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Cholera: Water Borne Disease: A Review

Haleema Sadia^a, Iqra Mujeeb^b, Arifa Tahir^c, Ayesha Alam^d, Shahid Raza^{d*}

^aDepartment of Biotechnology, Baluchistan University of Information Technology, Engineering and Management Sciences, Quetta, Pakistan

^bDepartment of Microbiology, Baluchistan University of Information Technology, Engineering and Management Sciences, Quetta, Pakistan

^cDepartment of Environmental Sciences, Lahore College for women University, Lahore Pakistan.

^dDepartment of ORIC, Lahore Garrison University, Lahore, Pakistan

Abstract

Cholera is pandemic, food and water borne disease caused by bacteria named *Vibrio cholera*. It is an intestinal disease which is mainly identified by severe diarrhoea and vomiting. It is transmitted through food and water contaminated with *V. cholera*. *Vibrio cholera* is found on crustaceans, copepods, plants surfaces etc. which spread from waters for the search of food and leave the organism there. Here it causes disease by contaminating the food and water. This bacterium has many serotypes but O₁ and O₁₃₉ is mainly known to be the causing agents of cholera disease. The disease is simply treated with ORS (Oral Rehydration Solution), a solution or may be powder form to mix in specific amount, recommended by WHO. The disease can also be treated by antibiotics. The origin of cholera is thought to be Ganges Delta region (in Asia). *Vibrio* bacteria attack on the small intestinal wall and secrete its toxin 'CTX' also called as Cholera toxin. This toxin is the virulence factor of cholera. This toxin is the constituent of phage which make the non-infected *Vibrio cholera* an infected bacterium. The infected bacterium must acquire VPI (*Vibrio* Pathogenicity Island) which contain a gene required for attachment with the mucosa of small intestine. In Pakistan, serotype O₁ and O₁₃₉ cause endemic cholera. Cholera spreads because of unsafe water supply and contaminated food as well as ignoring hygienic conditions. This disease can be controlled if sanitary conditions are kept in balance.

Keywords: cholera; *vibrio cholera*; O₁; O₁₃₉; cholera toxin.

Introduction

Cholera is an intestinal disease in which a person suffers from severe diarrhoea ^[1]. The origin of this disease is found in Asia (Ganges Delta Region). The first pandemic began in 1817 to the west through trading routes ^[2]. Then cholera pandemic occurred in UK, Africa, America and Australia ^[3]. Because of this disease many people were dead so it became a public health concern ^[4]. With the past few years ratio of cholera disease is increased due to poor environmental conditions and floods and earth quack like natural disaster. It is like an indicator for those countries which are under development. If an area has refugees and poor health conditions then surely cholera is present in that area. The causative agent is found to be bacteria named *Vibrio cholera* ^[1]. One of its serotype E1 Tor isolated in 1905 from Indonesian pilgrims who were going to Mecca at the quarantine station of a village name E1 Tor, Egypt, so this sero group was named after this place ^[2]. E1 Tor belongs to biotype of sero group O1. Another sero group was discovered in 1992 in Bangladesh ^[5-7]. It was named *V. cholera* O139. Now O1 and O139, together, are causing disease worldwide ^[1].

1. Epidemiology

1.1 Transmission

Cholera can be simply defined as water or food borne disease. The contaminated food and water transmit the bacteria ^[8-10].

1.2 Risk factors

Cholera is found in 3 in 100 individuals ^[11,12]. Many factors are involved like:

Low amount of stomach acid: *V. cholera* is tending to be killed in stomach by HCl acid but with low quantity of acid cannot kill the bacteria and it will cause disease in the body.

O blood group: the person with O blood group is susceptible towards E₁ Tor. The reason is unknown ^[13-15].

Children of 2-4 years in endemic areas are more susceptible than other people but cholera in newly entered area affect the adult person ^[16].

1.3 Clinical aspects

Symptoms

Vibrio cholera's incubation period is about 5 days and 18 hours ^[1]. After this period symptoms start to appear with:

Dehydration

Watery diarrhoea: the stools will be in huge amount and resemble with the rice water. The odour is appeared to be as fish smell.

Vomiting: the heave usually contains alkaline clear and watery fluid ^[1].

It leads to severe dehydration in which:

Poor skin turgor, undetectable blood pressure, wrinkled hand and feet and sunken eyes, extreme thirst, hypoglycaemia ^[17] and hypokalaemia ^[18]. After these symptoms patient will be unconscious and die in few hours if he will not be rehydrated.

1.4 Complications

Miscarriage can occur due to shock and poor supply of liquids by placenta ^[19].

Severe muscle cramp is also common because of electrolyte deficiency.

These both issues can be solved with good rehydration. ^[1]

1.5 Treatment

Treatment is very simple. The person suffering from cholera must be supplied with a lot of fluids. These fluids should contain the electrolytes which are being lost because of the disease. After rehydration blood volume will be restored and the lost components will be replaced ^[1].

1.5.1 Oral Rehydration Solution ORS

This is a solution for maintaining dehydration. It is used for eliminating the issues of:

Potassium deficiency, fluid losses, shortage of fluid and metabolic acidosis. ORS is necessary for the rehydration so it is highly recommended to provide it as fast as possible. If ORS is not available, a person can prepare himself. In one Litter water, add 2.6g NaCl, 13.5g glucose, 1.5g KCl and 2.9g trisodium citrate. Instead of glucose rice powder can be used. Water should be clean and pure and leftover solution should be discard after twenty-four hours ^[1].

1.5.2 Antibiotics

Antibiotics helps in recovery. The intake of intravenous fluids and the stay at hospital can be shorten by antibiotics. Usually doxycycline is recommended for adults. ^[1]

1.6 Cholera Resistance towards Drugs

In the past few decades, V. cholera O1 has been found to be resistant towards antibiotics including: Ampicillin, kanamycin, streptomycin, gentamycin, trimethoprim, tetracycline and sulphonamides ^[20].

Fluor quinolone resistant strains of V. cholera (against Quinolones) have been informed from Kolkata, India ^[21,22].

1.6.1 Clinical microbiology

Vibrio cholera, a gram-negative bacterium with monotrichous flagella (polar). A non-spore forming bacteria found in curved rod. It is oxidase positive and produce ATP by fermenting mannitol, sucrose, and glucose and it is positive in ornithine and lysine decarboxylase tests.

It is classified on the bases of O antigen. It has 200 sero groups ^[23] but only O139 and O1 cause pandemic and endemic diseases. If Vibrio cholera specie do not agglutinate with O139 and O1 antisera then they termed as non-cholera vibrio or non-agglutinable vibrio. These non-cholera vibrio's can cause disease like intestinal infections ^[24-27].

1.6.2 Growth on agar

They are in faeces so the faeces is put on to thiosulphate citrate bile salts sucrose agar. This agar inhibits other normal flora of faeces and let Vibrio cholera grow. This specimen (faeces) should also be inoculated in the alkaline peptone water and high pH which also supports the growth of bacteria. This plate will be incubated for 6-12 hours and a second plate will be inoculated after these 6-12 hours.

After 18-24 hours, both plates have equal yellow colonies with a little higher centre. These colonies will be

agglutinate with O139 or O1 antiserum and oxidase positive ^[1].

1.6.3 Rapid Test

A sample of stool can be studied under dark field microscopy ^[28].

PCR and DNA probes and rapid immunoassay is also available for the confirmation but these are not use commonly ^[1].

1.7 Division of *Vibrio cholera*

There are many types of vibrio but two serotypes are considered as the causative agent of cholera. The two types are O139 and O1 ^[29].

Sero group O1 has two biotypes: Classical and E1 Tor

These can be distinguished by the use of phage, polymyxin B sensitivity, hemolysis, hemo-agglutination etc. O1 biotype is further subdivided into: Ogawa and Inaba serotype

Table 1: The serotype of *V. cholera* ^[30,31]

	Antigen A	Antigen B	Antigen C
Ogawa	Present	Present	Small amount present
Inaba	Present	Not present	present
Hikojima (rare and unstable)	Present	Present	present

1.8 Clinical pathophysiology

When a person ingests food and water contaminated with vibrio, the bacteria must pass through the stomach where stomach acid is present. If it passes through stomach, it will now colonize the small intestine (upper part). Toxin co regulated pilus (TCPA) is a fimbria that aid in colonization. It attaches with the receptor on the mucosa ^[32]. Because of its flagella, it can penetrate the mucus which overlying the mucosa. Attachment with mucosa, with high concentration of vibrios, can deliver enterotoxin sufficiently ^[33].

Koch suggested in 1884 that bacteria cause disease by toxin. This hypothesis was demonstrated by Dutta and De. They isolated this toxin from culture filtrates of rabbit and purified and sequenced it ^[34-37].

The toxin consists of five 'B' subunits and one 'A' subunit ^[38,39]. Inactive 'B' subunit binds holotoxin with GM1 ganglioside receptor which is present in the mucosa of small intestine. 'A' subunit is sent into cell where it stimulates adenylate cyclase ^[40,41]. It increases the cyclase AMP which leads to increase the amount of chloride secretion and inhibit the absorption of neutral sodium chloride. This disruption cause flood of fluid rushing into the small intestine ^[42]. Because of high quantity of fluids in the small intestine, the bowels are not able to absorb more than normal fluid and excrete it in the form of diarrhoea ^[43].

This excretion contains high amount of sodium, chloride, bicarbonates and potassium and very few amounts of protein and blood cells ^[44]. Large number of isotonic fluid containing electrolytes cause blood pressure and shock. It also leads to metabolic acidosis and potassium deficiency. Cholera bacteria in the diarrheal fluid are highly infectious (present in high concentration in the stools). When they transfer in the environment, they can contaminate water and food sources ^[1].

1.9 Virulence factor

Cholera toxin (CT) is the virulent factor of *Vibrio cholera* O1 and O139 which are toxigenic strains of *Vibrio cholera*. CT is produced by a gene (ctxAB) that has at least 6 genes: orfU, cep, ctxAB, zot and ace ^[45]. These all established the genome of filamentous bacteriophage (CTXφ) that is the carrier of cholera toxin gene and vibrio pathogenicity island (VPI), contain genes for pilus colonization factor TCP ^[46,47]. The representative CTX genome have two distinct areas:

1: The core ^[47]: it is involved in encoding cholera toxin. It also contains other genes which encodes protein that participates in phage packing and secretion (Ace, Cep and OrfU) and CTX assembly (Zot) ^[47].

2: RS2 region ^[47]: it encodes gene required for regulation (rstR), replication (rstA) and integration (rstB) of CTX ^[48].

1.10 The ecology of cholera

It is found attached on the crustaceans, copepods, insects ^[49], filamentous algae ^[50], and surfaces of plants. These organisms go for the food and spread these bacteria. The infected strains are isolated from the contaminated environment which contain infected individuals. Non-infected strain is found far from the infected places. A non-infected strain must acquire the VPI, CTXφ receptor and infected with CTXφ so that it can cause cholera ^[46,48,51].

1.11 Prevention and Vaccine

As contamination of food and water is the source of cholera so one must be careful about the food by cooking it carefully (especially sea food), safe supply of water, improved sanitation and create awareness about cleanliness and the disease.

1.11.1 Vaccine

Dukarol was found efficient for the disease. It consists of killed vibrio cholera and B subunit. Two doses are given for two to six weeks ^[52].

Another vaccine was also found to be effective against cholera that is Sanchol. It is for children of five years as well as for adults. It was used in Bangladesh ^[53].

1.12 Cholera in Pakistan

Cholera is defined as endemic in Pakistan by WHO. Many cases are reported to WHO by Ministry of Health, Pakistan and published in Weekly Epidemiological Records. In 1971, 1185 cholera cases and 43 deaths were reported. Also, in 2011 537 cases and 219 deaths were reported. Cholera occurs seasonally. *Vibrio cholera* O1 Ogawa was found high in summer. It was also isolated in very high amount between June and August. In 1993 and 1994, epidemics occurred by sero group O₁ (in May to August) and serogroup O₁₃₉ (August to October). O139 re-emerged in 2000 and remained till 2000. It was discovered that O139 was affecting age around 40 years. Inaba and Ogawa was found as main infectious serotype in Pakistan between 2004 and 2005. Drugs were found sensitive towards cholera like Quinolones which was effective for many years but many drugs like Tetracyclines, Cortimoxazol, Chloramphenicol and Ampicillin never remained constant. ORS was

found effective for the treatment of cholera.

The disease is spreading because of many factors for example: behavioural practices like hand washing, maintenance of hygiene, practices of garbage disposal and sanitation has never been studied. It is also found that malnutrition individual has high chances of having cholera disease ^[54].

2. Conclusion

Cholera is sporadic, endemic or epidemic disease cause by vibrio cholera. This is a serious threat to human survival as it can cause shock that leads to death. The affected person should be rehydrated as it kills half of the affected individuals. The awareness among people should be assured about sanitation as even today many people do not think that washing hands after using toilet is necessary. Without taking any precaution, one can face more tough and hard situation in the future. As *Vibrio* bacteria found normally in aquatic life, we cannot eradicate it completely. Without being harmed, it is necessary to found solution which will help us living with this organism.

Recommendation

- I. Take care of hygiene.
- II. It should be assured by government that the sewage water line and drinking water line are separate. If some damage occurs in these pipelines then the repairmen should be assured.
- III. Good quality of sewage water pipe line and drinking water pipe line are needed to be kept in mind as a preventing measure.
- IV. Drink boiled or filtered water.
- V. Conduct seminar and awareness through all type of media (social networks, television, public service message through mobile phones, radios, print media etc.)
- VI. There should be a topic in school text books regarding importance of drinking clean water and hygienic food as well as keeping cleanliness so kids will be aware of good hygiene. As we all know, kids are more prone to suffer from cholera.

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