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Chapter 6

Cholera – Epidemiology, Prevention and Control

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Abstract

Cholera is an important public health problem, causing substantial morbidity and mortality especially in the developing countries. It is an indicator of socioeconomic problems and is a global threat to public health. Worldwide, approximately 3–5 million cholera cases and 100,000–120,000 deaths due to cholera occur annually. Cholera is transmitted by drinking water or eating food, which is contaminated with the *Vibrio cholerae*. Approximately 5–10% of persons suffer from severe cholera and if untreated, 50% of severe cases are fatal. The frequency, severity, and duration of cholera infection vary and keep on changing in different parts of the world. Environmental factors such as climate variability, temperature, and rainfall play an important role in cholera transmission. Population density, urbanization, and overcrowding also influence cholera transmission. It is also closely associated with the social and behavioral aspects of individuals as well as communities. Each year, many cholera outbreaks are reported from different regions of the world. These outbreaks have negative impact on social and economic conditions of the affected countries. An integrated, multisectoral program, designed on evidence-based interventions, is required to prevent and control cholera.

Keywords: Cholera, foodborne diseases, outbreaks, public health, *Vibrio cholerae*

1. Introduction

Cholera is an acute diarrheal illness, caused by the toxigenic strains of the bacterium *Vibrio cholerae* serogroups O1 or O139 [1, 2]. It is one of the important public health problems in Asia and Africa and causes substantial morbidity and mortality [3]. Since centuries, cholera has been a subject of interest for epidemiologists. The studies regarding cholera helped in the development of new epidemiological methods which led to the understanding of not only cholera transmission but also helped in the development of the science of infectious disease epidemiology [4]. The purpose of this chapter is to discuss this important infectious disease, i.e., its historical aspects, clinical features, epidemiology, and the outbreaks caused by cholera.

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Moreover, the preventive measures for cholera and methods of control of cholera outbreaks will also be discussed.

1.1. Historical aspects of cholera

For centuries, cholera remained one of the most horrific diseases [5]. It was first described by Hippocrates in the fifth century BC. Traditionally, the Ganges Delta region in Asia is considered the home of cholera. It is believed that cholera spread throughout the world from this region. Several epidemics occurred in Asia during the fifteenth and eighteenth centuries. Seven major pandemics of cholera have occurred since 1817 [3, 6].

Historians believe that the impact of cholera epidemics on the cultural evolution of Western Europe, was far reaching and it altered the social matrix of European culture. During the nineteenth century cholera was not only considered a terrifying disease, but was also a challenge to national identity and national economy [7].

John Snow performed pioneer work on cholera in London in the 1800s. He established an association between cholera transmission and contaminated water [4]. He discovered the method of prevention and control of cholera by tracing its source back to drinking water. Due to his work on the Soho cholera outbreak in 1854, John Snow has become a legend in epidemiology [5]. Later, in 1883, Robert Koch described the causative agent for cholera as a curved bacillus, *V. cholerae* [3].

In 1892, a major cholera outbreak occurred in Germany, killing 10,000 people. It was found to be caused by a defect in the design in the German waste removal system [7]. Seven cholera pandemics occurred during the nineteenth and twentieth centuries. The seventh pandemic began in Indonesia in 1961, reached West Africa in 1970 and the Americas in 1991 [3, 6].

In the United States of America, the risk of cholera is very low. However, in 2005, the floods caused by Hurricane Katrina, created the fear of a cholera epidemic for the first time in a century. The US Centers for Disease Control and Surveillance had 11 confirmed cases of people becoming ill from *Vibrio* sp. infection. However, only one of those cases had *V. cholerae*, which was not from the two epidemic-causing serogroups, i.e., O1 and O139 [5].

1.2. General burden of cholera on human population

Cholera is an indicator of a lack of social development and is a global threat to public health. With rapidly increasing population in developing world, the populations living in unsanitary conditions are increasing and the re-emergence of cholera has also been noted [8].

Every year, approximately 3–5 million cholera cases occur, worldwide. An estimated 100,000–120,000 deaths due to cholera occur every year. The number of cholera cases reported to the World Health Organization (WHO) continues to rise. In 2011, a total of 589,854 cholera cases including 7816 cholera deaths were reported from 58 countries, with a case-fatality rate of 1.3% [8, 9]. A total of 838,315 cases belonging to the period 2004–2008 had been notified to the WHO, as compared to 676,651 cases notified from 2000 to 2004 [1]. In 2006, 52 countries reported 236,896 cholera cases including 6311 deaths with a case fatality rate of 2.7% [10].

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The above-mentioned numbers are an underestimation of the real picture as the true number of cholera cases is thought to be much higher. Many cases may not be reported due to limitations in health-care systems and the surveillance systems. There are inconsistencies in cholera case definitions and there is a lack of standard vocabulary. Notified cases are often diagnosed on clinical grounds, leading to a number of undiagnosed and unreported cases. Some countries notify only laboratory-confirmed cases. It is a challenge in the estimation of disease burden due to the dearth of microbiology laboratories capable of detecting *V. cholerae* O1 and O139 in the countries where the disease is prevalent. Fear of sanctions regarding travel and trade may also result in underreporting of cholera cases [10, 11].

2. Causative agent

The causative agent of cholera, *V. cholerae*, is a waterborne and foodborne gram-negative bacterium. *Vibrio cholerae* can cause global pandemics which makes it unique among the diarrheal pathogens [12]. The serotype O1 or O139 colonizes and multiplies within the human small intestine [13]. There are two biotypes of *V. cholerae* O1: Classical and El Tor. Each of these biotypes has two serotypes: Inaba and Ogawa. Both these biotypes cause similar symptoms, however, El Tor biotype mostly causes asymptomatic infection or causes a mild illness [9]. Until 1992, only *V. cholerae* serogroup O1 was responsible for causing epidemics. However, in 1992, a previously unrecognized serogroup of *V. cholerae*, labeled as O139, was found to be responsible for large outbreaks of cholera in India and Bangladesh [3]. Multiple antibiotic-resistant strains of *V. cholerae* have also emerged and the severity of the disease appears to be intensifying [1].

2.1. Mode of transmission

Cholera is transmitted by drinking water or eating food contaminated with the *V. cholerae*. Fecal contamination of water or foods may result in large epidemics. The disease may also be transmitted through eating contaminated raw or undercooked shellfish [9]. Before the late 1970s, it was believed that person-to-person transmission of cholera is the main mode of transmission. Now, *V. cholerae* is found in riverine, estuarine, and coastal waters throughout both temperate and tropical regions of the world. It is recognized as a component of coastal and estuarine microbial ecosystems [14].

2.2. Incubation period

The disease has a short incubation period of 18 hours to 5 days, and it can spread rapidly through a population [12].

3. Clinical features of cholera

The infection may be mild or asymptomatic in most of the cases, but sometimes it can be severe. Approximately 5–10% of persons suffer from severe cholera. In severe cases, the clinical

features include profuse watery diarrhea, vomiting, increased heart rate, loss of skin elasticity, dry mucous membranes, low blood pressure, feeling of thirst, muscle cramps, metabolic acidosis, and restlessness or irritability. These patients can develop acute renal failure, severe electrolyte imbalances, and coma, leading to hypovolemic shock and death [3, 15]. If untreated, 50% of severe cases are fatal, while proper treatment and fluid replacement reduce mortality to less than 1% [3, 12].

3.1. Diagnosis

The confirmatory test for cholera is done by culture of a stool specimen or rectal swab. For transport of specimen, Cary Blair media is the most appropriate, and for isolation and identification of the organism, the selective thiosulfate–citrate–bile salts agar (TCBS) is the medium of choice. Commercially available rapid test kits should not be used for routine diagnosis as they cannot determine the subtypes and are not able to isolate the antimicrobial susceptibility. However, they are useful during epidemics [16].

3.2. Treatment

Rehydration by oral rehydration salts and, if required, intravenous fluids and electrolytes, is the cornerstone of cholera treatment. In addition, antibiotics may be needed for severe cases. Commonly used antibiotics include tetracycline, doxycycline, furazolidone, erythromycin, or ciprofloxacin [17].

4. Epidemiology of cholera

Cholera is said to be a 'forgotten disease' which mainly affects 'forgotten people' of the world. It comes into limelight when an extensive cholera outbreak occurs, although some neglected populations continually suffer from the recurrent episodes of cholera [10]. Cholera is the main cause of epidemic diarrhea in the developing countries. For the last four decades, there is an ongoing global pandemic in Asia, Africa, and Latin America [9].

4.1. Person distribution

In endemic regions, the majority of cases occur among children less than 5 years of age and in reproductive-age women [3]. However, various studies conducted in different parts of the world have reported varying age distribution for cholera patients. A study conducted in Pakistan during the period 2000–2001 found the mean age of patients infected with *V. cholerae* O139 as 40 years as compared to those infected with *V. cholerae* O1 strains where the mean age was 23 years [18]. Tamang et al (2005) conducted a study in a teaching hospital in Nepal between May 1, 2004 and October 31, 2004. They investigated 148 stool samples from patients with acute diarrhea and found out that 46 cases (31%) were positive for *V. cholerae* serogroup O1, biotype El Tor, serotype Ogawa. In their study, younger age group of less than 30 years was mostly affected. Males and females were equally affected [19]. During a cholera

outbreak in southwestern Nigeria from November 20, 2005 to January 1, 2006, a total of 115 cases and 11 deaths were reported. Overall case fatality rate was 9.6% with a case fatality rate in males of 11.9% as compared to 7.1% in females. During this outbreak, the age group of 15 years and above was the most affected comprising of 68.3% cases and 90.9% deaths [20]. A study conducted in southeast of Iran examined 3,178 patients with watery diarrhea, referred to a teaching hospital over a period of 4 years. A total of 362 (11.4%) samples contained *V. cholerae* strains; 336 (92.8%) were *V. cholerae* O1 Ogawa strain. A majority of the cases (270) were referred from rural areas. In this study, the patients ranged in age from 1 to 65 years. Approximately one-fourth (26%) were children under the age of 5 years [21]. In Mexico, the distribution of cholera cases by gender was reported to be similar. Individuals aged 25–44 years had the greatest proportion of cases while individuals aged over 65 years had the highest rates of infection. The authors state that this distribution differs from the distribution of cholera cases in endemic regions. The authors interpret this difference because of the occupational exposure and eating habits of the older individuals [3]. Most of the studies have mentioned a pattern of disparities between richer and poorer people with a higher incidence of cholera in lower socioeconomic groups [22]. Malnourished children and people with low immunity, such as HIV cases, have a higher mortality risk from cholera infection as compared to the normal population [8].

4.2. Place distribution

The frequency, severity, and duration of cholera infections vary and keep on changing in different parts of the world [13]. Cholera is endemic in Africa, south and southeast Asia [23]. In contrast, cholera is almost eradicated from most of the developed countries [5]. Incidence is as low as 0–5 cases per year in the United States [9].

In some countries such as Bangladesh and India, cholera infections occur every year [13]. Cholera reached West Africa and Ghana during the seventh pandemic [24]. In East Africa, cholera epidemic was first reported in 1836 but no cases were reported across Africa between 1870 and 1970. Cholera returned to Africa in 1970 as a result of seventh cholera pandemic. In 1974, cholera cases were reported for the first time in Tanzania, and then reported each year since 1977 [12]. In 1970, the first cholera case was reported in Ghana, after which cholera has been endemic in Ghana. Between 1999 and 2005, Africa accounted for about 90% of the cholera cases and 96% of the cholera-related deaths worldwide [24]. In contrast, other regions such as parts of South America have historically had only sporadic epidemics [13].

During 2013, a total of 56,329 cases were reported from Africa, which shows a decrease of 52% as compared to 2012 when 117,570 cases were reported. Africa accounted for 43.6% of the total cases in 2013 as compared to 93–98% of the total cases during the period 2001–2009. In contrast, 11,576 cases were reported from Asia, representing an increase of 57% as compared to 2012 when 7367 cases were reported from Asia [11].

In 2013, a total of 26 countries reported deaths due to cholera; 17 of these countries belonged to Africa. The case fatality rate was <1% in 4 countries, 1–5% in 17 countries, and >5% in 5 countries. In 2013, a majority (65%) of the deaths were reported from the African continent. A total of 1366 deaths were reported with a case fatality rate of 2.43% [11].

Various studies have reported differences in incidence of cholera in rural and urban areas. Sepúlveda et al (2006) reported high incidence of cholera in rural and suburban areas due to lack of basic sanitation infrastructure [3]. Other studies have reported cholera predominance in the urban areas, due to overcrowding and unsanitary living conditions. In urban communities in Ghana, intermittent water supply along with indiscriminate sanitation practices increases the risk of cholera. Urban slum areas are also at high risk of cholera infection as a lack of safe drinking water, poor sanitation, high population density, and crowding are common features in these areas; all of which are the risk factors for cholera [12, 24].

Bompangue et al. (2008) explored geographic proximity of the cholera cases [25]. The number of cases was found to be statistically significantly higher in the presence of a lake, a main road, or a harbor. Proximity to surface water, high population density, and low educational status were also identified as the predictors of cholera in an endemic area of Bangladesh. Poverty, urbanization, and proximity to coastal areas were important geographic predictors of cholera in Mexico. Proximity and density of refuse dumps also play a significant role in cholera transmission [6]. Epidemiological studies have demonstrated an inverse relationship between diarrhea and access to tube well water, and positive associations with canal water compared with river or pond water [13].

4.3. Time distribution

Vibrio cholerae are found in seas, rivers, and ponds of coastal areas of the tropical countries. It is postulated that environmental factors such as climate variability, temperature, and salinity play an important role in cholera transmission. Cholera is also associated with rainfall patterns. Recurrence of epidemic cholera has also been related to climatic factors [6, 13, 14].

Even in endemic areas, the magnitude of cholera incidence varies from year to year. In rural Bangladesh, there is a premonsoon epidemic almost every year. Cholera is rare during the winter as the temperature is low and there is little rainfall. Gradually, the temperature gets hotter till the monsoon arrives. The incidence of cholera is low in the actual monsoon period as compared to premonsoon period. This lower incidence in the monsoon period is explained by the dilution effect reducing the amount of bacteria in the aquatic environment. However, postmonsoon epidemics are much larger than the premonsoon epidemics [22].

A regular seasonal cycle for cholera outbreaks related to the different strains: classical, El Tor and O139, is described for Bangladesh. El Tor is reported to be most incident from September to November. Some studies have reported two annual El Tor cholera peaks; smaller peak in April followed by a larger outbreak from September to December. *Vibrio cholerae* O139 has a similar seasonal pattern [13].

In Pakistan, the incidence of cholera increases from November to January and from April to May, while in India, cholera cases peak in April, May, and June. In South America, cholera peaks in summer months, January to February and in the rainy season. In eastern African countries such as Kenya, Somalia, Uganda, and Tanzania, cholera outbreaks occur following summer rainfall. From 1979 to 1983, two cholera peaks were reported from Tanzania; from October to December; and from March to May. Both of these peaks coincide with increased

rainfall. In southern Tanzania, the highest incidence of cholera is reported in June and July, while during 2002 the northern parts of southern Africa reported maximum cholera cases from the last week of January to mid-March. In Mozambique, peak of cholera cases occurs from December to May [13].

Cholera outbreaks occur more commonly closer to the equator than at higher latitudes and do not follow a clear seasonal pattern near the equator. Although annual peaks are evident, it is difficult to determine distinct seasonal patterns in cholera outbreaks across regions. However, grouping countries by latitude range, rather than region, makes these seasonal peaks more obvious. Countries near the equator have higher and more constant temperatures, and have a greater incidence of cholera outbreaks [13].

The seasonality of cholera outbreaks may also be explained by secondary transmission. Several studies find that the severity of secondary transmission is associated with local environmental variables, predominantly water sources for household consumption. People who use contaminated surface water for drinking, cooking, and bathing are more likely to contract cholera than those who do not [13].

4.4. Social and behavioral epidemiology of cholera

Cholera transmission is closely associated with the social and behavioral aspects of individuals as well as communities. There are many demographic factors which predispose an individual or community to cholera infection. An increase in population density can result in overburdening existing water supply and sanitation systems. Thus, population density, urbanization, and overcrowding influence intensity of the cholera outbreak [24].

With increasing world population, urbanization is expected to increase. Most of this urban growth will occur in the developing countries. Because of economic issues, most of urban growth in the developing countries is the expansion of squatter settlements. These settlements comprise of households that lack access to safe drinking water and sanitation facilities. These conditions are of particular concern in the spread of infectious diseases which have been associated with conditions prevalent in urban squatter settlements [12].

There are obvious socioeconomic disparities in the occurrence of cholera. Even in the developing countries, the incidence of cholera is higher in socially deprived communities as compared to economically privileged class [13]. Among vulnerable groups living in areas at high risk for cholera, the case fatality rate is high. The secondary cases of cholera occur through fecal–oral transmission, and are related to poor hygiene, poor water, and sanitation environment [6, 22]. The water and sanitation environment as well as proper hygiene and educational level are associated with socioeconomic status of individuals as well as communities. Individuals with low socioeconomic status lack financial resources to install an appropriate sanitary system or obtain cleaner water sources. It is reported that cholera is more common in poorer households without safe water and proper sanitation system as compared to those having appropriate water and sanitation systems [22].

Surface water is contaminated with human excreta and sewage at place where rivers pass through overcrowded cities. In some African countries such as Ghana with multiethnic

population, the traditional laws for protection of water bodies are no longer obeyed. Thus, waste dumps are a common sight at the banks of surface water bodies in urban communities. These urban inhabitants have to use such polluted water at the times of water shortage. The urban slums and squatter settlers have lack of accessibility and affordability to safe drinking water and sanitation. Sometimes, public utility providers are not bound legally to serve the urban slums because of technical and service regulations. In addition, many urban slums are located at low lying areas leading to higher vulnerability to floods, making them more prone to cholera infection. Once the disease is introduced in a population, these demographic and social variables further aggravate the situation [6, 24].

Rapid urbanization can lead to overcrowding, unprotected water sources, and improper disposal of solid waste, liquid waste, and human feces. All these conditions make the environment conducive for cholera transmission. In urban communities, cholera outbreaks have been attributed to poor waste management and sanitation systems [24].

The behavioral aspects of community regarding cholera are important because if cholera is recognized as a serious and life threatening condition by the community, it will be more receptive to community health education program. Human behavior is also important in the acceptance of vaccine program [2].

A humanitarian crisis in a country or region can result in cholera outbreaks. The risk of cholera epidemics also increases after large-scale natural disasters. Some areas of Democratic Republic of Congo have been the site of large scale disasters including invasion and occupation by foreign forces, civil war, population displacements, and earthquakes. These areas have also shown high incidence of cholera [26].

Outbreaks of cholera have negative impact on social and economic conditions of the country as it leads to widespread fear and travel sanctions. Moreover, within the cholera-affected countries, resources are diverted to the care of cholera patients. Certain countries such as Peru and Mexico suffered economically as a result of cholera outbreaks, because of a decrease in tourism and decreased exports by other countries [3].

5. Cholera outbreaks

Cholera outbreaks have always proved challenge for the resource limited health-care systems of countries that usually suffer from these outbreaks. During 2014, cholera outbreaks were reported from South Sudan while in 2013 Mexico reported cholera outbreak [27]. Since October 2010, there is an ongoing outbreak in Haiti and the Dominican Republic. During 2013, the cholera cases during this outbreak accounted for 47.3% of all reported cases [11]. In 2013, outbreaks were also reported from other Central African countries such as Angola, Burundi, and Congo [11]. Namibia reported 1557 cholera cases including 17 deaths while Congo reported 1624 cases and 221 deaths in an outbreak which started in November 2012 [11]. In Cuba, an outbreak started in July 2012, and a total of 181 cholera cases were reported in 2013 [11].

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6. Prevention and control

6.1. Cholera prevention

For the prevention and control of cholera, it is important to understand the factors that are responsible for initiating and sustaining cholera infection in a community [28]. Measures for the prevention of cholera include provision of clean water and proper sanitation to the cholera-endemic communities.

6.1.1. Health education

Health education regarding personal hygiene and food hygiene should be provided to these communities. Media, community leaders, and religious leaders should participate in health education and social mobilization campaigns [29].

CDC has listed five basic cholera prevention messages. These include drinking and using safe water; washing hands with soap and water; using latrines or proper sanitation methods; proper cooking of food, covering it, and eating it hot; proper cleaning up of places used for bathing and washing clothes [30].

6.1.2. Vaccines

Currently, there are two oral cholera vaccines available: Dukoral and Shanchol. Dukoral is a killed whole cell vaccine including V. cholerae O1 serogroup and recombinant B subunit of cholera toxin. It can be given to children ≥2 years and to adults. For children 2–5 years of age, three doses, 1–6 weeks apart, are given orally, and booster dose is given after 6 months. For adults and children ≥6 years, 2 doses, 1–6 weeks apart, are given orally while booster dose is given after 2 years. The earliest onset of protection is 7 days after the second dose, and the protection at 6 months is 85–90% [31]. Shanchol is a killed bivalent (O1 and O139 serogroups) whole-cell vaccine suspension. It can be given to ≥1 year of age; 2 doses, 2 weeks apart, are given orally. The earliest onset of protection is 7–10 days after the second dose, and there is 65% protection for at least 5 years [31].

In cholera-endemic regions and those at high risk for outbreaks, cholera vaccines should be used along with other prevention and control strategies. In these regions, high risk population may be targeted for vaccination. The high risk groups include preschool and school-aged children, pregnant women, and HIV-infected individuals [23].

6.2. Cholera control

Cholera-endemic areas should prioritize cholera control measures [23]. Countries facing complex emergencies and displacement of internally displaced people (IDP) on a large scale or refugees to places where the provision of safe water and proper sanitation is compromised, and they are vulnerable to cholera outbreaks. In such situations, it is critical to depend on surveillance data to watch for an outbreak and to implement appropriate intervention

measures [32]. Thus, strengthening of surveillance system and early warning system is vital in places at high risk of cholera outbreak [29].

The main strategies for cholera control include appropriate and prompt management of cholera cases; strengthening laboratories; training and capacity building of health-care workers; and availability of adequate medical supplies for management [3, 29]. In addition, access to safe water, proper sanitation, appropriate waste management; personal hygiene and food hygiene practices; improved communication and public information are needed for the control of cholera outbreaks.

6.2.1. Cholera vaccines

Oral Cholera Vaccine should always be used as an additional public health tool in complex emergencies and should not replace usually recommended control measures such as improved water supplies, adequate sanitation, and health education. Once a cholera outbreak has started, the vaccine is not recommended as it takes time to provide protection and is also not cost-effective [33]. Reyburn et al (2011) estimated that an organized mass vaccination campaign could prevent 34,900 (40%) cholera cases and 1695 deaths (40%) in Zimbabwe. However, the cost of the vaccines was an important barrier along with other logistic issues [34].

A well-organized, multisectoral approach is required to control cholera outbreaks. The effectiveness of public health interventions depends on an efficient surveillance system. There must be frequent and timely information-sharing at local as well as global level [11]. The administration of cholera vaccines may be considered for high risk population in high risk areas. Funds and resources should be provided to the deserving countries to improve cholera prevention and preparedness activities.

6.2.2. International travel and trade

Currently, there is no obligation of cholera vaccination for international travel. It is learned with experience that quarantine and restrictions on travel and trade are not very effective in controlling the spread of cholera. However, the travelers should be provided information regarding signs, symptoms, and prevention of cholera. The neighboring countries of cholera-affected areas should be advised to enhance their surveillance system for early detection and prompt response if any outbreak occurs [11].

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