

BMJ Open Descriptive epidemiology of the cholera outbreak in Zimbabwe 2018–2019: role of multi-sectorial approach in cholera epidemic control

Tapfumanei Mashe ^{1,2}, Blessmore V Chaibva,³ Parvati Nair,⁴ Khalil A Sani,⁵ Musa Jallow,⁶ Andrew Tarupiwa,⁷ Alexander Goredema,⁸ Manes Munyanyi,⁸ Anderson Chimusoro,⁹ Nkosilathi Mpala,¹⁰ Kudzai P E Masunda,¹¹ Clemence Duri,¹¹ Prosper Chonzi,¹¹ Isaac Phiri⁸

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For numbered affiliations see end of article.

Correspondence to

Dr Tapfumanei Mashe;
mashe2006@yahoo.co.uk

ABSTRACT

Objectives This study was conducted to explore the epidemiology and microbiological pattern of the cholera outbreaks that occurred in Zimbabwe from 2018 to 2019.

Study setting and design This descriptive study used secondary data of 9971 out of 10 730 suspected cases from the Zimbabwean National Diseases Surveillance system and microbiology data of 241 out of 371 patients from the National Microbiology Reference Laboratory in Harare, for the period 5 September 2018 and 3 January 2019. Descriptive analysis was performed to describe the characteristics of the outbreak in terms of person, place and time.

Results A cumulative total of 10 730 suspected, 371 laboratory-confirmed cholera cases and 68 deaths were reported in Zimbabwe through the situation analysis report (sitrep). The attack rate during the outbreak was 174.6 per 100 000 with a case fatality rate of 0.63%. Most cases seen were among adults from Harare province. Antimicrobial sensitivity testing results showed that a multidrug resistant strain of *Vibrio cholerae* O1, Ogawa serotype was responsible for the outbreak. The treatment of cases was changed from the standard recommended medicine ciprofloxacin to azithromycin as confirmed by the antimicrobial sensitivity test results. Strategies employed to contain the outbreak included mass oral cholera vaccination in the hotspot areas of Harare, provision of improved and appropriate sanitation measures, provision of safe and adequate water, chlorination of water and improved waste management practice.

Conclusions The recurrence of a cholera outbreak is a global concern, especially with the emergence of multi-drug resistant strains of the causal organism. Improving water, sanitation, hygiene infrastructure, health system strengthening measures and inter-sectoral collaboration in responding to the cholera outbreak was key to controlling the outbreak.

BACKGROUND

Cholera is an acute diarrhoeal disease caused by toxigenic *V. cholerae*. It can lead to death within hours if untreated, but when properly

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ Large sample size with data from all cholera affected suburbs in Harare from 5 September 2018 to 3 January 2019.
- ⇒ The data are largely complete as regards time place and person.
- ⇒ The article has a strong regional focus.
- ⇒ The outbreak continued up to March 2019 but data are available only until 3 January 2019 and is for Harare (the epicentre of the outbreak).
- ⇒ Only 241 out of the 371 laboratory-confirmed cases were analysed in the study.

managed, the case fatality rate is below <1%.¹ Zimbabwe first reported cholera in 1972 with sporadic outbreaks occurring in subsequent decades.² The largest cholera outbreak in Zimbabwe occurred between August 2008 and July 2009, which recorded 98 592 cases and 4288 deaths.³ The cumulative case fatality ratio (CFR) was 4.3% which is well above the World Health Organization (WHO) recommended threshold of less than 1%. The scale and severity of the outbreak were attributed to poor sanitation and limited access to healthcare, indicative of social inequality in the country and region.

On 5 September 2018, 25 patients were admitted to Beatrice Road Infectious Disease Hospital (BRIDH) located in Harare, with symptoms typical of cholera, such as excessive vomiting, rice water diarrhoea and dehydration. One of these patients, a woman in her early 20s, died on the day she was admitted. Her stool sample was culture positive for *V. cholerae* O1 serotype Ogawa.

More patients subsequently presented to the hospital and suspected cases rose to 52 by the morning of 6 September 2018. Out of

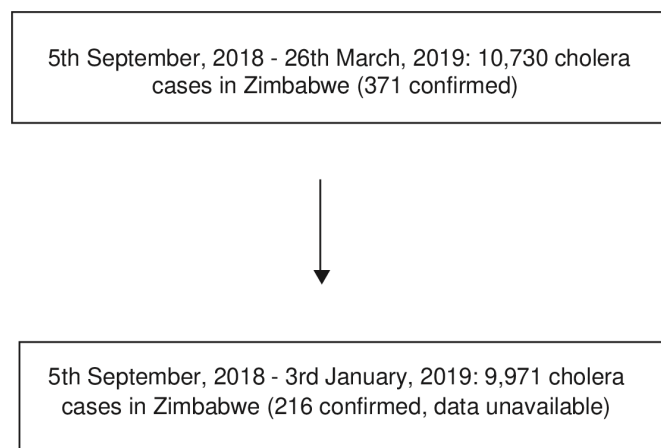


Figure 1 Selection of study population.

39 stool samples collected during these 2 days, 17 tested culture-positive for *V. cholerae* O1 serotype Ogawa. Due to the rapid increase in the number of cases, the outbreak was declared a state of emergency on 12 September 2018. Over the next few months, the outbreak spread and affected other provinces of Zimbabwe. The knowledge gained from this outbreak played an important role in the formulation of a cholera elimination plan in Zimbabwe (2018–2028) in line with the global 2030 cholera elimination plan. The study aim was to describe the epidemiology and microbiological pattern of the cholera outbreaks that occurred in Zimbabwe from 2018 to 2019.

METHODS

Outbreak data collection

The outbreak spanned 6 months from 5 September 2018 to 15 March 2019. Retrospective data of suspected cases that is routinely collected during provision of services and collected from health facilities across the country between 5 September 2018 and 3 January 2019 was reviewed. A total of 9971 suspected cholera cases that presented to Harare city's health facilities outpatient department and inpatients admitted within Cholera Treatment Units (CTU) were included in the study. The data from other provinces (for the duration of the outbreak) and Harare cases reported after 3 January 2019 was excluded from analysis due to the national surveillance system's inability to collect consolidated datasets. Cholera cases were detected through the national surveillance system using the case definitions: *Suspected case*: Any person aged 2 years or more with acute watery diarrhoea, with or without vomiting. *Confirmed case*: A suspected case in which *V. cholerae* serogroups O1 or O139 was isolated from a stool sample.⁴

The selection of the study population is described in figure 1.

The data collected were as follows:

1. Sociodemographic: age, sex, and place of residence.
2. Clinical: date of symptom onset and outcome of treatment, specifically death.

3. Diagnostic: *V. cholerae* culture result and antimicrobial susceptibility, if available.

Indicators derived were: attack rate and case fatality rate

Attack rate (AR)=(Total reported cases/population) 100 000 and case fatality ratio (CFR)=(Total reported deaths/total reported cases)×100.

Bacterial isolates

Samples were collected at the healthcare facility, processed at district health centres as described previously, and then through the public health laboratory network, isolates were sent to the National Microbiology Reference Laboratory (NMRL) in Harare using Cary Blair transport media, for further analysis. Serogrouping and serotyping were determined via the slide agglutination method with polyvalent antisera and mono-specific Inaba and Ogawa antisera (Mast Group Ltd, Bootle, UK).

Antibiotic susceptibility testing

The following antibiotics were used for the disk diffusion method: tetracycline (30 µg), cotrimoxazole (25 µg), ciprofloxacin (5 µg), ampicillin (10 µg), ceftriaxone (30 µg) and chloramphenicol (30 µg) (Oxoid, UK). The Clinical and Laboratory Standards Institute (CLSI) interpretative criteria for antibiotic susceptibility testing of *Vibrio* spp (M45 document) was used when available. For ceftriaxone, kanamycin, nalidixic acid and ciprofloxacin, the interpretative criteria for Enterobacteriaceae/*Salmonella* spp (M100-S27 document) was used. The presence of extended-spectrum β-lactamase activity was investigated using the combination disk methodology (double disk synergy test); ceftazidime (30 µg), cefotaxime (30 µg) and cefpodoxime (30 µg) alone and ceftazidime and cefotaxime in combination with clavulanate (10 µg) was used, as per CLSI guidelines.

Disks were manufactured by Mast Group. *Escherichia coli* ATCC 25922 was used for internal quality control purposes.

Patient and public involvement

None

As this is a purely descriptive study, all of the above was described in terms of time, place and person. Proportions were derived for all categorical variables.

RESULTS

V. cholerae O1 serotype Ogawa was the causative agent of the 2018 cholera outbreak in Zimbabwe

Case identification during routine consultation followed the cholera case definition, based on which a sample was collected for confirmation of the case and outbreak.

Following the confirmation of a case, national, provincial and district rapid response teams were activated to facilitate response during the outbreak. A total of 10 730 cholera cases (suspected: 10 359 and confirmed: 371) and 68 deaths were recorded between 6 September 2018 and

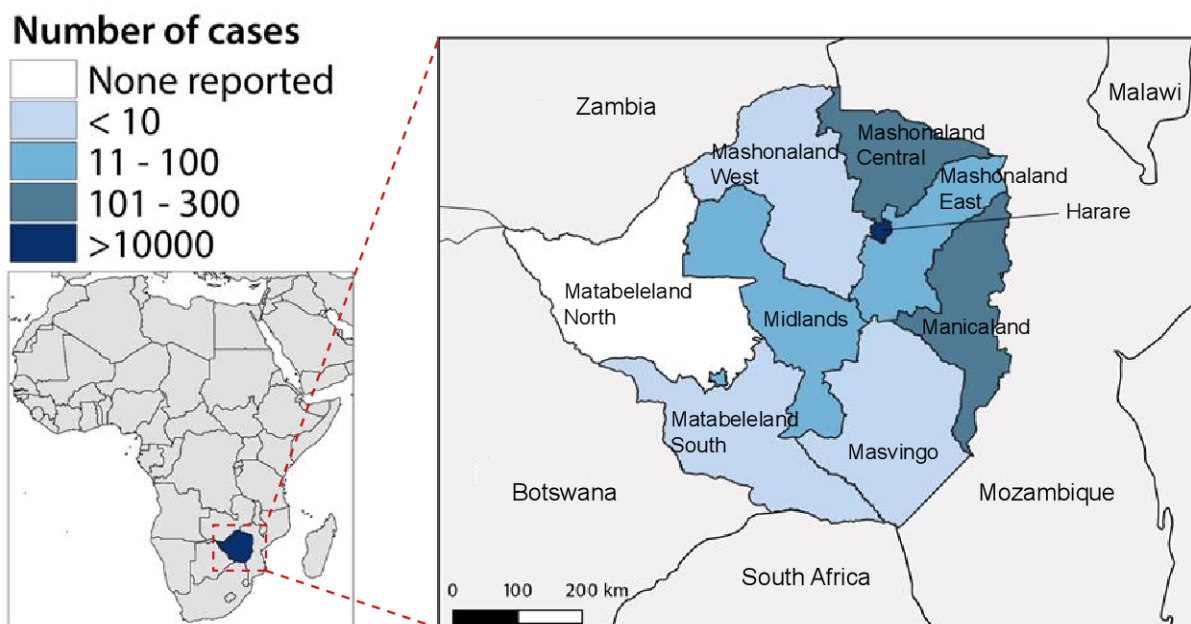


Figure 2 Geographic distribution of suspected cholera cases per province for the period 2018 to 2019.

26 March 2019 (figure 2, table 1). Overall, the CFR was 0.64% and AR was 174.6 per 100 000 (table 1).

A total of 10 730 suspected cases were recorded, but only 9971 of the suspected cases had complete information needed for analysis. Similarly, 371 cases were confirmed to be infected with cholera, but only 241 cases had complete information, more so, out of 68 mortalities, only 46 had complete information for analysis. Therefore, only complete information in the data set was extracted for analysis. Adults were the most affected, with 58.7% (5851/9971) of the suspected cases being greater than 15 years of age. The male-to-female ratio was approximately 1:1, across all age groups (table 2). Of the 46 deaths, the majority 76.1% (35/46) died within 24 hours of presenting at a health facility, 8.7% (4/46) within 2–3 days and 4.3% (2/46) occurred >1 week after admission and 10.9% (5/46) had no date of death.

The burden of the outbreak was higher in Harare province (consisting of Harare City and Chitungwiza). The cholera outbreak began in the districts of Glenview (4426/9971=44.4%) and Budiriro (2866/9971=28.7%) within Harare Province. The cases started declining during week 5 (4.10.2018) since the first case was reported. Beyond week 5 it was under control as there were no recorded cases above those that were recorded before week 5. Out of the 216 confirmed cholera cases, 112 (56.5%) were from Budiriro and 68 (31.5%) were from Glenview. Nine additional provinces were affected across the country during the outbreak. Only one travel-related case was reported in South Africa. Attack rates across the affected areas in Zimbabwe ranged from 0.6 to 105.8 per 100 000 population as shown in table 1, figures 2 and 3 respectively.

The source of the outbreak within Harare was identified to be contamination of water sources, such as

boreholes and wells from blocked and damaged sewage systems which were visible in the affected suburbs.⁵ This does align with the epidemiological analysis which shows 9971/10 730 cases occurring in Harare. The outbreak persisted in Harare due to the challenges associated with the water and sewer system.

Multisectoral response

The multisectoral measures put in place by the administration lead to a decrease in the likely number of cases during the epidemic. With help from United Nations International Children's Emergency Fund (UNICEF), water, sanitation and hygiene (WASH) interventions were introduced, such as the distribution of chemicals for at-home water treatment and monitoring of water quality were implemented within the first week of the outbreak. Furthermore, as the number of cases decreased, community engagement was carried out by teams of governmental and nongovernmental environmental stakeholders. This included health education and the distribution of soap and water treatment products (with guidelines on their use) to the cases and their neighbours. Additionally, point-of-collection chlorination was carried out at water points.

Azithromycin was the drug of choice for the management of the 2018 highly resistant cholera outbreak in Zimbabwe

National guidelines, specifically the Zimbabwe Essential Medicines List and Standard Treatment Guidelines (EDLIZ 2015) and National Cholera Control Guidelines (2011), which included oral rehydration therapy and antimicrobials, were used for case management. The guidelines recommended the empirical use of ciprofloxacin for severe cholera cases and this was followed during the first days of the outbreak. However, antimicrobial

Table 1 Cholera indicators by province and affected area for the Zimbabwe September 2018 to March 2019 outbreak

Province	Affected area	Population (2018 estimates)	Total cases	AR (per 100 000)	Cumulative deaths	CFR (%)
Harare	Harare City	1 576 603	9971	632.4	46	0.5
Harare	Chitungwiza	378 793	114	30.1	0	0
Bulawayo	Bulawayo City	693 530	38	5.5	1	2.6
Mashonaland Central	Shamva	131 257	4	3.1	0	0
Mashonaland Central	Mazowe	247 812	8	3.2	0	0
Mashonaland Central	Rushinga	78 595	18	22.9	0	0
Mashonaland Central	Mt Darwin	225 812	239	105.8	5	2.1
Mashonaland East	Seke	106 955	6	5.6	0	0
Mashonaland East	Marondera	65 812	13	19.8	0	0
Mashonaland East	Murehwa	211 887	51	24.1	7	13.7
Mashonaland East	Mutoko	155 117	8	5.2	1	12.5
Mashonaland East	UMP	119 539	2	1.7	0	0
Mashonaland East	Wedza	75 334	4	5.3	0	0
Mashonaland East	Chikomba	125 899	4	3.2	0	0
Mashonaland West	Kadoma	98 158	2	2.0	0	0
Manicaland	Buhera	261 004	74	28.4	6	8.1
Manicaland	Makoni	289 094	4	1.4	1	25
Midlands	Gokwe North	255 133	10	3.9	0	0
Midlands	Mberengwa	185 787	28	15.1	2	7.1
Manicaland	Mutare City	199 163	128	64.3	0	0
Masvingo	Masvingo	224 209	2	0.9	1	50
Masvingo	Bikita	162 356	1	0.6	0	0
Masvingo	Chiredzi	172 344	6	3.5	0	0
Matabeleland South	Beitbridge	108 050	1	0.9	0	0
Total		6 148 243	10730	174.6	69	0.6

AR, attack rate; CFR, case fatality rate; UMP, Uzumba Maramba Pfungwe.

susceptibility testing was also conducted as part of routine management.

Among the study population (9971 cases), 216 cases were confirmed to have cholera and were all tested for antimicrobial susceptibility (table 3). Of 216 cases, the majority were determined to be intermediate to full resistance to the antimicrobials tested (table 3).

As reported by Mashe *et al*⁶ genomic analysis of 11 isolates obtained during the 2018 Zimbabwe cholera outbreak showed that the isolates belonged to sublineage T13 of the 7PET lineage. However, these isolates differed from previous T13 isolates by having 14 additional antimicrobial resistance genes carried on a 160 kb InCA/C2 plasmid, resulting in a broader resistance profile. The use of genomic analysis enabled the country to rapidly adapt national guidelines for cholera based on the antimicrobial susceptibility of the causative pathogen. This would have had a maximum impact on the treatment of severe cholera where the antimicrobials have a role in reducing the severity and potentially reducing the CFR.

The country's major interventions to control the outbreak included improved WASH measures (including the provision of potable drinking water and household

water treatment products, chlorination facilities and waste management) and the rollout of the mass campaign for oral cholera vaccination (OCV) to the populations most at risk.

OCV as an outbreak mitigation measure

The target population for the two-dose vaccination (in individuals >1 year of age) was estimated to be 1 512 642 people living in 17 high-density suburbs of Harare. Starting 2 October 2018, nearly 1.3 million people were vaccinated during the campaign giving coverage of 86% and over 2.5 million doses of OCV (Euvichol) were administered. The multisectoral measures put in place by the administration led to a decrease in the likely number of cases during the epidemic.

DISCUSSION

Cholera affects approximately 1.3 billion people globally, the majority of whom are in sub-Saharan Africa.⁷ Cholera epidemics can only be prevented by improving the availability of safe drinking water and sanitation facilities. A timely, well-coordinated and effective

Table 2 Sociodemographic and clinical characteristics of patients presenting from 5 September 2018 to 3 January 2019 (9971 cases)

Characteristic	Total (%)
Age	
<2 years	1072 (10.8%)
2–5 years	1128 (11.3%)
5–15 years	1860 (18.7%)
15–25 years	1840 (18.5%)
25–35 years	1854 (18.6%)
35–45 years	1174 (11.8%)
45–55 years	551 (5.5%)
>55 years	492 (4.9%)
Gender	
Male	4948 (49.6%)
Female	5023 (50.4%)
Health facility	
Glenview Poly	5410 (54.3%)
Beatrice Road Infectious Diseases Hospitals	2702 (27.1%)
Budiriro Poly	1849 (18.5%)
Harare Hospital	5 (0.1%)
Not stated	4 (<0.1%)
Hatcliffe	1 (<0.1%)
Symptom onset	
September	7760 (77.8%)
October	1671 (16.8%)
November	392 (3.9%)
December	148 (1.5%)
Case definition	
Confirmed	
Suspected	216 (2.2%)
Others	9755 (97.8%)
Deaths	
within 24 hours after admission	35 (76.1%)
2 to 3 days after admission	4 (8.7%)
> week after admission	2 (4.3%)
no date of death	5 (10.9%)

response to the cholera outbreak is paramount to contain its spread, reduce morbidity and mortality and mitigate the threat to international trade and travel.^{8 9} The period from detection and verification of the 2018 cholera outbreak was in line with national guidelines. The cases were suspected, tested and confirmed to be caused by *V. cholerae* within 24 hours. This increased sensitivity allowed national authorities to declare an emergency earlier on during the outbreak based on the increased number of cases. Simultaneously, training of the identified rapid response team at various levels, and healthcare workers on the outbreak identification, preparedness, investigation and response were conducted.

After declaring the cholera outbreak emergency, the Ministry of Health and Child Care (MoHCC), Zimbabwe in collaboration with WHO, Médecins Sans Frontières and other stakeholders coordinated the outbreak response. This was achieved by setting up CTUs in affected areas as well as rapid response teams at various levels, additionally, a large number of healthcare workers received Integrated Disease Surveillance and Response training.

The 2018 cholera outbreak stretched over 6 months with a CFR of 0.64%, 58.7% of cases was recorded among adults (>15 years) and 22.1% in children <5, no significant difference was recorded based on gender. The findings are consistent with findings from other low-income and middle-income countries, like what was reported by a study conducted in Bangladesh in 2008 which reported children <5 to be 2.7 times more likely to develop an infection from *V. cholerae* O1 subtype when compared with adults.¹⁰

All the recorded deaths were recorded in the first month (September) of the outbreak, and most deaths (72.2%) occurred within 24 hours of arrival at a health facility. This high number of deaths may be attributed to the initial lack of familiarity with early detection and management of cholera cases among healthcare workers. It could also be linked to a lack of awareness about the disease by the patients and thus a delay in seeking treatment/ late presentation to health facility, resulting in complications.

In the early phase of the outbreak (1–3 days of the outbreak), case management initially followed the Essential Medicines and Standard Treatment Guidelines of 2015, which recommended the empirical use of ciprofloxacin for severe disease. The strain was subsequently proved to be resistant to ciprofloxacin and it is speculated that the use of ciprofloxacin among the deceased cases might have contributed to increased morbidity and hospital stay in the initial stages of the outbreak. Similar findings were illustrated in a Zambian study by Mutale and colleagues.¹¹

The majority of the cases occurred in Harare province. Harare province had a population of >2.1 million thus, overcrowding and unsanitary living conditions are common. This is a known risk factor for the propagation of cholera epidemics as discussed in other cholera studies in Africa.^{12 13} This was further exacerbated by water shortages in Harare city leading to the use of unsanitary water supply, especially in the densely populated suburbs of Glenview and Budiriro, the epicentres of the outbreak. Harare has a huge growth/influx of people creating a huge burden on dilapidated underground pipes which were duly replaced in Glenview and Budiriro as a mitigation measure. Eighteen kilometres of underground pipes were laid in collaboration with a private sector organisation (Econet, a telecom company).

The decline in cases was attributed to the early identification of the outbreak, a multipronged strategy employed

Table 3 Antimicrobial susceptibility patterns of the *V. cholerae* in Zimbabwe, 2018 to 2019 outbreak

Antibiotic name	Number (n)	% R (n)	% I (n)	% S (n)
Ceftriaxone	216	99.6 (215)	–	0.5 (1)
Ciprofloxacin	216	36.6 (79)	60.2 (130)	3.2 (7)
Trimethoprim/Sulfamethoxazole	216	96.8 (209)	–	3.2 (7)
Chloramphenicol	216	13.9 (30)	79.6 (172)	6.5 (14)
Tetracycline	216	24.1 (52)	66.2 (143)	9.7 (21)
Ampicillin	216	100 (216)	–	–
Azithromycin	216			100 (216)

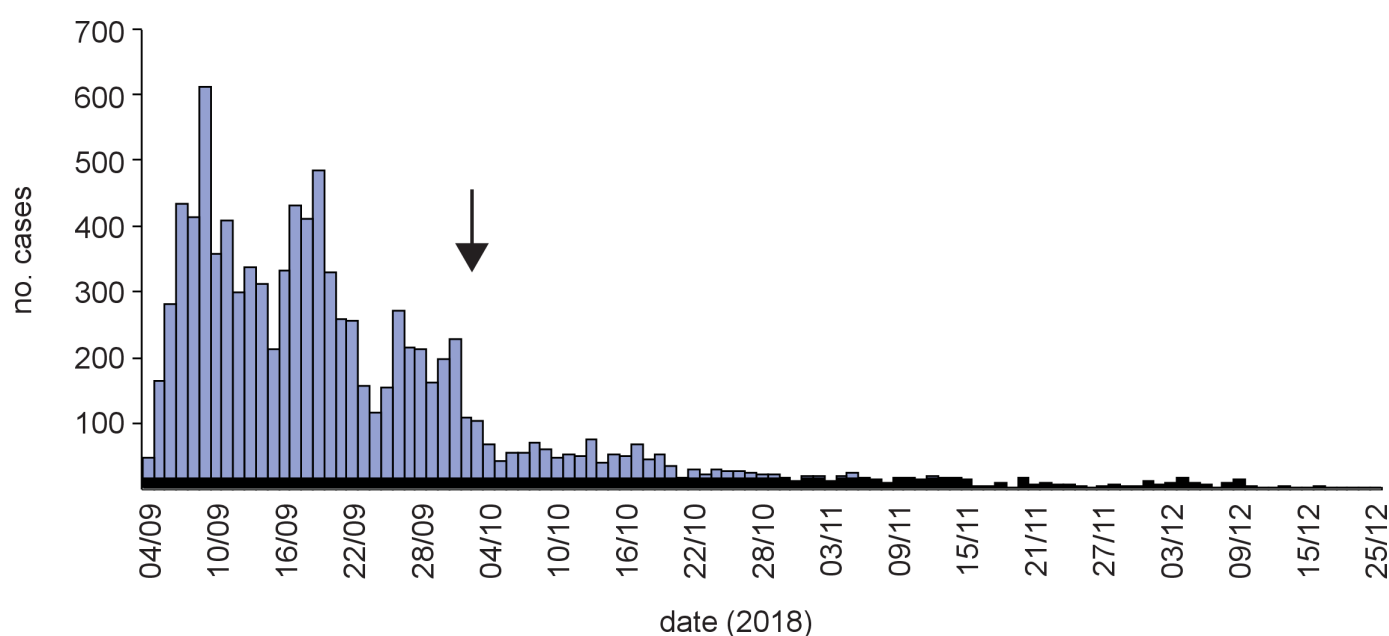
I, Intermediate; R, resistance; S, sensitive.

by the MoHCC, Zimbabwe. These interventions were followed up by an OCV campaign. This is in line with the advice from the Strategic Advisory Group of Experts in 2009, to consider reactive vaccination campaigns in response to large cholera outbreaks as highlighted by a study on the use of cholera vaccination in non-endemic and endemic settings.¹⁴ The net result of these interventions was that, unlike a similar study in Nigeria¹⁵ which showed four waves of disease, the epidemic curve in Zimbabwe showed a consistently decreasing trend.

Genomic analyses showed that the 11 isolates obtained during the 2018 cholera outbreak in Zimbabwe belonged to T13 of the 7PET lineage which was recently introduced from South Asia into East Africa and from there to Yemen. However, the 2018 Zimbabwean outbreak isolates differed from previous T13 isolates by having 14 additional antimicrobial-resistance genes, leading to a broader resistance profile. Specifically, the isolates were intermediate resistant or resistant to tetracycline and ciprofloxacin and produced the extended-spectrum beta-lactamase CTX-M-15.

This study highlights the great progress in the Zimbabwean response between the two outbreaks, that is, between 2008 and 2018. The caseload and mortality rate was much lower in 2018. Also, in 2008, the case fatality rate was 4.3% which was well above the threshold acceptable to the WHO while in 2018, it was <1%. The 2008 epidemic also showed a large second wave, a phenomenon which was conspicuously absent in the 2019 outbreak. The reasons for this are varied and will be discussed in the next paragraph.

In 2008, reports of the outbreak were reported by the media before the first official case in August 2008 and it took the MoHCC 4 months to declare a state of emergency. The health system at the time was at its weakest with high health worker attrition and limited knowledge and surveillance capacity. In the decade spanning 2008–2018, donor funding was used to retain human resources in healthcare, development of treatment guidelines and improve the availability of medications like oral rehydration salts, training of healthcare workers and revival of the previously defunct Community Health Worker

**Figure 3** Epidemic curve (4 September 2018–3 January 2019).

Programme which increased access to healthcare services for the population. All of these interventions put the country in good stead at the time of the 2018 epidemic resulting in speedy control of the outbreak. It is unfortunate, however, that the cause of the outbreak viz gaps in sanitation and hygiene is a common factor in both outbreaks. This is addressed in the National Cholera Elimination Plan (2018–2028) and it is hoped that this will prevent a repeat of such tragic outbreaks.

The case fatality rate of 0.64% indicated the country employed relatively effective measures to mitigate the outbreak at the earliest. First, deaths occurred only during the first 2 weeks of the outbreak. Second, the country implemented a mass OCV campaign in hotspot areas to limit the current outbreak and as a prevention measure. The high coverage of the OCV campaign during the outbreak provided protection for at-risk populations. Third, other well-proven control strategies related to WASH, provision of potable water, water treatment, attending to leaky pipes and improvement of sanitation were implemented to manage the outbreak. In addition, the efforts of governmental and international and local non-governmental organisations working together in a coordinated manner helped contain the outbreak relatively early with low mortality as compared with the previous outbreak a decade earlier. The key limitations of our study include the retrospective nature of the analysis, dependence on only data routinely reported in the healthcare system and incomplete data for the period from mid-January to March 2019 which led to the exclusion of data from that period in the analysis. Finally, only about 65% of the confirmed cases recorded in the outbreak were analysed in our study.

CONCLUSION

Zimbabwe managed the outbreak, maintained the case fatality rate below 1% and brought down the number of cases during the cholera outbreak. The following lessons were learnt from this experience:

- ▶ Strengthening of health systems and surveillance is essential to enable prevention and if not possible, early detection of cholera outbreaks.
- ▶ Creation of awareness and dissemination of information by appropriate authorities.
- ▶ The epidemic curve illustrates the role of cholera vaccination to reduce mortality and morbidity during an outbreak though it is to be noted that WASH improvement must also take place concurrently.
- ▶ Political will and multisectoral approach, leveraging on the strengths of both governmental and non-governmental organisations are required, to implement effective mitigation measures during an epidemic. In Zimbabwe, this gave rise to an effective control strategy that tackles all aspects of a cholera outbreak. Case management, WASH measures, and vaccination campaigns are of prime importance to control a cholera outbreak.

Author affiliations

- ¹One Health Office, Ministry of Health and Child Care, Harare, Zimbabwe
- ²Health System Strengthening Unit, World Health Organization, Harare, Zimbabwe
- ³Directorate of Pharmacy, Ministry of Health and Child Care, Harare, Zimbabwe
- ⁴Médecins Sans Frontières, Amsterdam, The Netherlands
- ⁵Department of Public Health, Federal Ministry of Health, Abuja, Nigeria
- ⁶Medical Research Council (MRC) Unit, London School of Hygiene and Tropical Medicine (LSHTM), Banjul, Gambia
- ⁷Bacteriology Department, National Microbiology Reference Laboratory, Harare, Zimbabwe
- ⁸Epidemiology and Disease Control, Ministry of Health and Child Care, Harare, Zimbabwe
- ⁹Communicable and Non-communicable Diseases, World Health Organization, Harare, Zimbabwe
- ¹⁰Emergencies, World Health Organization, Harare, Zimbabwe
- ¹¹Health Services Department, City of Harare, Harare, Zimbabwe

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Contributors While TM was the guarantor, BVC, IP, and TM shared leadership and supervision duties. PN, KAS, MJ, AT, AG, MM, AC and NM were responsible for data analysis and interpretation. TM, KP, CD, PC, BVC, PN, KAS, MJ, AT, MM, AC and NM were responsible for the writing of the manuscript.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval All data were reviewed retrospectively, and ethical approval was waived as routinely collected surveillance (secondary) data was used. No specific consent was required from the patients whose data were used in this analysis as the NMRL has the authority to handle patient data for public health monitoring under section 46 (notifiable diseases) of the Zimbabwe Public Health Act. However, no data on specific patients' identification was presented.

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Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information.

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ORCID ID

Tapfumane Mashe <http://orcid.org/0000-0001-6481-4095>

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