventions (Refugee camps, Cameroon 2015) have also been tested and provide evidence of the feasibility of conducting OCV campaigns in a variety of scenarios.

To help developing country vaccine manufacturers, the International Vaccine Institute (IVI) engaged in a technology transfer development strategy (Table 3). Long-term efficacy of Shanchol [13] and safety and immunogenicity of Euvichol [14] have already been assessed. Cholvax is currently under evaluation in a non-inferiority trial to Shanchol in Bangladesh. In parallel, an individually randomized placebo-controlled trial to evaluate the use of a single dose in an endemic setting was completed [15].

**Workshop session**

To elicit more consideration for the prevention and control of cholera in participating countries, a brainstorming breakout session was held. The first part of the session was focused on what should countries aim at in terms of cholera prevention and control. There were two clusters of countries in terms of mid-term objectives depending on where they currently stand in cholera prevention and control (Fig. 1). Cambodia, Malaysia, Thailand and Vietnam aim at eliminating cholera in the coming years while recognizing cholera as a public health problem was the main mid-term objective for others.

Participants identified five main areas of strategic intervention to bridge the gaps and hence to reach the objectives of countries in terms of cholera prevention and control.

**Implementation/reinforcement of surveillance systems** (Fig. 2)

Currently, surveillance systems are patchy or minimal. Countries must strengthen the existing surveillance systems both in terms of coverage and capacity (e.g. laboratory diagnostic tests). This would allow early case detection and immediate response. Regular analysis and dissemination of data at the national and neighborhood level is also believed to act as a driver in the prevention and control of cholera.

**Water, sanitation and hygiene promotion** (Fig. 3)

WASH is universally recognized as a major component of preventing several infectious diseases [16]. Implementation of successful proactive WASH campaigns requires political will and community engagement. Tailored messages should be developed to increase awareness of open defecation, food and environmental safety and hygienic practices. Special attention should be given to schools. Engagement of political leaders could help in funding WASH priorities and in implementing food and water safety laws.

**Deployment of oral cholera vaccine** (Fig. 4)

OCV is considered as a supplementary tool for cholera prevention and control [17]. Pre-emptive and reactive OCV vaccination programs in cholera hot spots in several African and Asian countries have shown promising results [9–11] and should be sustained. Cost-effectiveness

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**Fig. 1** Countries’ aims for cholera prevention and control

| Cambodia, Malaysia, Thailand, Vietnam |
|-----------------------------|
| Eliminate cholera by 2020 / 2025 / 2030 |
| No local transmission for three years in a row |

| Bangladesh, India, Indonesia, Nepal, Pakistan, Philippines |
|-----------------------------|
| Recognize cholera as a public health issue Set-up robust surveillance systems to better understand cholera design adequate action plan |
analysis of mass cholera vaccination campaigns is a key consideration for optimizing OCV deployment.

Social mobilization and health promotion (Fig. 5)
To be effective, community mobilization should be based on outreach and awareness campaigns that improve knowledge on the disease, prevention and existing treatment. They should provide transparent sharing of information and proper education about routes of transmission and prevention measures. Appropriate involvement of media and schools could ensure fast spread of the information.

Collaboration (Fig. 6)
Cholera preparedness and responses should include inter-sectoral partnership between health authorities at national and international level, civil society and other stakeholders. Cholera epidemics commonly occur in a cross-border manner, emphasizing the importance of cross-border cooperation to control and prevent the spread of the disease.

Conclusions
Cholera remains a continuous threat with high health and economic burden in several South Asian countries. Despite tremendous efforts, prevention and control of cholera suffers from a number of challenges and issues in Asia. Inadequate WASH was identified as a major barrier in the prevention and control of cholera. Countries believe that WASH responses were often reactive and the criteria to trigger WASH responses were often unclear. Funding of WASH priorities remains also a challenge. This might be due to the difficulties related to measuring quantitatively the effectiveness and sustainability of WASH, as compared to vaccination which is precisely measured and evaluated using immunological or surveillance data, or directly by determining vaccination status. The group recommended that priority WASH interventions in emergency situation should include: i) increased water supply, ii) improved quality of water supplied, iii) increased access to excreta disposal facilities, solid waste collection and disposal, hand washing facilities, soap and water storage vessels and iv) hygiene education and social mobilization.
Weak surveillance systems, underreporting and limited laboratory capacities have been reported by country representatives who advocated for reinforcement of active and passive cholera surveillance system: capacity building, training, guidelines, and equipment facilities. Participating countries recommended that the Cholera Prevention and Response National Road Map should also be endorsed urgently.

OCV have the added advantage of herd protection which further decrease significantly the number of cases. Thanks to technology transfer, the OCV stockpile will grow with more vaccines being manufactured by different companies. Vaccine price could also be positively impacted by multiplying manufacturers. The group concluded that OCV should be introduced and used in different ways according to the country situation (special populations, integrated in the existing immunization programs or used in emergency situations). The use of one-dose OCV regimen could also be a promising solution during emergency situations. Other innovative OCV delivery strategies are also being tested. This includes:

✓ A self-administered second dose for the fishermen in “floating homes” living on Lake Chilwa is carried out by MSF. The second dose is given together with first dose that will be home-based self-administration.

A community-led self-administrated second dose on the six islands of Lake Chilwa carried out by AMP. The second dose is given to community leaders and kept in large cool boxes to be administrated under direct observation of the leader.

Evidence supports that killed whole cell vaccines are stable at high temperature for long periods [9, 18, 19]. Therefore, vaccine can be kept under cold chain in central stock but used out of the cold chain during distribution in hard-to-reach areas.

Provision of necessary supply will have the greatest impact on cholera burden if it is coupled with educational programs, community engagement and mobilization. The efficacy of a number of actions (e.g. door-to-door visits, placards, slogans, banners, special annual campaign) has already been tested and ought to be sustained. Outbreaks should be investigated and controlled as rapidly as
possible by means of communication. Low-cost nudges behavior changes with a preventive approach can help to increase compliance to hand-washing. In a nudge-based intervention study (i.e. positive reinforcement to influence people's behavior) carried in rural Bangladesh, hand-washing with soap increased from 4% at baseline to 68% the day after nudges were completed and 74% at 2 and 6 weeks post intervention [20].

Cholera still causes stigma as it is said to be a ‘forgotten disease’ mainly affecting ‘poor people’. Outreach meetings including public and private stakeholders and the general population are warranted to recognize that cholera is not only a health problem but also the direct consequence of poor WASH, linked to various environmental, climatic and socio-economic situations. Cholera can be prevented and controlled via complementary, synergistic and multidisciplinary interventions including access to safe water supply, end of open defecation, increased hygiene, political engagement, community mobilization, prompt case management and vaccination.

Perspective
Integrated multi-sectoral approaches have proven to be the best mechanism to implement effective strategies for the prevention and control of infectious diseases. Coordinated stakeholder activities are key components of disease control success. In this perspective Fondation Mérieux hosting organization along with present stakeholder during the meeting announces its full commitment to the coordinated strategy and join its cholera activities along with other partners within the Global Task Force on Cholera Control to implement the renewed strategy for cholera control while building on existing achievements.

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