



Is Cholera Still Posing Global Health Challenge?

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Diarrhea caused by diverse etiologies, such as viruses, bacteria, protozoa and helminths, is the main clinical manifestation of food and water borne diseases. Many bacterial diseases like aeromoniasis, campylobacteriosis, colibacillosis, salmonellosis, shigellosis, *Vibrio parahaemolyticus* infection and yersiniosis transmitted through contaminated food and water, are reported from developing as well as developed nations. These diseases can occur in sporadic and epidemic form resulting into significant morbidity and mortality, especially in children, elderly and immunocompromised persons. Among these, cholera is an acute infectious life threatening bacterial disease that still remains a major public health threat to many countries of the world. The recorded history of cholera goes back to year 1854 when the etiologic agent *Vibrio cholerae* was isolated by Filippo Pacini of Italy. John Snow, a British Physician in 1854 was the first to establish a connection between cholera and water. The first cholera vaccine was developed by Waldemar Haffkine in 1892. The first pandemic of cholera, which occurred in 1817 spread through Middle East to Europe. Due to lack of surveillance and poor laboratory facility in developing nations, the actual burden of cholera is not well defined. In this context, the World Health Organization has mentioned that only 5 to 10% of cholera cases are officially reported each year. In cholera endemic countries, about 1.3 billion people are at risk of acquiring the infection. It is estimated that around 1.3 to 4 million cases and 21,000 to 1,43,000 deaths due to cholera are reported worldwide each year. The financial burden of cholera costs around US Dollar 2.0 billion annually. Globally, 2.4 billion people do not have basic sanitation and 844 million people lack clean water for drinking. Many countries of Africa and Asia, which do not have access to improved sanitation, are at risk of getting cholera. The cases and deaths of many persons due to cholera in several countries, such as Afghanistan, Angola, Bangladesh, Bhutan, Burundi, Cambodia, Cameroon, Chad, China,

Cosmos, Democratic Republic of Congo, Djibouti, Eritrea, Ethiopia, Gabon, Gambia, Ghana, Indonesia, Jamaica, Mali, Mozambique, Namibia, Nepal, Niger, Pakistan, Papua New Guinea, Peru, Philippines, Rwanda, Senegal, Somalia, Sudan, Swaziland, Tajikistan, Tanzania, Togo, Uganda, Yemen, Zambia and Zimbabwe clearly show that the disease still poses challenges to public health. It is important to mention that 98% of cases and 99% of all deaths are reported from African countries alone.

Outbreaks of disease are recorded from many nations including Bangladesh, Democratic Republic of Congo, Ethiopia, Haiti, India, Kenya, Nigeria, Tanzania, Uganda and Yemen. The massive epidemic of cholera in Haiti after the devastating earthquake in 2010 was responsible of 500,000 cases and 6600 deaths. The world's biggest outbreak of cholera with over 600,000 suspected cases and more than 2000 deaths was reported in 2016 from Yemen. A very recent epidemic of cholera, which occurred in Zambia during 2018 involved 3,077 persons and killed 70 patients. The drinking of unsafe water from shallow wells and insufficient waste management were identified as main causes of cholera outbreak in Zambia. Cholera is rarely encountered in industrialized countries because of easy access to potable drinking water, better waste disposal and improved environmental sanitation. However, the developing nations are vulnerable to cholera due to unsafe drinking water, poor sanitation and overcrowding. The epidemic of cholera in poor resource nations caused mounting stress as it inflicts high morbidity and fatality.

Disease is caused by *Vibrio cholerae*, a gram negative, non-acid fast, curved shaped, aerobic, motile, non-sporulated and non-capsulated organism. The bacterium is positive for oxidase, catalase, nitrate, methyl red, indole, but negative for Vogues Proskauer and urea hydrolysis. It ferments maltose, glucose, sucrose, mannitol and

mannose. The organism grows well at 37°C and can survive in salty water for long periods of time. *Vibrio cholerae* is susceptible to common disinfectants (1% sodium hypochlorite, 2% glutaraldehyde, 2.5% phenol, 4% formaldehyde and 70% ethanol), heat and drying. The infection can be experimentally established in dogs and rabbits.

A plethora of factors, which include lack of access to clean safe water, contamination of water sources, poor environmental sanitation, heavy rain fall, severe flooding, inadequate personal hygiene, inefficient waste management, scarcity of chlorine, overcrowding and temporary movement of people during flood, famine, war etc., are implicated in the epidemics of cholera. Climate change may also increase the burden of cholera worldwide. Humans act as the principal reservoir for cholera. The source of cholera infection is exogenous. The transmission of infection occurs through drinking of contaminated water and also ingestion of raw and undercooked fish, shellfish and sea foods. Occasionally, laboratory acquired infection is also recorded. The spread of infection from person to person is rarely observed. Hitherto, the transmission of cholera through inhalation is not documented. The vegetables grown in water containing human waste, ice cream prepared from municipal water and drinks sold by street vendors can also be potential source of the bacterium. Most cases are reported from low income nations. Though the disease can strike at any age group, young children are frequently affected with cholera.

The incubation period of cholera varies from few hours to 5 days. Clinical manifestations of disease in affected persons include watery diarrhea, vomiting, acidosis, dry mouth, muscular cramps, decreased skin elasticity, cold skin, sunken eyes, dehydration, weakness, intense thirst, oliguria, low blood pressure, rapid heart rate, renal failure, seizures, coma and death. The skin becomes bluish as a result of dehydration. The profuse watery diarrhea with flecks of mucus is called "Rice Water Stool", which is considered the hallmark of cholera. The disease lasts for 4 to 6 days. Cholera can be serious in malnourished children and AIDS patients. In severe cases, the prognosis of disease is poor. In order to save the life of patient, timely management of dehydration is highly imperative.

Diagnosis of cholera can be confirmed by isolating the bacterium from fresh diarrheic stool or rectal swab from patients on several media such as nutrient agar, MacConkey agar, blood agar, bile salt agar (BSA) and thiosulphate citrate bile salt sucrose (TCBS). It is advised that stool and rectal swab should be collected in Cary Blair transport medium and alkaline peptone water, respectively for bacteriological examination. The identification of *V. cholerae* can be done by string test.

Cholera can be managed by giving oral rehydration therapy, which is safe, effective and easy to administer to the patient. In severe cases, intravenous fluid is given to maintain glucose electrolyte balance. A number of antibiotics, such as azithromycin, chloramphenicol, ciprofloxacin, doxycycline, furazolidone, erythromycin, tetracycline and trimethoprim sulfamethoxazole can be used in severe cases to lessen the duration of diarrhea and diminish the excretion of organisms and thus will help to check the spread of infection. One study from Bangladesh mentioned that many cases showed resistance to erythromycin, tetracycline and trimethoprim sulfamethoxazole. It is recommended that poor people who are unable to afford expensive oral rehydration powder from market, can easily prepare oral rehydration solution at home by adding 6 teaspoon of sugar, half teaspoon of table salt, one meshed banana in one liter of boiled water. This solution should be given orally to the chorea patients to check fluid loss. Most of the infected persons, who are either asymptomatic or show mild symptoms can be easily treated with oral rehydration solution. However, in severe cases, early treatment with parenteral administration of fluids and antibiotics is essential. It is pertinent to mention that in the absence of treatment, renal failure and death may occur with 3 to 4 hours. Several vaccines, namely Dukoral, Euvichol, Shanchol and Vaxchora are available. It is advised that immunization should be done in young children and HIV persons living in cholera endemic regions. In USA, Food and Drug Administration approved immunization by Vaxchora, a live vaccine, which is given orally as a single dose. This vaccine claims to reduce the chance of diarrhea in people by 90% after ten days of immunization. However, some side effects, such as nausea, vomiting, diarrhea, headache, anorexia and tiredness are observed with Vaxchora vaccine. The World Health Organization has recommended that immunization with oral cholera vaccine should be made a part of an integrated strategy in the control of cholera, which is widely prevalent in many countries of world.

The disease can be controlled by employing multifaceted approaches, such as water purification, effective sewage disposal, environmental sanitation, surveillance, social mobilization and immunization. In addition, health education to the public about the mode of transmission, severity of disease, personal hygiene, use of potable water, safe storage of water, chlorination of water, washing of fruits and vegetables with clean water and consumption of cooked fish and sea foods will be very helpful to mitigate the incidence of cholera. Furthermore, early detection and quick response to contain outbreaks of cholera in endemic regions is warranted.

It is emphasized that person showing profuse watery diarrhea and dehydration with a history of consuming sea food or travelling in endemic area should immediately seek medical advice. It is highly imperative to institute prompt hydration and antibiotic therapy, especially in children and immunocompromised person to avert the severe complications as delay in treatment can be fatal. As cholera is endemic in over 45 countries of the world, it is emphasized that cholera surveillance should be made as a part of integral disease surveillance programme. The persons travelling to endemic areas are advised to take vaccine as a preventive measure against cholera. Since the current cholera vaccine gives protection for short time, further attempts should be made to develop a safe, potent and low cost vaccine to confer lifelong immunity to the susceptible population as cholera remains an important global health challenge.

Dedication

This paper is dedicated in the memory of Shri Atal Bihari Vajpayee, former Prime Minister of India who was recipient of Bharat Ratan, the highest Indian Civilian Award. He was a great statesman, veteran politician, visionary leader, an ardent defender of democracy and honest, generous, kind person with high moral value and character.

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