

## Review of Trends in Cholera

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Received date: November 26, 2014, Accepted date: January 26, 2015, Published date: January 30, 2015

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### Abstract

Cholera is not only a matter of developing countries but also of developed ones. Its causative agent is toxigenic *V. cholerae* having a filamentous bacteriophage (CTXΦ) cause cholera. It finds mostly in bile aquatic surroundings. This disease spreads through contaminated water and food materials. Oral rehydration is enough as treatment for cholera dehydration. Its cases may depend upon season, climate and distance of refuse dumps.

**Keywords:** *V. cholerae*, Enterobacteriaceae; *V. mimicus*

### Background

Internationally, Cholera is a significant matter, that is emerging as the integer of countries affected continues to increase in its cases [1,2]. Cholera, is an acute secretory diarrheal infection which is rare in industrialized countries; however, the disease is still globally prevalent including the subcontinent of India and sub-Saharan Africa including India, Pakistan, Bangladesh, Latin and Central American countries (like Haiti) and African countries (Zimbabwe, South Africa, Mozambique, Botswana and Zambia). Epidemic infection sometimes occurs in south-eastern of Iran in the border of Pakistan and Afghanistan [3,4]. In global health, there is always an incomplete outline leftover regarding to manage diarrheal diseases and worldwide support still stands to make an important impact in the burden [5]. Developed countries with high quality water and its dirt management, have no cholera gear more than a century. But the causative agent (*Vibrio cholera* O1 and O139) exists within jam-packed environment [1].

### Causative Agent

Discovery of *V.cholerae* is credited to Robert Koch a German bacteriologist, who identified the micro-organism during 1883's outbreak in Egypt and due to the vibratory movement of organism the genus was named as *Vibrio* [3].

A study of Nepal, Haiti, and Bangladesh showed that all strains from these three countries shared a common ancestor, three Haitian and three Nepalese strains were almost the same, with only 1 or 2 nucleotide dissimilarities in their core genome [5]. A new strain of *V. cholera* serogroup O139 (Bengal) observed in the fall of 1992 caused outbreaks in Bangladesh and India in 1993. Now, this strain is endemic in at least eleven countries. The current seventh pandemic of cholera, began in 1961 and continued to 1991 caused by serogroup O1, El Tor biotype and originated from the Celebes Islands and Indonesia [3,6].

It is declared by a study that 'indigenous non-O1-O139 Haitian strains were involved in the outbreak, published on June 18, 2012 by Hasan and colleagues [6]. In some endemic countries, in higher

absolute latitudes cholera outbreaks were occurred in a significant seasonal pattern while in tropical countries outbreaks of cholera do not depends upon seasonal pattern. Hashizume et al. and Huq et al. defined from the data on four rural regions of Bangladesh, an important relationship of water temperature, water depth, and rainfall with the incidence of cholera.

### Prevalance

Prevalence of *V. cholerae* is highly temperature and season dependent. The genomic affinity of the Haitian and Nepalese strains were noticeably different from isolates circulating elsewhere in the world, showing strains have some relation with climate [7]. The WHO has recommended an early warning system for cholera epidemics, due to the sensitivity of *V. cholerae* to climate changing, using climate parameters [2,7-9].

Favour by the micro-environment, increases growth of the bacterium which ultimately raise the cholera cases. According to study, the frequency of cholera is difficult to calculate from data on climate, and depending on the local surroundings and may hit the highest point once or twice a year [10].

*V. cholera* is a comma-shaped, gram-negative curved motile bacterium by a single flagellum, aerobic and sometimes facultative anaerobic [3,4]. The natural habitat of *V. cholera* is the aquatic environment, can survive within and outside the aquatic environment and inadequate ecological management makes cholera a complex health problem to manage [11,12]. Humans are more infected by Halophilic (requires NaCl for growth) pathogen in moist salty conditions. It grows with a range of 10 to 43°C but rapidly in most favorable temperature at 37°C. The organism can be inactivated at pH values less than 4.5 at room temperature and it grows in optimum pH of 7.6, with a range of 5.0 to 9.6 [4].

### Biochemical Tests

Variable in size from 1-3 µm in length and 0.5-0.8 µm in its diameter with two different antigenic structures; a flagellar antigen (H) and a somatic O antigen, non-acid resistant with infectious dose 10<sup>3</sup>-10<sup>6</sup> and 10<sup>2</sup>-10<sup>4</sup> organisms ingested with water and food respectively. *V. cholerae* is not fastidious in nutritional requirements

for growth though, organism needs an adequate buffering system. Non toxigenic strains of *V. cholerae* are also present in environment, only strains encoding cholera toxin, haven a filamentous bacteriophage (CTX $\Phi$ ) cause cholera. Colonies of *V. cholera* are lactose-negative, but sucrose-positive. Contrasting other Enterobacteriaceae, *V. cholera* is oxidase-positive. The differentiation of the somatic antigen leads to pathogenic and nonpathogenic strains. Among more than 200 serogroups of *V. cholerae*, *V. cholerae* O1 and *V. cholerae* O139 are the most common serogroups associated with epidemic cholera [3,4].

## Death Rates

Comprehensive nationwide statistics regarding cholera outbreaks presenting yearly synopsis maintains in Weekly Epidemiological Record by the World Health Organization (WHO) [1,2]. There is fast increase in cholera cases, As due to lack of insufficient epidemiological observation systems, laboratory facilities, financial supporting and social disincentives to case reporting through one estimation, among actual numbers of cholera worldwide only 5-10% cases befall as account [1]. Showing annually about 100 000 to 120 000 deaths globally along with 3 to 5 million cases. The mortality rate in Bangladesh and India is about 6.3 deaths, in the Eastern Mediterranean region which includes Pakistan and Somalia is 0.1 deaths and in Western Pacific Region 1.2 deaths per 100,000 people. Amongst all group ages mortality rate is high. According to Lanata et al; 2002 calculation, globally per year 11 million cholera cases occur, amid under 5 years children [1,13]

## Haiti's Study

More than 700,000 cases and more than 8,000 deaths were reported by the end of 2013. From 2011 all the way through 2013, the reported cases of cholera in the world accounted for more than half gear from Haiti only. Eventually, to develop a national designed plan for cholera eradication and cholera vaccines, CDC worked with other partners and establishes a laboratory-enhanced observation system. The number of cases during the first 4 months of 2014 is 97% below, mention cases of cholera have waned noticeably [14]. Field Survey of the slums of Bahawalpur (February-April 2010) showed that cholera is major disease of Bahawalpur, especially in young ones [15].

## Vaccines

Due to harmful and short timed impacts, the use of cholera vaccine is not recommended by most of physicians; according to them, improved personal and environmental hygiene can replace the vaccine administration [16].

Two types of oral cholera vaccines (OCV), namely Dukoral and Shanchol two oral cholera vaccines (OCV) are currently available and are whole-cell killed vaccines (8). Due to interest in the use of vaccines as a measure to control cholera, one new generation of oral cholera vaccine has also created, cheap oral vaccine which is under assessment for WHO pre-qualification [1,7]. For areas of cholera outbreak threat mass vaccination especially of children for cholera immunization is particularly important [1,17].

## Kolkata's Study

A study in Kolkata, India showed that a single dose of live oral cholera vaccine VA 1.4 ( $1.9 \times 10^9$ ) is safe and immunogenic in adults [18]. Cholera infection may be asymptomatic or calm, while dryness,

renal malfunction and death may occur within hours of onset in severe cholera cases caused by only cholera toxin-producing (toxigenic) strains of the bacterium *Vibrio cholerae* [3,4].

## South Sudan's Study

Cholera spreads through eating food, other factors that increase the risk of cholera cases in the capital Juba of South Sudan showed that its spread is due to water from unsafe sources and poor community handling of dead bodies [11].

## Sindh's Study

According to one study in Khairpur, Sukkur and Rohri of Sindh, Pakistan the cause of cholera is the presence of *Vibrio* species *V. cholerae* and *V. mimicus* in drinking water of these areas [19]. The prevalence of cholera is due to use of polluted water, there is an inverse spatial relationship between cholera prevalence and distance to refuse dumps [12,20].

## Risk Factors

Everyone is at risk of contracting cholera but malnutrition increases the chance of infection and then clinical diseases [3,11]. With unknown reason, the incidence of cholera is twice in people with type O blood compared with other blood groups. *Vibrio cholerae* O139 cause a major epidemic and infection with *V. cholerae* O1 does not lead to immunity against *V. cholerae* O139 [3].

## Symptoms

Children are more symptomatic than adults, while second infections in adult patients rarely occur or are mild because of earlier infection with classic biotype of *V. cholera* which usually produce antibodies that protect them against recurrent infection. Two new subclades (PSC-1 and PSC-2) of O1 E1 Tor strains have originated in Pakistan, according to one study, geologically, PSC-1 isolates originated from the shore, while PSC-2 isolates originated from inland areas flooded in August 2010 by the Indus River [3, 19,21].

Incubation period is one or two days, symptoms can begin as soon as a few hours or as long as five days after the infection, are often mild to severe with sudden onset of a painless watery diarrhea with vomiting which can quickly lead to dehydration. Hallmark of disease is abundant watery diarrhea characterized by profound fluid and electrolyte losses in the stool and the rapid development of hypovolemic shock. One of 20 patients infected with dehydration, remain untreated can lead to a severe shock and death in a few hours, While administration of appropriate rehydration therapy reduces the mortality of severe cholera from over 10 percent to less than 0.5 percent. Although many infected people can spread out the infection. The typical cholera stool is opaque white and usually has a "rice water" appearance which is not aromatic. Patients with severe cholera have a stool volume of more than 250 mL/kg of body weight during 24 hours [3,4].

*V. cholerae* can be recognized in microbiology laboratories using selective media and biochemical tests by eagerly grown-up from clinical specimens, including stool and rectal swabs [4]. For identification of microorganism and epidemiological purposes laboratory diagnosis is required, for this purpose, direct microscopic

examination of stool including dark-field examination, gram staining, culture, serotype and biotype identification are performed [3].

Polymerase chain reaction (PCR) has a high sensitivity and specificity has been developed to identify for screening of *V. cholera* in food samples. As vibrio grows at a high pH or in bile salts that's why many of the selective media used for enteric pathogens do not support the growth of *V. cholerae*. On thiosulfate-citrate-bile-sucrose-agar (TCBS), the sucrose-fermenting *V. cholera* grows as large, smooth, round yellow colonies. By using specific antiserum, positive immobilization test can be observed for the *V. cholera* [3].

## Treatment

Treatment with oral rehydration is enough [2]. In conjunction with suitable oral or intravenous hydration, treatment with antibiotics prescribed for all hospitalized patients and who lost a large volume of stool during the rehydration therapy, is also recommended. Antibiotics susceptibility patterns should follow for choice of antibiotic but mostly, doxycycline is suggested as the first-line treatment for adults and azithromycin which is more effective than erythromycin and ciprofloxacin for pregnant women and children. Trimethoprim-sulfamethoxazole (TMP-SMX), erythromycin, and ciprofloxacin are other antibiotics effective against *V. cholera*. Antibiotics should be administered along with aggressive hydration, antibiotic use can reduce secondary transmission of cholera. Antibiotic recommendation for patients resistance to tetracycline or other antimicrobial agents can be treated with a single 300 mg dose of doxycycline [3].

## Therapeutic Study

In one study screening the antimicrobial activities of extracts extracted with methanol and water of leaves and stems of *Adiantum capillus veneris* and *Tagetes patula* against *V. cholerae*, showed that Leaves methanol extract (LME), Leaves water extract (LWE), stem methanol extract (SME) and stem water extract (SWE) of *Adiantum* and *Tagetes* showed maximum Zone of Inhibition (ZI) against *V. cholerae* and needs further studies for utmost benefits [22].

## Prevention

Cholera is a killer but preventable disease [11]. For the prevention of cholera adequate hygienic condition, safe water and sanitation are important and critical but for much of the cholera-affected rising countries, major improvements are a far-off objective [7].

## Full Text

"Policymakers need to know the burden of disease and the population at risk." Dr. Ali said. "If cases are not reported then resources cannot be allocated to deal adequately with the disease" [13].

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