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Review Article

Epidemiology and Burden of Cholera in Nigeria

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ABSTRACT

Cholera is an acute diarrhoeal infection caused by ingestion of food or water contaminated with bacterium Vibrio cholera. It is a significant public health concern globally, particularly in low-income countries like Nigeria and resulting in mobility and mortality every year. Several factors including socioeconomic and environmental among other factors drive this trend. Some regions in the country have been identified as hot spots most especially the north where insurgency has worsened outbreaks and management/control difficult. This review examines the occurrence, geographical distribution, seasonal patterns, risk factors and associated mortality rates with cholera outbreaks highlighting the key findings and trends observed in the epidemiology of cholera and the challenges faced in the prevention and control of cholera in the country such as; inadequate sanitation and water supply, limited healthcare resources and low community awareness. Furthermore, It highlight the need for improved surveillance systems, access to clean water and sanitation facilities, improved education on the importance of handwashing and good hygiene practices with effective public health intervention to mitigate the burden of cholera especially in the northern part of Nigeria where the outbreaks are more frequent. It contributes to the existing literature on cholera epidemiology in Nigeria and provides valuable insights for future research and intervention strategies.

Keywords: *Cholera, Epidemiology, Vibrio cholerae, Risk factors, outbreaks.*

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INTRODUCTION

Fear of cholera was a major factor in the creation of modern sanitary systems (Luby *et al*., 2020). Its outbreaks in the middle of the 19th century in London caused thousands of fatalities (Luckin W., 1866; Tien JH, 2010). It remains a major public health threat in developing countries where safe water, good infrastructure, hygiene and sanitation facilities are poor or unavailable (Jutla *et al*., 2013; Talavera & Pérez, 2009). According to the World Health Organization (WHO) estimates, about 3 to 5 million people are affected annually by cholera worldwide and over 100,000 cases result in death (WHO, 2012) Cholera is an acute watery diarrheal syndrome caused by the bacterium Vibrio cholerae which normally lives in aquatic environments along the coast. People become infected by consuming water that has been contaminated, shellfish, or other foods, and once infected, the bacterium is expelled in the stool. Thus, the infection can spread rapidly, particularly in areas where human waste is left exposed or untreated (Olutola *et al*., 2012). This disease is endemic in Africa, parts of Asia, the Middle East, and South and Central America with 1.3 billion people at risk (Shaikh *et al*., 2020a). The world's worst cholera outbreak in fifty years hit Haiti in 2010, infecting over 600,000 people and killing around 8000 (Scopus, 2011). As of July 2017, a recent cholera outbreak in Yemen that began in October 2016 has 275,987 probable cases of the disease and 1634 fatalities related to it (Ferences, 2008). According to WHO, almost 94% of reported cholera cases is from Africa (WHO, 2012). The estimated number of cholera cases in Nigeria is currently the second highest in Africa (Lessler J, 2007) and it has experienced many large outbreaks of this disease resulting in much human sufferings and death (Dalhat, 2021). The high burden is likely due to the present of several underlying social and environmental risk factors, including a favorable climate (Abdussalam, 2016), high proportion of the population living in poverty (62% at <$1.25/day) (Leckebusch & Abdussalam, 2015). Water, sanitation and hygiene (WASH) (Bompangue, 2011; D'Mello-Guyett, 2020) reliance on hand dug wells and contaminated ponds as source of drinking water. In addition other cholera patients are also a typically source of the contamination when their untreated diarrhea discharge is

permitted to enter water systems (Igomu, 2023). In 2016, it was predicted that there will be a rise in the number of cholera cases worldwide, from 3,046,238 in 2015 to 3,787,385 in 2030, with Asia and Africa bearing the greatest burden (Kim *et al*., 2016).

In Nigeria, the first series of cholera outbreak was reported between 1970-1990. Despite the long record of cholera, understanding the disease's epidemiology that might help it deal with in epidemic circumstances is still inadequate. In this Review, knowledge gaps of the infection and various updated facts and phenomena related to the epidemiology and burden of this disease in Nigeria was discussed based upon the extensive searches in several biomedical science journals and web-based official organization reports.

METHOD

A thorough electronic search was conducted in various online databases and search engines, such as PubMed, ScienceDirect and Google scholar for available literature on Cholera. The search was carried out in June 2023. The following key words were used in all the database with no language restrictions: Cholera, Cholera in Nigeria, Cholera in Africa, epidemiology of cholera, epidemiology of cholera in Nigeria, Burden of Cholera, and Cholera outbreaks in Nigeria. The search terms were used separately and also were connected using Boolean operators such as "AND", "OR", "NOT". We also used Google search or citation matcher to look for specific papers that were discovered in the bibliographies or references of other articles.

Eligibility criteria: There was no restriction for the time the studies were conducted or the article was published. Studies were considered eligible if they were published in English, focused on Cholera, used scientific methods such as surveys, case-control, trials, review, prevalence and surveillance studies with good methodological standards. These studies were further considered if they were original publications and were carried out in community and healthcare facilities. The review excluded articles that were not available in full text, articles without abstract and duplicate studies

Data Screening and Extraction: The data screening and extraction process involved removal of duplicate articles, initial screening of the titles and abstracts based on the eligibility criteria and full text screening of selected studies. All the articles that met our inclusion criteria were retained for data extraction using an electronic standardized data extraction template designed by the team. A narrative summary of the extracted data was performed to address the research aims of the review

RESULTS

Search yield: The search from the databases and manual search from Google retrieved 370 articles and 287 were retained after removal of duplicates. After screening title, abstracts and references, 174 papers were removed. Full text was obtained for 113 papers of which 76 papers were eliminated as they did not meet inclusion criteria and finally, a total of 40 articles were considered for this review. The flow diagram as shown in Figure 1 presents the inclusion and exclusion process.

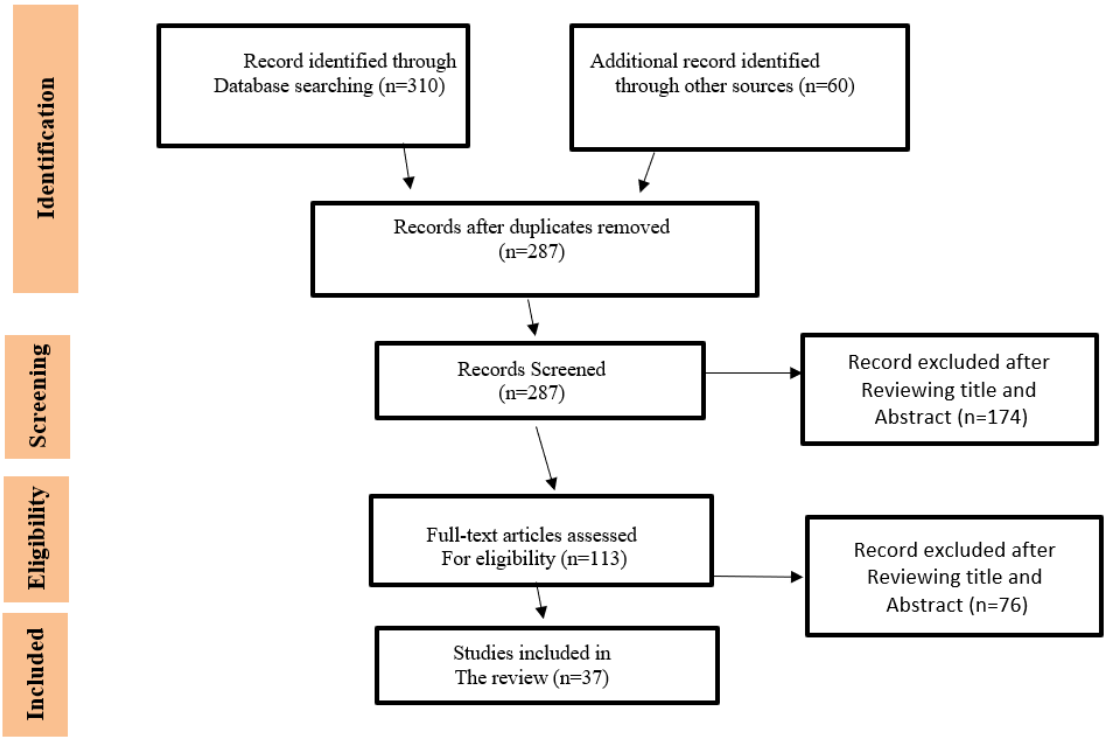

Figure 1:
Flow diagram of the article selection procedure

Description and Characteristics of *Vibrio cholera*: *Vibrio cholerae* is a highly curved Gram-negative bacillus rod which belongs to Vibrionaceae family and is characterized by the presence of a single polar flagellum that aids in its locomotion (Olutola et al., 2012). The biochemical profiles for *V. cholerae* include positive tests *viz*., nitrate reduction, indole production, catalase production, citrate utilization, ornithine decarboxylase production and lysine Decarboxylase production, and tests such as arginine dihydrolase production and urea hydrolysis (Mandal et al., 2011a).The primary surface antigen (O) from lipopolysaccharide of *V. cholerae* is divided into roughly 206 serogroups. Only two serogroups of *V. cholerae*, O1 and O139, are regarded causal agents of cholera epidemic (Sharma, 2007). V cholerae O1 is divided into classical and El Tor biotypes, and into three serosubtypes - Ogawa, Inaba, and Hikojima. Vibrio cholera O139 has characteristics in common with the El Tor biotype but differs from O1 in its polysaccharide surface antigen (López-Gigosos, 2011) Unknown strains of *V. cholerae* have been reported to have caused the first four pandemics while the seventh pandemic strains contain the El Tor variant toxins, the fifth and sixth pandemics were produced by the traditional O1 biotypes (Chowdhury, 2022). Serogroup O139 additionally became a contributing factor in South East Asia in 1992 (Safa, 2008). The O139 biosynthetic genes have taken the position of the O1 biosynthetic genes in this strain, which is a genetic derivation of the El Tor biotype. The most prevalent strain of Vibrio cholerae in Nigeria is 01 Eltor (Opajobi, 2004; Utsalo, 1999). The cholera toxin (ctx), which has been attributed to a toxin co-regulated pilus (TCP), is the most significant virulence factor associated with V. cholera O1 and O139. They also have the capacity to attach to and colonize the small intestine (Olutola et al., 2012). All of these important virulence-related genes are located in clusters (Hacker, 1997).

History Of Cholera: Cholera spread across the world from its original reservoir in Bangladesh and West Bengal (WHO, 2011), millions of lives have been lost across all continents since then, but mainly in Africa and Asia. The first pandemic was recorded starting in 1817 through 1824 and eight pandemics have occurred globally since then (Ruiz-Moreno, 2010). Africa first experienced the current (seventh) cholera pandemic in 1970, which spread quickly (Shaffer, 1988). African nations reported more than 4 million cases of cholera to WHO in the roughly five decades before 2017 (Lawoyin, 1999; Umoh, 1983). Explosive outbreaks occurred in Nigeria, Democratic Republic of the Congo (DRC), Ethiopia, Somalia, South Sudan, Sudan, and Zambia in 2017 (Deen et al., 2020). The WHO received official reports of 179,835 cases and 3,220 fatalities from cholera in Africa that year, with reported case fatality rates varying from 0 in various countries to 3.2% in Zambia, 5.2% in Angola, and 6.8% in Chad (Griffith, 2006). These high case fatality rates are a direct result of severe barriers to proper case management in many regions of the African continent.

Signs And Symptoms: Cholera is a destructive disease that causes extreme and intense water loss (Ayenigbara, 2019. About 70 to 80% of people infected with cholera do not develop any symptoms, although the bacteria are present in their faeces for 7-14 days after infection with the potentially of infecting other people by shedding it back into the environment (Shaikh et al., 2020b). When symptoms do appear, 80% of those affected have mild or moderate symptoms, whereas 20% experience severe dehydration and acute diarrhea which is often refer to as rice water stools because of its appearance (Kim et al., 2016). Just one diarrhea stool can cause a one-million increment of *V. cholerae* in the environment and Onset of illness is usually sudden with incubation periods varying from 6 hours to 5 days (Clemens, 1983; Colwell, 1999). More than one quart of water and salts is lost per hour(Olutola et al., 2012) and serious cases without treatment could result in life-threatening dehydration can become severe, causing intense thirst, vomiting, kidney failure, shock, coma, and death(Azman et al., 2013; WHO, 2004). Also, when infected with cholera, a person's skin may turn bluish-gray from extreme loss of fluids (Adagbada, 2012). In addition, blood pressure may drop because of dehydration, peripheral pulse is rapid, and urine output diminishes with time (Chizindu, 2012).

Outbreaks in Nigeria: In Nigeria, Cholera was first notified on December 1970 which led to an epidemic of 22,931 cases and 2,945 deaths with intermittent outbreaks occurrence since then.(Griffith, 2006). However, reports of cholera outbreaks have not been steady, but the infection is unique because it affects many states since the onset. Table 1 shows several outbreaks that have occurred since the first epidemic in which five significant epidemics recorded: 1991(Ayenigbara, 2019a), 1995-1996(Gangarosa, 2004), 1997(Ramamurthy et al., 2020)**,** 2017-2018(Azman et al., 2020a) and 2021(Ali et al., 2015) with highest number of cases reported in 1991 and 2021. In 1991, 59,478 suspected cases were reported with 7,654 deaths; in 2021, a total of 103,589 suspected cases including 3,566 deaths were reported from 401 LGAs across the country (Ayenigbara, 2019b). Like the global prevalence, the high rate of confirmed cases by Nigeria Centre of Disease Control (NCDC) was among the pediatric population, with 63.2% between 5 and 14 years and the proportion of affected males and females was the same (50% each)(Opajobi et al., 2004).

GEOGRAPHIC DISTRIBUTION OF CHOLERA IN NIGERIA

Although there have been inconsistent reports of cholera outbreak in the country and reported cases are not limited to specific regions of the country. However some states have been identified as hotspots of the disease having a history of frequent epidemics. Northern Nigeria has recorded more and severe outbreaks than other regions of the country overtime. According to a report released by (UNICEF (2015), Cholera cases reported between 2004 and 2014 in Nigeria had five states (Bauchi, Borno, Katsina, Gombe and Kano) contributing 66% of the entire cases. In addition, the largest outbreak in the history of cholera in Nigeria was the 2021 outbreak in which the northern part of the country is also responsible for 55% of the total reported cases (Global Task Force, 2017). Risk factors associated with cholera in any endemic location is largely at play in this regions, some of this

factors includes; absolute poverty, unwashed hands after using the toilet and before meals (Saheed, 2018), open defecation, improper sewage and waste disposal, (Oyedepo, 2019; Popoola, & Ogunshola, 2015) dependent on hand-well and contaminated water, (Hutin, & Pauet, 2003) poor sanitation and hygiene. However, the long-lasting turmoil caused by the terrorist organization (Boko Haram), banditry, farmers and herders crises, which forces people of impacted villages to escape to overcrowded internally displaced person (IDP) camps which become the epicenters of epidemics have all amplified some of these risk factors (Abubakar and Nguku, 2015)

Table 1:
Some Cholera Cases in Nigeria from 1970 Till 2022

Time Period	Reported No. Of Cases	CFR (%)	Source
1970-1971	22,931	12.80%	(WHO, 2021)
1991	59,478	12.90%	(WHO, 2021b)
1995-1996	5,600	6.10%	(Hutin, 2003)
1999	26,358	7.9%	(NCDC, 2019)
2001	2,050	3.90%	(WHO, 2012))
2008-2009	18,831	3.60%	(WHO, 2013)
2010-2011	60,086	3.60%	(NCDC,2019)
2014	35,996	2.1%	(David, 2015)
2015	5,301	3.51%	(NCDC, 2017)
2016	768	4.17%	(NCDC, 2017)
2017	1,198	2.67%	(Bayode, 2019)
2018	50,719	2.2%	(WHO, 2021)
2021	103,589	3.4%	(WHO, 2021)
2022	12,496	3.2%	(WHO, 2023)
2023	1366	5.91%	(Racheal, 2023)

Seasonality: Endemic cholera, which occurs frequently yearly and its association with seasonal circumstances is a major public health problem in many areas in Southeast Asia (Ayenigbara, 2019). Extreme environmental variables, such as frequent and widespread flooding that can contaminate water sources and displace communities, or droughts that impact water supplies, can cause cholera epidemics in places with poor water and sanitation facilities. Cholera generally manifests itself during the raining season. Pascual and colleagues emphasized the significance of rainfall as a driver of the seasonal cycle of cholera due to its watery transmission, its dose-dependent nature of infection, and the increase in incidence during the rainy season (Pietroni et al., 2020). In Nigeria, higher number of outbreak cases have been reported in Kano and some other northern parts of the country occurred during the rainy season (Adagbada, 2012b). In Calabar, southern part of the country, outbreaks tended to be more common during the dry season, declining as the rainy season got underway (Ndon, 1992). Since infections have been observed during both the wet and dry seasons, seasonality of infection is not a serious problem in Nigeria.

Transmission And Risk Factor: Transmission of cholera is primarily through the fecal-oral route of contaminated food or water caused by poor sanitation (Pietroni, 2020). Primary transmission of *V. cholerae* is known to occur from aquatic reservoirs in the environment, and secondary transmission is known to occur from people who have already contracted the disease. Once primary transmission has started an outbreak, secondary transmission causes epidemics in the endemic areas (Olukoya, 1995). Water is usually the main vehicle of transmission in endemic areas, although this may also occur via food while most cholera cases in non-endemic areas is more commonly associated with the consumption of contaminated food**,** such as undercooked or raw seafood, imported from cholera-endemic regions (Mandal et al., 2011b). People infected with cholera suffer acute diarrhea and excrete watery stool loaded with toxigenic *V. cholera*, when this diarrhea stool enters public waterways, groundwater or drinking water supplies, contamination and transmission of cholera will occur. As such, drinking any contaminated water, eating any food washed in the contaminated water or eating shellfish living in the contaminated conduit all predispose to becoming infected. Foodborne transmission of cholera is less common than waterborne transmission (WHO, 2017) In Nigeria, almost all the cholera outbreak was attributed to contamination of potable water source, poor sanitation and water supply. An example was the outbreak that happened in Ibadan (southwest) and Kano state in 2001 respectively (Bolade, 2008; Sinclair et al., 2011). Population migration, which accelerates the dissemination of the infectious agent to additional people and to new locations is another factor that may significantly increase the risk of cholera transmission [54]. Overcrowding also increases the risk of cholera transmission and spread, particularly in regions with inadequate sanitation and insufficient water sources, including prisons and camps for internally displaced individuals (Ayenigbara et al., 2009).

Management of Cholera: No one should die of cholera. It is an eminently preventable and treatable disease (Umoh, 1982b). Effective case management of cholera involves a combination of measures at treating the symptoms and rapid early intervention with strict attention to detail including infection control processes. The case fatality rate exceeds 50% without proper clinical management but can be less than 1% with prompt rehydration and antibiotics (Hutin, 2003) Fluid replacement is the treatment's mainstay (Olutola et al., 2012). Fluid replacement is an incredibly efficient therapy that greatly reduces mortality since the majority of cholera fatalities are caused by severe dehydration and electrolyte loss. Those who are suffering from cholera often have greater fluid loss (10 to 20 ml/kg/hr) and are more likely to be dehydrated than those who are experiencing other gastrointestinal illnesses (NCDC, 2018). The most common mistake in the treatment of cholera is under-administration of fluid (Hutin, 2003b). Most patients with mild to moderate cholera can be managed with Oral rehydration treatment (ORT) which reduces the need for intravenous fluids. This involves the administration of a solution containing water, salts, and sugars to replace fluids and electrolytes lost through diarrhea. ORT is an effective and inexpensive treatment for cholera that has been widely implemented in cholera-endemic areas (Ayenigbara et al., 2019). Those with severe cholera usually require 200 ml/kg of intravenous fluid replacement in the first 24 hours of therapy. Additionally, antibiotics can be

used to reduce both the severity and duration of cholera symptoms as well as the disease's transmission. They are suited for usage in settings with minimal resources since they are efficient at treating cholera and may be taken orally. Antibiotics can delay the excretion of vibrio by 1-2 days in patients with moderate or severe dehydration, as well as minimize the length of sickness and fluid loss (Musa et al., 2021). As a result, they shorten the amount of time that patients need to stay in the hospital and how much liquids they need. However, *Vibrio cholera* strains from endemic and epidemic situations during the past ten years have demonstrated intriguing patterns of antibiotic resistance to widely used antimicrobial drugs (Olutola et al., 2012). Eighty six strains of *Vibrio cholera* O1 (79 Ogawa serotype and 7 Inaba serotype) from 1992 outbreak in Nigeria were less sensitive to cloxacillin, cotrimoxazole, streptomycin, ampicillin, penicillin and tetracycline (Adagbada, 2012a) Hence, Azithromycin or doxycycline was recently suggested by the World Health Organization as the first-line medicines for treating cholera (WHO, 2009). The implementation of these measures has led to significant reductions in the morbidity and mortality associated with cholera in many endemic countries.

Prevention and Control: Cholera may be dangerous and life-threatening, but if basic sanitation procedures are followed, the disease tends to be easily preventable. Global Task Force on Cholera Control (GTFCC) and partners lunched a Global Roadmap policy in 2017, which aim to decrease cholera-related mortality by 90% and eradicate cholera infection in at least 20 out of the 47 endemic countries by 2030, considered a multi-sectoral approach to cholera control and prevention as essential (Legros, 2018). Nigeria has been taken strategic actions since then, which include campaigns in the country mostly in the northern region, creation of a national strategic action plan and implementation of oral cholera vaccination (NCDC, 2019). 5-year National Strategic Plan of Action for Cholera Control was also devised towards achieving the worldwide goal of eradicating cholera by 2030, the plan includes a commitment to reduce cholera morbidity and death by 67% by the year 2023 (WHO, 2010). In order to achieve these objectives, the OCV administration was carried out in seven cholera hotspots spread over four different regions, including Borno, Bauchi, Yobe, and Adamawa which are states in the northern part of Nigeria. Furthermore, Cholera prevention and control measures mainly rely on the implementation of adapted WASH solutions to ensure use of safe water, basic sanitation and good hygiene practice, (Colwell, 1999) which mainly depends on economic growth and universal access to clean water. These steps safeguard against cholera epidemics and other water-borne illnesses (WHO, 2004).

Vaccine: The World Health Organization (WHO) advises that immunization with presently available cholera vaccines can be used in conjunction with the typically advised control measures in places where cholera is prevalent as well as in areas at risk of outbreaks (Azman et al., 2020b). With little adverse effects, oral vaccines have been proven to give short-term protection against *V. cholera* O1 of 85–90% across all age categories at 4-6 months after inoculation (Adagbada, 2007;Umoh, 1983). Three oral cholera vaccines (OCVs) are prequalified by WHO, namely Dukoral, Sanchol, and Euvichol, all three vaccines requires for doses for full protection (Umoh, 1983b). Dukoral consist of killed whole cell of *V. cholerae* O1 strain in combination with a recombinant B-subunit of cholera toxin which provides strong protection with 2 doses given 1–6 weeks apart (Chowdhury et al., 2022). It can be given to all individuals over the age of 2 years and those between 2-5 years require a second dose, it is mainly used for travelers and two doses can provide protection against cholera for 2 years (WHO, 2010.). Sanchol and Euvichol are essentially same vaccines produced by two different manufacturers. They are oral cholera vaccine that contains whole killed *V. cholerae* cells without the addition of the B subunit (GMS, 2019). It can be given to all individual over the age of one year and two doses provide protection against cholera for 3 years while a single dose provides a short term protection (WHO, 2010).

Recommendation: A multi-sectoral strategy to cholera prevention and control is crucial since there are many different yet functionally interconnected factors that contribute to cholera transmission in Nigeria. Firstly, Monitoring and Surveillance is necessary for any interventions to be implemented. This will assist in having precise data based on epidemiologic and laboratory monitoring systems that can quickly identify, confirm, and track the presence of disease. Cholera is one of the diseases that must be reported to the WHO via the country's Disease Surveillance and Response system. Unfortunately, there are sometimes underreported data gaps due to a lack of case definition understanding and diagnostic capability**.** In addition, the healthcare facility setting plays a crucial role in preventing and managing cholera transmission. As a result of this, it is essential that this be continually strengthened, especially at the primary care and other care levels while not ignoring the community since environmental and socioeconomic elements to which Nigeria is prone to certainly play a part in transmission of the disease. Although the NCDC has developed ways to address the problem, open defecation practices should be outlawed, particularly in the Northern areas. To decrease the prevalence of infectious diseases spread by direct physical contact, it is also important to raise awareness among the populace about the importance of good hygiene practices like proper latrine use, digging wells far from sewage systems, and proper food handling. However, our proposal is to concentrate epidemiological research on collecting comprehensive data on the sources of infection and modes of transmission because studies and information on the prevalence of the disease and the characteristics of circulating strains in Nigeria are limited. Finally, we urge the government to provide clean water for drinking as well as better sanitary and hygienic conditions for state residents.

CONCLUSION

Cholera spreads quickly across a population and can kill within hours. In Nigeria, it continues to be an imminent threat to public health, particularly in regions where residents are exposed to high levels of human waste. fatality rates can be

nearly eliminated with proper case care, particularly the early use of ORS and quick intravenous rehydration in patients with severe dehydration and its prevention would be aided by a combined comprehensive water, sanitation, and hygiene (WASH) development strategy and OCVs deployed in identified susceptible locations, prioritizing the greatest risk populations. However, it is clear that the danger for cholera will continue to rise without prompt intervention in Nigeria due to the country's rapid urbanization and increase in population, which create rising and conflicting needs for water and standard healthcare services.

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