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Original Article

Cholera Outbreaks in South and Southeast Asia: Descriptive Analysis, 2003–2012

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SUMMARY: We conducted descriptive analysis of available information regarding the epidemiology of cholera outbreaks in South and Southeast Asia during 2003–2012. Information from 58 articles, 8 reports, and World Health Organization databases were analyzed. Overall, 113 cholera outbreaks were studied in South and Southeast Asia during the past 10 years. The majority of the outbreaks (69%) occurred in Southeast Asia, including India (52%). The highest number of outbreaks was observed in 2004 (25.7%). The most commonly identified source was contaminated water: however, in some countries, the spread of cholera was facilitated via contaminated seafood (e.g., Myanmar, Thailand, and Singapore). Several genotypes and phenotypes of *Vibrio cholerae*, the causative agent of cholera, were identified in the outbreaks, including *V. cholerae* O1 El Tor (Ogawa and Inaba) and *V. cholerae* O139. The emergence of multidrug-resistant *V. cholerae* strains was a major concern. Cholera-related mortality was found to be low across the outbreaks, except in Orissa, India (currently Odisha) during 2007, where the case fatality rate was 8.6%. Potential limitations included underreporting, discrepancies, possible exclusion of nonindexed reports, and incomprehensive search terms. The provision of safe water and proper sanitation appear to be critical for the control of further spread of cholera in South Asian and Southeast Asian regions.

INTRODUCTION

Cholera is a potentially life-threatening acute diarrheal disease caused by the toxigenic bacterium *Vibrio cholerae* (1,2). It is a major public health challenge, mostly affecting developing countries with limited access to safe drinking water and inadequate sanitation (2). According to the World Health Report 2012, cholera is considered to be a major indicator of social development (2). Globally, an average of approximately 53 countries reported cholera cases and cholera-related deaths per year between 2000 and 2006 (3). The disease is characterized by a sudden onset and painless passage of a large volume of rice-water stools, leading to severe dehydration, and it can be life-threatening in the absence of prompt and proper treatment (1,2). Approximately 75% of persons infected with *V. cholerae* O1, the causative agent of cholera, do not show any symptoms (2). It is a water-borne disease and shows seasonality (1). The impact of environmental correlates of cholera varies across studies. Analysis of World Health Organization (WHO) data for 32 years (1974–2005) on the global cholera pandemic indicated latitude-dependent temporal variations in cholera outbreaks (in terms of severity and duration), which are partially explained by environmental and climatic factors (4). In Bangladesh, an environmental association (particularly heavy rainfall) and clear seasonality (bimodal, peaking in spring and monsoon) were observed (5,6). Higher relative humidity ($>80\%$) during the monsoon season was associated with cholera infection in Kolkata, India, and analysis of data collected between 2000 and 2006 showed definite seasonal patterns (first peak in July and second peak from August to October) (7).

The risk of cholera is associated with poverty and poor sanitation (1). As per the World Health Report 2012, it is estimated that approximately 3–5 million cholera cases occur every year globally: however, only a small portion of these cases are reported to WHO (2). It is also estimated that 4.2% of the total cholera cases reported globally originate in Asian countries (3). The highest number of cases has been reported in India (52.9%), followed by Afghanistan (29%) and Indonesia (22%) (3). There is a huge disparity in the reporting system of cholera cases owing to lack of motivation by both healthcare providers and governments. Over the years, reporting has improved in some countries; however, in most countries, the cholera surveillance system remains very poor. According to the WHO Technical Report, Bangkok, 2008, it was observed that the number of cholera cases reported in Thailand showed a 30-fold increase from 2006 to 2007, mostly arising from Tak Province (3). These discrepancies indicate the potentially vast underreporting of cholera cases and in-

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dicate the need for a marked improvement in the cholera surveillance system in most countries in this part of the world.

V. cholerae has been historically classified into two serogroups: O1 and non-O1 (8). Based on the number of phenotypic traits, *V. cholerae* O1 is considered to have two biotypes: classical and El Tor (9). Each biotype has been further categorized (on the basis of antigen factors) into two major serotypes, namely Inaba (expressing A and C antigens) and Ogawa (expressing more A and B antigens and less C antigen), as well as one minor serotype, Hikojima (expressing all three antigens; rare and unstable) (8). Before 1992, all cholera epidemics were associated with *V. cholerae* O1 or *V. cholerae* non-O1 serogroups, with mild isolated cases of diarrhea (8). However, at that time, a new serogroup emerged, designated as *V. cholerae* O139 Bengal, which caused severe epidemics in India (Chennai and Kolkata) and Bangladesh between 1992 and 1993 (8). Since 1994, *V. cholerae* has been reclassified into three serogroups, namely *V. cholerae* O1, *V. cholerae* O139, and non-O1 non-O139 *V. cholerae*; the third serogroup includes all other major serogroups of *V. cholerae* except O1 and O139. This non-O1 non-O139 *V. cholerae* rarely produces cholera toxins and other virulent factors, thereby causing diarrhea that is less severe and has no epidemic potential (8).

Most disease manifestations are caused by cholera toxins produced by *V. cholerae* O1 and O139 (9). Being influenced by the environmental activation signals, the TcpPH gene affects the ToxT protein, which attaches with the toxbox region of the *ctxAB* gene, resulting in the expression of the ctxAB toxin (10). Cholera epidemics are usually associated with toxigenic strains of serogroups O1 with classical and El Tor biotypes and with derivatives of *V. cholerae* O139, which carry the virulence cassette (carrying at least six genes, including *ctxAB*, *zot*, *cep*, *ace*, and *orf*) along with the cholera toxin (8,11,12). In some strains of El Tor biotypes, the presence of a repetitive sequence of elements in the virulence cassette may be associated with varying degrees of toxigenic potential (8).

Although the mechanism underlying the onset of cholera is unclear, a multitude of studies have demonstrated the development of new toxigenic clones of *V. cholerae*, leading to the reemergence of cholera epidemics affecting vulnerable populations residing in unhygienic conditions (1,2). In Malaysia, the periodic cholera outbreaks were found to be linked with a single clone of *V. cholerae*; 35% of the isolates were found to be multidrug resistant (13). In Vietnam, an outbreak occurred because of a genetically altered isolate of *V. cholerae* O1 El Tor Ogawa, which affected large numbers of people (14). Since 1992, the new strain *V. cholerae* O139 has caused cholera outbreaks in Bangladesh, China, and Thailand (3).

Cholera has been identified as an important cause of diarrhea, and it still remains a global threat despite recent advances in oral rehydration therapy and disease management. The reemergence of the cholera epidemic and the evolution of multidrug-resistant *V. cholerae* strains over the last decade, particularly in Asian countries, pose a great threat to the clinical diagnosis and treatment of this disease. Despite this trend, residents of these countries have been found to be less aware about cholera and its preventive measures. To our knowledge, no descriptive analysis of available information about cholera in South and Southeast Asia has been performed till date. Such analysis may be helpful in designing a blueprint for surveillance standards, comprehensive intervention strategies, and preparedness activities.

The present study aimed to perform descriptive analysis of available information regarding cholera outbreaks in South and Southeast Asia over the past 10 years (2003–2012) to explore their epidemiological characteristics.

MATERIALS AND METHODS

We mainly searched two databases for relevant literature: Google Scholar and PubMed. The following search terms were used in PubMed in various combinations: (''cholera'' [MeSH Terms] OR ''cholera'' [All Fields]) AND (''disease outbreaks'' [MeSH Terms] OR (''disease'' [All Fields] AND ''outbreaks'' [All Fields]) OR ''disease outbreaks'' [All Fields] OR ''outbreak'' [All Fields]) AND ((''2002/01/01'' [PDAT]: ''2012/12/31'' [PDAT]) AND ''humans'' [MeSH Terms]). The search included all work related to cholera outbreaks that occurred between 2003 and 2012. Altogether, the search retrieved 762 articles in PubMed. Of these, 33 articles and 1 weekly epidemiological record issued by WHO in 2008 met our inclusion criteria. In Google Scholar, the following key terms were used in various combinations: cholera, outbreak, South Asia, Southeast Asia, and diarrhea. This search resulted in 299 citations, of which we included 20 relevant articles, 8 newspaper reports on cholera-related outbreaks, 1 report by the Global Emerging Infectious Surveillance and Response System (2010), and 1 WHO report on cholera (2004). During the process of review and analysis, 5 more articles that reported research findings on drug response and the emergence of drug resistance among cholera cases were evaluated and outbreak-related information from these was also included in analyses.

In total, 58 articles and 8 related reports on cholera outbreaks from various data sources during 2002–2012 were included in this analysis. We acknowledged that despite extensive literature search, there may be exclusion of some relevant articles owing to poor reporting or nonexistence of disease surveillance systems in some regions.

Peer-reviewed original articles related to cholera outbreaks in South and Southeast Asia published in English during 2003–2012 were considered for this analysis. A newsprint covering cholera outbreaks during the abovementioned period was included. Reviews of literature, proposals, and editorials were excluded. Two independent researchers validated the selected articles and any conflict.

In addition, information available in the WHO database was reviewed, and data on all cholera outbreaks, cases, and deaths notified to WHO during 2003–2012 were incorporated in analyses.

From each eligible identified article or report, we extracted data, including the first author and year of publication, time of occurrence, area affected, number of cholera cases diagnosed, number of deaths related to cholera, specific strain of *V. cholerae* involved, routes of transmission, methods for control, and sanitation and water supply conditions of the affected area. This information was entered into a master framework using Microsoft Excel, in which tables were constructed. Endnote X4 was used proper data management and referencing.

RESULTS

The articles and reports (58 articles and 8 reports of 1,061 citations [762 from PubMed and 299 from Google Scholar] and 5 additional articles included during the review process) used in this analysis indicated that 113 cholera outbreaks occurred in South and Southeast Asian countries during the past 10 years. We have grouped the study findings into the following subheadings for a comprehensive understanding of the epidemiological characteristics of cholera outbreaks in South and Southeast Asia.

Geographic distribution: Out of 113 cholera outbreaks, 78 (69.03%) occurred in South Asia and 35 (30.97%) were reported in Southeast Asia (Table 1). Overall, more than half of all cholera outbreaks occurred in India (59 outbreaks, 52.21%), followed by Thailand (11 outbreaks, 9.73%), Bangladesh (8 outbreaks, 7.08%), Vietnam (7 outbreaks, 6.19%), and Nepal (6 outbreaks, 5.31%). In the remaining countries in South and Southeast Asia, the occurrence of cholera outbreaks was found to be less than 5%. The fewest outbreaks were reported in the Philippines and Indonesia.

Years of occurrence: The highest number of cholera outbreaks was observed during 2004 (29 outbreaks, 25.66%), followed by 2005 and 2007 (17 outbreaks each, 15.04%) and 2010 (11 outbreaks, 9.73%) (Fig. 1). Surprisingly, no cholera outbreaks were reported during 2011.

Routes of transmission: Cholera is a water-borne disease, and contamination of water by any means remains one of the most important factors contributing to cholera outbreaks (Table 2). In India, most cholera outbreaks have been caused by the consumption of contaminated drinking water (39,43,44,46). In some studies in India, cholera outbreaks were found to be associated with the handling of contaminated water from a pond-connected tube well (15,22,50). One water-borne cholera outbreak occurred after the impact of Cyclone Aila in West Bengal, India, in May 2009 owing to the resulting disruption of the water distribution system in the affected areas (37,38). The existence of poor drainage systems and leaky pipelines has been identified as common sources of water contamination in India, particularly during the monsoon season and during other natural calamities (20,21,30,38). Contaminated water sources have also been identified as a major route of cholera transmission in Nepal and Laos (16,33,34,48).

In Malaysia, a cholera outbreak occurred in July 2012 because of handling contaminated seafood and accessing contaminated river water for washing clothes (47). Many people were affected by another cholera outbreak in Thailand between May and December 2007 because of the consumption of contaminated seafood (3,36). Contaminated imported seafood products were identified as a major source for a cholera outbreak in Singapore in October 2004 (23). An additional 44 people suffered from two consecutive cholera outbreaks in Tak

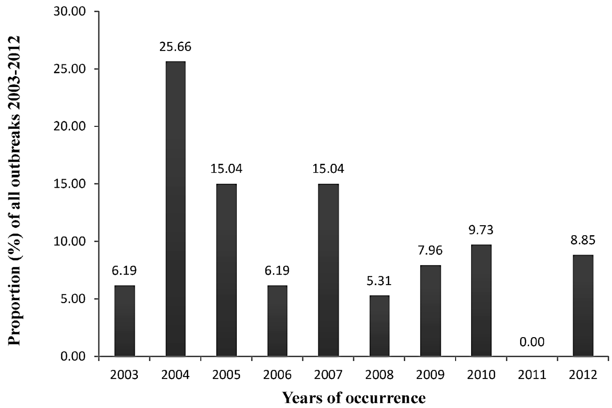

Fig. 1. Year-wise distribution of cholera outbreaks in South and Southeast Asia, 2003–2012.

Table 1. Country-wise distribution of cholera outbreaks in South and Southeast Asia, 2003–2012

Region	Country	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	Total no. (%)
South Asia	India	4	17	12	6	5	1	4	5	0	5	59 (52.21)
	Nepal	0	1	0	0	0	0	1	1	0	3	6 (5.31)
	Bangladesh	0	3	3	1	0	0	1	0	0	0	8 (7.08)
	Pakistan	1	2	0	0	0	0	0	1	0	0	4 (3.54)
	Afghanistan	0	0	1	0	0	0	0	0	0	0	1 (0.88)
Southeast Asia	Thailand	0	1	0	0	5	1	1	3	0	0	11 (9.73)
	Vietnam	1	0	0	0	3	3	0	0	0	0	7 (6.19)
	Laos	0	0	0	0	3	0	0	1	0	0	4 (3.54)
	Malaysia	0	0	0	0	0	1	2	0	0	1	4 (3.54)
	Myanmar	0	2	0	0	1	0	0	0	0	0	3 (2.65)
	Singapore	0	2	0	0	0	0	0	0	0	0	2 (1.77)
	Philippines	0	1	1	0	0	0	0	0	0	1	3 (2.65)
	Indonesia	1	0	0	0	0	0	0	0	0	0	1 (0.88)
Total		7	29	17	7	17	6	9	11	0	10	113 (100)

Table 2. Summary of the information regarding transmission and control of cholera outbreaks in South and Southeast Asia, 2003–2012

Reference no.	Year	Site of occurrence	Route of transmission	Control measure
(15)	2003	Orissa, India	Contaminated well water	Chlorination of public wells
(16)	2003	Miri, Indonesia	Contaminated water	
(17)	2003	Karachi, Pakistan	Contaminated water	
(18)	2004	Mathbaria, Bangladesh	Contaminated water	
(18)	2004	Mathbaria, Bangladesh	Contaminated water	
(18)	2004	Bakherjanj, Bangladesh	Contaminated water	
(19)	2004	Bhind, India	Contaminated water	
(20)	2004	Kolkata, India	Contaminated water from leaked pipelines	
(21)	2004	Kashmir, India	Contaminated water	
(22)	2004	South 24 Parganas, West Bengal, India	Contaminated pond water	
(21)	2004	Myanmar	Heavy rainfall leading to contamination of water	
(21)	2004	Singapore	Contaminated food	
(23)	2004	Bedok and Tampines, Singapore	Contaminated imported seafood	Screening of food handlers
(18)	2005	Mathbaria, Bangladesh	Contaminated water	
(18)	2005	Bakherjanj, Bangladesh	Contaminated water	
(24)	2005	Delhi, India	Contaminated water	
(25)	2005	Sangli, Maharastra, India	Contaminated water	
(26)	2005	Orissa, India	Contaminated food products and water	
(27)	2006	Kolkata, India	Contaminated water	Discarding unsafe water and chlorination
(28)	2006	Orissa, India	Contaminated water	
(22)	2006	South 24 Parganas, West Bengal, India	Contaminated pond water	
(29)	2006	Andaman and Nicobar Island, India	Contaminated pond water	Chlorination of water
(30)	2006	Garulia, West Bengal, India	Contamination of water and low chlorine content	Repair of leakage and chlorination of water
(22)	2007	South 24 Parganas, West Bengal, India	Contaminated pond water	
(31)	2007	Orissa, India	Contaminated water	
(32)	2007	Orissa, India	Contaminated water	
(33,34)	2007	Thateng and Lamam, Laos, PDR	Contaminated water, interpersonal transmission	Providing safe water, improving water, sanitation, and health education
(35)	2007	Xekong province, Laos	Contaminated water	
(36)	2007	Thai-Myanmar border	Contaminated sea-food	
(3)	2007	Tak province, South and Northeast Thailand	Consumption of contaminated squid, not washing hands	
(22)	2008	Rural Nadia, West Bengal, India	Contaminated pond water	
(37)	2009	Sundarban, West Bengal, India	Water contaminated following Cyclone Aila	Chlorination of water and repair of water pipes
(38)	2009	Medinipur, West Bengal, India	Water contaminated following Cyclone Aila	
(39)	2009	Secunderbad, India	Contaminated water	
(40)	2010	Lalpur, Gujrat, India	Contaminated water	Repair of leaking water-pipes
(22)	2010	Howrah, West Bengal, India	Contaminated pond connected tube-well	Closure of tube-well and disinfection of other wells
(41)	2010	Tamil Nadu, India	Contaminated water	
(42)	2010	Tak province, Thailand	Consumption of contaminated Hainanese chicken rice	Active case finding, shop closure, screening, treatment, and health education
(42)	2010	Tak province, Thailand	Consumption of contaminated Hainanese chicken rice	Active case finding, shop closure, screening, treatment, and health education
(43)	2012	Sadalaga, Chikodi, Karnataka, India	Contaminated water	
(44)	2012	Baramulla, North Kashmir, India	Contaminated water	
(45)	2012	Badungar colony, Punjab, India	Contaminated water	Repair of leaked water pipes
(46)	2012	Dhanera, Gujrat, India	Contaminated water	Repair of leaked water pipes, provision of safe water
(47)	2012	Bintulu, Sarawak, East Malaysia	Contaminated water and contaminated food	Screening of food handlers, provision of safe water and food
(48)	2012	Kathmandu, Nepal	Contaminated water	
(49)	2012	Kathmandu, Nepal	Contaminated water	

Table 3. Characteristics of the cholera outbreaks in South and Southeast Asia, 2003–2012

Reference no.	Time of occurrence	Site of occurrence	Case	Death	Strain
(59)	July–Sept '03	Chandigarh, India	40		*V. cholerae* O1 El Tor Ogawa
(60)	2003	India	2,893	2	*V. cholerae*
(15)	Nov '03	Orissa, India	41		*V. cholerae* El Tor O1 Ogawa
(61)	June–Oct '03	Nagpur, India	198		*V. choleare* O1 El Tor Ogawa (152), Inaba (3), Hikojima (4), Non-agglutinating vibrios (39)
(16)	2003	Miri, Indonesia	15		*V. cholerae* O1
(17)	June '03	Karachi, Pakistan	37		*V. cholerae* O1
(62)	May–Sept '03	Hue, Vietnam	115		*V. cholerae* O1 El Tor Inaba
(18)	Apr '04	Mathbaria, Bangladesh	24		*V. cholerae* O1
(18)	Nov '04	Mathbaria, Bangladesh	2		*V. cholerae* O1
(18)	Oct–Dec '04	Bakherganj, Bangladesh	21		*V. cholerae* O1
(20)	Mar–Apr '04	Kolkata, India	89		*V. cholerae* El Tor O1 Ogawa
(19)	May '04	Delhi, India	105		*V. cholerae* Ogawa (36) and *V. cholerae* Inaba (69)
(19)	May '04	Ludhiana, India	48		*V. cholerae* Ogawa (23) and *V. cholerae* Inaba (25)
(19)	May '04	Tripura, India	6		*V. cholerae* Inaba
(19)	May '04	Bhind, India	2		*V. cholerae* Inaba
(19)	July '04	Chandigarh, India	2		*V. cholerae* Ogawa (1) and *V. cholerae* Inaba (1)
(19)	July '04	Madurai, India	26		*V. cholerae* Ogawa (25) and *V. cholerae* Inaba (1)
(19)	Sept '04	Uttar Pradesh, India	6		*V. cholerae* Inaba (6)
(19)	Sept '04	Haryana, India	5		*V. cholerae* Inaba (5)
(19)	Oct '04	Trivandrum, India	2		*V. cholerae* Inaba (2)
(19)	Oct '04	Ahmedabad, India	56		*V. cholerae* Ogawa (29) and *V. cholerae* Inaba (27)
(63)	May '04	Northern Tripura, India			*V. cholerae* O1 El Tor, Ogawa
(21)	Nov 15, '04	Tamil Nadu, India	40		*V. cholerae*
(21)	Aug 29, '04	Kashmir, India	1	1	*V. cholerae*
(21)	Jan–Apr '04	India	21		*V. cholerae*
(22)	2004	South 24 Parganas, West Bengal, India	55	2	*V. chlorerae*
(60)	2004	India	4,695	7	*V. cholerae*
(21)	Oct 6, '04	Myanmar		4	*V. cholerae*
(21)	Sept 27, '04	Myanmar	10/wk		*V. cholerae*
(64)	May–Oct '04	Kavre, Nepal	46		*V. cholerae* El Tor O1 Ogawa
(21)	July 11, '04	Nawab Shah, Pakistan		4	*V. cholerae*
(21)	June 25, '04	Spin Boldak Afghan refugee camp, Pakistan		25	*V. cholerae*
(21)	Oct 18, '04	Singapore	9	1	*V. cholerae*
(23)	Oct 3–10, '04	Bedok and Tampines, Singapore	10	1	*V. cholerae* O1 El Tor Ogawa
(21)	Feb 25, '04	Thailand	9		*V. cholerae*
(65)	2004	Philippines	533	3	
(18)	March '05	Mathbaria, Bangladesh	10		*V. cholerae* O1, and *V. cholerae* O139
(18)	Mar–Apr '05	Mathbaria, Bangladesh	22		*V. cholerae* O1 (12), and *V. cholerae* O139 (10)
(18)	Apr '05–May '05	Bakherganj, Bangladesh	9		*V. cholerae* O1
(24)	Jan–Sept '05	Delhi, India	40		*V. cholerae* O1 Inaba
(66)	May–Oct '05	Orissa, India	56		*V. cholerae* O1 Inaba (37) and Ogawa (19)
(25)	Feb–Mar '05	Sangli, Maharastra, India	81		*V. cholerae* O1 El Tor Ogawa
(19)	Feb '05	Goa, India	16		*V. cholerae* Ogawa (7) and *V. cholerae* Inaba (9)
(19)	Apr '05	Kolkata, India	4		*V. cholerae* Inaba (4)
(19)	Apr '05	Berhampur, India	4		*V. cholerae* Inaba (4)
(67)	May–Jun '05	Kabul, Afghanistan	30		*V. cholerae*
(19)	July '05	Chennai, India	47		*V. cholerae* Ogawa (44) and *V. cholerae* Inaba (3)
(19)	July '05	Hyderabad, India	34		*V. cholerae* Inaba (34)
(19)	July '05	Manipal, India	27		*V. cholerae* Ogawa (9) and *V. cholerae* Inaba (18)
(19)	Nov '05	Alleppy, India	12		*V. cholerae* Inaba (12)
(26)	Sept–Oct '05	Orissa, India	113	1	*V. cholerae* El Tor O1 Ogawa
(60)	2005	India	3,155	6	*V. cholerae*
(68)	2005	Philippines	139	2	
(69)	2006	Bakherganj and Mathbaria, Bangladesh	74		*V. cholerae* O1 El Tor
(27)	2006	Kolkata, India	22		*V. cholerae* O1
(28)	Mar '06	Orissa, India	19		*V. cholerae* O1 El Tor Ogawa
(22)	2006	South 24 Parganas, West Bengal, India	56		*V. cholerae*
(29)	2006	Andaman and Nicobar Island, India	10		*V. cholerae* O1 El Tor Inaba

Table 3. (Continued)

Reference no.	Time of occurrence	Site of occurrence	Case	Death	Strain
(60)	2006	India	1,939	3	*V. cholerae*
(30)	Apr '06	Garulia, West Bengal, India			*V. cholerae* O1 Inaba
(3)	July–Sept '07	Orissa, India	7,565	159	*V. cholerae* O1 El Tor Ogawa
(22)	2007	South 24 Parganas, West Bengal, India	32	1	*V. cholerae*
(22)	2007	Howrah, West Bengal, India	63		
(31)	July–Sept '07	Orissa, India	62		
(32)	Aug–Sept '07	Orissa, India	32		*V. cholerae* O1 El Tor Ogawa
(3)	Dec 23, '07	Sekong province, Laos	254	3	*V. cholerae* O1 El Tor Ogawa
(56)	2007	Southeast Myanmar, Northern Thailand	877	7	*V. cholerae*
(56)	June–Aug '07	Tak, Northern Thailand	344		*V. cholerae* El Tor Inaba
(57)	Mid-Sept–Oct '07	Northeastern Thailand	235		*V. cholerae* El Tor Ogawa
(36)	May–Oct '07	Mae Sot district, Tak province, Thai-Myanmar border	477		*V. cholerae* O1 El Tor Inaba
(54)	2007	Northeastern Thailand	3		*V. cholerae* O1 El Tor Ogawa, MLVA type 2
(3)	Aug–Dec '07	Tak province, Southern region, Northeastern region, Thailand			*V. cholerae* O1 El Tor Ogawa (Southern and Northeastern region) and *V. cholerae* O1 El Tor Inaba (Tak province)
(58)	Oct '07	Northern provinces, Vietnam	38		V. cholerae O1 Ogawa
(14)	Oct–Dec '07	Hanoi, Vietnam	295		*V. cholerae* O1
(3)	Nov–Dec '07	Hanoi, Vietnam	1,940		*V. cholerae*
(33,34)	Dec '07–Jan '08	Thateng and Lamam, Laos, PDR	18		*V. cholerae* O1 Ogawa
(35)	Dec '07–Jan '08	Xekong province, Laos			*V. cholerae* O1 El Tor Ogawa
(22)	2008	Rural Nadia, West Bengal, India	71	0	
(70)	2008	Kota Bahru, West Malaysia and Labuan, East Malaysia	5		*V. cholerae* O1
(54)	2008	Northeastern Thailand	6		*V. cholerae* O1 El Tor Ogawa
(57)	Apr '08	Northern provinces, Vietnam	32		*V. cholerae* O1 Ogawa
(58)	Mar–Apr '08	Vietnam	377		*V. cholerae* O1 Ogawa
(14)	Dec 24–Feb 6, '08	Hanoi, Vietnam	33		*V. cholerae* O1
(37)	May '09	Sundarban, West Bengal, India	2		*V. cholerae* O1 El Tor Ogawa
(38)	May '09	Medinipur, West Bengal, India	21		*V. cholerae* O1 El Tor Ogawa (17), non-O1 non-O139 (4)
(39)	May '09	Secunderbad, India	10		*V. cholerae* O1 El Tor Ogawa
(55)	May '09	Hyderabad, India	34		*V. cholerae* O1 El Tor Ogawa
(72)	Nov '09	Terengganu, Malaysia	187	1	*V. cholerae* O1 El Tor
(13)	Nov–Dec '09	Kelantan, Malaysia	20		*V. cholerae* O1 El Tor Ogawa
(72)	Oct '09	Nepal			*V. cholerae*
(54)	Jul '09	Northeastern Thailand			*V. cholerae* O1 El Tor Ogawa
(73)	2009	Bangladesh	86		*V. cholerae* O1
(51)	Mar '10	Solapur, South Western India	41		*V. cholerae* O1 El Tor Ogawa
(40)	Dec '10	Lalpur, Gujrat, India	19		*V. cholerae* O1 El Tor Ogawa
(50)	May '10	Howrah, West Bengal, India	91	3	*V. cholerae* O1 Ogawa
(52)	Sept–Oct '10	Raygada, Orissa, India	32		*V. cholerae* O1 El Tor Ogawa
(41)	May '10	Tamil Nadu, India	37	1	*V. cholerae* O1 El Tor Ogawa
(53)	July '10	Attapeu, southern Laos	237	4	*V. cholerae* O1 El Tor Ogawa
(72)	Apr '10	Nepal	14		*V. cholerae*
(42)	Apr '10	Tak province, Thailand	33		*V. cholerae* O1 El Tor Ogawa
(42)	Apr '10	Tak province, Thailand	11		*V. cholerae* O1 El Tor Ogawa
(54)	2010	Central Gulf area, Thailand	10		*V. cholerae* O1 El Tor, MLVA type 4
(67)	Oct '10	Sindh and Khyber Pakhtunkhwa, Pakistan	99		
(43)	Oct 22, '12	Sadalaga, Chikodi, Karnataka, India		4	*V. cholerae*
(44)	Sept 24, '12	Baramulla district, North Kashmir, India	238		*V. cholerae*
(45)	July 21, '12	Badungar colony, Punjab, India	7		*V. cholerae*
(46)	July 5, '12	Dhanera, Gujrat, India		5	*V. cholerae*
(74)	June 9, '12	Assam, India		4	*V. cholerae*
(47)	July 27, '12	Bintulu, Sarawak, East Malaysia	33		*V. cholerae*
(48)	Dec 17, '12	Kathmandu, Nepal	15		*V. cholerae*
(49)	Aug 4, '12	Kathmandu, Nepal	10		*V. cholerae* O1 El Tor Ogawa
(75)	July 22, '12	Doti, Nepal	401	12	*V. cholerae*
(76)	Jan 1–Jun 13, '12	Virac, Catanduanes, Philippines	748	8	*V. cholerae*

Province, Thailand following the consumption of contaminated chicken fried rice during April 2010 (42).

Causative organisms: Microbiological analysis of rectal swabs revealed that the same organism, *V. cholerae* O1 El Tor Ogawa, was responsible for the majority of cholera outbreaks in Nepal, India (30,39–41,50,51–55), Thailand (42,54,56), Malaysia (13), Vietnam (57,58), Laos (3,33–35), and Singapore (23) (Table 3). In addition, non-O1 non-O139 *V. cholerae* was detected in a cholera outbreak in West Bengal during May 2009 (38), while *V. cholerae* O1 El Tor Inaba was linked with cholera outbreaks in Thailand during 2007 (56), the Myanmar border (36), and India (24,29,30). Both *V. cholerae* O1 El Tor Ogawa and *V. cholerae* O1 El Tor Inaba were identified in cholera outbreaks in Thailand during 2007 (3) and India during 2005 (19,66). In addition, both *V. cholerae* O1 and O139 were isolated from suspected cholera cases at a hospital in Bangladesh following an acute diarrheal outbreak in 2005 (18).

Cholera-related deaths: Cholera-related mortality in the identified studies was found to be relatively low (3,21,22,41,43,46,50,53,60,71,74) (Table 3). A notable exception was an outbreak in Orissa (currently Odisha), India between July and September 2007, in which 159 out of 7,565 cases died, the case fatality rate (CFR) being 8.6% (3). In another outbreak in northern Tripura, India, during May 2004, the CFR was observed to be 0.69% (63). In the Philippines, 8 out of 748 cases died (CFR 1.07%) in a cholera outbreak between January 1 and June 13, 2012 (76). In the Doti district in far-western Nepal, 12 out of 401 affected cases were reported to die (CFR 2.99%) from cholera during July and August 2012 (75). In Northern Thailand and Southeastern Myanmar, 7 out of 877 cases died (CFR 0.79%) in a cholera outbreak during 2007 (56). Finally, in Pakistan, approximately 25 people staying in the Spin Boldak Afghan refugee camp died in a cholera outbreak in June 2004 (21).

Control measures: Most cholera outbreaks reported in the literature were controlled by ensuring access to safe drinking water and through proper sanitation. Contaminated foods were discarded and screening of food handlers was instituted while controlling an outbreak in Singapore (23). Chlorination of public wells and other water sources was used to combat an outbreak in Orissa, India (26). Other reported measures taken include improving sanitation, raising awareness through health education, and repairing leaky pipelines in Laos (33,34) (Table 2).

Cholera cases and outbreaks that were reported to WHO from South and Southeast Asian countries during 2003–2012 are presented in Table 4. The WHO numbers

Table 4. Cholera cases and deaths reported to WHO by South and Southeast Asian countries during 2003–2012

Country		2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
	Reference no.	(77)	(78)	(65)	(68)	(79)	(80)	(81)	(82)	(83)	(84)
Afghanistan	Case	41	—	33	—	—	4,384	662	2,369	3,733	12
	Death	7	—	—	—	—	22	11	10	44	—
Iran	Case	96	94	1,133	—	19	72	—	—	1,187	53
	Death	—	1	11	—	—	4	—	—	12	—
India	Case	2,893	4,695	3,155	1,939	2,635	2,680	—	5,155	—	—
	Death	2	7	6	3	3	1	—	9	—	—
Nepal	Case	—	—	—	—	264	—	82	1,790	12	34
	Death	—	—	—	—	—	—	—	9	—	—
Pakistan	Case	—	—	—	—	—	—	—	164	527	144
	Death	—	—	—	—	—	—	—	—	219	8
Cambodia	Case	—	57	—	—	—	—	39	588	—	—
	Death	—	1	—	—	—	—	—	1	—	—
Laos	Case	—	—	—	—	169	201	—	237	—	—
	Death	—	—	—	—	3	—	—	4	—	—
Myanmar	Case	—	—	—	—	—	45	—	—	16	174
	Death	—	—	—	—	—	1	—	—	—	—
Thailand	Case	—	—	—	35	1,428	436	315	1,974	279	29
	Death	—	—	—	—	7	3	2	15	4	—
Vietnam	Case	—	—	—	—	1,946	853	471	606	3	—
	Death	—	—	—	—	—	—	1	—	—	—
Malaysia	Case	—	16	—	237	—	—	187	443	586	282
	Death	—	—	—	1	—	—	1	6	10	1
Brunner	Case	—	—	—	—	—	—	—	—	3	—
	Death	—	—	—	—	—	—	—	—	—	—
Indonesia	Case	—	—	1,338	—	—	1,007	—	—	—	—
	Death	—	—	19	—	—	27	—	—	—	—
Philippines	Case	—	533	139	66	—	—	—	33	120	1,864
	Death	—	3	2	1	—	—	—	2	3	14
Singapore	Case	1	11	—	—	—	—	—	—	2	2
	Death	—	1	—	—	—	—	—	—	—	—

were grossly different from those available from the published scientific literature.

DISCUSSION

Seven cholera pandemics have been recognized in human history (12). The first six were associated with the classical biotype, while the seventh one, caused by an El Tor biotype (12,85), started in Indonesia and spread to other parts of Asia, Europe, Africa, and Latin America during 1961–1991 (12,39). Based on genetic studies involving the identification of the phylogeny of lineage, researchers have argued that the most recent pandemic spread from the Bay of Bengal in at least three waves and was greatly influenced by antibiotic resistance (SXT family) (12).

Globally, there has been a steady increase in incidence of cholera since 2005 (86). However, cholera epidemics in South and Southeast Asia have shown diverse patterns in recent years. In some of these countries, the incidence of cholera has declined (e.g., in Laos since 2001) (87); in some countries, there has been a reemergence of previously identified strains (e.g., *V. cholerae* O139 in Bangladesh during 2002) (88), while in others (e.g., Thailand [89], Vietnam [90], and Bangladesh [91]), new strains have emerged with different phenotypic and genotypic expressions that seem to be associated with the development of multidrug resistance, disease severity, and epidemic potential.

In 2001, Nair et al. identified a new ''hybrid type'' cholera strain: a distinct variety of *V. cholerae* O1 that is an El Tor biotype but possesses certain traits of the classical biotype. The strain was isolated from patients admitted to hospitals in Bangladesh (9,92). Interestingly, the cholera toxin of the classical biotype has been produced by all strains of *V. cholerae* El Tor since 2001 (92). The cholera toxin produced by this variety showed both epitypic and genotypic transitions that might be associated with cholera epidemics in Bangladesh (9). A distinct genetic transition was also observed with *V. cholerae*-associated diarrhea in Northeastern Thailand during 2007, 2010, and 2011 (89). All the isolated strains belonged to serogroup O1, biotype El Tor, serotype Inaba or Ogawa, and most strains had toxigenic altered El Tor, *ctxA* and *ctxB* genes. Clonally related, altered El Tor with distinct signatures were observed in Thailand, Vietnam, and Bangladesh (89). This was reconfirmed by another study on the genetic characteristics of a strain of multidrug-resistant *V. cholerae* O1 El Tor in Dhaka, Bangladesh. These findings demonstrated a genetic transition of *ctxB* genotype 1 to genotype 7 in *V. cholerae* El Tor that probably occurred because of a point mutation during 2008–2010, resulting in endemic cholera (91). Similar findings were also reported in a study on multidrug-resistant *V. cholerae* O1 conducted in Vietnam during 2007–2010, where cholera outbreaks reemerged as a major public health concern (90). The predominant strain identified in that study was multidrug-resistant *V. cholerae* expressing phenotypic traits of both O1 El Tor Ogawa and an altered El Tor (*rstR* El Tor and *ctxB* classical biotypes) (90).

The coastal areas of the Bay of Bengal have been recognized as a significant reservoir of both *V. cholerae* O1 El Tor and O139 serogroups with varying degree of epidemic potential (18). A review of reported cholera cases over a 10-year period in India identified overall 222,038 cases involving 68 cholera outbreaks in 18 states during 1997–2006 (60). In addition, the cholera epidemic in India was found to be further jeopardized by the recent emergence of multidrug-resistant strains of *V. cholerae* in different parts of India (Delhi, Kerala, and Kolkata) since 2000 (93–96). Analyses of several *V. cholerae* isolates collected during different time periods (1992–1997, 2004–2005, and 2007–2009) from hospitalized patients in Kolkata, West Bengal (eastern part of India) showed a gradual shifting of multidrug resistance from *V. cholerae* non-O1 non-O139 serogroups to *V. cholerae* O1 (Inaba and Ogawa) and O139 strains (95,97). The recent increase in the number of cholera cases among children younger than 2 years of age in Kolkata, as evidenced from active surveillance (2007–2009), is another point of concern (94).

Reports of cholera outbreaks in Bangladesh during 2003–2012 are limited (66). Since 1996, the majority of cholera cases in Bangladesh have been found to be associated with *V. cholerae* O1 El Tor, with few cases involving the O139 serogroup (88). However, a recent change in the cholera epidemic was observed in Bangladesh (88): approximately 2,350 people were affected by a *V. cholerae* O139 strain (possessing both ctx^{Calc} and ctx^{ET} prophage) in Dhaka during March–April 2002 (88). In 2006, a different strain of *V. cholerae* O1 El Tor, secreting cholera toxin of the classical biotype was identified from two outbreaks in rural sites in Bakerganj and Mathbaria (69). An additional concern was the emergence of multidrug-resistant strains isolated from patients in Bangladesh since 2006 (15,19,30,50,51,79, 98).

This analysis has clearly indicated that cholera is still a major public health challenge in South and Southeast Asian countries. More than 50% of cholera outbreaks occurred in India, followed by Thailand. The major route of transmission is contaminated drinking water: however, in some regions of Southeast Asia such as Thailand, Myanmar, and Singapore, the consumption of contaminated seafood resulted in cholera outbreaks. The peak number of cholera outbreaks occurred in 2004, followed by 2007. All *V. cholerae* isolates were identified during these outbreaks. The emergence of multidrug-resistant *V. cholerae* is of great concern in developing countries, where the burden of diarrheal diseases is the highest. Nevertheless, cholera-related mortality was found to be relatively low. Most of these outbreaks were controlled through water chlorination treatment, provision of safe drinking water, discard of contaminated food, screening of food handlers, and increase in public awareness regarding cholera. Controlling cholera outbreaks is understandably very difficult in areas with poor access to safe drinking water and inadequate sanitation. To better understand how these outbreaks occur, it is necessary to gather information on the main source of the water supply in the affected areas, sanitation, the use of hygienic practices such as hand-washing, and the awareness level of individuals regarding cholera and its preventive measures.

Similar findings across a diverse array of global sites in this analysis indicate that there is an urgent need for multilevel, comprehensive intervention strategies to prevent the dissemination of cholera. Further research activities and initiatives from governments and nongovernmental organizations are also required to determine the policy and to address the sociocultural contexts related to cholera outbreaks.

Some limitations were identified during this analysis. It is estimated that 500,000 to 700,000 cases of acute watery diarrhea that occurred in Central and Southeast Asia were not reported to WHO in 2012 (15), while more than 2 million cases of acute watery diarrhea were being registered every year in Bangladesh alone. The proportion of these cases attributable to *V. cholerae* remains unknown (30), and the scenario is not much different in many other countries in this part of the globe (Table 4).

Surprisingly, the numbers of cholera outbreaks, cholera cases, and cholera-related deaths reported to WHO conflicted with the numbers derived from articles published in journals or newspapers during 2003–2012. For example, although a significant number of cholera cases was officially reported to WHO from Afghanistan during 2008–2011, no information on any cholera outbreaks that occurred in Afghanistan during 2003–2012 was retrieved from a search of published journal articles. Similarly, contradictory findings were observed for countries such as Iran and Cambodia.

Even the reported figures pertaining to cholera cases and deaths during outbreaks occurring in the same geographic locations and time periods significantly differed across data sources, including the scientific literature, country-wise cholera profiles published by WHO, and newspaper reports. Moreover, the proportions of total cholera cases and deaths reported to WHO during 2003–2012 that occurred during outbreaks remain largely unclear in most of these countries.

Furthermore, country-specific numbers of cholera cases reported to WHO considerably fluctuated from year to year in South and Southeast Asian countries during 2003–2012. These dramatic variations probably lack legitimate scientific justifications. For example, the numbers of cholera cases reported to WHO from Afghanistan were as follows: 12 in 2012, 3,733 in 2011, 2,369 in 2010, 662 in 2009, 4,384 in 2008, 33 in 2005, 41 in 2003, and none in 2007, 2006, and 2004. Similarly, the corresponding figures for India were quite high during 2003–2008 and 5,155 in 2010; no cases were reported in 2012, 2011, and 2009 (Table 4).

These discrepancies may have resulted from underreporting or misreporting of cholera cases and deaths owing to poor or even nonexistent surveillance systems (15,26,30); they may also be attributable to inconsistent case definitions because some countries reported only laboratory-confirmed cases, while others used the WHO standard case definition. The comparability of data between studies was thus potentially limited. The lack of uniform availability of laboratory support for the diagnosis of cholera further hindered the case detection process. In the majority of studies, only a subset of the study sample was tested for *V. cholerae*, thereby complicating the estimation of the actual burden of cholera. Moreover, only few studies reported the specific serotypes and biotypes of *V. cholerae* isolates, which are essential in detecting the changing pattern of global cholera epidemics over time.

Another important factor contributing to this potential underreporting, as pointed out by WHO, may be the fear of losing income from the tourism industry and concern about trade-related sanctions (30). The change in the revised International Health Regulations (adopted in 2005 and enforced in 2007 by WHO), which stipulated that notification of cholera cases was no longer mandatory, may also explain the decline in the reporting of cholera cases from some of these countries in recent years (30,51).

Surprisingly, cholera-related mortality was very low across our database, with the exception of few studies. In general, cholera-related CFRs varied between 1% and 5%, mainly depending on patients' accessibility to treatment facilities (58). It is not clear whether it is a result of the death of patients before reaching treatment facilities or the underperformance of cholera surveillance systems, thereby resulting in the underreporting of death or the true incidence of cholera mortality has declined over the past 10 years in South and Southeast regions.

Finally, the data available for this analysis were very likely affected by the operational principles of the databases used and the comprehensiveness of the search terms employed. It seems impossible to claim that search terms utilized were sufficiently exhaustive, and the probability of missing nonindexed reports is also high.

Despite all these limitations in the quality of the data collection process across studies, the results of this analysis give a clear indication of the reemergence of a cholera epidemic in this region from 2004 onward.

Some recommendations identified from this analysis and those suggested by WHO (99) to control cholera epidemics include establishing multidisciplinary, well-coordinated cholera preparedness programs; conducting risk assessments and communicating the results; raising awareness regarding the importance of personal hygiene; utilizing proper sanitation techniques; and ensuring access to safe drinking water. The identification and timely dissemination of information regarding the incidence of cholera, the epidemiological characteristics, and the geographic distribution may help design appropriate preventive programs. Cholera surveillance programs should be integrated with the ongoing health-related surveillance systems in each country. For better comparability of data across studies, a standardized case definition of cholera as recommended by WHO should be followed. Multi-sectoral, well-coordinated, sustainable response and cross-border collaboration are required to control such outbreaks. The development of risk assessment tools through continuous surveillance is essential to identify the at-risk groups in vulnerable populations. Care should also be taken to enhance prevention strategies in anticipation of seasonal cholera outbreaks, including preparedness plans, training of healthcare staff, and uninterrupted flow of supplies.

Cholera is a preventable disease, and the provision of safe water and proper sanitation are clearly essential for the control of the further spread of cholera in these South Asian and Southeast Asian regions. Further, we need the interplay of preparedness plans and prompt responses during anticipated outbreaks along with a robust surveillance system for mitigating such health hazards. It is also recommended to continue extensive cholera outbreak investigations, which will help in justifying the investments in new intervention programs.

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Conflict of interest None to declare.

REFERENCES

1. Faruque SM, Albert MJ, Mekalanos JJ. Epidemiology, genetics, and ecology of toxigenic *Vibrio cholerae*. Microbiol Mol Biol Rev. 1998;62:1301-14.
2. World Health Organization. Cholera (South-East Asia Region). 2012. Available at <http://www.who.int/topics/cholera/about/en/index.html>. Acceseed August 21, 2013.
3. Bayugo Y. Cholera: Global and Regional Update. Bangkok: WHO Country Office for Thailand; 2008. Available at <http://dse.healthrepository.org/handle/123456789/59>. Accessed September 2, 2013.
4. Emch M, Feldacker C, Islam MS, et al. Seasonality of cholera from 1974 to 2005: a review of global patterns. Int J Health Geogr. 2008;7:31.
5. Hashizume M, Faruque AS, Wagatsuma Y, et al. Cholera in Bangladesh: climatic components of seasonal variation. Epidemiology. 2010;21:706-10.
6. Hashizume M, Armstrong B, Hajat S, et al. The effect of rainfall on the incidence of cholera in Bangladesh. Epidemiology. 2008;19:103-10.
7. Rajendran K, Sumi A, Bhattachariya M, et al. Influence of relative humidity in *Vibrio cholerae* infection: a time series model. Indian J Med Res. 2011;133:138.
8. Nair GB. *Vibrio cholerae*. Guidelines for drinking-water quality. Available at <http://www.who.int/water_sanitation_health/dwq/admicrob6.pdf>. Accessed September 11, 2013.
9. Raychoudhuri A, Mukhopadhyay A, Ramamurthy T, et al. Biotyping of *Vibrio cholerae* O1: time to redefine the scheme. Indian J Med Res. 2008;128695-8.
10. Amin Marashi SM, Rajabnia R, Imani Fooladi AA, et al. Determination of *ctxAB* expression in *Vibrio cholerae* classical and El Tor strains using real-time PCR. Int J Mol Cell Med. 2013 Winter;2:9-13.
11. Chun J, Grim CJ, Hasan NA, et al. Comparative genomics reveals mechanism for short-term and long-term clonal transitions in pandemic *Vibrio cholerae*. Proc Natl Acad Sci U S A. 2009;106:15442-7.
12. Mutreja A, Kim DW, Thomson NR, et al. Evidence for several waves of global transmission in the seventh cholera pandemic. Nature. 2011;477:462-5.
13. Ang GY, Yu CY, Balqis K, et al. Molecular evidence of cholera outbreak caused by a toxigenic *Vibrio cholerae* O1 El Tor variant strain in Kelantan, Malaysia. J Clin Microbiol. 2010;48:3963-9.
14. Anh DD, Lopez AL, Thiem VD, et al. Use of oral cholera vaccines in an outbreak in Vietnam: a case control study. PLoS Negl Trop Dis. 2011;5:e1006.
15. Das A, Manickam P, Hutin Y, et al. An outbreak of cholera associated with an unprotected well in Parbatia, Orissa, Eastern India. J Health Popul Nutr, 2009;27:646-51.
16. Benjamin PG, Gunsalam JW, Radu S, et al. Factors associated with emergence and spread of cholera epidemics and its control in Sarawak, Malaysia between 1994 and 2003. Tonan Ajia Kenkyu [Southeast Asian Studies]. 2005;43:109-40. Available at <http://hdl.handle.net/2433/53820>. Accessed March 3, 2013.
17. Siddiqui FJ, Bhutto NS, von Seidlein L, et al. Consecutive outbreaks of *Vibrio cholerae* O139 and *V. cholerae* O1 cholera in a fishing village near Karachi, Pakistan. Trans R Soc Trop Med Hyg. 2006;100:476-82.
18. Alam M, Hasan NA, Sadique A, et al. Seasonal cholera caused by *Vibrio cholerae* serogroups O1 and O139 in the coastal aquatic environment of Bangladesh. Appl Environ Microbiol. 2006;72:4096-104.
19. Dutta B, Ghosh R, Sharma N, et al. Spread of cholera with newer clones of *Vibrio cholerae* O1 El Tor, serotype Inaba, in India. J Clin Microbiol. 2006;44:3391-3.
20. Sur D, Sarkar B, Manna B, et al. Epidemiological, microbiological & electron microscopic study of a cholera outbreak in a Kolkata slum community. Indian J Med Res. 2006;123:31-6.
21. Astrium.com. Cholera Outbreaks 2004. Africa. Asia. North America. South America. Available at <http://www.astrium.com/uploads/pdf/cholera2004.pdf>. Accessed August 28, 2013.
22. Mukherjee R, Halder D, Saha S, et al. Five pond-centred outbreaks of cholera in villages of West Bengal, India: evidence for focused interventions. J Health Popul Nutr. 2011;29:421-8.
23. Wong CS, Ang LW, James L, et al. Epidemiological characteristics of cholera in Singapore, 1992-2007. Ann Acad Med Singapore, 2010;39:507-12.
24. Rajeshwari K, Gupta A, Dubey A, et al. Diarrhoeal outbreak of *Vibrio cholerae* O1 Inaba in Delhi. Trop Doct. 2008;38:105-7.
25. Kulkarni R, Patil S, Kulkarni V, et al. An outbreak of cholera in the Sangli District of Maharashtra. Indian J Med Microbiol. 2007;25:76-8.
26. Das A, Manickam P, Hutin Y, et al. Two sequential outbreaks in two villages illustrate the various modes of transmission of cholera. Epidemiol Infect. 2009;137:906-12.
27. Sur D, Dutta S, Sarkar B, et al. Occurrence, significance & molecular epidemiology of cholera outbreaks in West Bengal. Indian J Med Res. 2007;125:772-6.
28. Khuntia HK, Samal SK, Kar SK, et al. An Ogawa cholera outbreak 6 months after the Inaba cholera outbreaks in India, 2006. J Microbiol Immunol Infect. 2010;43:133-7.
29. Sugunan AP, Roy S, Shahina M, et al. Emergence of *Vibrio cholerae* O1 Inaba in Andaman & Nicobar Islands, India. J Public Health. 2007;29:308-9.
30. Bhunia R, Ramakrishnan R, Hutin Y, et al. Cholera outbreak secondary to contaminated pipe water in an urban area, West Bengal, India, 2006. Indian J Gastroenterol. 2009;28:62-4.
31. Pal B, Khuntia H, Samal S, et al. Epidemics of severe cholera caused by El Tor *Vibrio cholerae* O1 Ogawa possessing the *ctxB* gene of the classical biotype in Orissa, India. Int J Infect Dis. 2010;14:e384-9.
32. Kumar P, Jain M, Goel A, et al. A large cholera outbreak due to a new cholera toxin variant of the *Vibrio cholerae* O1 El Tor biotype in Orissa, Eastern India. J Med Microbiol. 2009;58:234-8.
33. Lenglet A, Khamphaphongphane B, Thebvongsa P, et al. A cholera epidemic in Sekong Province, Lao People's Democratic Republic, December 2007–January 2008. Jpn J Infect Dis. 2010;63:204-7.
34. Phongmany S. Cholera outbreak, Xekong, 2007, Laos. In: Health Challenges in Southeast Asia: 8e Congrés international de la Societe de Pathologie Exotique. 2010 Jan 25-28, Vientiane, R.D.P. Lao. p. 27. Availabe at <http://www.pathexo.fr/docfiles/vol.resumes.laos.final.pdf>. Accessed September 30, 2013.
35. Sithivong N, Izumiya H, Munnalath K, et al. Cholera outbreak, Laos, 2007. Emerg Infect Dis. 2010;16:745-6.
36. Swaddiwudhipong W, Peanumlom P. A case of nosocomial cholera during a community outbreak in a Thai-Myanmar border area. J Med Assoc Thai. 2010;93:1112-4.
37. Bhunia R, Ghosh S. Waterborne cholera outbreak following Cyclone Aila in Sundarban area of West Bengal, India, 2009. Trans R Soc Trop Med Hyg. 2011;105:214-9.
38. Panda S, Pati KK, Bhattacharya MK, et al. Rapid situation & response assessment of diarrhoea outbreak in a coastal district following tropical cyclone Aila in India. Indian J Med Res. 2011;133:395-400.
39. Sinha A, SenGupta S, Ghosh S, et al. Evaluation of a rapid dipstick test for identifying cholera cases during the outbreak. Indian J Med Res. 2012;135:523-8.
40. Shah H, Shah V, Desai A. An epidemic outbreak of *Vibrio cholerae* El Tor 01 serotype Ogawa biotype in a Lalpur town, Jamnagar, India. J Postgrad Med. 2012;58:14-8.
41. Sekar R, Amudhan M, Sivashankar M, et al. An outbreak of cholera among a rural population in south India: is it time to vaccinate the children in endemic areas? Indian J Med Res. 2012;135:678-9.
42. Swaddiwudhipong W, Hannarong S, Peanumlom P, et al. Two consecutive outbreaks of food-borne cholera associated with consumption of chicken rice in northwestern Thailand. Southeast Asian J Trop Med Public Health. 2012;43:927-32.
43. Deccan Herald. Sadalaga cholera-hit. Updated Ocotober 22,

2012. Available at <http://www.deccanherald.com/content/287024/sadalaga-cholera-hit.html>. Accessed August 31, 2013.
44. Greater Kashmir. Manzoor-Ul-Hassan. 238 diagnosed with cholera in north Kashmir Updated September 25, 2012. Available at <http://www.greaterkashmir.com/news/2012/Sep/25/238-diagnosed-with-cholera-in-north-kashmir-73.asp>. Accessed April 5, 2013.
45. Hindustan Times. Vasudeva, R. Cholera scare in Badungar colony. Updated July 21, 2012. Available at <http://www.hindustantimes.com/Punjab/Patiala/Cholera-scare-in-Badungar-colony/SP-Article-893116.aspx>. Accessed September 15, 2013.
46. DNA. 5 die of cholera in Dhanera, 200 ill. Updated July 5, 2012. Available at <http://www.dnaindia.com/india/report_5-die-of-cholera-in-dhanera-200-ill_1711081>. Accessed March 30, 2013.
47. Borneo Post Online. Chia, J. Wong confirms cholera outbreak in Bintulu. Updated July 27, 2012. Available at <http://www.theborneopost.com/2012/07/27/wong-confirms-cholera-outbreak-in-bintulu/>. Accessed March 30, 2013.
48. The Himalayn Times. 15 confirmed cholera cases in Kathmandu. Updated August 12, 2012. Available at <http://www.thehimalayantimes.com/fullNews.php?headline = 15 + confirmed + cholera + cases + in + Kathmandu + &NewsID = 343294>. Accessed April 2, 2013.
49. Crofsblogs.typepad.com/h5n1/. Nepal: more on the Kathmandu cholera outbreak Updated August 5, 2012. Available at <http://crofsblogs.typepad.com/h5n1/2012/08/nepal-more-on-the-kathmandu-cholera-outbreak.html>. Accessed April 2, 2013.
50. Datta SS, Ramakrishnan R, Murhekar MV. A rapidly-progressing outbreak of cholera in a shelter-home for mentally-retarded females, Amta-II Block, Howrah, West Bengal, India. J Health Popul Nutr. 2012;30:109-12.
51. Jain M, Goel A, Bhattacharya P, et al. Multidrug resistant *Vibrio cholerae* O1 El Tor carrying classical *ctxB* allele involved in a cholera outbreak in South Western India. Acta Trop. 2011;117:152-6.
52. Kumar P, Jain M, Goel AK, et al. Tetracycline resistant *V. cholerae* O1 biotype El Tor serotype Ogawa with classical *ctxB* from a recent cholera outbreak in Orissa, Eastern India. J Infect Public Health. 2012;5:217-9.
53. Sithivong N, Morita-Ishihara T, Vongdouangchanh A, et al. Molecular subtyping in cholera outbreak, Laos, 2010. Emerg Infect Dis. 2011;17:2060-2.
54. Okada K, Roobthaisong A, Nakagawa I, et al. Genotypic and PFGE/MLVA analyses of *Vibrio cholerae* O1: geographical spread and temporal changes during the 2007-2010 cholera outbreaks in Thailand. PLoS One. 2012;7:e30863.
55. Goel AK, Jain M, Kumar P, et al. Molecular characterization reveals involvement of altered El Tor biotype *Vibrio cholerae* O1 strains in cholera outbreak at Hyderabad, India. J Microbiol. 2011;49:280-4.
56. Kimball AM, Moore M, French HM, et al. Regional infectious disease surveillance networks and their potential to facilitate the implementation of the international health regulations. Med Clin North Am. 2008;92:1459-71.
57. Nguyen BM, Lee JH, Cuong NT, et al. Cholera outbreaks caused by an altered *Vibrio cholerae* O1 El Tor biotype strain producing classical cholera toxin B in Vietnam in 2007 to 2008. J Clin Microbiol. 2009;47:1568-71.
58. World Health Organization. Outbreak news-severe acute watery diarrhoea with cases positive for *Vibrio cholerae*, Viet Nam. Wkly Epidemiol Rec. 2008;83:157-8.
59. Kaistha N, Mehta M, Gautam V, et al. Outbreak of cholera in & around Chandigarh during two successive years (2002, 2003). Indian J Med Res. 2005;122:404-7.
60. Kanungo S, Sah B, Lopez A, et al. Cholera in India: an analysis of reports, 1997-2006. Bull World Health Organ. 2010;88:185-91.
61. Mishra M, Mohammed F, Akulwar S, et al. Re-emergence of El Tor vibrio in outbreak of cholera in & around Nagpur. Indian J Med Res. 2004;120:478-80.
62. Thiem VD, Deen JL, Von Seidlein L, et al. Long-term effectiveness against cholera of oral killed whole-cell vaccine produced in Vietnam. Vaccine. 2006;24:4297-303.
63. Gupta D, Mondal S, Sarkar B, et al. An El Tor cholera outbreak amongst tribal population in Tripura. J Commun Dis. 2004;36:271-6.
64. Tamang M, Sharma N, Makaju R, et al. An outbreak of El Tor cholera in Kavre district, Nepal. Kathmandu Univ Med J. 2005;3:138-42.
65. World Health Organization. Cholera annual report 2005. Wkly Epidemiol Rec. 2006; 81:297-308. Available at <http://www.who.int/cholera/statistics/en/>. Accessed September 4, 2013.
66. Pal BB, Khuntia HK, Samal SK, et al. Emergence of *Vibrio cholerae* O1 biotype E1 Tor serotype Inaba causing outbreaks of cholera in Orissa, India. Jpn J Infect Dis. 2006;59:266-9.
67. World Health Organization. Global Alert and Response (GAR), Cholera. Available at <http://www.who.int/csr/don/archive/disease/cholera/en/index.html>. Accessed September 9, 2013.
68. World Health Organization. Cholera annual report 2006. Wkly Epidemiol Rec. 2007;82:273-84. Available at <http://www.who.int/cholera/statistics/en/>. Accessed August 24, 2013.
69. Siddique A, Nair G, Alam M, et al. El Tor cholera with severe disease: a new threat to Asia and beyond. Epidemiol Infect. 2010;138:347.
70. Teh CSJ, Chua KH, Thong KL. Multiple-locus variable-number tandem repeat analysis of *Vibrio cholerae* in comparison with pulsed field gel electrophoresis and virulotyping. J Biomed Biotechnol. 2010;2010:817190.
71. Teh CSJ., Suhaili Z, Lim KT, et al. Outbreak-associated *Vibrio cholerae* genotypes with identical pulsotypes, Malaysia, 2009. Emerg Infect Dis. 2012;18:1177-9.
72. The Armed Forces Health Survellace Center. Global emerging infections surveillance & response system. Fiscal year 2010. Available at <http://www.dtic.mil/cgi-bin/GetTRDoc?AD = ADA550147>.
73. Alam M, Hasan NA, Sultana M, et al. Diagnostic limitations to accurate diagnosis of cholera. J Clin Microbiol. 2010;48:3918-22.
74. Crofsblogs.typepad.com/h5n1/. India: four dead in Assam cholera outbreak. Updated June 9, 2012. Available at <http://crofsblogs.typepad.com/h5n1/2012/06/india-four-dead-in-assam-cholera-outbreak.html>. Accessed April 1, 2013.
75. Chinadaily.com.cn. Nepal: cholera outbreak in Doti. Updated August 7, 2012. Available at <http://www.chinadaily.com.cn/life/2012-08/07/content_15649180.htm>. Accessed October 2, 2013.
76. Crofsblogs.typepad.com/h5n1/. Philippines: Cholera outbreak declared in Virac, Catanduanes. Updated June 15, 2012. Available at <http://crofsblogs.typepad.com/h5n1/2012/06/philippines-cholera-outbreak-declared-in-virac-catanduanes.html>. Accessed April 1, 2013.
77. World Health Organization. Cholera annual report 2003. Wkly Epidemiol Rec. 2004;79:281-8. Available at <http://www.who.int/cholera/statistics/en/>. Accseed August 24, 2013.
78. World Health Organization. Cholera annual report 2004. Wkly Epidemiol Rec. 2005;80:261-8. Available at <http://www.who.int/cholera/statistics/en/>. Accseed August 24, 2013.
79. World Health Organization. Cholera annual report 2007. Wkly Epidemiol Rec. 2008;83:261-84. Available at <http://www.who.int/cholera/statistics/en/>. Accseed August 24, 2013.
80. World Health Organization. Cholera annual report 2008. Wkly Epidemiol Rec. 2009;84:309-24. [cited 2013 Aug 24]. Available at <http://www.who.int/cholera/statistics/en/>. Accseed August 24, 2013.
81. World Health Organization. Cholera annual report 2009. Wkly Epidemiol Rec. 2010;85:293-308. Available at <http://www.who.int/cholera/statistics/en/>. Accseed August 24, 2013.
82. World Health Organization. Cholera annual report 2010. Wkly Epidemiol Rec. 2011;86:325-40. Available at <http://www.who.int/cholera/statistics/en/>. Accseed August 24, 2013.
83. World Health Organization. Cholera annual report 2011. Wkly Epidemiol Rec. 2012; 87:289-304. Available at <http://www.who.int/cholera/statistics/en/>. Accseed August 24, 2013.
84. World Health Organization. Cholera annual report 2012. Wkly Epidemiol Rec. 2013; 88:321-36. Available at <http://www.who.int/cholera/statistics/en/>. Accseed August 24, 2013.
85. Chin CS, Sorenson J, Harris JB, et al. The origin of the Haitian cholera outbreak strain. N Engl J Med. 2011;364:33-42.
86. World Health Organization. Global Health Observatory (GHO), Cholera. Available at <www.who.int/gho/epidemic_diseases/cholera/en/index.html>. Accessed September 11, 2013.
87. World Health Organization. Global task force on cholera control. Cholera country profile: Laos. Available at <http://www.who.int/cholera/countries/LaosCountryProfile2008.pdf>. Accessed September 11, 2013.
88. Faruque SM, Sack DA, Sack RB, et al. Emergence and evolution of *Vibrio cholerae* O139. Proc Natl Acad Sci U S A.

2003;100:1304-9.
89. Chomvarin C, Johura FT, Mannan SB, et al. Drug response and genetic properties of *Vibrio cholerae* associated with endemic cholera in north-eastern Thailand, 2003-2011. J Med Microbiol. 2013;62:599-609.
90. Tran HD, Alam M, Trung NV, et al. Multi-drug resistant *Vibrio cholerae* O1 variant El Tor isolated in northern Vietnam between 2007 and 2010. J Med Microbiol. 2012;61:431-7.
91. Rashed SM, Mannan SB, Johura FT, et al. Genetic characteristics of drug-resistant *Vibrio cholerae* O1 causing endemic cholera in Dhaka, 2006-2011. J Med Microbiol. 2012;61:1736-45.
92. Nair GB, Qadri F, Holmgren J, et al. Cholera due to altered El Tor strains of *Vibrio cholerae* O1 in Bangladesh. J Clin Microbiol. 2006;44:4211-3.
93. Das S, Saha R, Kaur IR. Trend of antibiotic resistance of *Vibrio cholerae* strains from East Delhi. Indian J Med Res. 2008;127:478.
94. Nair GB, Ramamurthy T, Bhattacharya MK, et al. Emerging trends in the etiology of enteric pathogens as evidenced from an active surveillance of hospitalized diarrhoeal patients in Kolkata, India. Gut Pathog. 2010;2:4.
95. Roychowdhury A, Pan A, Dutta D, et al. Emergence of tetracycline-resistant *Vibrio cholerae* O1 serotype Inaba, in Kolkata, India. Jpn J Infect Dis. 2008;61:128-9.
96. Sabeena F, Thirivikramji G, Radhakutty G, et al. *In vitro* susceptibility of *Vibrio cholerae* O1 biotype El Tor strains associated with an outbreak of cholera in Kerala, Southern India. J Antimicrob Chemother. 2001;47:361-2.
97. Garg P, Chakraborty S, Basu I, et al. Expanding multiple antibiotic resistance among clinical strains of *Vibrio cholerae* isolated from 1992-7 in Calcutta, India. Epidemiol Infect. 2000;124:393-9.
98. Tarantola A, Quilici M. *Vibrio cholerae* O1 strains with decreased susceptibility to fluoroquinolones in travellers returning from India (Rajasthan) to France, April 2007. Euro Surveill. 2007;12(18):pii = 3186.
99. World Health Organization. Global task force on cholera control. Prevention and control of cholera outbreaks: WHO policy and recommendations. Available at <http://www.who.int/cholera/technical/prevention/control/en/>. Accessed September 23, 2013.