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Combating Cholera Re-Emergence in Nigeria

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Abstract:- Throughout African countries, infectious diseases have long been widespread and have been recognized as one of the main causes of death. The bacterium *Vibrio cholerae* serogroup O1 or O139 is the cause of cholera, an acute diarrhoeal disease that poses a significant public health risk to both adults and children. Acute, watery diarrhoea affects about 20% of infected individuals; severe diarrhoea, which includes vomiting, affects 10% to 20% of these individuals. Severe dehydration and death within hours can occur from the large loss of fluid and salt in these individuals if they are not appropriately and quickly treated. Between 28,000 and 150,000 people die from cholera each year, and there are 3 to 5 million cases worldwide. Nigeria is one of the three primary cholera hotspots in the world at the time. In 2012, Sub-Saharan Africa accounted for 71% of all cases and 86% of fatalities from the disease. This paper evaluates the literature on the occurrence of cholera in sub-Saharan Africa, with a focus on Nigeria. It also explains the disease's treatment options, diagnostic procedures, and containment strategies that incorporates all necessary elements including education, WASH, immunization, monitoring, and nutrition).

I. INTRODUCTION

➢ *Background*

For a long time, infectious diseases have been raging throughout the African nations; in addition, they have been identified as one of the leading causes of mortality. The number of deaths related to communicable diseases has decreased (by 1% annually) since 2010[1]. The World Health Organization (WHO) predicts that before 2050, the number will occasionally rise and that the figures will probably fluctuate. The latest Ebola virus, cholera, Zika, hepatitis A and B, measles, dengue fever, rabies, Hantavirus infection, smallpox, and acquired immunodeficiency syndrome are a few of the infectious diseases. The second and third-world countries are still fighting these diseases, even if the first-world countries have managed to eradicate some of them[2]. To provide additional clarification, we will concentrate on the current cholera outbreak in Nigeria in this study.

Cholera is an acute diarrhoeal illness of public health significance, it is caused by the bacteria *Vibrio cholerae* serogroup O1 or O139 and affects both adults and children[3]. About 20% of infected people experience acute, watery diarrhoea; and 10% to 20% of these people also experience severe diarrhoea that includes vomiting. The loss of so much fluid and salt can cause severe dehydration and death in a matter of hours if these people are not appropriately and quickly treated[4]. Untreated cases may have a case-fatality rate of 30 to 50%, but therapy is simple (rehydration essentially) and should keep the rate below 1% when administered correctly[5].

The symptoms of cholera typically begin with cramping in the stomach, vomiting, and diarrhoea. If untreated, these symptoms can worsen and result in fluid losses of up to one liter per hour, which can lead to metabolic acidosis and severe dehydration, which can ultimately cause kidney failure, shock, coma, and death. Of all cholera cases, around half had no symptoms. People who don't exhibit any symptoms can spread the infection to others by passing on vibrio in their feces. Before the onset of the disease, patients with symptoms may also shed vibrio, which they will continue to shed for one to two weeks[6].

Cholera transmission is via the fecal-oral route; it involves contaminated food, carriers, and unhygienic surroundings. Outbreaks of cholera usually develop from the introduction of *Vibrio cholerae* organisms into food or water as a result of inadequate personal hygiene, unsanitary environmental circumstances, and a lack of drinkable water supplies. It has also been documented that internal displacement brought on by man-made and natural disasters can result in unstable living conditions, contaminated food, and contaminated water supplies, which can contribute to cholera outbreaks[7].

Since cholera prevention and treatment are related, the primary goal of this study is to explore the factors that contribute to the endemicity of cholera in Nigeria. This will be accomplished by identifying potential treatment strategies and developing a method for remote access to early detection

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and management of the disease. Through this study, the government and donor agencies will be able to better plan for the future by identifying the disease's trends and patterns. Additionally, by concentrating their attention on the places and individuals who are most susceptible, the government, charitable organizations, and medical facilities may be able to better address the results of this study.

➢ *Epidemiology of Cholera*

An estimated 3 to 5 million cases of cholera and 28,000 to 150,000 deaths occur each year worldwide. Nonetheless, developing nations with high human poverty indexes located in tropical and subtropical regions are commonly infected[8]. Tropical and subtropical developing nations with high human poverty index are more likely to have the infection. In Africa, certain regions of Asia, the Middle East, and South and Central America, cholera is endemic[8]. There have been multiple cholera epidemics in Africa, each with a high case-fatality rate and a significant disease burden. Between 1970 and 2012, the WHO received reports of 3,316,201 (46%) suspected cases of cholera from African nations. Sub-Saharan Africa accounted for 86% of cholera deaths and 71% of all cases reported in 2012[9].

The World Health Organization (WHO) estimates that the officially recorded cases only make up 5–10% of the entire illness burden, even though 129,064 cases from 47 countries were documented in 2013, including 2102 deaths. It is possible to attribute the disparity between the estimated illness burden and the reported numbers to subpar laboratory and surveillance systems. There have also been implicated political motives, such as fear of trade and travel penalties[9].

According to reports, Nigeria is one of the three main global cholera hotspots at the moment[10]. Nigeria had its first documented cholera epidemics from 1970 to 1990. Subsequent outbreaks occurred again after that[11]. A 4.1% case fatality rate (CFR) was recorded in Nigeria in 2010 for a total of 41,787 cases from 18 northern states, resulting in 1716 deaths. This rate of CFR above both the WHO-acceptable limit of 1% and the average general rate of 2.4% observed in Africa between 2000 and 2005[12]. The 2010 outbreak was mostly linked to untreated cholera patients' diarrhoeal discharge during the rainy season contaminating water supplies. Consequently, this highlighted the susceptibility of rural communities in Nigeria[6].

The cholera pandemic in Nigeria is dynamic and seems to be endemic in Northern Nigeria, despite inconsistent reporting of the disease. According to the cholera report for Kano State, Northern Nigeria, between 2010 and 2019, the state experienced recurrent cholera outbreaks at the following frequencies and distributions: 1608, 778, 0, 1678, 7058, 1094, 226, 948, 2982, and 89 respectively[13].

➢ *Chronology of Cholera Epidemic in Nigeria*

The World Health Organization reports that Lagos, Nigeria, saw the first cholera cases ever, with 22,931 infections and 2,945 deaths. The pandemic subsequently claimed approximately 260 lives in four northern states in the late 1970s, primarily affecting the local government councils of Maiduguri, Jere, Gwoza, Biu, and Dikwa[14].

➢ *Seasonal Variation in Transmission*

Since cholera is a disease influenced by climate, research has indicated that changes in the environment or climate do affect the illness's ability to spread[15]. The seasonal distribution of the outbreak based on age and gender is not stable, according to epidemiological observations of multiple cholera epidemics in Nigeria[16].

There are two distinct seasons in Nigeria: the rainy and the dry seasons. As cholera is a seasonal infection, it is well known that the rainy season is linked to floods that raise the water level, a characteristic that promotes the growth and spread of bacteria and certain other vector species[17]. But climate change has the potential to raise air pollution levels, which would raise the infection rate[18,19].

➢ *Risk Factors*

Some risk factors, including poor food hygiene (e.g., street foods), tainted drinking water, and inadequate sanitation are linked to poverty and the likelihood of contracting cholera. There is a lower risk if you wash your hands with soap before, after, and after urinating[20]. Certain biological factors have been identified as risk factors for cholera, including female gender, blood group O, retinol deficiency, and hypochlorhydria (i.e., those taking proton pump inhibitors, antacids, and histamine receptor blockers, which increases the risk of cholera)[21].

Susceptibility is increased by malnutrition, particularly in young children. Due to their lower levels of acquired immunity than adults, children under the age of five have the highest incidence of cholera in endemic nations.[22] It is advised that women residing in endemic regions breastfeed their infants exclusively for the first six months of life because secretory immunoglobulin A (SIgA), which is released in breast milk, offers protection against severe cholera[23]. The risk of contracting *Vibro cholerae* is increased when the gut is simultaneously infected with pathogens such as parasites or enterotoxigenic *Escherichia coli* (ETEC)[24].

➢ *Clinical and Metabolic Manifestations*

The signs and symptoms of a cholera infection can range from mild to severe. In the initial stages of the infection, cholera patients' diarrhoea is typically painless and may contain feaces or bile. Only those suffering from cholera can have "rice water stools." They resemble uncooked rice or water used to wash rice because of their starchy color, fishy smell, and appearance[25].

The word "cholera gravis" refers to the condition in which an adult cholera patient can generate up to 1,000 mL of loose, watery feaces per hour, which can cause hypovolemia, shock, and death. In children with severe cholera, the excretion rate of feaces typically ranges from 10 to 20 milliliters per kilogram per hour[26]. Sodium, potassium, and bicarbonate are present in this feaces. When there is frequent watery diarrhoea, there are symptoms of dehydration (such as sunken eyes, tears, dry mouth, thirst, fast heartbeat,

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sluggishness, cold skin, skin elasticity loss, or crinkled hands and feet). One of the most noticeable symptoms of severe cholera is acidosis, or the loss of bicarbonate in the stool, and deep and rapid breathing caused by hyperventilation (Kussmaul breathing). Within two days to two weeks of infection, patients with symptoms of cholera can release germs in their feaces, while carriers show no symptoms for a short period (less than seven days)[27].

A significant amount of water can be quickly lost from the body through increased frequency of watery stools and vomiting, causing severe dehydration in 5 to 10% of patients. If treatment is not received, this can result in kidney failure, shock, sepsis, and even death in a matter of hours. Cholera frequently results in electrolyte imbalance, which can cause hypo- or hypernatremia, hypocalcemia, and hypokalemia[25]. Children also frequently get aspiration pneumonia and renal failure brought on by decreased urine production[28].

➢ *Diagnosis of Cholera*

Cholera should be suspected in the following situations, under the World Health Organization's (WHO) criterion for reporting cases[29,30].

- Any individual over the age of two who presents with acute watery diarrhoea (AWD; defined as three loose or watery, non-bloody stools in 24 hours), severe dehydration, or AWD-related death in locations where a cholera outbreak has not been proclaimed.
- Anyone who presents with or passes away from AWD after a cholera outbreak has been proclaimed.
- Volume-depleting diarrhea in children can be caused by several bacteria, while in adults, *Vibrio cholerae* is typically the cause.

In most situations, individuals with severe acute watery diarrhoea are diagnosed with cholera presumptively. But there aren't any telltale signs or symptoms that can definitively differentiate cholera from other infectious causes. Isolating *Vibro cholerae* from stool cultures conducted on particular selective media can confirm the diagnosis of cholera. Rapid diagnostics like stool dipsticks or darkfield microscopy can help confirm the diagnosis in situations where stool culture is not easily accessible[31].

➢ *Stool Culture*

The culture of the organism from a clinical sample—such as feces or rectal swabs—is the basis for a conclusive cholera diagnosis. Selective media, such as taurocholate tellurite gelatin agar or thiosulfate citrate bile sucrose agar, can be used to isolate *Vibro cholerae* from stool. *Vibro cholerae* can be identified biochemically once it has been grown, and specific antibody testing can be used to determine the serogroup and serotype[32].

➢ *Rapid Antigen Detection Test*

There are numerous commercially available fast antigen detection-based cholera diagnostic tests. The O1 or O139 antigen can be detected using the antibody-based immunochromatographic dipstick tests Crystal VC and Cholkit (which only detect the O1 antigen). These assays can be used on feces or rectal swabs[33].

➢ *Darkfield Microscopy*

Using darkfield microscopy at 400x magnification, rice-water stools may be examined for the presence of extremely motile *Vibro cholera*. These bacteria can be stopped from moving like shooting stars by adding certain antibodies later on. Although darkfield microscopy is quite specific for *Vibro cholerae*, it is not sensitive enough to be employed in everyday diagnosis[34].

Stool sample rapid diagnostic tests (RDTs) are cheap and can be conducted without special training in poor or rural healthcare settings when resources for culture medium/PCR and/or trained personnel are scarce[35]. Additionally, when a cholera outbreak is about to occur, RDTs can alert public health professionals in advance. There is a broad range of sensitivities and specificities among the various RDT types that are sold. Both *Vibro cholerae* O1 and O139 serogroups' lipopolysaccharide (LPS) antigens are readily detectable by monoclonal antibodies in Crystal VC (Span Diagnostics Ltd., Surat, India). 97% sensitivity and 76% specificity have been reported with Crystal VC[36].

II. MANAGEMENT OF CHOLERA

➢ *Fluid Therapy*

Prompt detection and prompt treatment of dehydration are essential for optimizing results. Oral rehydration solutions (ORS) are a simple way to treat the majority of mild to moderate cases of cholera. Low-osmolarity ORS, which is now advised by UNICEF and the WHO, is made with sodium, chloride, potassium, citrate, and anhydrous glucose and prepared in 1,000 mL of sterile water. This enhanced ORS recipe reduces stool production, lowers hypertonicity, and is safe[37].

ORS can also be made at home by combining 1,000 mL of sterile water with 1/2 teaspoon salt and 6 tablespoons of sugar. For infants older than six months, rice-based saline—that is, rice powder—is also utilized; however, its preparation is more challenging. To counterbalance the amount of stool loss, ORS is administered based on age groups following each purge of watery stool. Breastfeeding and hydration replacement are essential for infants up to two years old. To treat cholera, several nations have combined zinc and low-osmolarity oral rehydration solution (ORS)[38,39].

In patients vomiting more than three times in a single hour or cases where ORS is not helping, IV fluid treatment may be necessary. The foundation of rehydration therapy is the immediate restoration of fluid and electrolyte deficiencies to offset continuous losses. IV fluid is needed in severe instances of cholera[40]. Since Ringer's lactate solution contains more potassium and bicarbonate than normal saline (which has sodium chloride at 154 mmol/L and potassium bicarbonate at 154 mmol/L and pH of 4.5), the WHO recommends it over normal saline (which has sodium chloride at 154 mmol/L and potassium bicarbonate at 4

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mmol/L, Cl− at 109 mmol/L, HCO3− at 28 mmol/L, and Ca+ at 1.5 mmol/L)[21].

Extremely dehydrated patients require an immediate intravenous fluid infusion lasting three hours, with a bolus dosage of 100 mL/kg of body weight administered over the first thirty minutes. Patients one year of age and older require 70 mL/kg in the next two and a half hours after the initial 30 mL/kg. For children under one year old, rehydration takes place over six hour[41]. ORS is restarted for hydration once a patient can consume fluids. In all patients, if warning signals (hypovolemia, low radial pulse.) persist even after initiating an intravenous infusion as bolus therapy, the fluid infusion should be administered repeatedly. To prevent hypoglycemia, hyponatremia, and hypokalemia, malnourished children must be fed a high-energy diet after their fluid deficit is corrected[21].

➢ *Antibiotics Therapy*

Antibiotics are used to treat cholera infections to shorten the illness's duration and severity and prevent its spread to other people. To achieve synergistic efficacy, ORT and antibiotics are used to treat acute infections accompanied by severe dehydration. The three medications tetracycline, azithromycin, and doxycycline work well to treat cholera. When individuals receive numerous doses of 12.5 mg tetracycline over three days, their symptoms can be reduced from four to two days, and their average stool volume can decrease from 21L to 8L[42]. As effective as several doses of tetracycline, a single dose of doxycycline (300 mg for adults and 6 mg for children) is available. Conversely, individuals treated with tetracycline experienced a one-day reduction in diarrhoea length and a much larger reduction in stool volume, according to a study of significantly more trials involving indirect comparisons between tetracycline and doxycycline[43].Similarly, a single 20 mg dose of azithromycin can reduce the frequency of vomiting and terminate the symptoms of diarrhoea in less than 48 hours—24 hours quicker than with ciprofloxacin while also enabling the passing of an average of 36 stools with volumes of roughly 5L. Adults can use tetracycline, but pregnant women and small children should take azithromycin. Compared to erythromycin and ciprofloxacin, they are both more beneficial[44].

➢ *Vaccine*

Since oral cholera vaccines (OCVs) are effective when used in conjunction with other correlative treatments like antibiotics, ORT, and health management, the World Health Organization (WHO) recommends their use as a temporary protection during outbreaks or in endemic areas. This includes both live-attenuated and inactivated oral whole-cell (WC) vaccines[43]. The main mechanism via which OCVs induce mucosal protection against the virus is through antibodies, specifically IgA. Antigens including O1-specific polysaccharide and CT are targets of these antibodies. Though the circulation of IgA is limited (less than six months), memory B cells, which guard against cholera infection, endure and can proliferate rapidly, differentiating into plasmablasts and ultimately into plasma cells. These cells can then reseed protective antibodies when they are activated by antigen contact. In addition, OCVs may give unvaccinated persons herd immunity; however, more research is needed to determine how this would affect unvaccinated adults[44].

A popular vaccination against WC strains is called Dukoral (CTB-WC), which combines recombinant B subunits of CT (CTB) with inactivated/dead *Vibro cholerae* O1 (El Tor and classical biotypes). Due to its short half-life, high cost, and need for cold-chain circulation, Dukoral is not recommended for use by populations living in endemic areas. Its effectiveness ranges from 55% to 88%. Dukoral is effective for only six months between the ages of two and five, and it takes at least two doses to be effective. Nevertheless, in vaccinated individuals over the age of five, it can offer protection against infection for up to two years.[45,46]

In addition to the inactivated *Vibro cholerae* vaccines, the US Food and Drug Administration has licensed the single-dose oral live-attenuated vaccine Vaxchora (CVD 103-HgR), which comprises CTB from both the classical and El Tor biotypes and protects against the Inaba or Ogawa serotype. Vaxchora has a strong, quick cell-mediated immunity, which helps it fight cholera. Its effectiveness is predicted to be about 90% after vaccination and 80% three months later in travels to high-risk cholera locations[47].

To effectively prevent or control cholera outbreaks, epidemiological research is essential since different endemic locations require different vaccines to target the various circulating strains. In addition, optimal cholera vaccinations won't rely on cold-chain transportation. Novel methods of treating or preventing cholera infections are being developed in addition to the three already available treatments[44].

➢ *Probiotics*

The host microbiome's capacity to prevent or reduce illnesses is a newly recognized idea in microbiology. This is a relatively new idea for *Vibro cholerae*, and it's being investigated as a preventative or therapeutic measure against cholera infections. *Vibro cholerae* causes a significant change to the gut microbiota during infection as a result of the excessive fluid accumulation; as a result, most of the bacteria discovered in the distinctive rice-water stools are *Vibro cholerae*[48]. Additionally, the type VI secretion system of *Vibro cholerae* can modify host cells or transport effector toxins to the gut microbiome, both of which change the gut microbiota to promote colonization. These factors make probiotic therapy, which restores the gut microbiome or prevents colonization, a promising treatment for cholera infections.[44, 48, 49]

Probiotics are frequently used with antibiotics and a variety of other medications, such as adjuvants for inflammation, but the negative effects of the medications on the probiotics call for additional research. However, probiotics that lessen cholera may restrict the use of antibiotics, therefore limiting the number of strains of *Vibro cholerae* that are resistant to them[50].

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➢ *Micronutrients*

Children under five years old who take zinc supplements can also experience shorter bouts of diarrhoea and smaller stools. International research has demonstrated that adding zinc to ORS lessens the intensity of diarrhea, which in turn minimizes the need for antibiotics. Zinc blocks cAMP-induced chloride-dependent fluid secretion, hence inhibiting basolateral potassium channels. Along with increasing enzyme secretion, water and electrolyte absorption, and intestinal epithelium regeneration, zinc also strengthens the immune system[51]. To prevent diarrhoea in children between the ages of 6 months and 5 years, vitamin A supplementation is advised. Even when diarrhoea is present, a high-calorie diet can help lower hypokalemia, hypoglycemia, and malnutrition[21].

III. INTEGRATED CONTROL

➢ *Water and Sanitation Hygiene (WaSH)*

In the developing world, water, sanitation, and hygiene, or WaSH, are crucial for the prevention and management of cholera and other enteric illnesses[52]. The sickness cannot be stopped by treating the water at the source since contamination can happen at any point from collection to consumption. Contamination is another consequence of storing water. Prioritizing which WaSH components need to be implemented and taking multidisciplinary action is essential when an epidemic is announced to contain the disease. When combined with other behavioral modification techniques, such as handwashing, using soapy water, and chlorinating household drinking water, studies have demonstrated an increase in the preventive efficacy of oral cholera immunization[53,54].

High rates of cholera disease are seen in Bangladesh, Pakistan, Nepal, and India. These nations also have low levels of piped water in many locations, little access to potable water in rural areas, impoverished urban populations sharing latrines, open defecation in rural areas, and low handwashing compliance[55]. There have been published reports on the effectiveness of household water treatment in lowering the incidence of cholera; however, in high-risk families, the treatment is ineffective because of low education levels, financial restrictions, and behaviors that lead to low adoption of interventions[56]. Merely 12% of high-risk families in Nigeria, 19% in Nepal, and 24% in Haiti have disclosed their usage of water treatment techniques, such as filtration, boiling, UV purification, or the use of chlorine disinfectants[21].

A modest reduction in the number of cholera cases has been observed in community trials using low-cost WaSH interventions like solar power water purifiers, handwashing stations, soapy water dispensers, Aquatabs (hypochlorous acid) for water purification, and safe storage containers. Emergency WaSH measures are essential for lowering mortality during epidemics and averting more ones. These interventions may include low-cost WaSH techniques, health education, and media coverage[21].

IV. CONCLUSION

In several parts of the world, *Vibro cholerae* periodically cause cholera epidemics. In individuals with moderate to severe cholera, the disease can be fatal in a matter of hours, so prompt medical attention is needed. Progress to severe dehydration and mortality has been significantly decreased with the introduction of intravenous fluids, ORS, and Zn treatment. Supplemental aid in healing may come from probiotics, vitamins, and antibiotics. The most difficult aspects of treating *Vibro cholerae* are the complexities that come with living in endemic or unstable areas, such as unstable economies, unstable natural disasters, unstable political environments, weak national security, and inadequate infrastructure. These difficulties mean that treating cholera requires a multifaceted strategy that can adapt to the unique requirements of a given outbreak. Because ORT is affordable, user-friendly, and consistently reduces the severity of infection, it has been and will remain the first line of defense for patients who have already contracted *Vibro cholerae.*

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