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***Vibrio cholerae*: A historical perspective and current trend**Mary Oyenike Oladokun^{1,2*}, Ifeayin Anthony Okoh^{1,2}¹SAMRC Microbial Water Quality Monitoring Centre, University of Fort Hare, Alice, South Africa²Applied and Environmental Microbiology Research Group, Department of Biochemistry and Microbiology, University of Fort Hare, P Bag X1314, Alice 5700, South Africa

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ABSTRACT

Vibrio cholerae (*V. cholerae*) is a Gram-negative, curved, rod-shaped bacteria with two of its strains *V. cholerae* O1 and *V. cholerae* O139 known to cause cholera, a deadly diarrheal disease that has repeatedly plagued the world in pandemics since 1817 and still remains a public health problem globally till today. The pathogens' persistence in aquatic milieu during inter-epidemic periods is facilitated by the production of a biofilm, thus evolving from being an infection of oral-fecal transmission to a more composite ecological framework of a communicable disease. The outbreaks of cholera spread rapidly in various intensities within and among countries and even continents and the World Health Organization estimates that 3–5 million cases outbreak and over 200000 die yearly from cholera. Also, the impact of a cholera epidemic is not limited to its high morbidity and mortality rates alone, but also the grievous impact on the economy of the countries experiencing the outbreaks. In this review, we carried out an overview of *V. cholerae* including its isolation and detection, genetics as well as a comparison of the toxigenic and non-toxigenic determinants in the human host and the host defences. Furthermore, the history of global pandemics, cost implications, conflict and ecological methodologies of cholera prevention and control. The management of disease and antibiotic resistance in *V. cholerae* are also highlighted.

1. Introduction

Vibrio cholerae (*V. cholerae*) belongs to the family of Vibrionaceae, a facultative anaerobe with a flagellum used for mobility[1]. It is Gram-negative, bean-rod shaped, and oxidase positive, but it does not form spores[2]. Fresh isolates are prototrophic, and in suitable media they breed very fast within a maximum growth rate of 30 min. They exhibit maximum growth in an aerobic condition, though they are facultative organisms. *V. cholerae* fare well in an alkaline medium but are destroyed in any condition below pH 6 and can be found mainly in aquatic habitats (freshwater, saltwater or brackish water) or in the intestine, vomit and stool of a human host[3].

The bacterium is distinguished serologically on the O antigen of its lipopolysaccharide into cholera vibrio (pathogenic) and non-cholera vibrio (non-pathogenic) variants. Cholera toxin-producing strains, O1 and O139 serogroups, cause cholera disease (acute enteric human diarrhoea), while the non-toxigenic O1/O139 group causes non-epidemic periodic diarrhoea, wound infection, gastroenteritis, septicemia and skin infections[4]. *V. cholerae* O1 is further classified into Ogawa, Inaba and Hikojima biotypes that may either be classical or El Tor serotypes.

Although, all *Vibrio* strains exist in an aquatic environment, the non-toxigenic strains are more dominant in this environment[5]. In their aquatic habitations, these bacteria are found mostly attached to the exoskeletons of phytoplanktons and zooplanktons to improve their adaptation to the aquatic habitat. Because they have to be modified to suit both environments (aquatic habitats or in the intestine of a human host), many *V. cholerae* structures, such as their pili, have to be strongly heritably structured, with the ability to colonize surfaces. The organism has different ways of colonizing surfaces. This depends on the presence and characters of both preserved and mutable genetic factors[6]. In the marine

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environs, different surfaces are accessible for colonization (biofilm development). These include suspended mineral particles that are made up of majorly negatively charged silicates, cellulosic plants and the exoskeletons of crustaceans, which include zooplankton organisms and they consist principally of chitin[7]. Ecological reports reveal that an add-on to the chitin outer walls is a fundamental habitual routine of *V. cholerae* in the aquatic habitat and biofilm development establishes an efficacious endurance device[7,8]. Biofilms formation is critical for the ecological existence, spread and infectivity of the *Vibrio* species[9].

Previous project reported a universal model for *V. cholerae* biofilm growth, consisting of distinctive forms of transcript inside plankton with a layer of a molecule thick[10]. Planktonic phase involves transitory exchanges and with a surface which may be umpired by mannose-sensitive haemagglutinin. This shallow relationship brings about flagella genetic copy suppression leading to an enduring add-on of the organism to the external layer of the plankton. Once fashioned, this add-on leads to the establishment of a well-developed biofilm comprising packs of bacteria colonizing the surface[8,10].

Extended incubation in the course of a biofilm assay can lead to a rugose morphotype of *V. cholerae*[11]. The occurrence of the rugose variant makes the organisms, as biofilms, predation resilient[12]. Actually, it is a vital protection mechanism that contributes immensely in preserving the *Vibrio* species attached to floating materials, chitin and other surfaces[13]. Hence, the presence of biofilm in water bodies promotes the endurance and perseverance of the organism as well as serving as a nutrient source[10]. It is also responsible for the survival of the pathogenic *V. cholerae* against the acidic medium of the stomach of the infested human host. Persat *et al.* described *V. cholerae* in biofilm-clumps as well as in a planktonic form in stool samples of cholera patients[13]. The regular contamination of clusters like biofilm in water, always exceeds those that exist in planktonic form, and also that evolution instigates an increase in the infectious character of *V. cholerae* in biofilm; hence biofilms are more significant in the infection process[13]. The development of biofilm rests solely on the reaction of exopolysaccharides, proteins and nucleic acids. among which exopolysaccharides are the key portion of the biofilm matrix and their absence diminishes the development of biofilm[14,15].

V. cholerae can exist as free-living bacteria in aquatic environments, especially warmer water, hence, it is more prevalent in Africa and Southeast Asia[16]. As a result of this environmental factor, cholera can remain dormant in water, attaching to plankton and the chitin in the shells of mollusks and other crustaceans, resulting in seasonal outbreaks[16].

2. Segregation and identification of *V. cholerae*

2.1. Collection of samples

Samples collection for isolation of *V. cholera* depends on the scope of the study and could be from water, faeces, food or aquatic animals. Samples are taken at different sites according to the justification of the study, in order to have good standard results. In

non-cholera epidemic areas or developed countries, determination of the concentration of *V. cholerae* in sea animals such as oysters, the water bodies where the oyster is harvested and the underlying sediment should be of paramount importance[17].

Water collection bottles should be washed and autoclaved for 20 to 25 min at 121 °C preceding their use. For water sampling, polypropylene bottles must be used while glass bottles are standard for plankton sampling[18]. Collection of adequate volume and sample size is crucial to ensure the completion of all appropriate analyses. Also the simple physiochemical parameters of water should be determined on site at the same time and samples are collected and these parameters may include temperature, salinity, pH, dissolved oxygen and conductivity of the water, depending on study targets[18]. The nature of the water current when sampling, the water depth, and rainfall can also be measured if necessary[18].

2.2. Isolation and identification of *V. cholerae*

In recent time, modern science have improved technologically in the area of isolation, identification and characterization of *V. cholerae*. Both the virulent and non-virulent strains can be found throughout the year in aquatic environments, not necessarily in cholera epidemic environment[19]. Unless appropriate methods are used, the organisms may not be detected especially if they are in their viable but non-culturable (VBNC) state *i.e.* the VBNC *V. cholerae* will not form colonies on culture plates when a traditional culturing method is used but can cause disease[20,21].

To detect these organisms irrespective of their cultivability, two methods can be used. These are fluorescence *in situ* hybridization, which is used to identify the arrangements of DNA genes specific to all serogroups of *V. cholerae* and fluorescent antibody plus direct viable count (FA-DVC). These are direct detection methods which can only detect serogroups associated with cholera epidemics and cholera toxin-producing vibrio[18]. Fluorescence *in situ* hybridization is a quantification method that can give an accurate estimation of vibrio cells in an environmental water sample. This is accomplished by visualizing a fluorescently-labelled oligonucleotide probe using epi-fluorescence or con-focal laser scanning microscopy.

The FA-DVC method used for the fast discovery of virulent *V. cholerae* is also direct, without any culturing. When carried out with the direct viable count according to the method of Kogure *et al.*, it can be used to differentiate between the cells that can be cultured and VBNC cells of *V. cholerae*[22,23]. It can also distinguish the pathogenic strains from the non-pathogenic serotypes. Direct FA-DVC is accurately used to detect the presence of *V. cholerae* within 8 h out of which 6 h is used for incubation.

Xu *et al.* introduced the indirect fluorescent antibody method for the enumeration of *V. cholerae* serogroup O1 in conservational water samples[24]. It is used mostly when commercial direct fluorescent antibody kits are not available. It is also very useful in counter checking the presence of non-culturable organisms in negative cultured samples[25]. PCR is another method for evaluating directly the existence of *V. cholerae* in ecological samples or after the sample has been enriched with alkaline peptone water. These methods work

by first detecting species-specific nucleotide sequences, amplifying them, and then visualizing them on agarose gel.

2.3. Uncovering of *V. cholerae* by standard technique

In traditional procedures, according to Huq *et al.*, the sample can be streaked on one or two of the three selective media for *V. cholerae* isolation, namely, thiosulfate citrate bile salts sucrose (TCBS) agar, tellurite taurocholate gelatin agar (TTGA), also known as Monsur medium and CHROMagar™ *Vibrio* after pre-enrichment with alkaline peptone water[18,24,26]. For water samples, the sample must first be filtered and the residue on the filtered paper should be washed with distilled water or 1× phosphate buffer saline and then centrifuged for 5 min. About 1 mL of the mixture can then be plated directly on TCBS and/or TTGA/CHROMagar™ *vibrio*, using the pour plate method and incubated for 24 h for TCBS and CHROMagar™ *vibrio*, but 48 h for TTGA. The direct pour plating method can be used alongside streaking methods of the pre-enrichment sample.

Following incubation, *V. cholerae* shows as yellow colonies on TCBS, colourless on TTGA and turquoise colonies on CHROMagar™ *Vibrio*[27]. Thereafter, the presumptive *V. cholerae* is purified on non-selective media such as amended nutrient agar, or Luria Bertani agar with 1% NaCl and PCR could be used for the confirmation of the target *Vibrio* isolates. The confirmed isolate can then be serogrouped using a slide agglutination assay with specific antisera for the O1 and O139 antigens or by PCR using specific primers targeting O1 and O139 serogroups.

2.4. Confirmation of assumed *V. cholerae* isolates using molecular technique

Molecular testing replaced the time consuming biochemical tests previously used for the confirmation of presumptive isolates. This is done using species-specific primers for *V. cholerae* targeting the internal transcribed spacer region between 16S and 23S rDNA and the outer membrane protein subunit W. Positive and negative controls are run concurrently in the PCR assay. Verified isolates can be vetted for specific virulence genetic make-up of each isolate[28].

2.5. Non-O1/non-O139 *V. cholerae* with less toxicity compared to O1/O139

The numbers of non-O1/non-O139 serogroups in aquatic milieu exceed that of *V. cholerae* O1 even in the regions that experience a cholera epidemic[4]. They can be isolated from water surfaces such as marine, sewage contaminated rivers and streams, estuarine brackish waters, seafood, chironomid egg masses, water plants and clinically from stool samples of patients not showing any sign of cholera/diarrhoeal disease and domestic animals[1,29,30]. Studies have reported a high magnitude of non-O1/O139 strains in stool samples of gastroenteritis patients in Asia, Africa and Europe[31,32]. Recently, the isolation rate of *V. cholerae* non-O1/O139 serotypes from diarrhoea patients is growing[33]. A study carried out in Thailand between 1993 and 1995 reported that non-cholera strains sequestered are either

the same rates with or more in number than O1/O139 biotypes. Most reported cases of diarrhoea are usually associated with different ranges of serotypes[2,33]. However, certain serotypes have been more frequently isolated. For example, in Peru in 1994, the O10 and O12 serogroups were dominant, while the O6 and O14 serogroups were dominant among Khmers in a refugee camp in Thailand and the O10 serogroup was dominant in India[2,34,35]. An upsurge of cholera was triggered by the O37 strain in Czechoslovakia and Sudan. Although it is conveyed commonly in O1 and O139 serogroups, the cholerae originates from the environmental non-virulence group universally, together with other *Vibrio* species[35,36].

3. Virulence factors of pathogenic *V. cholerae*

The main virulence factor, vibrio pathogenicity island (VPI), which has several genetic properties are predominantly seen in pathogenic *V. cholerae* strains and are linked with widespread cholera[37]. ToxT is a soluble transcriptase that magnifies itself. When ToxR, a transmembrane protein associates with ToxS of the toxRS operon, it leads to the activation of toxT, the gene encrypting the cytosolic protein ToxT, that controls how the cholera toxin (CT) is encrypted by a unified CTX phage and other genetic factors which include *aldA*, *tagA*, *acfA*, *acfD* and *tcpI* in the VPI cluster[38,39]. Other genes such as toxin co-regulated pilus (TCP) are responsible for the colonization of the small intestine[40]. The majority of the vibrio serogroups lack CT and TCP naturally whereas the genes for ToxR are common[41].

The VPI segment also includes AldA and TagA. These proteins are responsible for the encryption of aldehyde dehydrogenase and metalloprotease actions[42]. The accessory colonization factor which is a part of the VPI is responsible for CT and AcfB expression as well as helping in intestinal colonization[42].

4. Differences between VPI of O1/O139 group and non-O1/non-O139 group

Vibrio cholerae O1/O139 strains naturally encrypt dangerous virulence elements: cholerae and TCP, which is linked to their virulence potential[43]. Cholerae and TCP are principally liable for the diarrheal purge and intestinal colonization of the wall of intestine respectively, whereas the non-pathogenic group conveying TCP can capably obtain the CT genetic factor (*ctxAB*) through lysogenic alteration with cholerae, a filamentous phage that encrypts cholerae and uses TCP as its receptor and/or it may be through the horizontal transfer of the VPI, CT gene and exchange of O antigen biosynthesis genes[39,43].

Nevertheless, the mere acquisition of these genetic factors does not necessary on them the ability to cause cholera disease, and most likely, they may need extra genetic characters that are exclusive to pathogenic *V. cholerae*. Though, the pathogenicity mechanisms of non-cholera vibrio are not yet understood, there are reports from many studies showed a hemagglutinin protease, but few other proteases and toxins in the pathogenicity of these strains[44].

A dynamic 4.5 kilobytes core region, a virulence cassette found in *V. cholerae* O1 and O139 strains is absent in non-O1 and non

O139 strains and is recognized to convey a minimum of six genetic factors, including *ctxAB* (encrypting the A and B subunits of CT), *zot* (encrypting zonula occludens toxin *cep* (encrypting core-encoded pilin, *ace* (encrypting accessory cholera enterotoxin and/or *fU* (encrypting a product of unknown function[45,46]. These are responsible for the virulence potential of the O1/O139 *V. cholerae* serogroup. Apart from the clear importance of CT (cholera toxin) in a cholera infection course, it is now obvious that the secretion of cholera toxin by *V. cholerae* is significant in the acquisition of the ability of a serogroup to cause epidemics. The evidence is seen in the advent of *V. cholerae* O139.

The virulence devices of the non-cholera serogroup are diverse. Several of them convey the CTX and TCP genes, whereas a number of them encrypt a contaminant known as RTX, and yet others encrypt a heat-stable enterotoxin (nag-ST)[47]. Even though the CT and TCP clone of the pathogenic non-O1/O139 serogroups are widely distributed globally, most strains are unable to cause endemic disease and are vastly different[39]. The non-O1/O139 strains such as O141, O10 and O12 are responsible for the occurrences of gastroenteritis infection by a system different from the pathogenic type and are referred to as entero-pathogenic *V. cholerae*[48].

Dziejman *et al.* reported for pathogenic groups, including CTX and TCP non-cholera *vibrio* groups[49]. They establish differences between each organism and also from CT producing strains, and their genomes were found to carry a Type III secretion system (TTSS) which correlate to that of *Vibrio parahaemolyticus* TTSS gene cluster[50,51]. Their analysis also shows the presence of TTSS in most non-O1/O139 strains and so they came to the conclusion that TTSS is the virulence factor of non-O1/O139 and is responsible for ecological capability of the strains.

The TTSSs are a genetic factor responsible for virulence in many bacteria such as *Salmonella*, *Pseudomonas*, *Yersinia*, *Shigella*, and enteropathogenic and enterohemorrhagic bacteria, *Escherichia coli*[52]. Some earlier studies showed that the reference strain (AM-19226) takes the possession of the suckling mouse guts and causes disease in mature rabbits[49,53]. These are traits usually related to the production of TCP and CT in O1 strains, respectively, but the analysis of the genome sequence showed that the genes that encode CT and TCP are absent in the AM-19226, and only the genome that encodes a TTSS is present[49].

TTSSs are responsible for translocation of effector proteins, in Gram-negative bacteria, directly into the host cytosol[54]. The effector protein translocated controls cellular processes such as those manipulating the actin cytoskeleton in the host[55]. The two effector proteins in AM-19226 TTSS are known as: 1) VopF, which stimulates actin nucleation and is needed for AM-19226 to proficiently inhabit suckling mouse guts, and 2) VopE, which stimulates actin depolymerisation[53,56].

Tam *et al.*[53], and Dziejman *et al.*[49], reported that AM-19226 TTSS is liable for the colonization of non-O1/O139 strains in the guts of the suckling mouse and for diarrhoea in adult rabbits. The peculiarity of pathogenicity of AM-19226 was revealed by using suckling rabbits which were inoculated orally with the strain. This led to rapid development of severe diarrhoea disease in the infant rabbit. A

functional TTSS of AM-19226 invaded the small intestine, which led to the histopathology and infection in this exemplary host.

Obliteration of AM-19226 TTSS effectors, such as vopE, or vopF, or mcfV and, or tcdB, showed a decrease in AM-19226 intestinal colonization and in the austerity of the infection. This showed that all AM-19226 effectors are associated to virulence. Compared to CT and TCP producing *V. cholerae* strains (O1/O139 serogroup), AM-19226 (non-O1/O139 serogroup) causes distinct impairment to the epithelium of the wall of the rabbit's intestine. In conclusion, the investigators collectively agreed that AM-19226 and other vibrio that harbor TTSSs to cause enteric disease via mechanisms that are totally different from TCP and CT producing *V. cholerae* O1/O139[53,55]. When pathology, the effect and pattern of intestinal colonization with the disease kinetics of TTSS *V. cholerae* were measured and compared to toxigenic *V. cholerae* (O1/O139), they showed clearly that the virulent gene TTSS of non-cholera causing *V. cholerae* (at least AM-19226) causes rapid infection as well as mortality faster than cholera causing *Vibrio* strains[57]. It also inhabits both the nearest and farthest part of small intestine compared to TCP producing *V. cholerae* that colonizes only epithelial cells of the small intestine. Furthermore, it was discovered that the population density of the TTSS producing strain is higher than that of TCP producing strains. Lastly, TCP and CT producing *V. cholerae* O1/O139 strains are virulent and cause disease but do not destroy or invade the small intestine and that is to say, the intestine is recoverable after treatment.

In contrast, TTSS producing *V. cholerae* causes noticeable damage to the epithelium and induces excretion of pro-inflammatory cytokines[57]. In summary, it was suggested that TTSS producing *V. cholerae* can make the infant rabbit bowel imperceptible such that it prevents other bacteria colonization and creates a conducive environment for itself to spread all over the small intestine and colonize it using a group of effectors supplied by the TTSS-dependent strain to the epithelial cells of the bowel. These effectors include VopF and VopE, together with newly identified McfV and TcdB. According to Tam *et al.* in their tissue culture-based studies, VopF modifies the association of the eukaryotic actin cytoskeleton, while VopE in conjunction with VopF stimulates a protein that encourages the epithelial cell barricade function[53,56]. The intense interruption of the villi as found in AM-19226-infected rabbits may be caused by the reaction of the afore mentioned effectors. Furthermore, newly identified effectors (McfV and TcdB) contribute to the AM-19226 virulence, since the deletion of mcfV or tcdB reduces the brutality and occurrence of diarrhea. Both McfV and TcdB correspond with toxins that have insecticidal properties[58]. Though most of the non-cholera vibrio lack cholera toxin found in CT producing vibrio, quite a few other innate virulence factors contribute to their pathogenicity.

5. Pathogenicity of *V. cholerae* in human hosts

V. cholerae infections in humans start by ingesting polluted water and/or food. Once the organisms have successfully escaped from the acerbic hurdle of the abdominal cavity, the pathogenicity of *V. cholerae* is exhibited in their ability to invade human hosts and their ability to secrete cholera toxin from their TCP production[40].

Other elements that may influence colonization include diverse haemagglutinins, adjunct colonizing elements and a core-encoded pilus. All these may assist in enhancing adhesion and intestinal colonization[40]. The secreted cholera toxin also known as CT induces frequent and watery bowel movements[59]. The binding of the cholera toxin to the plasma membrane of epithelial cells results in the discharge of dynamic enzymes that lead to an increase in cyclic adenosine 5'-monophosphate production which causes an enormous emission of electrolytes and water into the intestinal cavity, ultimately, leading to loss of as much as 20 L of fluid (rice water stool) daily. This eventually leads to death if not treated early.

6. Human host defences

The contagion of cholera vibrio species in a human host can lead to a range of responses. These range from classic to serological responses. The serological response is associated with individual differences in gastric acidity. People suffering from hypochylia, have high potential of being infected by *V. cholerae*. Intestinal receptivity of *V. cholerae* O1/O139 strains differs in people, for the CT depends on the previous immunologic status or experience of the individual. The existence of a local immunoglobulin A antibody in an individual provokes resistance against *V. cholerae* O1/O139 and/or cholera toxin. Colonization of the mucosal surface is prevented by the intestinal immunoglobulin A antibody. This can also defuse or inhibit the binding of the cholera enterotoxin. The classic response is associated with symptomatic cholera infection that can be cured by administering oral replacement solutions and intravenous replacement solutions in severe cases. Patients can recover by purging the vibrio species using antibiotics or by personal immunity retorting and rejuvenation the damaged bowel cells.

7. History of spread of epidemic O1/O139 *V. cholerae*

According to history, Indian subcontinent had experienced so many deaths due to severe dehydrating diarrhoea for centuries with no idea of the organisms responsible. In 1849, a London physician named Snow proved that cholera is naturally transmitted through water[60]. Aberth was the first scientist who isolated the causative agent of cholera from the stool of a cholera patient[61]. The Europeans and the Americans first experienced the force of cholera in 1817, when the disease became rampant and eventually spread all over the globe.

Until 1992, the CT-producing strains were categorized to be classical and El Tor. The classical biotype was discovered earlier in 1883, while El Tor was first isolated in the Sinai Peninsula from one of the Mecca-bound pilgrims. El Tor was looked exactly like classical *V. cholerae* but was different, in that it caused blood haemolysis in a Greig test. The carrier of El Tor did not show any symptom even after discovery hence it was disregarded as unimportant. In the 1930s, similar haemolytic *Vibrio* species were isolated in an outbreak of diarrheal disease in the Celebes, called Para-Cholera, which later broke out in 1991 in Hong Kong and from there became pandemic.

Classical strains are associated with earlier pandemics that occurred between 1899 and 1923, while the seventh pandemic was

ascribed to El Tor, from 1961 to 1970[62,63].

The epidemic virulence of El Tor strains is more grave and pandemic compared to classical strains due to the following: 1) El Tor strains stay longer in the host after infection and are asymptomatic compared to the classical strain which gives room to further spread to unaware victims. The carriers are extremely contagious, polluting anything they touch, which can lead to devastating epidemics. It also endures harshness after it has been released to the environment from the human intestine. 2) El Tor is more resilient to adversarial ecologically harsh conditions, and displays a superior resistance to antibiotics and chlorine compared to the classical biotype.

Also, the behaviour of El Tor cholera is totally different from that of the classical and causative agents in the earlier six pandemic areas[64]. Firstly, the seventh pandemic area showed a different behaviour compared to earlier pandemics along the spatial dimension of globalization. The pandemics spread wider through a larger geographical area, including regions that had always been cholera free. In addition, the form of the spreading was not normal. It was not going from one country to another as expected; instead it skipped continents, appearing in one country in a particular continent and then suddenly breaking out in a faraway continent[65].

The second important difference is the speed at which the infection had spread and the duration of the epidemic[65]. In the nineteenth century, cholera spreads as fast as people travelled across countries and continents. The twentieth century, which is characterized by advanced technologies, with faster means of transportation at reasonable costs and higher speed of travelling by aircraft, vehicles, ships and trains, enables the faster spread of diseases. The last pandemic which is the seventh was the longest pandemic in the history of cholera epidemics. It raged for 40 years with no appearance of declining, even with the recent advances in Medicare and public health schemes[65].

A classical strain of toxigenic *V. cholerae* re-appeared in 1982, in Bangladesh, with a severity which overshadowed the El Tor biotype that was believed to be deep-rooted[64]. This classical biotype re-appearance was restricted to Bangladesh and other countries did not experience any serious outbreak[64].

Peru in 1991, experienced an explosive outbreak of El Tor strains following 100 years of a cholera epidemic free period[66]. The infection spread into the inland of Peru, following the trade itineraries to Ecuador, Colombia, Brazil, Chile, and then central Mexico. After a year, Peru experienced the severity of a cholera outbreak and some Southern and Central American countries recounted cases of cholera epidemics that recurred in 1992 and 1993 which led to a total of 1 041 422 cases and 9 642 deaths. A total incident casualty rate of 0.9% was reported to the Pan American Health Organization. In 1993 alone, 204 543 cases and 2 362 deaths were reported[67]. Concurrent with the cholera incidence in Peru was a warm event that occurred which was related to El Niño in the tropical Pacific from 1990 to 1998[63].

The Latin American facsimile of cholera causing vibrio strains were compared to other identified global copies of *V. cholerae* O1, and it was discovered that the multi-locus enzyme electrophoresis makeup of the Latin American clone was distinctive from formerly

recognized cholera causing vibrio strains. It was suggested that cholera caused by vibrio strains was present in the sea environs long before the cholera outbreak started in Peru. The spread of the Peruvian cholera demonstrates the significance of planning ahead for a cholera outbreak.

The emergence of the Bengal serotype O139 in 1993 in Bangladesh and India increased the concern of the scientific community because the organism was a non-O1 strain that was not virulent but through genetic transfer became virulent and caused the epidemic^[68-70]. In 1993, epidemic cases of O139 *V. cholerae* outnumbered those of the O1 serotype, with 170 000 cases reported and a 2 000 death toll estimated^[71]. In 1994, a dramatic drop in the occurrence of cholera outbreaks triggered by O139 strains was witnessed in regions where it dominantly occurred in the previous decade. The O139 was supplanted by O1 strains, but studies revealed genomic diversification between the two strains^[72,73]. In August 1996, O139 reappeared with a reformed antibiogram in Calcutta and in different regions of India, displacing the current O1 serogroup to become the principal serogroup in this part of the sub-continent^[68]. Molecular studies have again revealed that the O139 strains that recurred in August 1996 indicated modifications at the genomic level and were diverse from the O139 strains that occurred in 1992^[73]. In 1995 alone, 50 921 cases and 1 145 deaths were recounted from 18 nations in Asia. The incident-casualty percentage increased from 1.3% in 1994 to 2.2% in 1995^[74].

In April 1997, a cholera epidemic befells 90 000 Rwandan refugees leaving provisionally in three refugee camps between Kisangani and Ubuntu, in the Democratic Republic of Congo. In 12 days, 1 521 deaths were recounted, most of which happened due to lack of health-care services, and overall 53 000 deaths were recorded from 21st of April 1997 to May, 1997^[75]. Although it is not often so deadly, cholera occurrences remain civic health problem worldwide, causing extensive socioeconomic disorder as well as loss of life. For almost 4 years, 698 304 alleged cholera cases and 8 562 cholera related deaths were recounted by the Government of Haiti in 31st of January, 2014^[76]. Roughly, the daily death rate estimated ranged from 7 to 14 per 10 000 people with a daily mean of 9.9 per 10 000 people^[2].

8. Mode of cholera epidemic transmission

Cholera, an acute enteric diarrheal infection, has spread intermittently worldwide since 1817^[75]. Globalization contributes to the spread of cholera now that distant continents are a plane ride away, as exemplified by the vast epidemic spread during the 2010 cholera outbreak in Haiti^[76]. Peru experience in 1991 was another clear pointer to effect of globalization on epidemic transmission, an outbreak that began in Peru, was transmitted to Ecuador within 2 months and to Colombia, Brazil, and Chile within 5 months^[76]. Throughout the decade, it spreads to Mexico and through Central America affecting a total of 21 countries with over 775 000 cases by the end of 1992^[76]. Countries did not report the actual number of cholera cases and deaths because it would have adverse effect on their national economic growth as in the case of Latin America, that declared that cholera cases was more than 1 000 000 and deaths

rate was 10 000. This was small fragment of the real number of contagions in 1994^[77].

Cholera can be curbed by preventing initial infection of the host. It is crucial to know exactly the way that the organism is spread. Snow proved that cholera spread through water during an explosive outbreak of cholera in London in 1856^[78]. He, among others, believed that there are other important ways to spread cholera. An epidemiologic surveyed during the 17th pandemic documented a variety of particular food and water corridors by which the bacteria reach the host, some of which were new and unimagined^[79].

In the spread of disease generally, hydrological controls are the leading actor in the transmission of the disease^[80]. Cholera pathogens can easily be spread from watercourse passageways or coast to interior regions, spreading to neighbouring cities through dynamic and inert transference mechanisms as in the case of the Indian cholera epidemic in 1817. According to the interim report of the acute infectious disease, Agency for International Development, task force on cholera, (1971) there was a cholera outbreak in Calcutta Indian in 1817 during India's customary, great Kumbh festival at Hardwar in the Upper Ganges. The fiesta lasted 3 months, attracting pilgrims worldwide. The place was crowded with people who interacted and camped on the banks of the Ganges river. At the end of the festival, the attendees carried cholera back to their homes within India and foreigners to their countries of residence. There was no proper record of the death rate in India, but the British army counted 10 000 mortalities among its groups. Cholera is also spread to Iran, Baku and Astrakhan and up the Volga into Russia via the trade routes to where the businessmen met for an autumn fair in Nijni-Novgorod. The infection followed the businessmen to their residences in Russia, Europe and other areas of abode. Cholera travelled in water from harbour to harbour. The angel of death-pathogenic *V. cholerae* moved in infested barrels of water conveyed by itinerants. By 1827, cholera was pandemic, the most dreaded infection of the century^[81].

Constructing the longitudinal, embedded, mean-field epidemiological prototype projected by Jutla *et al.*^[82], Bertuzzo *et al.*^[80], built a plain structure to exemplify cholera transmission during epidemics through surface waters, suggesting that cholera spread is facilitated by waterway connection networks.

Nevertheless, the pattern of space and time of cholera epidemics can be influenced naturally by humanoid movement. Vulnerable individuals who need to commute daily for their businesses may contract the disease unknowingly from a place they visited and then transmit it to the people they live with. Most infected individuals are asymptomatic, especially those infected by El Tor biotype, yet they may excrete the bacteria into the environment through their faeces, thereby infecting other vulnerable people^[83]. This shows that movement of people promotes cholera transmission more than endemic breeding grounds, and therefore is the leading cause of the spread of cholera^[83]. This also shows the main dynamic forces of any infectious diseases^[64].

Mari *et al.* analyzed the connection between human movement and cholera transmission via a reaction-diffusion approach, and reported diffusive activities of cholera patients and the disease spreading along an easy, one-dimensional river network edifice^[84]. Nevertheless, the

movement forms of pathogens in humans are somewhat complex due to the interlacing of short- and long-distance mobility of people. Most times, mobility involves temporary movement of the hosts from their home locations which is different from what is indirectly presumed by diffusion mock-ups. More importantly, human mobility as a matter of fact is associated with transportation networks such as air-travel, train and road networks that link communities rather than restricted by the edifice of the underlying hydrological matrix or narrowed to the originating river basin[84].

The scourge of the pathogenic *Vibrio* species is not peculiar to man alone because it also causes a great deal of loss in aquaculture farms leading to the colossal death of fresh water prawn cultured in Taiwan[85]. The symbiotic relationship between vibrio pathogens and chitinous exoskeletons of some aquatic animals provides the bacteria with abundant carbon and nitrogen sources, thereby enhancing the ability of the microorganisms to thrive the aquatic milieu and their ability to cause infection in man via consumption of seafood[64]. The ability of *V. cholerae* to adhere strongly gut of shell fish such that removal by rinsing is almost impossible which has been recognized as one of the factors that aid its ability to cause infection via consumption of contaminated seafood[64].

It has been reported that the heat used to remove shellfish from the shell was not strong enough to kill *Vibrio* pathogens and proper cooking does not guarantee the protection against vibrio illness in cases of recontaminations[86]. This is what resulted in the major cholera epidemics in USA in 1978, where, in Louisiana, cooked shrimps were transferred into boxes where raw shrimp had been shipped and were held at warm temperatures before being served[86]. Many outbreaks in Thailand were linked to the consumption of mussels containing *V. cholerae*, which had been smuggled into the country and 10 outbreaks in US between 1973 and 1992 were associated with vibrio contaminated seafood such as crab harvested from Gulf Coast[87]. Outbreaks among travellers were linked to consumption of contaminated seafood served in aircraft[88].

Prevention and control of cholera outbreaks depend mainly on intercepting its spread using measures that prevent continual infection and spread. The use of an oral vaccine for example may give long-term protection against cholera infection[89]. Another way to control cholera is blocking every means of transmission to prevent the organism from getting into human hosts. This prevention methodology is the most effective way of controlling cholera and many epidemic diseases in the industrialized world, before vaccines or antibiotics were developed.

Industrialized countries constructed a massive engineering infrastructure, which provided a clean treated tap water and modern functioning waste treatment plants in every part of their nations, which made the sustained transmission of cholera in those countries extremely unlikely. Regardless of intermittent occurrences along the U.S. Gulf Coast and the periodic introduction of the pathogenic *V. cholerae* by travellers, cholera outbreaks were not experienced in America for decades until recently following a flood disaster in Haiti[90].

9. Economic implications of epidemic cholera

The outbreaks of highly infectious diarrhoea disease spread rapidly within and between countries and even continents in various intensities. The World Health Organization (WHO) estimates 3–5 million cases and over 200 000 deaths yearly due to cholera outbreaks. The disease is deadly because 75% of the population can be infected and it is asymptomatic, leading to more spreading of the disease, especially when people travel through regions and countries, since the disease is highly infectious[91].

The impact of cholera is not limited to only morbidity and mortality rates. It also has grievous impact on the economy of the nation experiencing the outbreak. The effect of economic costs can be direct or indirect. The effect of indirect costs of cholera includes the economic losses in incomes and production due to disease and demise of members of the work force, and losses to the economy due to its interference with trade and tourism.

Cholera affects transnational trade when countries enforce a restriction on commodities normally imported from cholera infected countries. They may also ban their ships from visiting cholera-infected countries, thus reducing both their imports and exports. For instance, during the cholera outbreak in Iran in 1965, Switzerland stopped all the airmail coming from Iran from entering their country while Russia stopped chromate ore importations from Iran. These extreme actions harmed and destabilized the economy of the countries affected, especially if the banned material is consumable. In 1970, Ethiopia prematurely declared the country cholera free because of setbacks being suffered by her economy.

Cholera can also have a serious effect on the tourism industry especially in a country where tourism is the main earner. Hong Kong lost more than 10 000 tourist visits in 1962 as a result of a cholera epidemic and tourist traffic resumed its growth very slowly following the control of the epidemic.

The effects of direct cost of cholera include the cost of treatment and hospitalization of the severely infected cholera patients. Often times, a cholera outbreak affects the lower socioeconomic groups, particularly those living in unhygienic conditions. The set of population lives in dire financial conditions; hence it can bear neither the cost of treatment nor hospitalization.

The mean cost of treating severely ill patients differs from country to country and the costs depend on many variables. For instance, intravenous replacement therapy is costlier than oral replacement therapy. However, intravenous solutions must be administered first until the vital signs are stabilized and acidosis is corrected, and the patient is able to drink. Antibiotics can also be administered in severe cases to reduce the duration of treatment. This results in the reduction of the cost of fluids and hospitalization (interim report of acute infectious disease task force on cholera, 1971).

Several studies have reported on the financial implications of a cholera epidemic in some countries. Suarez and Bradford studied the estimated economic loss experienced in Peru during the 1991 cholera outbreak[92]. The fund channels were traced and three effective demands were described by Kirigia *et al.*, namely, tourism revenue, revenue from food, good exportation and domestic consumption

of the suspected medium of infection such as fish and other sea foods[93]. They found that there was a significant reduction in the tourism channel leading to the loss of about 72% of the revenue generated the year before 1990. In food exportation, only the trade of fresh fish was affected, with 0.5% drop in total trade compared to the previous year. They also established that the consumption of fresh fish dropped by 33.6%, and street food hawkers were affected as regular consumers substituted hypothetically infected food with safe alternatives, and most shunned eateries[92]. WHO attributed the loss of 770 million dollars from Peruvian gross domestic product (GDP) in 1991 (around 2% of GDP) to the epidemic, suggesting that an embargo on food exports and the effect of low tourism were the main channels. Kimball *et al.* calculated the loss of trade rates due to cholera epidemics (1997 to 2002) in four countries, Mozambique, Kenya, Tanzania and Uganda[94]. Using data generated from these countries, they found that these African nations lost around 4% of their total export earnings in 1998 but recorded a 10% increase in 2002.

Kirigia *et al.* carried out an investigation on the total expenditure on cholera by WHO Africa Region in 2005[93]. This expenditure included the cost of hospital admissions, test centre findings, treatment of the disease, salary loss of patients and low yield in production as a result of inadequate strength to work and untimely death. The lump-sum economic loss of 53.2 million dollars was estimated following the 125 018 cases reported in the WHO Africa Region in 2005. It was less than 1% GDP equivalence.

10. Cholera and conflict

This relationship between cholera and conflict or natural disasters presents a major global health challenge. In the past, cholera was often carried along trade routes by merchants and travellers. In recent times, displaced populaces in refugee camps have had the same precarious potential. Often times, outbreaks within refugee camps do not stay contained; they spread outwards, becoming epidemic. The risk of the spread of cholera disease after disasters or conflict is connected mainly to the size and physical characteristics of the displaced populace, especially the proximity of safe potable water and operational toilets, the nutritive position of the moved population, the level of invulnerability to vaccine- avoidable diseases such as measles, and access to healthcare facilities[95].

Epidemics are more commonly found in conflict-affected populaces, where more than half of the morbidity rates are the result of contagious diseases compared to disaster-affected populations[96]. The upsurge of malnourishment and the threat of death from contagious infections like cholera are rampant in conflict-affected populations, especially if their displacement is connected to long-term conflict, as the crisis of 1997 in Rwanda, where 48 000 cases and 23 800 deaths were recorded within a month in the refugee campsites at Goma in the Congo[95].

Natural disasters, such as floods, storms *etc.* can endanger people's access to safe water. After flooding, cholera epidemics are inevitable due to the contamination of water sources, as in the case of a Bangladesh cholera epidemic after a flood disaster in 2004 which

led to more than 17 000 cases where *V. cholerae* (O1 Ogawa and O1 Inaba) and entero-toxigenic *Escherichia coli* were isolated[97]. A cholera epidemic caused by *V. cholerae* O1, Ogawa serotype reported in West Bengal in 1998, involving more than 16 000 cases was linked to previous floods, and torrential rain in Mozambique in January–March 2000 resulted in an upsurge in the occurrence of cholera disease[98,99]. The major part of all recounted cholera outbreaks in 1994, and 42% of all mortality recounted internationally due to cholera in the same period, were in Africa[100]. The effect of conflict and civil turmoil on cholera outbreaks is exemplified plainly by the Rwanda experience. In December 1996, 26 countries had recounted the number of cholera and Nigeria, Senegal, and Somalia recorded more than 1 000 cases each and showed very high casualty rates[100].

Cholera outbreaks in populations displaced by conflict or natural disasters present a global health crisis due to their high menace, elevated degrees of mortality, and their ability to transmit cholera abroad[100]. In case of an emergency cholera eruption in heavily populated refugee camps, some simple methods of intervention can help lower the severity of the attack. These include the provision of sufficient potable water, adequate sanitation and public health education. The broadest tactic in the management of cholera is to ensure both the quality and quantity of available water. Assuring the quality of water is more easily practicable and most essential. World Health Organization found that point-of-use water disinfection was the cheapest method to decrease the disease problem connected to the dangers of an unclean water supply and sanitation[101]. The dissemination of point-of-use water treatment such as chlorine tablets or flocculants-disinfectant power (PURTM) which is not only cheap, but also highly effective to reduce the incidence of diarrhoea by 90%[102]. The biggest obstacle is access, the ability to bring the supplies needed. Funding and provisions necessary for these strategies to control cholera transmission are not great, as there are no wildly expensive medicines to purchase or high-tech instruments needed.

Another measure to control the spread of cholera in refugee or internally displaced person camps is provision of proper sanitation. A regular supply of soap is the most important part of improving the general sanitation and hygiene in these camps, but there is also the necessity of the proper elimination of excreta. Building more latrines to reduce the number of people sharing one, can decrease the spread of cholera[100].

However, all these processes like the sharing of point-of-use water treatment and soap are only efficient when they are used to their full potential. To achieve this, the refugees must be trained and educated on the importance of hygiene and sanitation measures to curb the outbreak[103]. In a study done on the awareness and approaches on prevention practices around a public health crusade in the capital of Haiti, Port-au-Prince, during the 2010 outbreak, the purification of domestic water practiced by different household improved from 30.3% to 73.9%[104]. This study shows the monumental significance of public health education as a complement to the distribution of precautionary measures in the effective prevention of the spread of cholera.

11. Monitoring and surveillance of *V. cholerae*

Cholera is the most devastating waterborne disease in the history of mankind and it has proved to be one of the most virulent killers. It strikes so suddenly that a healthy man earlier at the dawn of the day could be dead by nightfall. Since cholera is caused by ingesting water and food polluted by the wastes discharged by cholera patient, contacted with polluted wares, poo, bedding, water even food can result in cholera infection. The disease can be so quick and rapid that it can kill within 12 to 48 h^[105]. Cholera continues to lead to disease and death rate worldwide with an estimation of more than 100000 deaths each year^[91]. However, earlier occurrences of cholera outbreaks led epidemiologists to discover the connection between sanitation and public health, which led to the discovery of modern day water and sewage system.

Despite the efforts of the scientists was conducted to control cholera, the global frequency of occurrence is on the rise. It was discovered that cholera is also linked to socio- cost-effective factors such as the population density and financial paucity. It is also associated with unsanitary environments and an untreated water supply^[83]. Scientific research has described ways of improving water quality. These include the purification of water through boiling, chlorination and filtration. However, these are economically impracticable for the masses in rural or peri-urban communities; hence, public health issues remain unsolvable in undeveloped nations especially in Asia and Africa^[106]. The cost of paraffin or wood for boiling water makes the boiling method uncommon especially in poverty stricken communities. The correlation of cholera and poverty still remains a problem worldwide, specifically in undeveloped countries^[106]. In rural areas, people depend mostly on water sources such as surface and ground water for drinking and domestic use. In a situation where a water resource is contaminated, disease can be transmitted to the communities through flowing. In municipalities, cholera outbreaks are commonly triggered by breakdowns in wastewater treatment plants, pipes and contaminated public water supplies as suggested by the Broad Street episode in the Soho District of London, England in the year of 1854, that led to 616 deaths in the space of 3 months. The Broad Street water taps were polluted through the leakage of sewage pipes which led to an explosive occurrence of cholera^[60].

The WHO approximated the percentage of population in the third world countries with drinkable water to 22% and 15% to those with suitable sewage treatment, leading to recurrent and continuous cholera outbreaks in some parts of the world^[91].

Over two decades ago, Americans succeeded in eliminating cholera by making a great effort to improve water and sanitation^[107]. Operational interferences used in America for many years to tackle cholera outbreaks comprise operational laboratory methods for disease analysis (operative cure with hydration restoration through oral or intravenous means and antibiotics in severe dehydration

cases; setting up treatment plants to supply drinkable tap water and modern wastewater treatment plants and a sanitary environment)^[108]. Unfortunately, the implementation of all these measures happened in Latin America in the 1990s. To address this issue, in October 2011, the Bill & Melinda Gates Foundation presented a donation to form an Alliance to fight against cholera and to fast-track the progress of a broad tactic worldwide to check and control cholera. The grant was awarded to The Task Force for Global Health and Harvard Medical School/Partners in Health.

12. Assessment of all preventive approaches

The efficacy of all intervention assessments determines success in the reduction of the impact of cholera, such as morbidity and mortality cases. For quick and successful cholera intervention, diligence must be the watch word that must be espoused by the organisers and the management involved, using recommended procedures laid down by WHO, and the results should immediately be reported to Ministries of Health and WHO. Furthermore, the information and procedures or guidelines for effective responses should be shared with other countries experiencing the same cholera scourge.

13. Alliance among nations prone to cholera

Every country should have cholera prevention guidelines especially those neighbouring endemic areas. They should form an alliance with their neighbours and work as a team to fight the cholera epidemics^[109]. Cross-border teamwork is not yet common in many nations in Africa which have experienced cholera. This should not be the case. The health consultants in control of cholera outbreaks amongst the countries should come together and form cross-border partnerships involving disease control departments and national reference laboratories. They should meet occasionally to form a forum to prepare for, as well as take action in case of a cholera outbreak or outbreaks of other vital infectious diseases along their shared boundaries^[91]. A cholera pandemic cuts across boundaries; therefore, team surveys should be adopted by the governments of neighbouring countries.

Key actions relay the diverse stages of a cholera epidemic, in addition to the primary phases of an outbreak (handling cases, curtailing spread), the epidemic itself and checking and assessing interferences, such as water, sanitation, hygiene and oral cholera vaccine. Management of a cholera epidemic encompasses a diverse set of participants that need to be assessed (Centers for Disease Control).

14. Responsibility of governments at the community level

Governing councils must adhere to the specifications recommended

by Program for Appropriate Technology in Health/WHO in their reports and description of the incident. They should avoid ambiguity at all cost and should update the summary of zones and regions with cholera and or are in danger of a cholera outbreak and organize workshops and in-service training for physicians and paramedical personnel on cases and treatment management of cholera before and during an epidemic as well as community health education. In terms of treatment, bulwark stocks of necessary drugs such as rehydration solutions must be conserved and preserved in case of emergencies and the provision of free health services and treatment should be considered.

For long- term purpose, the planning and construction of healthy structures for disposing of human excreta that will suit local conditions, such as building of pit toilet are very important. The government should also ensure the provision of boreholes for the community to have access to clean drinkable water and encourage community made chlorine to prevent scarcity. Individual responsibility in the community is to avoid the following: eating seafood from polluted waters, unless they are cooked thoroughly; eating raw vegetables unless washed with vinegar; drinking raw milk, unless pasteurized or boiled; eating partially cooked food and cold food; eating without thorough washing of hands and more importantly avoiding indiscriminate use of antibiotics.

15. Antibiotic resistance of *Vibrio* family

Antagonism of bacteria to antimicrobials has become an essential civic health issue that is mainly connected to disease management and control[110]. *Vibrio* spp. was earlier reported to be highly sensitive to most clinically used antibiotics[111]. However, emergence of antibiotic resistance strains has occurred and is escalating as the years go due to the abuse of antibiotics intake and assortment stress triggered by the use and misuse of antimicrobials in aquaculture, food production and animal farms[112]. Treating animals, especially those eaten by man, with antibiotics has become a public health concern because it may result in the resistance of human pathogens to such antibiotics, which may be the only vital human drug available to treat a particular human infection[113].

Resistance of the *Vibrio* family to frequently used antimicrobials is growing both in the farm animal and in humans, and has become a worldwide problem. The increase in the rate of recurrence of antibiotic resistant *Vibrio* has been recounted often because the resistance determining factor can be transmitted to other bacteria of human clinical importance[110,114].

Bacteria such as *V. cholerae* are globally known to be resistant to common antibiotics such as doxycycline, tetracycline, streptomycin and erythromycin used for the treatment of different bacterial diseases[115]. Many researchers reported in their studies on the antibiotic susceptibility of the causative agent of cholera, *V. cholerae* O1/O139 that has found the organism to be resistant to a

group of antibiotic such as chloramphenicol, tetracycline and oxy-tetracycline, ampiciline, amoxycillin clavulanate, sulfamethoxazole, trimethoprim, chloramphenicol, nalidixic acid, kanamycin, streptomycin and tetracycline[116,117]. Raissy *et al.* in their research on the antibiotic resistance pattern of some *Vibrio* strains isolated from seafood reported that of 72 strains tested, 70 were resistant to ampicillin (97.2%), 60 to gentamycin (83.3%), 56 to penicillin (77.7%), 18 to streptomycin (25.0%) and five to erythromycin (6.9%) and 13 to tetracycline (18.1%)[118]. All isolates were susceptible to sulfamethoxazole[118]. Also antibiotic resistant *Vibrio parahaemolyticus* strain was reported in Thailand, Malaysia and China[119-121].

Naturally, autochthonous organisms in aquatic habitats produce antibiotics, just for gesturing or signalling and controlling reason in their ecological environment[122]. However, when contaminated waste water consisting of pathogenic organisms and genomic antimicrobial resistance are discharged into receiving waters and it makes the autochthonous organisms safeguard themselves from the contamination by procuring and conveying antibiotic resistance genes, thereby serving as cisterns of resistance genes and those genes are responsible for the development and spread of antibiotic resistance in aquatic environments[123,124].

16. Conclusion

Globally, the track record of illness and death because of cholera is enormous, especially in developing countries. It results from ingesting *V. cholerae* through the oral-faecal route. Cholera is mainly associated with poverty, unsanitary environments as well as the inaccessibility of a clean water supply. The impact of a cholera epidemic is not limited only to morbidity and mortality rates. It also has grievous impact on the economy of the nation experiencing the outbreak. This organism also plays a key role in emergent and recurring infections as well as rising drug-resistance trends. Prevention and control of cholera outbreaks lie mainly in intercepting its spread using measures that prevent continual infection and spread. Hence, it is important to survey and monitor the root causes and ways of communication of cholera diseases in order to control and prevent outbreaks. Children, expectant mothers, the aged and immune-compromised people form a considerable percentage of the populace that are mostly susceptible to cholera disease. Therefore, a collective effort to combat cholera is vital globally.

Conflict of interest statement

We declare that we have no conflict of interest.

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