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# Vibrio cholerae: Understanding a persistent pathogen in Sub-Saharan Africa and the East Mediterranean Region

Beenzu Siamalube<sup>1</sup> and Emmanuel Ehinmitan<sup>1</sup>

Department of Molecular Biology and Biotechnology, Pan African University Institute for Basic Sciences, Technology and Innovation, P.O. Box 62000-00200, Nairobi, Kenya

\*Corresponding author. Department of Molecular Biology and Biotechnology, Pan African University Institute for Basic Sciences, Technology and Innovation, Nairobi, P.O. Box 62000-00200, Kenya. E-mail: [siamalube.beenzu@students.jkuat.ac.ke](mailto:siamalube.beenzu@students.jkuat.ac.ke)

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## Abstract

*Vibrio cholerae* remains a significant public health threat in Sub-Saharan Africa and the East Mediterranean Region, where recurrent outbreaks are driven by inadequate water, sanitation, and hygiene infrastructure, climatic variability, and socio-political instability. This review explores the persistence of the pathogen in these regions, examining its epidemiology, environmental reservoirs, and genomic adaptations that enhance its survival and transmission. We highlight the impact of antimicrobial resistance and the role of climate change in cholera dynamics. Furthermore, we discuss current prevention and control strategies, including advancements in oral cholera vaccines, genomic surveillance, and microbiome-targeted interventions. Addressing these challenges requires a multi-faceted approach that integrates sustainable sanitation improvements, strengthened disease surveillance, and innovative vaccination strategies. Understanding the persistence of *V. cholerae* in these high-risk regions is critical for developing effective, long-term mitigation strategies to reduce cholera morbidity and mortality.

**Keywords:** Sub-Saharan Africa; East Mediterranean; antimicrobial resistance; climate change; oral cholera vaccines; public health intervention

## Introduction

*Vibrio cholerae* is a Gram-negative bacterium that causes cholera. The infectious disease is characterized by severe vomiting and severe diarrhoea (Siamalube et al. 2025), with significant public health implications, particularly in Sub-Saharan Africa (SSA) (Dor-sainvil 2021) and the East Mediterranean Region (EMR) (Buliva et al. 2023). These regions experience recurrent outbreaks driven by inadequate water, sanitation, and hygiene (WASH) infrastructure (Bose et al. 2024), climate variability (Asadgol et al. 2020), and socio-political instability (Merrill et al. 2021). Despite advances in public health, cholera remains endemic, with environmental reservoirs and antimicrobial resistance (AMR) complicating control efforts (Chettri et al. 2024). *Vibrio cholerae* is both a foodborne and a waterborne pathogen (Subedi et al. 2024). It can navigate through the aquatic surroundings due to its single polar flagellum, contributing to its persistence in cholera-prone zones (Kokashvili et al. 2013). Additionally, it is a rod-shaped and curved facultative anaerobe bacterium that thrives in salt or brackish water and for endemic regions it can also survive in freshwater ecosystems, where it attaches itself to shellfish containing chitin (Montero et al. 2023).

There are over 200 serogroups of *V. cholerae*; the O139 and the O1 have been associated with causing most cholera pandemics (Pal et al. 2010). However, recent studies (Jia et al. 2025) have shown that non-O139/non-O1 strains are also emerging (Ceccarelli et al. 2015). Their transmission is often associated with seafood consumption (Hill et al. 2011) and lacks the cholera toxin (CT) but still causes significant gastroenteritis outbreaks (Marin et al. 2013).

The O1 serogroup is comprised of two biotypes, namely El Tor (Mukhopadhyay et al. 2014) and Classical, the former being linked to the ongoing seventh cholera pandemic (Mwaba et al. 2021). The production of the CT is the hallmark of cholera infection, it fuels the 'rice-water stools' and the life-threatening profuse watery diarrhoea (Keely and Barrett 2022). CT is an enterotoxin AB<sub>5</sub> multimeric protein complex (Patry et al. 2019), the adenylate cyclase is activated by the A subunit in the intestinal cells of the host, this results in a mass production of cyclic AMP (Khannpnavar et al. 2020, Sarker et al. 2023). Leading to the secretion of chloride ions into the intestinal lumen, subsequently stimulating massive water loss that causes rapid dehydration (Elsasser and Faulkenberg 2024).

Furthermore, *V. cholerae* possesses adherence factors that facilitate its survival and colonization within the intestines of the host (Djaouda et al. 2020). It activates adenylate cyclase, leading to excessive chloride secretion and water loss, resulting in severe dehydration. Another essential component is the toxin-coregulated pilus (Raskin et al. 2020), it is useful in the formation of biofilm and the attachment of the bacterium to the epithelial lining (Nielsen et al. 2010). *Vibrio cholerae* employs biofilm formation, phase variation, and antigenic switching to evade host immunity, ensuring persistence and transmission (Samanta 2023). A balanced gut microbiome can provide resistance against *V. cholerae* colonization (Merrell et al. 2002). Beneficial microbes such as *Lactobacillus* (Rollins-Smith et al. 2020) and *Bifidobacterium* contribute to gut homeostasis and immune defence (J. Worley 2023). Similarly, other virulence driving factors like neuraminidase and

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hemagglutinin protease, spearhead the bacteria's evasion of the immune responses, ultimately boosting pathogenicity (Mavhungu et al. 2023). This review explores the persistence of *V. cholerae* in these regions, highlighting its epidemiology, genomic adaptations, and intervention strategies, emphasizing the role of vaccines, WASH improvements, and genomic surveillance.

## Timeline of cholera pandemics

There have been seven cholera pandemics in recorded world history (Table 1), each caused by different strains of *V. cholerae*, predominantly the O1 serogroup. The seventh pandemic continues today, with endemic cholera in parts of Sub-Saharan Africa, South Asia, and the Middle East (Mutreja et al. 2011).

## Epidemiology and disease burden

### Global and regional cholera trends

Although significant improvements have been made in public health and preventive medicine, cholera is still a major threat to the health of humans globally (Dorsainvil 2021), with annual case estimates ranging between 1.3 and 4 million and deaths reaching up to 143 000 (Troeger et al. 2018). However, the actual numbers may be higher due to limited surveillance systems and some cases not being recorded. SSA and EMR account for a notable proportion of cases due to persistent vulnerabilities (Ali et al. 2012). Cholera outbreaks are particularly common in Nigeria (Eneh et al. 2024), the Democratic Republic of the Congo (DRC) (Ingelbeen et al. 2019), Malawi (Miggo et al. 2023), Lebanon (Melhem and Hamdan 2025), Yemen (Nasr et al. 2024), and Afghanistan, where conflict and natural disasters exacerbate disease spread. Haiti in the regions of the Americas equally experiences significant cholera outbreaks (Pun 2011).

Since 1 January 2025 and as of 17 March 2025, the global cholera caseload has reached 76 919, with 969 reported deaths. New cases have emerged in 20 countries, including Pakistan, Ghana, and South Sudan (Izzoddeen et al. 2025), which tops the list with 19 122 cases. Other countries with significant caseloads include Afghanistan (14 403), Yemen (9 784), Democratic Republic of the Congo (8 056), and Angola (7 119) (Fig. 1). In terms of fatalities, South Sudan again leads with 262 reported deaths, followed by Angola (258), Democratic Republic of the Congo (171), Sudan (141), and Nigeria (28) (European Centre for Disease Prevention and Control 2025).

### Sub-Saharan Africa

In SSA, recurrent outbreaks occur in hotspot countries such as Zambia (Thelma et al. 2024), Sudan (Mohammed et al. 2024), Ethiopia (Endris et al. 2022), and Mozambique (Ansaruzzaman et al. 2004). These regions experience seasonal variations, with outbreaks intensifying during rainy seasons due to flooding and water contamination (Perez-Saez et al. 2022). While both regions share common challenges in combating cholera, there are distinct regional-specific obstacles that make controlling outbreaks particularly difficult. In SSA for instance, the vast geographic diversity presents localized barriers to cholera response efforts (Jackson 2013). Remote rural areas often lack access to adequate healthcare facilities and infrastructure, delaying diagnosis and treatment during outbreaks (Baddianaah et al. 2024). In contrast, urban centres face challenges such as overcrowded informal settlements, where poor drainage systems, inadequate waste manage-

ment, and contaminated water supplies create fertile conditions for the rapid spread of cholera (Mutale et al. 2020).

Economic instability further exacerbates these challenges, limiting governments' capacity to invest in sustainable public health infrastructure (Hsiao et al. 2022). Prolonged conflicts and insecurity in many SSA nations, such as in the DRC and Sudan (Abdel-Latif and El-Gamal 2024), lead to mass displacement of populations, forcing people into refugee camps or informal settlements where water and sanitation conditions are often dire (Casati et al. 2024). Natural disasters, such as the cyclones, cause widespread destruction of water systems, compounding the risk of cholera transmission by forcing communities to rely on unsafe water sources (Focus Adriano et al. 2023). In rural areas, the lack of standardized WASH services hinders preventive efforts. Many communities rely on untreated water from rivers, ponds, or wells, increasing exposure to *V. cholerae*. Together, these factors highlight the multifaceted and region-specific challenges that SSA must address to mitigate cholera outbreaks effectively (Ngoma et al. 2024).

### East Mediterranean Region

In the EMR, Yemen faces one of the largest cholera epidemics in history, largely due to the ongoing war and water scarcity (Al-Gheethi et al. 2018). Similarly, Pakistan and Lebanon experience outbreaks aggravated by climatic events and inadequate sanitation. The region faces unique challenges in controlling cholera outbreaks, largely driven by political instability and restricted access to conflict zones (Lopez et al. 2020). Prolonged conflicts, such as those in Syria and Afghanistan, have unstable healthcare and sanitation infrastructure, leaving large portions of the population without access to clean water or adequate healthcare (Ahmed et al. 2018). This disruption often leads to the collapse of public health systems, making it difficult to detect, respond to, and contain cholera outbreaks in a timely manner. The inaccessibility of conflict-affected areas further hinders humanitarian efforts, delaying the delivery of critical resources such as oral rehydration therapy, vaccines, and water purification supplies (Deen et al. 2008).

One of the primary causes of cholera outbreaks in these countries is the scarcity of clean water, exacerbated by the impacts of climate change and mismanagement of natural resources (Kruger et al. 2022). Droughts, irregular rainfall, and water shortages strain already fragile water systems, forcing communities to rely on contaminated water sources. Poor resource management compounds this issue, with limited investments in sustainable water infrastructure and overexploitation of available resources (Melhem and Hamdan 2025). Additionally, conflict-induced displacement leads to overcrowded conditions in refugee camps and informal settlements, where sanitation facilities are often inadequate (Diseases 2017). Open defecation and poor waste management further contaminate water supplies, creating a vicious cycle of cholera transmission (Shackleton et al. 2024). Addressing cholera in the EMR requires overcoming these deeply rooted structural and political challenges, alongside implementing sustainable water and sanitation solutions.

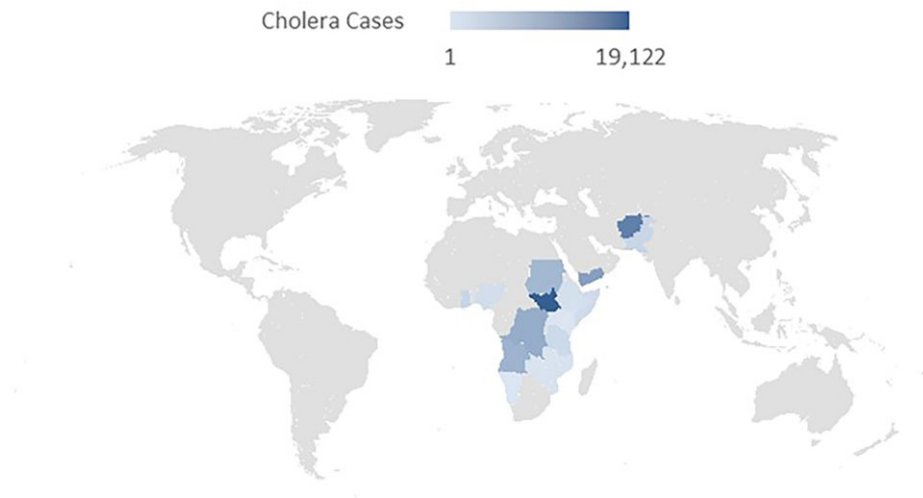
## Environmental and climatic factors influencing cholera persistence

### Aquatic reservoirs and faecal transmission of *V. cholerae*

*Vibrio cholerae* leads a two-way mode of life; it can flourish within human hosts as well as in water bodies (Feng et al. 2023). The

**Table 1.** Timeline of cholera pandemics in world history.

| Pandemic                    | Period       | Origin                     | Spread   | Key events and responses   | References                             |
|-----------------------------|--------------|----------------------------|--|--|--|
| <b>1st cholera pandemic</b> | 1817–1824    | Bengal, British India      | Southeast Asia, Middle East, Eastern Africa, Mediterranean | Spread via British trade routes; first global cholera pandemic. Declined in the 1820s but persisted in endemic regions   | Meltzer and Schwartz (2007)            |
| <b>2nd cholera pandemic</b> | 1829–1837    | India                      | Russia, Europe, North America, Latin America               | Reached London and Paris (1832); outbreaks in the U.S. and Canada. Quarantine efforts were ineffective   | Devault et al. (2014)                  |
| <b>3rd cholera pandemic</b> | 1846–1860    | India                      | Asia, Europe, North America, Africa, Latin America         | Dr. John Snow identified contaminated water as the mode of transmission (1854 London outbreak), laying the foundation for modern epidemiology  | Azizi and Azizi (2010)                 |
| <b>4th cholera pandemic</b> | 1863–1875    | Ganges Delta, India        | Middle East, Europe, Africa, North America                 | Major outbreak in Mecca among Hajj pilgrims. Improved sanitation efforts were introduced in some regions   | Huber (2020)                           |
| <b>5th cholera pandemic</b> | 1881–1896    | India                      | Europe, Africa, Americas                                   | Robert Koch isolated <i>V. cholerae</i> in 1883, proving the bacterial cause of cholera. Urban sanitation improvements in Western Europe helped mitigate its impact                          | Ramamurthy and Ghosh (2021)            |
| <b>6th cholera pandemic</b> | 1899–1923    | India                      | Russia, Ottoman Empire, Asia, Middle East                  | Largely avoided Western Europe due to better sanitation. Major outbreaks in the Philippines, Indonesia, and the Middle East. Quarantine and water sanitation improvements were introduced    | Healing (2024)                         |
| <b>7th cholera pandemic</b> | 1961–present | Indonesia (El Tor biotype) | Asia, Africa, Latin America, Middle East                   | Spread to Africa in the 1970s and Latin America in the 1990s. Ongoing outbreaks in Sub-Saharan Africa, South Asia, and the Middle East. WHO launched a global roadmap to end cholera by 2030 | Lam et al. (2010), Weill et al. (2017) |



**Figure 1.** Africa and Asia cholera cases: 1 January 2025 to 20 January 2025 (European Centre for Disease Prevention and Control 2025).

bacterium forms biofilms on plankton surfaces while in water, this increases its persistence in the environment (Martinelli Filho et al. 2020). Besides, environmental features including nutrient availability, temperature, and salinity can influence the proliferation of *V. cholerae* in aquatic sources (Islam et al. 2020). The bacterium enters a viable but non-culturable (VBNC) state under environmental stress, reviving under favourable conditions (Islam et al. 1995). Quorum sensing regulates biofilm dispersal and facilitates bacterial persistence (Wu et al. 2020). Recent genomic data highlight that the seventh pandemic lineage possesses unique defence systems, including clustered regularly interspaced short palindromic repeats—CRISPR-associated protein (CRISPR-Cas) and toxin-antitoxin modules, aiding rapid adaptation and persistence in diverse environments (Robins and Mekalanos 2014).

Cholera is primarily transmitted via the faecal–oral route, with *V. cholerae* spreading through contaminated food and water, especially in overcrowded living conditions and places with limited sanitation (Levine et al. 1988). CT plays a critical role in disease severity and bacterial shedding. A study was conducted at the University of Maryland in the United States of America and the results demonstrated that CT-deficient strains resulted in significantly lower bacterial excretion compared to wild-type strains, reinforcing the role of CT in enhancing transmission (Levine et al. 1988). Rivera-Chavez and Mekalanos (Rivera-Chávez and Mekalanos 2019) further illustrated how CT remodels gut metabolism, facilitating *V. cholerae* colonization and increasing shedding, which directly impacts cholera outbreak dynamics (Merrell et al. 2002).

### Climate change and cholera expansion

Climate change has facilitated the spread of *V. cholerae* to previously unaffected regions (Vezzulli et al. 2020). In recent years, cases have been reported in temperate zones such as the Baltic Sea, the United States of America Gulf Coast (Ceccarelli et al. 2015), and parts of Europe where cholera was historically absent. Rising sea surface temperatures and altered ocean currents are suspected to play a role in transporting *V. cholerae* to new environments (Pretzer et al. 2017).

Climate-induced flooding events have a direct impact on cholera transmission by overwhelming sanitation systems, con-

taminating drinking water sources, and facilitating the spread of *V. cholerae* (Lebu et al. 2024). Heavy rainfall and monsoons, common in cholera-endemic areas such as South Asia and Sub-Saharan Africa, flush the bacteria into rivers and groundwater, increasing the risk of large-scale outbreaks. In areas with poor drainage and inadequate WASH infrastructure, floodwaters mix with human waste, creating ideal conditions for faecal–oral transmission of cholera (Bockemühl et al. 1986).

Paradoxically, prolonged droughts also contribute to cholera outbreaks. In arid regions, water scarcity forces populations to rely on unsafe water sources, increasing exposure to *V. cholerae*-contaminated supplies (Ehinmitan et al. 2024). Additionally, stagnant water bodies formed due to drought-related changes in hydrology can serve as long-term reservoirs for the pathogen. Studies have shown that *V. cholerae* can persist in such environments in a VBNC state, reactivating when conditions become favourable (Wu et al. 2020).

### Role of WASH infrastructure in disease control

**Water Supply:** Access to safe and clean drinking water is essential for preventing cholera (Sikder et al. 2023). **Sanitation:** Proper waste management and sanitation facilities prevent the contamination of water sources (Libanda et al. 2024). **Hygiene:** Promoting hand-washing with soap and water, especially after using the toilet and before handling food (Adugna 2023). Proper WASH infrastructure reduces the transmission of cholera by preventing the contamination of water sources and reduces morbidity and mortality rates (Kim et al. 2024). Standard WASH infrastructure also helps communities prepare for and respond to cholera outbreaks, enhancing their resilience (Tseklevs et al. 2022).

Many communities in SSA (Parkman et al. 2008) and EMR lack access to safe WASH facilities. Or existing WASH infrastructure is often inadequate, poorly maintained, or non-functional. Additionally, conflict and displacement can lead to the destruction of WASH infrastructure, exacerbating cholera outbreaks (Diseases 2017). Nonetheless, governments and donors could invest in the development and maintenance of WASH infrastructure and empower communities to take ownership of their sanitation and hygiene practices. The coordination between WASH sector stakeholders could be strengthened to ensure a unified response to cholera outbreaks (Ladan et al. 2023).

## Genomic insights into *Vibrio cholerae* evolution and virulence

Recent genomic studies reveal distinct genetic signatures differentiating pandemic *V. cholerae* strains from environmental isolates (Mulikutla et al. 2024). These include virulence-enhancing genes and AMR determinants. The spread of AMR genes through mobile genetic elements complicates treatment options (Roque-Borda et al. 2024). Whole-genome sequencing (Jiang et al. 2021) has provided insights into *V. cholerae*'s evolving resistance patterns, informing targeted intervention strategies (Sharif et al. 2025). Furthermore, horizontal gene transfer facilitates the acquisition of virulence factors, enabling *V. cholerae* to rapidly adapt to new environments and hosts (Childers and Klose 2007).

## Cholera prevention and control strategies

### Oral cholera vaccines (OCVs)

The World Health Organization (WHO) has prequalified three whole-cell killed OCVs, namely: Euvichol (Matias et al. 2024), Shanchol (Ilboudo et al. 2021), and Dukoral (Dash et al. 2024). During mass vaccination campaigns in endemic regions, Shanchol is widely used to control humanitarian emergencies (Ng'ombe et al. 2022). The vaccine provides up to 3 years protection, although people living in high-risk areas may require booster doses (Song et al. 2021). Advances in genomic epidemiology have provided valuable insights into vaccine efficacy by tracking genetic shifts in circulating strains, enabling the design of improved vaccine formulations (Thompson and Duintjer Tebbens 2016). However, logistical constraints hinder large-scale vaccination efforts in endemic regions (Figueroa et al. 2024). Thus, plant-based edible vaccines are emerging as an innovative, cost-effective strategy for mass immunization campaigns (Siamalube et al. 2024). SSA and EMR may explore this biotechnology to develop region-specific green factory vaccines derived from local plant varieties (Tripurani et al. 2003).

### Probiotics and microbiome-based therapies

Dysbiosis, or microbiome imbalance, can increase disease severity by weakening gut barrier functions. Emerging research suggests microbiome-targeted therapies, such as probiotics and antimicrobial peptides (AMPs), as promising interventions for reducing cholera severity and enhancing vaccine responses (Macbeth et al. 2021).

Additionally, bacteriocins have been highlighted as alternative therapeutic strategies against *V. cholerae* (Huang et al. 2021). AMPs such as LL-37 and bacteriocins like nisin have demonstrated efficacy in inhibiting *V. cholerae* growth. Their mechanisms involve disrupting bacterial membranes and modulating immune responses (Bhattacharjya et al. 2024). Furthermore, the probiotic *Bacillus subtilis* has shown potential in reducing *V. cholerae* colonization in the gut, offering new avenues for probiotic-based interventions (Maftei et al. 2024).

### Climate-resilient and innovative sanitation technologies

Erecting flood-resilient designs such as raised water points, floating latrines, and improved drainage systems could prevent contamination during extreme weather events (Lebu et al. 2024). Alongside solar energy powers water treatment systems like solar desalination (Arunkumar et al. 2024) and UV purification in remote or resource-limited areas without external electricity (Unnarkat et al. 2022), as well as mobile systems for rapid water purifi-

cation, especially during emergencies, bypassing centralized facilities (Goodrich and Hall 2024).

In addition, container-based sanitation (Russel et al. 2019), like portable waste collection systems could be ideal for densely populated urban areas lacking traditional sewer infrastructure (Ouatara et al. 2023). Also, ecological sanitation, i.e. toilets converting waste into compost, providing sustainable waste management and resources for agriculture. Similarly, sanitation options for water-scarce areas, would reduce contamination risks and ensure proper waste management (Werkneh and Gebru 2023).

### Digital tools and community-driven approaches

Remote sensing and geographic information system involving mapping satellite imagery to track water quality and identify high-risk areas, especially in remote locations (Bari et al. 2023). And digital platforms for real-time reporting such as mobile applications and dashboards for communities to report sanitation issues (Gupta et al. 2023), would improve response times and accountability (Biswas et al. 2021). Also, predictive analytics forecasting can be initiated on WASH-related outbreaks by analysing climate (George et al. 2019), demographic, and health data to enable proactive interventions (Marcus 2022).

Consequently, incorporating community-driven WASH initiatives and health campaigns would educate the people on hand-washing, safe water storage, and hygiene tailored to cultural contexts for sustainable behavioural changes (Kim et al. 2024). Training men, women and youth in water resource management could boost community engagement and advocacy for WASH improvements (Tseklevs et al. 2022). Further, prioritizing health interventions for children by empowering research to align with the global roadmap to end cholera by 2030, could sensitize the community further on disease prevention and control (Ko et al. 2022).

### Prospects and research considerations

The fight against cholera is far from over. Increasing urbanization in vulnerable settlements and changes in climatic conditions may exacerbate the outbreaks of cholera (Asadgol et al. 2020) by heightening population density and modifying environmental reservoirs, respectively (Bastin et al. 2024). Likewise, the progression of *V. cholerae* strains that are resistant to antibiotics poses a substantial hazard to effective treatment, requiring ongoing research to delve more into strain-specific vaccine production studies. There has equally been a keen exploration in new strategies to reduce the burden that cholera poses on public health (Debes et al. 2021, Baltazar et al. 2022, Bwire et al. 2023, Hussen et al. 2024, Mbewe et al. 2024). These include the development of plant-based edible cholera vaccines (Yuki et al. 2021) that promise to render longer-lasting immunity and more affordable vaccines (Beenzu et al. 2024). Improved diagnostic tools for prompt detection and novel interventions addressing the environmental persistence of *V. cholerae* are additional mitigation measures (Specht et al. 2024).

### Conclusion

Cholera remains a persistent public health challenge in SSA and the EMR. A comprehensive approach integrating genomic surveillance, improved WASH infrastructure, vaccine innovations, and microbiome-based therapies is essential for long-term cholera control. Strengthening regional collaboration and sustained public health investments will be critical in achieving global cholera elimination goals.

## Author contributions

Beenzu Siamalube (Conceptualization, Formal analysis, Writing—original draft, Writing—review & editing) and Emmanuel Ehinmitan (Software, Validation, Writing—review & editing).

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