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Cholera Epidemiology, Management and Control in the Sub-Saharan Africa

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SUMMARY: Cholera is a very devastating disease caused by a mono-flagellated gram negative bacillus called *Vibrio cholera*. It is currently endemic in Africa most especially the sub-Saharan part where the organism thrives well under the favourable climatic condition of the region, thereby causing havoc especially among children and women. In spite of the various interventions, the disease poses a great burden in Africa as aggravated by many influencing factors present in the region. This review presents crucial aspects of the disease that are of importance to stakeholders. Specifically, it covers the history of cholera and the biology of *Vibrio cholera* including the serogroups and virulence factors. The etiology, transmission and prevalence of the disease are thoroughly reviewed. All the information obtained from past literatures which have been combined in this report have broadened our knowledge on the current approaches needed in the treatment and management of cholera as well as the various control mechanisms as standard guidelines in the alleviation of the disease in the sub-Saharan Africa.

KEY WORDS: Cholera, Control, Influencing factors, Management, Sub Saharan-Africa

INTRODUCTION

Cholera is one of the tropical diseases caused by *Vibrio cholera,* a gram negative motile bacterium. The organism belongs to the family Vibrionaceae that shares some characteristics with the family Enterobacteriaceae. There are more than 200 serogroups but *V. cholera* O1 and *V. cholera* O139 are the most common serogroups associated with epidemic cholera (Sharifi-Mood and Metanat, 2014). *Vibrio cholera* O1 is divided into classical and El Tor biotypes, and into three serosubtypes - Ogawa, Inaba, and Hikojima. The virulence factors are coded for in the genome, especially the large plasmid. Cholera toxin (ctx) is encoded by ctx genes (Nelson *et al.,* 2009; Adagbada *et al*., 2012). Cholera is spread through the fecal-oral route, either directly from person-to-person or indirectly through contaminated fluids from an environmental reservoir of varying duration, food and potentially flies and fomites (Ebob, 2019). Every year, approximately 3-5 million cholera cases occur, worldwide. During the nearly five decades until 2017, African countries reported over 4 million cholera cases to the WHO. Cholera infection rate, sex and age distribution and seasonality are not constant (Adagbada *et al*., 2012)

It has been described as a waterborne and foodborne bacterium that can cause global pandemics. This characteristic makes it unique among the pathogens that cause diarrhea (Jahan, 2016). Cholera has proven to be one of the deadliest diseases known in history. Although it is a global disease, Africa has been the worst hit in pandemic cases. It is now said to be endemic in Africa. Many factors account for the heavy burden of *V. cholera* in the Sub-saharan Africa. *Vibrio cholera* is a mesophile, that is it lives within an optimum temperature value of 37°C hence it is physiologically adapted to such an environment (Haneef *et al.,* 2015). Malnutrition is common among children in the less developed countries around the sub-saharan Africa, a factor that has been reported to promote cholera. This is associated with lowering of immunity of the children thereby allowing the pathogen to invade gastrointestinal tracts to cause cholera. In some cases, the presence of other pathogens of bacterial and viral origin such as HIV is a predisposing factor. Environment is a major determinant of cholera outbreak. Many outbreaks have been recorded in swampy and coastal environment across Africa (Ebob, 2019).

Other associated factors include contamination of water and food as a result of poor hygiene or poor sanitation. These are characteristics of densely populated environment where the number of people living in an area is beyond the carrying capacity of such an environment. Pressure is exerted in such an area which may lead to heavy pollution and contamination of water (Deen *et al.*, 2019). Also, there are evidences that raining season and flood aggravate cholera burden, thus both climate and season are implicated. Migration of people increase population density and further increase the spread of the pathogen to non

endemic regions. Poor socioeconomic status and deficient health system of an area may influence the outbreak of cholera. All these factors are characteristics of sub-Saharan African regions that probably account for the high burden of cholera (Ebob, 2019). This paper reviews crucial aspects of public health education on cholera outbreaks that are of significant importance to stakeholders. All the information obtained from past literatures which have been combined in this report would broaden our knowledge on the current approaches needed in the management and control of cholera in the sub-Saharan Africa.

HISTORY OF CHOLERA OUTBREAK

Cholera has proven to be one of the deadliest diseases known in history and it was thought that Hippocrates (460-377 BC) first gave a perfection description of the disease in the fifth century BC. Asia was reported as the home of cholera from where it spread to other parts of the world 1991 (Jahan, 2016). John Snow, a legendary epidemiologist, was the first person to work on cholera in the 18th century when he established a relationship between cholera disease and polluted water (Codeço and Coelho, 2006). Hence, his work especially on the Soho cholera outbreak of 1854 helped to gain insight into how cholera could be controlled by looking into the sources of water intake. Robert Koch, in 1883, stated that cholera was primarily caused by a curve shaped bacillus called *Vibrio cholera* (Sepulveda *et al*., 2006). As a result of defective waste management system, another cholera outbreak occurred in Germany where more than 10,000 people were killed in 1892. Cholera outbreaks were later reported in Indonesia in 1961; West Africa in 1970 and Americas in 1991 (Jahan, 2016). So far, seven cholera pandemics have been recorded globally. Africa was the worst hit in the seventh pandemic. The narration currently is the endemicity of the disease in Africa. Historically, it was first reported in Africa in 1836 killing more than 20,000 people in Zanzibar (Olago *et al*., 2007) followed by another occurrence in Egypt in 1848 with many casualties and in West Africa in 1868 (Mengel *et al*., 2014). Sub-Saharan African countries had experienced frequent cholera outbreaks that accounted for > 86% of reported cases and deaths worldwide in 2011. As at 2018, cholera outbreaks were reported in seven Sub-Saharan African countries including Cameroon, Democratic Republic of Congo, Tanzania, Kenya, Mozambique, Zambia and Zimbabwe (Gwenzi and Sanganyado, 2019). Major cholera epidemic recorded in Nigeria occurred in 1992, 1995 and 1997 with casualties. Although all parts of Nigeria are vulnerable to cholera infection, it is endemic in the Northern part (Adagbada *et al*., 2012).

BIOLOGY OF VIBRIO CHOLERA

Structure and Physiology of *V. cholera*

Vibrio cholera (family Vibrionaceae) is a curved or comma-shaped Gram-negative bacillus that shares some characteristics with the family Enterobacteriaceae. It is a bacillus of variable sizes ranging from 1-3 µm in length and 0.5-0.8 µm in its diameter (Adagbada *et al*., 2012; Sharifi-Mood and Metanat, 2014). As a motile bacterium, it has a single flagellum. *V. cholera* is aerobic and sometimes, facultatively anaerobic gram-negative bacterium. The natural habitat of *V. cholera* is the aquatic environment but it can survive within and outside the aquatic environment. It is halophytic (salt tolerant) and it grows with a temperature range of 10 to 43°C but optimally 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 (Haneef *et al.,* 2015). *Vibrio cholera* is the causative agent of cholera that has both human and environmental stages in its life cycle (Nelson *et al.,* 2009). It has been described as a waterborne and foodborne bacterium that can cause global pandemics which makes it unique among the diarrheal pathogens (Jahan, 2016).

Serogroups and biotypes

Vibrio cholera exists in different types based on serological characteristics. The organism is differentiated on the basis of the O antigen of its lilipopolysaccharide (Piarroux and Faucher, 2010; Sharifi-Mood and Metanat, 2014). There are two antigenic structures namely; flagellar antigen (H) and a somatic O antigen. The O-antigen confers pathogenicity to the organism. There are more than 200 serogroups but *V. cholera* O1 and *V. cholera* O139 strains are the most common serogroups associated with cholera (Piarroux and Faucher, 2010). Hence, toxigenic strains are found within these two groups. They are known to produce cholera toxin (Sharifi-Mood and Metanat, 2014). There are two distinct biotypes from the O1 serogroup: El Tor and Classical, which are further subdivided into two to three strains depending on source of the reports. Some authors reported only the Inaba and Ogawa strains while some reported three strains with the addition of Hikojima strain. The El Tor strain remains the dominant strain globally (Adagbada *et al*., 2012; Nelson *et al.,* 2009; Sharifi-Mood and Metanat, 2014).

The Genome and Virulence Factors

Pathogenicity of *V.cholera* has been confirmed to have genetic basis that encodes the secretion of choleragenic toxins (Heidelberg *et al.,* 2000). The organism has both large and small chromosomes (Ebob, 2019). The large chromosome encodes genes that that govern DNA replication, transcription and translation. It also carries genes for metabolic pathways and those encoding the surface antigens, pili and toxins (Heidelberg *et al.,* 2000). The small chromosome consists of a large plasmid which

is a self replicating circular choromosome that carries many virulence factors along the segments. The two chromosomes are similar to an extent by sharing the same type of genes coding for similar products (Ebob, 2019; Heidelberg *et al.,* 2000).

Virulence factors are present in all chloragenic *V.cholera* strains in form of toxins. Many factors may account for pathogenicity and virulence of the organism. However, toxin production is implicated in the manifested choleragenic symptoms of *V.cholera* such as diarrhea (Nelson *et al.,* 2009). Cholera toxin is in form of AB5-subunit that consists of structures which binds to the epithelial cells and releases certain enzymes (Burrus *et al.,* 2006). The organism possesses colonisation factor and toxin co-regulated pilus (TCP). The pilus colonisation factor is encoded by the tcpA gene (Adagbada *et al*., 2012). Apart from toxins that are the main virulence factors, some cholera toxin confers antibiotic resistance which is coded for by the large and small choromosome, especially the large plasmid (Nelson *et al.,* 2009). According to Adagbada *et al*. (2012), the most important virulence genes in *V. cholera* strains are ctx genes (ctxA and ctxB) that encode the production of the cholera toxin.

ETIOLOGY AND TRANSMISSION

The disease known as cholera has been described as an acute infectious, secretory, and painless diarrheal disease caused by *Vibrio cholera* (Ebob, 2019). It arises as a result of water or food contamination caused by the faeces of a *V. cholera* infected symptomatic or non symptomatic patients. Contaminated food or water intake by healthy persons may result in cholera. The bacteria may be found in the faeces between 7-15 days of exposure (Ebob, 2019; Horwood and Greenhill, 2013). Therefore, the route of spread is of cholera is fecal-oral (Deen *et al.,* 2019). It can occur from person-to-person or through contaminated water, food, flies and fomites (Sack *et al.,* 2004). Epidemic cholera often occurs in such a way that there is an interaction between the aquatic environment and fecal-oral route (Deen *et al.,* 2019). *V.cholera* cells in contaminated aquatic environment is hosted and disseminated by chironomid eggs, planktons, benthic biota and sediments as reservoirs. These reservoirs are transferred to aquatic birds and fishes which are taken up by man. Gwenzi and Sanganyado (2019) in their review presented a diagram sourced from Vezzulli *et al.* (2010) showing the reservoirs of *V.cholera* in an aquatic ecosystem and how the reservoirs affect man (Figure 1). Cholera infected persons excrete *V. cholera* in their stool. The organisms appear as a mixture of free-swimming aggregate of cells. The bacteria alternate between motile and biofilm forms to colonize the small intestine. The biofilm form is more resistant to stressful conditions in the host as a very effective strategy for adaptation (Faruque *et al.,* 2006; Silva and Benitez, 2016). The fecal-oral transmission may be facilitated by a transient hyperinfective state of *V. cholera* in fresh stool and this may increase the transmission within a short time especially in areas with high population density (Eisenberg *et al.,* 2013; Deen *et al.,* 2019).

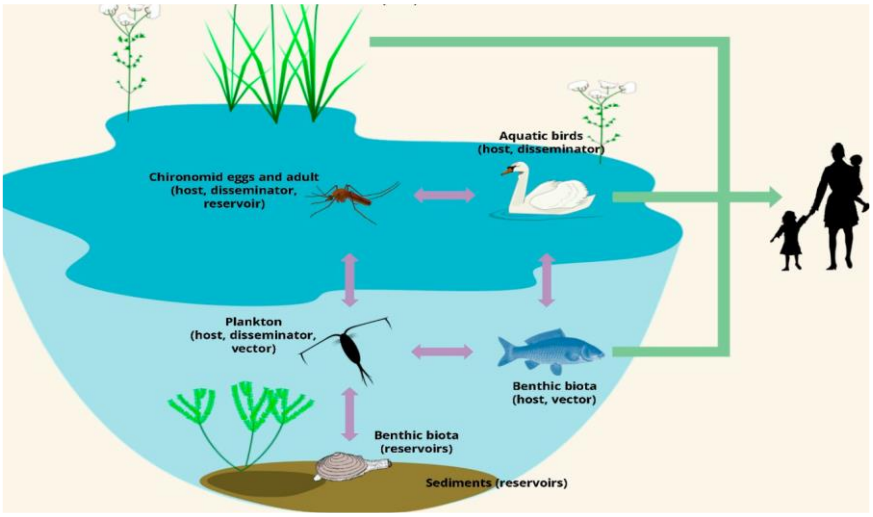

Figure 1: Host and reservoirs of V.cholera in a typical aquatic environment (adapted from Gwenzi and Sanganyado (2019) as sourced from Vezzulli *et al.* (2010)

SYMPTOMS AND COMPLICATIONS

Symptoms begin with sudden onset of a painless but voluminous watery diarrhea usually without vomiting. Symptoms may be mild or severe (Sharifi-Mood and Metanat, 2014). In many cases, there are no symptoms. In some symptomatic patients, severe dehydration may arise from acute diarrhea and vomiting. This is because a large volume of water and salts is frequently lost and it is characterized by gray or opaque white mucus stool. Dehydration is a serious matter that may cause of death if not quickly treated (Harris *et al.,* 2012). One out of 20 patients infected with *V. cholera* has severe watery diarrhea (Ebob, 2019). Patients with severe cholera may have a stool volume of more than 250 mL/kg of body weight in 24 hours (Sharifi-Mood and Metanat,

2014). Due to this large volume of diarrhea, there may be uncontrolled bowel movements that may cause total dehydration (Jackson *et al.,* 2013). Other symptoms may include intense thirst, muscle cramps, weakness, anuria, sunken eyes and consequently kidney failure, shock, coma, and death. Even after recovery, patients may exist in a carrier state (Sharifi-Mood and Metanat, 2014; Ebob, 2019). During dehydration there are complications of hypoglycemia, hypokalemia (potassium loss in stool) and bicarbonate loss in children. Hypokalemia is intense among children with existing malnutrition. Other complications associated with cholera in children are: hypocalcemia, hyperphosphatemia, accidemia and other unusual clinical presentation that may account for high mortality rate of cholera cases.

PREVALENCE AND BURDEN OF CHOLERA

Studies have shown an annual increase in cholera cases globally. For instance, there were 600,000 approximated cases between 2000-2004 whereas the figure rose to approximately 800,000 cases between 2004-2008, (Kanungo *et al.,* 2010). In 2006, 52 countries reported 200, 000 cases including 6000 deaths with a fatality rate of 2.7% (CDC, 2020). About 5 million cholera cases and 120,000 deaths were reported in the past few decades (Jahan, 2016) but Africa took the lion share. Between 2008 and 2012, the annual cholera burden was estimated at 2.86 million cases with about 95,000 deaths. Many authors have argued that the cholera cases are grossly underreported. Under-estimation of cases is likely to have taken places due to difficulty in data collection and presence of asymptomatic cases. The above figures are likely to have been obtained from laboratory data alone (Jahan, 2016). According to the WHO (2020), researchers have estimated that each year there are 1.3 million to 4.0 million cases of cholera and 21,000-143,000 deaths worldwide. According to WHO, cholera is now endemic in many parts of Africa. African countries had reported over 4 million cholera cases to the WHO in the last five decades. Explosive outbreaks had been confirmed in the Democratic Republic of the Congo (DRC), Ethiopia, Nigeria, Somalia, South Sudan, Sudan, and Zambia with fatality rates as high as 6.8% in some regions.. With underreporting and inadequate surveillance systems, the number of cholera cases in Africa is probably much higher than what is officially reported (Deen *et al.,* 2019).The temporal occurrence of cholera varies around Africa. In the DRC, cases occur year-round with a rise in incidence during the rainy season. Elsewhere in Africa, cholera generally occurs in explosive outbreaks, as in Zimbabwe, which reported 128,208 cases and 5634 deaths between August 2008 and mid- January 2009. An assessment of 78 cholera outbreaks in Mozambique from 2009 to 2011 showed an average duration of 7.2 weeks with 68% of cases and 89% of deaths occurring within the first six weeks of an outbreak (Deen *et al.,* 2019). As analysed in Adagbada *et al*. (2012), cholera cases in Nigeria varied from place to place across demographic parameters such as age groups, sex and seasonality. At a particular time, fatality rate was as high as 13% in Nigeria. In Abeokuta, South-western Nigeria, between November 2005 and January 2006, 11 deaths from the 115 cases with case fatality rate of 9.6% were reported. The 2010 outbreak was very devastating where fatality rate in Plateau State was 23.0%. Here, women and children accounted for 80% of reported cases..

FACTORS INFLUENCING CHOLERA OUTBREAKS

Existing reports in literatures have extensively discussed the interrelationship among some factors and cholera outbreaks generally. They are: Host susceptibility factors, environment, climatic factors, seasonal factors, high population density, poor hygiene, migration, socioeconomic status, health system deficiencies and type of regions. These factors are analysed below:

Host susceptibility factors

V. cholera is not acid-resistant therefore, use of antacids, proton pump inhibitors and histamine receptor blockers are likely to increase the risk of *V. cholera* infection (Sharifi-Mood and Metanat, 2014). Increase in the level of gastric acidity is reported to inhibit *V.cholera* and reduce the chances of cholera infection (Van Loon *et al*. 1990; Zuckerman *et al*. 2007). People who produce less stomach acid such as young children, older people, and those taking drugs that reduce stomach acid are also susceptible (Adagbada *et al*., 2012). Malnutrition is a major challenge in poor countries and it is a situation whereby people especially children do not have access to the right type of food needed for their growth and development (Harris *et al.,* 2008). Examples include, energy rich food, protein, fats and oil, minerals and vitamins. Malnourished children are susceptible to all types of infection including *V. cholera* due to weak immune system. Therefore, host nutritional status is a major factor. This is why infants that are not properly breast fed are predisposed to cholera in endemic regions (Clemens *et al.,* 1990; Deen *et al.,* 2019). The incidence of cholera is twice in people with type O blood compared with other blood groups. The reason for increased susceptibility in type O blood is unknown (Deen *et al.,* 2019; Kuhlmann *et al.,* 2016). The O phenotype corresponds to an unmodified H antigen and is associated with a decreased risk of infection with *V. cholera*. However, once the host is infected the O phenotype is associated with an increased risk of severe symptoms (Nelson *et al*., 2009). The host immune system is the critical defence mechanism against cholera. However, infection with cholera can result in a range of responses, from severe and life threatening diarrhoea to mild or unapparent infections (Adagbada *et al*., 2012). In endemic regions, the majority of cases

occur among children less than 5 years of age and in reproductive-age women (Jahan, 2016). Some studies showed that people infected with human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS), malaria, and tuberculosis often have weakened immunity, and are more susceptible to co-infections with other infectious diseases. Also, *Helicobacter pylori* infection increases individual susceptibility to cholera (Sharifi-Mood and Metanat, 2014).

Environment

Numerous cholera foci in Africa have been located in estuarine areas. The complex biological systems constituting the aquatic environmental reservoir are critical to long-term survival of epidemic *V. cholera*. Pathogenic vibrios are commensal with numerous organisms such as algae, crustaceans, floating aquatic plants like water-hyacinth (Feikin *et al*. 2010), phytoplankton, and zooplankton such as copepods (Reyburn *et al*., 2011; Acosta *et al*. 2001; Colwell *et al*. 2003). In response to nutrient deprivation, vibrios can enter a dormant state and persist in an aquatic environment; subsequent changes in water temperature, salinity, pH, and nutrients can resuscitate vibrios and lead to their multiplication, causing epidemics (Reyburn *et al*. 2011). In Africa, water likely plays a major role in triggering cholera outbreaks, with lagoons and estuaries contributing to coastal disease, and lakes and rivers contributing to inland disease (Mengel *et al*., 2014; Rebaudet *et al*., 2013).

Contamination and poor sanitation

Several factors influence the occurrence and development of epidemics in sub-Saharan Africa.

In sub-Saharan Africa, cholera frequently causes large outbreaks and epidemics presumably due to lack of safe water, poor sanitation and inadequate case management (Mengel *et al*., 2014). The onset of an outbreak in a new location can result from person to- person transmission when a symptomatic or asymptomatic carrier enters a susceptible population or when an individual comes in contact with contaminated environmental sources (Nelson *et al*. 2009). Once cholera has infected individuals in a new area, initial propagation depends on the extent of individual bacterial shedding, host and organism characteristics, and the likelihood of additional persons coming into contact with an infectious dose. Shedding may occur before and up to 7 months after symptom onset (Utsalo *et al*. 1999). Symptomatic persons shed substantially more (107–109 V. cholera per ml of stool) than asymptomatic persons (103 V. cholera/ml). The infectious dose for a susceptible individual is 104–1011 (Nelson *et al*. 2009; Kaper *et al*. 1995; Zuckerman *et al*. 2007). After excretion by the patient, V. cholera acquires a hyper-infectious state that lasts for at least 5 h in an aquatic environment (Merrell *et al*. 2002; Nelson *et al*. 2009; Morris, 2011). More virulent strains, or the introduction of equally virulent strains into an immunologically naïve population, can increase the risk of outbreaks and may have contributed to ongoing epidemics in Africa (Kaper *et al*. 1995; Keddy *et al*. 2007; Mengel *et al*., 2014; Quilici *et al*. 2010; Piarroux and Faucher 2012).

Food may become contaminated with V. cholera in the natural environment, during preparation of food or storage of leftovers (Kaper *et al*. 1995; Estrada-García and Mintz 1996; Albert *et al*., 1997). Because vibrios concentrate in the gastrointestinal tracts of mollusks, crustaceans, and fish that ingest copepods (Estrada- García and Mintz 1996), the consumption these seafoods has been incriminated in cholera outbreaks as shown in figure 1. Transmission of *V. cholera* O1 has been associated with eating of unwashed raw vegetables or fruits (Albert *et al*. 1997; Dubois *et al*., 2006) and with poor hygiene practices during meal preparation, as observed in fish gutting processes. Inadequately stored and reheated food has been shown to transmit cholera. In Africa, this has been observed, for example, with cooked rice in Guinea and cooked pigeon peas in Malawi (Mengel *et al*., 2014).

Climatic and Seasonal factors

Beside its seasonal variations, the burden of cholera has exhibited important interannual fluctuations in numerous costal African countries. For instance, early 1990s cholera epidemics in

Ghana, Togo, Benin, and Nigeria showed a significant synchrony with rainfall. Sometimes, these global climatic forces have provoked local hydrometeorologic disasters, which have been contemporaneous with several cholera epidemics (Gwenzi and Sanganyado, 2019; Rebaudet *et al*., 2013).Weather and climate play a critical role in cholera dynamics due to a variety of reasons (De Magny *et al*. 2012). In Africa, the climate influences cholera outbreaks in specific ways (Bompangue *et al*. 2011), with an increase in the frequency and size of outbreaks during the hot and rainy seasons, as has been documented in Zanzibar (Schaetti *et al*. 2009), the South Kivu district bordering Lake Tanganyika in DRC (Bompangue *et al*. 2009), Angola (Colombo *et al*. 1993), and five countries in West Africa. Climate may influence cholera dynamics by affecting water supplies. Heavy rainfall may increase contamination through overflow and disruption of water networks (Griffith *et al*. 2006; Guévart *et al*. 2006; Sasaki *et al*. 2009), as observed with rainfall in Dakar, Senegal, that exacerbated a cholera epidemic (De Magny *et al*. 2012). Flooding can cause draining of sewage into rivers and lakes Cholera Outbreaks in Africa and increase runoff from latrines or pit toilets, which then contaminates shallow and uncovered wells as noted in Senegal, Zambia, Cameroon, and Zimbabwe (Adagbada *et al*. 2012; Guévart *et al*. 2006; Mengel *et al*., 2014; Sasaki *et al*. 2008, Ako *et al*. 2009; De Magny *et al*. 2012; Luque Fernandez *et al*. 2012). Based on the report given by the WCAR (2020), heavy rains in August 2020 caused massive flooding in some countries of the

West and Central Africa region with nearly 1,660,000 people affected in Nigeria, Niger, Cameroon, Mali, Chad, Burkina Faso, Gambia and Guinea (OCHA). Most of the areas affected by the floods are cholera hotspots and some of them were already affected by cholera outbeak. The risk of new outbreaks and the spread of ongoing cholera epidemics are very high during this period of flooding (WCAR, 2020). Cholera is rare during the winter as the temperature is low and there is little rainfall. Gradually, the temperature gets hotter till the monsoon arrives. The incidence of cholera is low in the actual monsoon period as compared to pre-monsoon period. This lower incidence in the monsoon period is explained by the dilution effect reducing the amount of bacteria in the aquatic environment (Jahan, 2016).

High population density

High population density combined with poor quality informal housing may influence cholera incidence and outbreak amplification (Griffith *et al*. 2006; Penrose *et al*. 2010) by facilitating person-to-person transmission and increasing the burden on inadequate sanitation facilities. In Harare, 2008–2009, cholera attack rates ranged from 1.2 cases per 1,000 people in low-density residential suburbs to 90.3 per 1,000 in an overcrowded suburb (Luque-Fernandez *et al*. 2011), with similar trends observed in Ghana (Osei and Duker 2008) and Uganda (Legros *et al*. 2000). A strong association exists between increased cholera incidence and the absence of sanitation facilities (Sasaki *et al*. 2008; Griffith *et al*. 2006; Mahamud *et al*. 2012) or proximity to waste dumps (Osei and Duker 2008). In Africa, only 34 % of the population has access to improved sanitation facilities, ranging from 9 % in Niger, to 74 % in South Africa (WHO, 2020).

Poor hygiene

Poor hygiene practices, for example the absence of soap in the household, also increase cholera risk (Dubois *et al*. 2006; Guévart *et al*. 2006). Severe outbreaks can occur where a lack of functional hygiene and sanitation services coincides with high population density, such as in refugee camps (Boelaert *et al*. 1995; Shultz *et al*. 2009; Goma Epidemiology Group 1995; Griffith *et al*. 2006), during gatherings (Manga *et al*. 2008) and in prisons (Griffith *et al*. 2006). Markets, fairs, and other cultural and social events have been shown early on to provide a forum for increased food-borne cholera transmission. *V. cholera* can survive on produce for two to five days and easily spread because of crowding, and the absence of latrines and running water. In Lusaka, Zambia, 2004, raw vegetable consumption from the Soweto market was strongly associated with cholera, whereas water source contamination or treatment practices were not (Dubois *et al*. 2006); a similar situation has been observed in Guinea-Bissau (Luquero *et al*. 2011). Fecal-oral cholera spread is facilitated by sharing glasses and plates, as often occurs in traditional African settings. Funerals may propagate cholera spread through local rites such as washing the deceased's body followed by preparing and serving a large community meal (Germani *et al*. 1998; Gunnlaugsson *et al*. 1998; Griffith *et al*. 2006).

Cholera has been proven to be transmitted through fecal-oral route via contaminated food, carriers of the infection and inadequate sanitary conditions of the environment. The principal mode of transmission however remains ingestion of contaminated water or food. In Nigeria, the 1996 cholera outbreak in Ibadan (Southwest) was attributed to contaminated potable water sources. Street vended water and not washing of hands with soap before eating food are possible reasons for the 1995-1996 cholera outbreaks in Kano state. Drinking water sold by water vendors was also connected with increased risk of contracting the disease. In Katsina, the outbreak of the disease was linked to faecal contamination of well water from sellers. The recent 2010 outbreak of cholera was speculated to be directly related with sanitation and water supply. The hand dug wells and contaminated ponds being relied on by most of the Northern states as source of drinking water was a major transmission route during the outbreak. Perhaps, these wells were shallow; uncovered and diarrhoea discharge from cholera patients could easily contaminate water supplies (Adagbada *et al*., 2012).

Migration

Human travel via land, sea, rivers, and air drives the wide geographic spread of cholera (Mari *et al*. 2012; Manga *et al*. 2008; Duval *et al*. 1999). Susceptible people may become infected while traveling and introduce the disease in their home communities (Manga *et al*. 2008); inversely, through fecal shedding, asymptomatic or recovered cholera patients may be responsible for long-range dissemination of vibrios to a foreign environment (Mari *et al*. 2012). For example, fishermen on the Rift Valley lakes travel long distances and may return to their lakeside cities and trigger cholera outbreaks (Piarroux and Faucher, 2010). Additional overcrowding increases risk of contact with vomitus, excreta and contaminated water or food (Adagbada *et al*., 2012).

Socioeconomic status

In sub-Saharan Africa, risk factors for cholera infection, transmission and propagation are very specific to the local socioeconomic context and might vary among sub-regions and geographical areas. In more developed regions, natural contamination through infected seafood or vegetables are more likely to account for cholera cases, while in poor settings, risk factors will rather be a lack of potable water and proper sanitation (Griffith *et al*. 2006), mostly resulting from human crises and possibly exacerbated by natural disasters such as flooding. Political instability and civil wars have been shown to increase the risk

of cholera outbreaks especially in vulnerable populations such as refugees that have even less access to adequate water and sanitation facilities. Climatic factors periodically aggravate these difficult conditions and can lead to more frequent and more deadly cholera outbreaks. In Africa, cholera can be considered primarily as a disease of poverty (Bateman, 2009).

Health system deficiencies

Health system deficiencies contribute to outbreak magnitude. For example, poor surveillance can delay diagnosis and reporting and lead to delays in the implementation of control measures (Gunnlaugsson *et al*. 2000; Einarsdottir *et al*. 2001; Ahmed *et al*. 2011, Nguyen *et al*. 2014). Inadequate treatment facilities may lead to an increase in the risk of nosocomial transmission (Daniels *et al*. 1999; Kyelem *et al*. 2011).

Regions

The frequency, severity, and duration of cholera infections vary and keep on changing in different parts of the world. Cholera is endemic in Africa, south and southeast Asia. In contrast, cholera is almost eradicated from most of the developed countries. Between 1999 and 2005, Africa accounted for about 90% of the cholera cases and 96% of the cholera-related deaths worldwide. In contrast, other regions such as parts of South America have historically had only sporadic epidemics. During 2013, a total of 56,329 cases were reported from Africa, which shows a decrease of 52% as compared to 2012 when 117,570 cases were reported. Africa accounted for 43.6% of the total cases in 2013 as compared to 93–98% of the total cases during the period 2001–2009. In contrast, 11,576 cases were reported from Asia, representing an increase of 57% as compared to 2012 when 7367 cases were reported from Asia. In 2013, a total of 26 countries reported deaths due to cholera; 17 of these countries belonged to Africa. The case fatality rate was <1% in 4 countries, 1–5% in 17 countries, and >5% in 5 countries. In 2013, a majority (65%) of the deaths were reported from the African continent. A total of 1366 deaths were reported with a case fatality rate of 2.43% (Jahan, 2016).

DIAGNOSIS OF *V. CHOLERA*

Culture and Microscopy

Laboratory diagnosis is necessary not only for identification of microorganism, but also for epidemiological purposes. For definitive diagnosis, direct microscopic examination of stool including dark-field examination. *Vibrio cholera* exhibits variable sizes from 1-3 µm in length and 0.5-0.8 µm in its diameter (Haneef *et al.,* 2005). Isolation by stool culture is the gold standard method for the laboratory diagnosis (Sharifi-Mood and Metanat, 2014). Although, other causes of diarrhea may be considered, but the clinical picture of cholera is unlikely to be confused with any other enteric diseases. This is especially true in adults, in whom no other infectious disease causes such profound dehydration, quickly. 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. cholera*. 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*.

Biochemical Tests

two different antigenic structures; a flagellar antigen (H) and a somatic O antigen, non-acid resistant with infectious dose 103-106 and 102-104 organisms ingested with water and food respectively. *V. cholera* is not fastidious in nutritional requirements for growth though, organism needs an adequate buffering system. Non toxigenic strains of *V. cholera* are also present in environment, only strains encoding cholera toxin, haven filamentous bacteriophage (CTXΦ) 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. cholera *V. cholera* O1 and V. cholera O139 are the most common serogroups associated with epidemic cholera (Haneef *et al.,* 2005). *V.cholera* can be recognized in microbiology laboratories using selective media and biochemical tests by eagerly grown-up from clinical specimens, including stool and rectal swabs.

Molecular characterization

Polymerase chain reaction (PCR) has been developed to identify *V. cholera*. This test has a high sensitivity and specificity. However, this test is used only for screening of food samples (Sharifi-Mood and Metanat, 2014).

TREATMENT AND MANAGEMENT OF CHOLERA

Oral or intravenous hydration is the most important aspect in the treatment of cholera. In conjunction with suitable hydration, treatment with antibiotics is also recommended. Antibiotics should be prescribed for patients severely or moderately dehydrated and those who lost a large volume of stool during the rehydration therapy. Antibiotic therapy is also recommended for all hospitalized patients. Antibiotics should be selected using local antibiotic susceptibility patterns. In most countries, doxycycline is recommended as the first-line treatment for adults, and azithromycin as the first-line treatment for pregnant

women and children. Other antibiotics effective against *V. cholera* are trimethoprim-sulfamethoxazole (TMP-SMX), erythromycin, and ciprofloxacin. Azithromycin is more effective than erythromycin and ciprofloxacin. There are no guidelines to recommend antibiotics as prophylaxis for cholera prevention. All guidelines recommended that antibiotics should be administered along with aggressive hydration. Treatment with a single 300 mg dose of doxycycline has shown to be equivalent to tetracycline treatment for 3 days. Resistance to tetracycline and other antimicrobial agents among *V. cholera* has been reported in endemic and epidemic cholera settings (Sharifi-Mood and Metanat, 2014).

PREVENTION AND CONTROL OF CHOLERA IN SUB-SAHARAN AFRICA

Good hygiene

Basic hygiene measures such as hand washing with soap have shown protection against cholera in Nigeria (Hutin *et al*. 2003), Zambia (Dubois *et al*. 2006; Sasaki *et al*. 2008), Kenya (Mahamud *et al*. 2012) and Guinea-Bissau. Having access to a clean latrine in or outside the household also may decrease cholera risk (Mahamud *et al*. 2012; Mengel *et al.,* 2014). WHO recommends safe water supply and adequate sanitation and hygiene (WASH) as the main steps to prevent cholera.

Acidic food

Growth of V. cholera is inhibited in acidic foods. In an epidemic in Guinea, eating tomato sauce (pH 5.0) was shown to protect against symptomatic cholera. For similar reasons, lime juice, which has been used as prophylaxis in northern Indian regions during the cholera season (Anand 1995), had a strong protective effect when added to sauce, as exemplified in Guinea- Bissau, 1996 (Mengel *et al.,* 2014; Rodrigues *et al*. 2000).

Food with low moisture content

Vibrio survival is reduced in food with lower water content and higher osmolarity such as dried, salt-preserved, and sugarpreserved foods (Estrada-Garcia and Mintz 1996). Consumption of dried fish has been shown to have a protective effect (Dubois *et al*. 2006; Lucas *et al*. 2005; Mengel *et al.,* 2014).

Cholera modeling and forecasting tools

Climate teleconnections are linked to outbreaks of human and animal diseases. These results point to the fact that such relationships between cholera and hydroclimatic factors can be further developed into predictive modeling tools to forecast outbreaks of cholera and potentially other water-borne diseases. Such forecasting tools may provide key information to better target financial and public health resources in the control and prevention of cholera in SSA and other regions (Gwenzi and Sanganyado, 2019).

Health education

Health education is recommended for high-risk groups. Considering children and pregnant women and immune-compromised patients as high risk groups is very important (WHO, 2020).

Oral cholera vaccines

Official recommendations also include the use of oral cholera vaccines (OCVs) for control of cholera outbreaks. Two cholera vaccines are available and recommended by WHO. Oral cholera vaccines are safe, effective and currently licensed by WHO as follows: 1-Dukoral (Crucell, Leiden, Netherlands), and 2-Shanchol (Shantha Biotechnics Ltd., Basheerbagh, Hyderabad, India). Both vaccines are given as a two-dose regimen. Vaccines are safe and provide sustained protection for several years. In 2010, they were added to WHO recommendations to control cholera outbreak. However, doubts about feasibility, timeliness, and acceptability by the people at risk, and the fear of discouraging to use other preventative routes have discouraged their use during epidemics (WHO, 2020).

Efficient surveillance system

A well-organized, multi-sectoral approach is required to control cholera outbreaks (WHO, 2020). The effectiveness of public health interventions depends on an efficient surveillance system. There must be frequent and timely information-sharing at local as well as global level. The administration of cholera vaccines may be considered for high risk population in high risk areas. Funds and resources should be provided to the deserving countries to improve cholera prevention and preparedness activities (WHO, 2020).

International travel and trade

Currently, there is no obligation of cholera vaccination for international travel. It is learned with experience that quarantine and restrictions on travel and trade are not very effective in controlling the spread of cholera. However, the travelers should be provided information regarding signs, symptoms, and prevention of cholera. The neighboring countries of cholera affected areas should be advised to enhance their surveillance system for early detection and prompt response if any outbreak occurs (WHO, 2020).

CONCLUSION

Effective control of cholera in the Sub Saharan Africa requires integrated approaches of health education, intervention and good socio-economy. The influencing factors promoting the infections must be properly studied through research. Efforts must be made by stakeholders to enlighten the general public on public health and good hygiene. Improvement on health care facilities is important to ensure quick and accurate diagnosis of cholera and also to provide the needed treatment intervention. Vaccine must be made available and should be administered to all age groups in the rural and urban environment. There is need to intensify efforts on data collation and reporting on cholera outbreak for quick intervention being an infectious disease.

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