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Evaluating cholera vaccine effectiveness in Harare Western District amidst a new outbreak, 2023

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ABSTRACT

Following targeted oral cholera vaccination (OCV) in 2018/2019, cholera cases declined. However, by July 17, 2023, Harare Western District reported 98 cases and 3 deaths. We investigated the outbreak to assess the long-term effectiveness of OCV in Harare Western District. We conducted a 1:2 unmatched case-control study among 46 cases and 92 controls. A case was any resident of Harare Western District with laboratory-confirmed cholera infection between April 22, - July 20, 2023. Antimicrobial susceptibility data were analyzed and multivariable logistic regression identified independent factors. Vaccine effectiveness was calculated as (1-OR) x 100). OCV effectiveness was 72% (95% CI 39–87; p<0.001). The majority of participants were females (52.2%) cases and 51.1% controls. Experiencing a sewage burst [aOR 9.75, 95% CI (2.60 to 36.62)] was an independent risk factor. Handwashing with soap [aOR 0.03,95% CI (0.01 to 0.17)], cholera vaccination [aOR 0.17, 95% CI (0.04 to 0.64)], and having a handwashing facility [aOR 0.04, 95% CI (0.01 to 0.18)] were independent protective factors. A total of 47.2% of boreholes (42/89) and 66.7% of wells (2/3) had excessive coliforms. Cholera strains were largely sensitive to ciprofloxacillin (90%). The outbreak was driven by water, sanitation and hygiene factors. This study provides evidence on long-term effectiveness of two-doses of OCV in an endemic urban setting. Vaccination status relied on participant recall and vaccination cards due to the absence of a central register, and while the study was sufficiently powered to assess the effectiveness of the two-dose regimen, the number of cases limited evaluation of single-dose effectiveness. Implementation of targeted OCV campaigns is recommended.

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1. INTRODUCTION

Cholera remains a major global health threat, causing an estimated 2.9 million cases and 95,000 deaths annually, with many cases unreported [1]. Sub-Saharan Africa contributed nearly a quarter of reported cases between 2010 and 2019 [2]. To address this burden, the Global Task Force on Cholera Control (GTFCC) launched the Ending Cholera—A Global Roadmap to 2030, which promotes early detection, hotspot-targeted interventions, oral cholera vaccines (OCVs), and WASH improvements [3]. Zimbabwe has experienced recurrent epidemics since 1972, including major outbreaks in 2008 and 2018 [4]. During the 2018–2019 cholera epidemic, a mass OCV (Euvichol Plus vaccine) campaign was conducted in Harare, Epworth, and Chitungwiza reaching 1.3 million people with 86% coverage, contributing to a significant reduction in cases [5], [6].

On 22 April 2023, a confirmed cholera case was reported in Harare, and by July 17, 2023, 115 cases had been recorded, with Glenview and Budiriro identified as epicenters. This resurgence, occurring four years after a mass OCV campaign, highlights uncertainties regarding the long-term effectiveness of OCVs in urban African settings. Although World Health Organization (WHO) reports that two OCV doses provide at least three years of protection with an efficacy of over 60% [7], Bi *et al.* [8] found sustained effectiveness among adults who received the vaccine over five years of follow-up but low efficacy in children under five, while Ngombe *et al.* [9] highlighted waning immunity, poor coverage, and limited data on booster timing. The city's ongoing cholera risk is exacerbated by socio-economic and infrastructural factors, including intermittent water supply, reliance on unsafe water sources (boreholes and shallow wells), sewage contamination, water and sanitation infrastructure breakdown, rural–urban migration, growing vulnerability of the urban poor, and inadequate waste management [10]-[14]. Moreover, Zimbabwe has limited experience using OCVs in outbreak response, as was also the case in Haiti [15], and the role of vaccination in controlling urban cholera outbreaks remains poorly understood.

This study assessed the long-term effectiveness of OCV by analyzing the 2023 cholera outbreak in Harare in relation to the 2018–2019 vaccination campaign, focusing on immunity among previously vaccinated individuals. It also incorporated environmental surveillance to identify potential sources of *Vibrio cholerae* transmission and characterize antibiotic susceptibility patterns. The findings provide evidence on the duration of protection and performance of two OCV doses in a high-risk urban African setting. By linking vaccine effectiveness with environmental and epidemiological factors, this research informs national cholera preparedness, optimal timing of booster campaigns, and supports the integration of OCVs into the broader GTFCC strategy for sustainable cholera control.

2. METHOD

2.1. Study design

A 1:2 unmatched case-control study was conducted in Harare Western District, where cases were defined as residents of Harare Western District who were diagnosed with a confirmed cholera infection between the dates of April 22nd, 2023, and July 20, 2023. A confirmed cholera case was based on a culture-positive test that detects the presence of *Vibrio cholerae* in the patient's stool sample. Controls were defined as residents in the Harare Western District who were at risk of contracting cholera but did not develop the disease during the period from April 22, 2023, to July 20, 2023, and were not individually matched by age or sex. A case-control design was used to efficiently assess vaccination effectiveness and other risk and protective factors at the same time among individuals affected by the cholera outbreak.

2.2. Study setting

This study was carried out in Harare Western District, which includes the suburbs of Glenview and Budiriro. These are high-density suburbs in Harare urban, and 60% of the residents are in the informal economic sector, which includes vending and small-scale business [16]. The majority of cholera outbreaks in 2008 occurred in the high-density Zimbabwean suburb of Budiriro, which accounted for 50% of all cases reported. During the same outbreak, Glenview also recorded high cases of cholera, and it shares boundaries with Budiriro to the North, Glen Norah to the East. In the current cholera outbreak, both Glenview and Budiriro have the highest confirmed cases of cholera, with populations of a total of 303,579 when combined.

2.3. Study population

Our study population included case patients and controls in Harare Western District, who were at risk of cholera between April 22 and 20 July, 2023, regardless of vaccination status. Environmental Health Officers, Environmental Health Technicians and Nurses in charge at the cholera treatment centre for the district were key informants. Information was also retrieved from cholera line lists, reports, and laboratory results charts.

2.4. Sample size and sampling procedure

Sample size was calculated using the Fleiss method (unmatched case–control) in Epi Info 7.2.5 (StatCalc). We specified: two-sided $\alpha = 0.05$, power $(1-\beta) = 0.80$, case: control ratio = 1:2, and an expected vaccine effectiveness (VE) of 69% from Wierzba *et al.* [17], corresponding to an assumed odds ratio (OR) for OCV exposure of 0.31 (OR = 1 − VE). Using an assumed prevalence of OCV exposure among controls (p_0) = 40.5%, the required sample is 46 cases and 92 controls (total n = 138). Because p_0 was uncertain, we performed sensitivity analyses across plausible control exposure prevalences. Cases were chosen from the line list for Harare Western District using simple random sampling, where each case had a unique case number. The cases were randomly selected until the desired sample size was achieved. Controls were selected from Harare Western District by sampling two households next to those of cases. Key informants were purposively sampled.

2.5. Data collection and analysis

We used interviewer-administered questionnaires among cases and controls during the cholera outbreak to collect information on factors associated with contracting cholera. The primary outcome of the study was contracting cholera. The source of drinking water, water treatment, type of container for water storage, proximity to sewage bursts, type of toilet, garbage collection, vaccination status, handwashing and use of soap, eating food sold on the road, education, employment status, age, sex, marital status, and number of people in a household and contact with case were exposure variables. Age, sex, and occupation were predictor variables, sources of drinking water, type of toilet, and hand washing practices were potential confounders, and a potential effect modifier was the number of doses of the vaccine.

Interviews for key informants were conducted using a key informant interview guide to assess the presence of environmental surveillance (water and sewage sampling). Given the absence of a centralized vaccination register, vaccination status was determined by a combination of participant recall, official cholera line lists, and personal vaccination cards. This strategy employed data triangulation to minimize the risk of information bias and potential misclassification of exposure status resulting from reliance on self-report or incomplete documentation. For antibiotic susceptibility patterns, laboratory results on antibiotic sensitivity tests for cholera confirmed cases were used. For water surveillance data, WHO Guidelines for drinking-water quality (fourth edition published in 2011 and complemented by the first addendum in 2017) were used to interpret the total coliform counts (*E. coli* or thermotolerant coliform bacteria must not be detectable in any 100 ml sample) [18].

Data entry and all statistical analyses were performed in Epi Info™ version 7.2.5. The data analysis was done through descriptive statistics using univariate analysis to characterize the cholera outbreak by person, place, and time. Chi-square/Fisher's exact was used to evaluate the equality of cases and controls and to test for independence between categorical variables. Limit grouping was used for quantitative variables. Microsoft Excel™ was used to generate an epidemic curve. ArcGIS software was used to generate a spot map of the outbreak. Bivariate analysis on risk factors contributing to the cholera outbreak was conducted, and variables with $p<0.05$ were considered to be significant. Backward stepwise multivariate logistic regression analysis was performed on variables that were significant at $p\leq0.25$. Vaccine effectiveness was assessed by comparing cholera cases between vaccinated and unvaccinated groups using odds ratio (1-OR × 100), 95% confidence intervals (CI) derived from the OR 95% CIs using VE lower = (1-odds ratio upper CI) × 100% and VE upper = (1−odds ratio lower CI) × 100%. A thematic analysis of key informants' responses on environmental surveillance of cholera was done.

3. RESULTS AND DISCUSSION

3.1. Result

A total of 46 cases and 92 controls were examined for eligibility, included in the study, and the results were analyzed. Figure 1 presents a flowchart illustrating the selection process of cases and controls.

3.1.1. Outbreak description by person

The majority of study respondents were females, 24 (52.2%) cases and 47 (51.1%) controls (p = 0.904). The majority of the cases were in the 10-20 years age group, with a total of 15 (32.6) cases and 26 (29.2) controls (p = 0.608). The median age for cases was 26 years (Q1 = 17, Q3 = 34), whilst the median age of controls was 28 years (Q1 = 19, Q3 = 34). On occupation, 43.5% of the cases were not employed whilst on controls, 43.5% were self-employed (p = .0.000). More than half (52.2%) of the cases had a number of people in their household of more than 10 (p = 0.051) and 54.4% of controls had a number of people in their household between 5 and 10. Sixty-three percent (63.0%) of the cases were single, whilst 78.3% of the controls were married (p = 0.000).

3.1.2. Vaccination status

Most confirmed cases and suspected cases were from patients who were not vaccinated (92% of 98 confirmed cases and 98% of 1243 suspected cases, respectively). This led to the hypothesis that vaccination status was a protective factor against contracting cholera since fewer people with a history of vaccination were affected by the cholera outbreak, regardless of whether it was one dose vaccination or two doses.

3.1.3. Outbreak description by place

The spot map of the outbreak revealed two main epicenters, Budiriro and Glenview. These areas stand out with clusters of cases concentrated in these regions. Specifically, Budiriro 1, located near the

Budiriro Polyclinic, and Glenview 3, which is also in close proximity to Budiriro 1, were identified as the most heavily affected areas as shown in Figure 2.

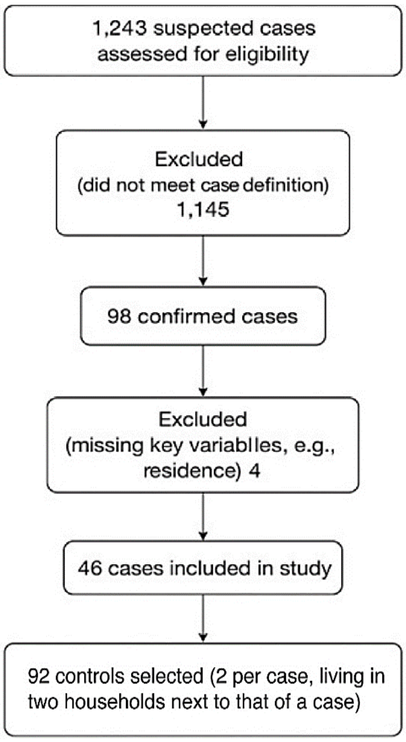

Figure 1. Selection of cases/controls, Harare Western District, 2023

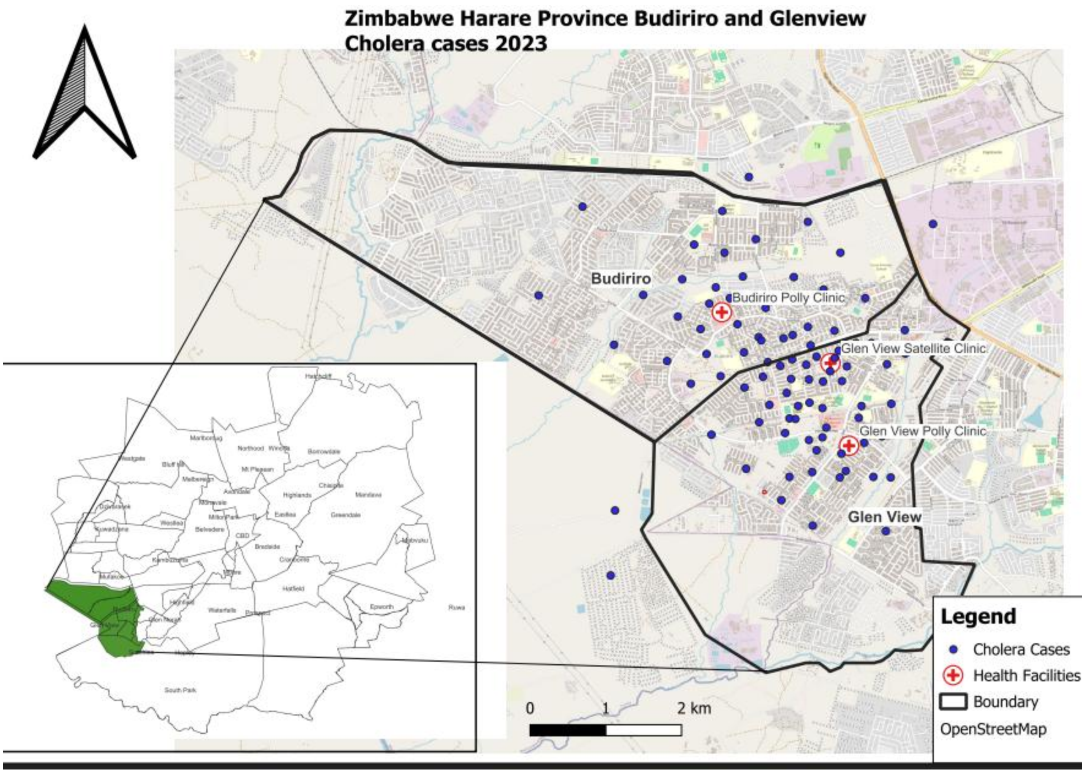

Figure 2. Cholera outbreak distribution of confirmed cases, Harare Western District, 2023

3.1.4. Outbreak description by time

The onset of the outbreak was on April 22, 2023. Cases gradually increased from 1 confirmed case on April 22 to 71 confirmed cases by May 15, 2023, with a peak of the cases on May 5 (N = 8) and May 8, 2023 (N = 8). Cases started decreasing from May 16 to July 11, 2023. As of July 17, 98 confirmed cases were recorded in Harare Western District, and a total of 114 confirmed cases in Harare. On September 23rd, 2023, another cholera outbreak started, and cases were detected in Harare Western District. The epidemic curve pattern resembled a continuous common source pattern, as shown in Figure 3.

3.1.5. Antibiotic susceptibility patterns

An antibiotic sensitivity test was conducted on stool samples that tested positive for *Vibrio cholera*. Laboratory results reviewed that ciprofloxacin displayed the highest susceptibility rate of 90.2% (101 out of 112 samples), followed by tetracycline, which also exhibited a relatively high susceptibility rate of 86.6% (97 out of 112 samples). On the contrary, cotrimoxazole demonstrated the lowest susceptibility rate of 1 % (1 out of 112 samples). Eighty out of 112 (71.4%) of the stool samples were susceptible to Azithromycin.

3.1.6. Environmental surveillance of cholera

Five key informant interviews were conducted. All participants reported that they conducted environmental surveillance, primarily through water sampling. Water sampling is being done routinely for testing water turbidity, chlorine levels, and pH levels for municipal water. During the outbreak, water sampling was carried out on boreholes, wells, and household water for consumption. One participant said, "There is currently no specific machine available for direct testing of *Vibrio cholerae*. However, the presence of *E. coli* is often associated with the presence of *Vibrio cholerae*."

A total of 92 water samples were collected from April to July 2023, comprising 89 borehole samples and 3 well samples as shown in Table 1. Among borehole samples, 42 (47.2%) were unsatisfactory for drinking water quality as they contained detectable total coliforms, and 5 (5.6%) were positive for *E. coli*. Total coliform counts in boreholes ranged from 1 to >100 cfu/100 ml. Well water showed higher contamination, 2 of 3 (66.7%) samples had detectable coliforms, and 1 (33.3%) was positive for *E. coli*. The total coliform counts in wells ranged from 61 to >100 cfu/100 ml, indicating heavy contamination.

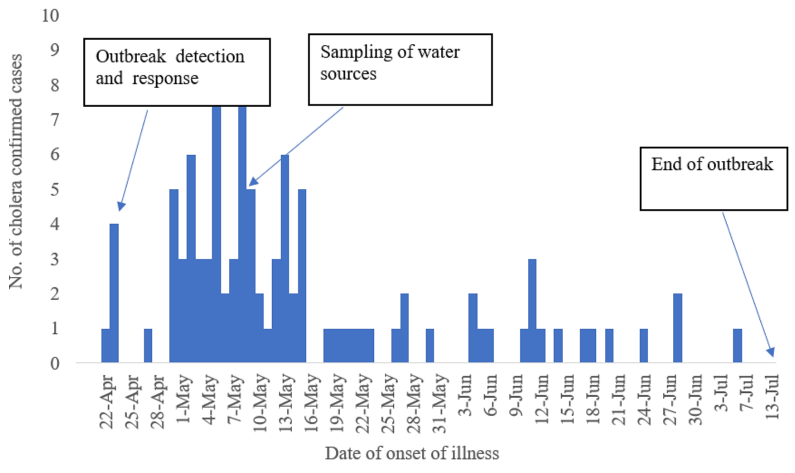

Figure 3. Epidemic curve for cholera outbreak, Harare Western District, 2023

Table 1. Summary of results on environmental sampling of water sources, Harare city, 2023

Water source	No. samples tested	n (%) Unsatisfactory (TCC >0)	n (%) *E. coli* positive	TCC range (cfu/100 ml)
Boreholes	89	42 (47.2)	5 (5.6)	(1 to >100)
Wells	3	2 (66.7)	1 (33.3)	(61 to > 100)

Water sources with unsatisfactory total coliform count were flushed, and some were installed with inline chlorinators. The municipal water had an adequate residual chlorine level and was found to be safe for drinking. These results helped in identifying cholera hotspots and guiding public health interventions. There was no sewage sampling and testing. During the implementation of environmental surveillance, several challenges were encountered. The Water Quality Monitoring Team faced difficulties due to limited transportation options and fuel shortages.

3.1.7. Analytical epidemiology

- Bivariate analysis on demographic factors associated with contracting cholera

Occupation showed a significant association, with employed individuals having a lower risk of contracting cholera (OR: 0.26, 95% CI: 0.12 to 0.55) compared to unemployed individuals. Marital status was significantly associated with contracting cholera, with married individuals having a lower risk (OR: 0.34, 95% CI: 0.16 to 0.70) compared to those who were single, as shown in Table 2.

- Bivariate analysis on water, sanitation, and hygiene-related factors associated with contracting cholera.

Bivariate analysis revealed several significant associations with factors associated with contracting cholera such as a sewage burst near their houses (OR 4.99, 95% CI 2.31 to 10.80), using pit toilets (OR 3.30, 95% CI 1.54 to 7.07) and those with a history of contact with a positive case of cholera (OR 3.91, 95% CI 1.70 to 8.99), drinking borehole water (OR 3.75, 95% CI 1.51 to 9.27) and eating food sold on the road (OR 2.44, 95% CI 1.04 to 5.69) were associated with increased odds of getting infected with cholera. On the other hand, washing hands with soap and water (OR 0.06, 95% CI 0.01 to 0.21) and having access to a hand washing facility (OR 0.17, 95% CI 0.08 to 0.38) were associated with lower odds of contracting cholera. There was a significant association between cholera vaccination status (OR = 0.28, 95% CI 0.13 to 0.61) and contracting cholera. Individuals who received the OCV vaccination had lower odds of contracting cholera compared to those who did not receive it. Furthermore, among those who received the vaccine, individuals who received two doses (OR=0.28, 95% CI 0.12 to 0.66) had a lower odd of getting infected with cholera compared to those who received no vaccine, as shown in Table 2.

- Vaccination effectiveness:

$$\begin{aligned}\text{Vaccine effectiveness (VE)} &= 1\text{-OR}\times 100\\ &= 1\text{-}0.28\times 100\\ &= 72\%\end{aligned}$$

The 95% confidence interval for VE was derived from the OR confidence limits (0.13– 0.61):
VE lower = (1−0.61) ×100 = 39% VE upper = (1−0.13) ×100 = 87%.
Thus, VE = 72% (95% CI: 39–87%; p = 0.001).

Table 2. Bivariate analysis for factors associated with contracting cholera, Harare Western District, 2023

Variable	Characteristics	Cases N = 46 (%)	Controls N = 92 (%)	Odds ratio	CI	p-value X2/F
Sex	Female	24 (52.2)	47 (51.1)	1.04	0.51-2.12	0.904
	Male	22 (47.8)	45 (48.9)	REF		
Age	<10 years	4 (8.7)	3 (3.4)	1.33	0.11-15.70	0.820
	10-20 years	15 (32.6)	26 (29.2)	0.58	0.37-4.53	0.601
	21-30 years	9 (19.6)	23 (25.8)	0.39	0.05-3.21	0.383
	31-40 years	13 (28.3)	31 (33.8)	0.42	0.05-3.30	0.409
	41-50 years	3 (6.52)	4 (4.5)	0.75	0.06-8.83	0.819
	>50	2 (4.4)	2 (2.3)	REF		
Occupation	Employed	15 (32.6)	60 (65.2)	0.26	0.12-0.55	<0.001
	Unemployed	31 (67.4)	32 (34.8)	REF		
Marital status	Married	20 (43.5)	64 (69.6)	0.34	0.16-0.70	0.003
	Single	26 (56.5)	28 (30.4)	REF		
Sewage burst 1 km near their house	Yes	26 (56.5)	19 (20.7)	4.99	2.31-10.80	<0.001
	No	20 (43.5)	73 (70.3)	REF		
Nature of toilet	Pit toilet	22 (47.8)	20 (21.7)	3.30	1.54-7.07	0.002
	Sit toilet	24 (53.2)	72 (78.3)	REF		
History of contact	Yes	18 (39.1)	13 (14.1)	3.91	1.70-8.99	0.001
	No	28 (60.9)	79 (85.9)	REF		
Drinking borehole water	Yes	39 (84.8)	55 (59.8)	3.75	1.51-9.27	0.003
	No	7 (15.2)	37 (40.2)	REF		
Washing hands with soap and water	Yes	3 (6.5)	50 (54.3)	0.06	0.02-0.20	<0.001
	No	43 (93.5)	42 (45.7)	REF		
Handwashing facility	Yes	19 (41.3)	74 (80.4)	0.17	0.08-0.37	<0.001
	No	27 (58.7)	18 (19.6)	REF		
Eating food sold on the road	Yes	14 (30.4)	14 (15.2)	2.44	1.04-5.69	0.036
	No	32 (69.6)	78 (84.8)	REF		
Vaccination against cholera	Yes	11 (23.9)	49 (53.3)	0.28	0.13-0.61	0.001
	No	35 (79.1)	43 (46.8)	REF		
Doses of vaccine received	Two	9 (19.6)	39 (42.4)	0.28	0.12-0.66	0.004
	One	2 (4.4)	10 (10.9)	0.25	0.05-1.20	0.082
	Zero	35 (79.1)	43 (46.7)	REF		

3.1.8. Multivariate analysis

Backward logistic regression analysis was performed on variables that were significant at p≤0.25. This reviewed that being employed (AOR 0.28, 95% CI (0.08 to 0.96), p-value = 0.043), washing hands with soap and water (AOR 0.03,95% CI (0.01 to 0.17), p-value = 0.0001) using a sit toilet (AOR 0.23, 95% CI (0.07 to 0.79, p-value = 0.020), being vaccinated against cholera (AOR 0.17, 95% CI (0.04 to 0.64), p-value = 0.008), and having a handwashing facility (AOR 0.04 95% CI (0.01 to 0.18), p-value = <0.001) were independent protective factors of contracting cholera. Experiencing a sewage burst (AOR 9.75, 95% CI (2.60 to 36.62), p-value = 0.001) was an independent risk factor of contracting cholera, as shown in Table 3.

Table 3. Multivariate analysis of independent factors associated with contracting cholera, Harare Western District, 2023

Variable		Cases N = 46 (%)	Controls N = 92 (%)	Crude odds ratio (CI)	Adjusted odds ratio (CI)	p-value X2/F
Occupation	Employed	15 (32.6)	60 (65.2)	0.26 (0.12-0.55)	0.28 (0.08-0.96)	0.043
	Unemployed	31 (67.4)	32 (34.8)	REF		
Sewage burst	Yes	26 (36.5)	19 (20.7)	4.99 (2.31-10.80)	9.75 (2.60-36.62)	0.001
	No	20 (43.5)	73 (79.3)	REF		
Washing hands with soap and water	Yes	3 (6.5)	50 (54.4)	0.06 (0.02-0.20)	0.03 (0.01-0.17)	0.0001
	No	43 (93.5)	42 (45.6)	REF		
Nature of toilet	Sit toilet	24 (47.8)	72 (21.7)	0.30 (0.14-0.65)	0.23 (0.07-0.79)	0.020
	Pit toilet	22 (52.2)	90 (78.3)	REF		
Vaccinated against cholera	Yes	11 (23.9)	49 (53.3)	0.28 (0.13-0.61)	0.17 (0.04-0.64)	0.008
	No	35 (76.1)	43 (46.7)	REF		
Presence of a handwashing facility	Yes	19 (41.30)	74 (80.4)	0.17 (0.08-0.37)	0.04 (0.01-0.18)	<0.001
	No	27 (58.7)	18 (19.6)	REF		

3.2. Discussion

3.2.1. Vaccine effectiveness

This study found an OCV effectiveness of 72% (95% CI 39–87; p<0.001) four years after vaccination, providing evidence of sustained population-level protection in Harare. Vaccinated individuals had lower odds of contracting cholera than those unvaccinated, and two-dose recipients were more protected than those who received no doses. This suggests that two-dose OCV regimens can maintain immunity for several years in high-risk urban populations, reducing susceptibility to outbreaks. From a public health perspective, these results support OCV as a key preventive tool in cholera-endemic or outbreak-prone areas, potentially lowering disease incidence and associated healthcare burdens.

These findings are broadly consistent with observations from other settings. In India, a cluster-randomized trial reported cumulative protective efficacy of the vaccine at 5 years was 65% (95% CI 52–74; p<0.0001) [19], while in Haiti, an extended case-control study by Franke *et al*. [20] found 76% effectiveness (95% CI 59–86) over four years with no evidence of waning. In contrast to our findings in Harare, a study in Bangladesh reported overall OCV protection of 36% (95% CI 19–49%) and total vaccine protection of 46% (95% CI 32–58%), with a significant decline (p = 0.0115) after three years among children vaccinated at 1–4 years of age [21]. Also, Bi *et al.* [8] found that OCV effectiveness remained stable in adults over five years; however, protection was lower in children under five. This lower and more rapidly waning protection in children may reflect age-specific differences in immune response, as younger children often exhibit poorer immune responses to cholera vaccines compared to older individuals. Additionally, higher exposure to cholera in endemic settings, coupled with potential nutritional deficiencies and underlying health conditions, may include differences in the level of effectiveness of the vaccine over time.

While these findings provide strong evidence of OCV effectiveness, several limitations should be noted. Multivariate logistic regression was used to adjust for key confounders, including age and sex. Vaccination status was verified using cholera line lists and vaccination cards to minimize misclassification and recall bias. Limited sample size prevented full quantification of the effect of a single vaccine dose. Despite these measures, residual confounding and measurement errors cannot be entirely excluded. Overall, this study emphasizes the importance of a multi-sectoral approach to prevent cholera outbreaks. The findings suggest the implementation of two-dose regimen booster campaigns every three to five years, particularly in urban cholera hotspots and among vulnerable groups such as children under five, to sustain population-level immunity and prevent outbreak resurgence. Alignment with the GTFCC Roadmap to 2030 is critical, ensuring that vaccine deployment is hotspot-driven and integrated with risk-based surveillance to optimize impact in high-transmission areas. Sustained vaccination must also be complemented by investment in water, sanitation, and hygiene (WASH) infrastructure to address structural drivers of cholera transmission and achieve long-term elimination.

3.2.2. Antimicrobial resistance

Ciprofloxacin, tetracycline, and to some extent azithromycin were effective antibiotics against cholera serotype Ogawa, which was the causative agent of this cholera outbreak. During the 2018/2019 cholera outbreak, *Vibrio cholerae* O1 serotype Ogawa isolates exhibited resistance to multiple drugs, particularly ciprofloxacin (36.6% resistance) and ceftriaxone (99.6% resistance) [22]. Nevertheless, these isolates remained susceptible to azithromycin (100%), which was effectively utilized as a treatment option during that particular outbreak.

Antimicrobial resistance may have been driven by the overuse and misuse of antibiotics, particularly when they are prescribed for infections and are not taken as directed. For example, azithromycin was one of the most prescribed antibiotics during the recent COVID-19 outbreak. A study by Abdelmalek *et al.* [23] demonstrated that azithromycin was misused by physicians, pharmacists, and the public in Jordan during the pandemic [23]. There are also issues with the agricultural use of antibiotics in livestock farming. And ultimately leads to the development of resistant bacteria that can be transmitted to humans through food or the environment, and several studies have mentioned or investigated this topic [24]-[26]. Cotrimoxazole and oxytetracycline are examples of the drugs mostly used in the veterinary sector. Addressing these factors is essential to combat antimicrobial resistance and preserve the effectiveness of these drugs for future generations.

3.2.3. Demographics, water, sanitation, and hygiene (WASH) and infrastructure

The cholera outbreak comparably affected both females (55.3%) and males (44.7%), especially the economically active, given the median age of 24 (15 to 39 years old) of cases and controls. This is also the same with findings by Mahanta *et al.* [27], where females were more affected than males. However, this contradicts with findings from Goswami *et al.* [28], who found that males were more affected by cholera than females. The varying impact of cholera on males and females, as well as the contrasting findings from different studies, can be attributed sociocultural factors, such as gender roles where women spend most of their time at home, making them more vulnerable to the impact of environmental factors such as water sources and living conditions, which can influence transmission patterns [29].

A sewage burst near the participants' houses was strongly associated with an increased risk of cholera infection. During the 2018 outbreak, the deteriorating sanitation infrastructure led to issues such as raw sewage flowing in Harare. Due to erratic water supply, people began to use unregulated wells and boreholes, leading to people drinking contaminated water [22]. This may be the same case for this cholera outbreak. Also, a study in Harare by Ayling *et al.* [30], where a geospatial analysis suggested that in Harare, the closer to the sewer network, the greater the association with increased cholera risk, for households with piped water. This finding highlights the importance of proper sanitation and sewage management (proper maintenance of existing pipes) in preventing the spread of the disease, and according to the Joint Monitoring Program of the WHO and United Nations Children’s Fund (UNICEF), sewered sanitation sits at the top of the improved sanitation ladder [31]. Additionally, using pit toilets was associated with contracting cholera, which is similar to a Zambian study by Nanzaluka *et al.* [32], where it was found that using pit latrines was associated with cholera contraction. These findings emphasize the role of personal hygiene and avoiding direct contact with infected individuals in preventing cholera transmission.

Occupation was found to be significantly associated with the risk of cholera infection, with employed individuals having a lower risk compared to unemployed individuals. This finding suggests that employment may provide individuals with better access to clean water sources at their workplaces and reduce their vulnerability to cholera. Washing hands with soap and water and having a hand washing facility were associated with lower odds of contracting cholera. These findings underscore the importance of proper hand hygiene in preventing cholera transmission. A study in Ethiopia by Dinede *et al.* [33] also found that washing hands with soap after visiting the latrine was an independent protective factor [33]. Handwashing is an easy behavior, but most people find it challenging to practice due to a lack of water and handwashing facilities.

4. CONCLUSION

This study demonstrates that oral cholera vaccination provides substantial and sustained protection, with a two-dose regimen showing 72% effectiveness four years post-vaccination in Harare, supporting its use as a key preventive measure in high-risk urban populations. Cholera transmission was also influenced by WASH conditions, occupation, and personal hygiene practices, while antimicrobial resistance remains an ongoing challenge for treatment. To achieve sustainable cholera control, a multi-sectoral approach is essential, including timely booster campaigns every three to five years, integration with the GTFCC Roadmap to 2030, and targeted improvements in sanitation and hygiene infrastructure, alongside strategies to promote rational antibiotic use in humans and animals. These combined efforts can reduce cholera incidence, prevent outbreak resurgence, and support progress toward long-term elimination.

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AUTHOR CONTRIBUTIONS STATEMENT

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C : **C**onceptualization
M : **M**ethodology
So : **So**ftware
Va : **Va**lidation
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R : **R**esources
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Su : **Su**pervision
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CONFLICT OF INTEREST STATEMENT

The authors declare no competing interests.

INFORMED CONSENT

Written Informed consent from the study participants was sought.

ETHICAL APPROVAL

Permission to conduct the study was sought from the Health Studies Office, Provincial Medical Director for Harare Metropolitan province, and Director of Health Services for Harare City. Written Informed consent from the study participants was sought.

DATA AVAILABILITY

The data that support the findings of this study are available from the corresponding author, [AC], upon reasonable request.

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