

The Health Press

Zambia's journal on public health, disease surveillance, prevention and control Vol. $02 \mid Issue\ 1 \mid 31\ January\ 2018$

The Health Press - Zambia is published by Zambia National Public Health Institute, Ministry of Health Zambia since Jan 31, 2017.

Address:

Plot 13, Reedbuck Road, Kabulonga, Lusaka.

Editor-in-Chief:

Ms Mazyanga L Mazaba

Managing Editor:

Dr Raymond Hamoonga

Editorial Team

Prof Paul Kelly

Prof Seter Siziya

Prof Mudenda Hangómbe

Dr Jeremiah Banda

Dr Alwyn Mwinga

Dr Victor Mukonka

Dr John S Moran

Email: editor.healthpress@znphi.co.zm **Website**: http://znphi.co.zm/thehealthpress/

Suggested Citation: [Author Surname, Initial].[Article title].Health Press Zambia Bull 2017;02(1):[inclusive page numbers].

ISSN: 2520-4378

Table of contents

FOREWORD

The Journey Continues by ML Mazaba	3
EDITORIAL EDITORIAL	
Outbreaks of Enteric Disease in Zambia by P Kelly	4
REVIEW	
A review of the epidemic-prone enteric diseases in Zambia: cholera, typhoid fever and bacterial dysentery by S Siziya	6
OUTBREAK REPORT	
Cholera Outbreak in Chienge and Nchelenge Fishing Camps, Zambia, 2017 by A Gama, P Kabwe, F Nanzaluka, N Langa, LS Mutale, L Mwanamoonga, G Moonga, G Chongwe, N Sinyange	12
Typhoid fever outbreak investigation in a malaria endemic community, Solwezi, North-Western province, Zambia, 2017 by FD Mwansa, A Gama, F Kapaya, E Yard, R Kumar, G Chongwe, N Sinyange	20

FOREWORD

The Journey Continues

By ML Mazaba

The Health Press Zambia (THP-Z) welcomes you to its Public Health Journal in 2018. While maintaining a broad scope THP-Z aims at intersecting various aspects in the field of public health through outbreak reports, perspectives, rapid communications, research articles, special features and surveillance reports.

Last year we managed to publish seven full issues, shared some press releases and some of the weekly bulletins from the Integrated Diseases Surveillance and Response program in Zambia. We dated some of you through our Facebook page and were happy to see the followings and likes on our page. We are also very excited that the journal has been attracting papers from a variety of individuals in the academia, research world and programs. This wide spectrum of publications was informative to the general public, researchers and academics as well as policy makers.

Through 2017, *The Health Press Zambia* themed its issues to have a minimum of one article relating to the celebrated health days. This was to ensure we published items which would support achievement of one of our objectives: to inform the public about health threats and what individuals can do to protect themselves and what the government is doing to reduce the threat.

This issue focuses on Outbreaks causing Enteric Diseases in Zambia, among them Cholera and Typhoid. Zambia continues to experience outbreaks of such a nature. In 2017 alone, Zambia experienced separate Typhoid outbreaks in three (3) districts. Currently, Zambia is experiencing a Cholera outbreak since 6th October 2017 affecting close to 4000 people, mostly in Lusaka, the capital city of Zambia.

As the journey continues, we promise you an exciting ride with various perspectives and research findings in Public Health. Look out for more interaction through our Facebook and twitter accounts. We maintain our vision to be a leading publication that will inform policy makers, public health practitioners, and the general public at large.

May I qualify our vision with a quote by Michael Bloomberg who said "You don't make spending decisions, investment decisions, hiring decisions, or whether-you're-going-to-look-for-a-job decisions when you don't know what's going to happen". Join us on this journey and you will, together with us, know what is happening.

To our authors, reviewers and readers, I must say it was a pleasure making your acquaintance. We look forward to a continued our symbiotic relationship.

EDITORIAL

Outbreaks of Enteric Disease in Zambia

By P Kelly

Blizard Institute, Barts & The London School of Medicine, Queen Mary University of London, London UK

Correspondence: Paul Kelly (m.p.kelly@qmul.ac.uk)

Citation style for this article:

Kelly P. Outbreaks of Enteric Disease in Zambia. 2017;2(1); pp4-5.

This issue, featuring some papers and a review on outbreaks of enteric disease, is a timely reminder that complacency is not a good strategy, and that we need to be watchful for outbreaks so that they can be reported and controlled. Typhoid is a case in point. Some years ago, I supervised a MPH student who wrote a dissertation on the acceptability of typhoid vaccine. The overwhelming response from physicians was that typhoid wasn't much of a problem in Zambia. Mothers of children were likewise unaware of typhoid as a potential problem, with 22% of respondents saying they had never heard of it (unpublished data). Surgeons, however, have for many years dealt with a steady trickle of bowel perforations, one of the severe consequences of typhoid. The evidence was there if we had we listened to the health care providers talking about their daily work. Now we are seeing the consequences of our unprepared state, with typhoid outbreaks occurring on a regular basis.

We have a national programme of rotavirus immunisation so we can congratulate the Ministry of Health heartily on this good work. The problem for surveillance and prevention of diarrhoeal disease is that there are so many enteric infections which may be responsible. We need to focus on those infections with the largest attributable risk or the worst impact on outcomes; rotavirus is responsible for 20-25% of childhood diarrhoea [1]. We also need to monitor the effects of our interventions, such as monitoring rotavirus vaccine effectiveness, and strategies are in place for that. Other high priority enteric infections include cholera, which causes large outbreaks and great anxiety among the public and cryptosporidiosis which is less obvious but which has a disproportionate effect on long-term health of children and people with AIDS.

Currently Zambia is experiencing an outbreak of cholera in Lusaka district. Close to 4000 cases including adults and children with 80 deaths have been recorded since 6th October 2017[2]. Many other countries within Africa and beyond are experiencing cholera outbreaks affecting atleast 47 countries across the globe, resulting in an estimated 2.9 million cases and 95,000 deaths per year worldwide [3]. On a positive note, the Global Task Force on Cholera Control (GTFCC) which brings together partners from around the world to support affected countries in mitigating the cholera outbreaks experienced has launched an effective platform hosted by Who through a strategy titles 'Ending Cholera: A Global Road Map to 2030'. The goal is to reduce cholera deaths by 90% ad if all stakeholders remain committed up to 20 countries affected

would eliminate Cholera by 2030. Zambia has endorsed this strategy and is putting in place activities to actualise the goal [4].

There are active research programmes in Zambia on rotavirus, cholera and cryptosporidiosis, at CIDRZ, in UTH and at UNZA vet school. More could be done, and we should encourage all front-line health care workers to be vigilant for those odd patterns of consultation that may herald outbreaks or just changing epidemiology. Such patterns might include unusually high numbers of patients presenting with diarrhoea, diarrhoea in unusual age groups, etc. We must also bear in mind that not all enteric infections cause diarrhoea: typhoid for example, is primarily a febrile illness, and hepatitis A and E which present with jaundice

are acquired through the gut. We should also learn from the very unusual outbreak of enterohaemorrhagic *E. coli* infection in Germany in 2011[5] that primarily affected adults, not children. Vigilance is the key. Be watchful!

References

- Xuan-Yi Wang, Zhi-Yi Xu, Lorenz von Seidlein, Ying-Lin Zhang, Shou-Jun Zhao et.al.; Incidence of Diarrhea Caused by Rotavirus Infections in Rural Zhengding, China: Prospective, Population-Based Surveillance. JID. 2005; 192(1): S100 – S105. https://doi.org/10.1086/431507
- 2.Unpublished MoH situational reports, October 2017 to January 2018
 3.Ali M, Nelson AR, Lopez AL & Sack DA. Updated Global Burden of Cholera in Endemic Countries. PLoS Negl Trop Dis 2015,9(6): e0003832. https://doi.org/10.1371/journal.pntd.0003832
- 4.World Health Organisation. URL: http://www.who.int/cholera/en/. Accessed 28 January 2018.
- 5.Frank C, et al. Epidemic profile of Shiga-Toxin–producing Escherichia coli O104:H4 outbreak in Germany — preliminary report. New Eng J Med 2011; 365: 1771-1780

REVIEW

A review of the epidemic-prone enteric diseases in Zambia: cholera, typhoid fever and bacterial dysentery

By S Siziya

Michael Chilufya Sata School of Medicine, Copperbelt University, Ndola, Zambia.

Correspondence: Seter Siziya (ssiziya@gmail.com)

Citation style for this article:

Siziya S. A review of the epidemic-prone enteric diseases in Zambia: cholera, typhoid fever and bacterial dysentery. 2017;2(1); pp6-11.

Enteric diseases caused by bacteria that are epidemic prone in Zambia include cholera, typhoid fever and dysentery. Common signs and symptoms of enteric diseases include diarrhoea and vomiting. There is scant information of the occurrence of enteric diseases other than cholera. Cholera is generally pandemic in Zambia with the most recent major outbreaks having occurred in 1990, 1999 and 2004. Cholera outbreaks mainly occurred in peri-urban areas of Lusaka, Luapula, Southern and Copperbelt provinces. Case fatality rates for cholera varied with epidemics indicating different responses to cholera epidemics. Factors that increase the risk factors for cholera include consumption of raw vegetables and contact with cholera cases. Factors that decrease the risk include hand washing with soap, availability of safe drinking water, and sanitation. Addition of oral cholera vaccines to strategies to control epidemics may curtail a seemingly explosive epidemic. More research is required on typhoid fever and dysentery outbreaks to monitor their occurrence and establish their risk factors for the purposes of designing interventions to prevent or curtail the epidemics. Improvement in health information systems to ensure timely, accurate, and complete reporting is needed. Ultimately, outbreaks of bacterial enteric diseases in Zambia can only be controlled once all Zambians have access every day to safe drinking water

Introduction

Enteric diseases caused by bacteria that are epidemic prone in Zambia include cholera, typhoid fever and dysentery [1]. Infections enter the body through the mouth. These diseases are contracted through contaminated food and drink, being in contact with contaminated faeces or vomitus [2]. Common signs and symptoms of enteric diseases in Zambia include diarrhoea and vomiting [3].

Cholera

The World Health Organization has documented the profile of cholera in Zambia from 1978 to 2010 [4]. Cholera was first reported in 1977 with major outbreaks occurring in 1990 and 1999 that lasted for 3 and 4 months, respectively. Another cholera outbreak occurred in 2004 that lasted until 2010 (Figure 1) and spilled over to 2012 (Figure 2), thus becoming pandemic. From 2013 to 2016, no cases of cholera were documented by WHO [5-8], although an outbreak of cholera occurred in Chibombo district between 9 February and 20 March 2016 in which 23 suspected and confirmed cases were seen with no deaths at the district health facility. Eight of the 18 stool cultures were positive for Vibrio cholerae [9]. Another outbreak occurred in Lusaka district between 5 February and 24 April 2016 in which 1079 cases and 20 deaths (case fatality rate [CFR] = 1.9%) were recorded. Yet another epidemic was recorded in Kapiri Mposhi district between 11 September and 21 October 2016 with 27 cases and 2 deaths (CFR = 7.4%) [10]. The same epidemic was documented for the period February to 31 May 2016 in which 1054 cases were reported with a CFR of 1.9% [11]. During the same epidemic, 1139 cases and 20 deaths (CFR = 1.8%) were reported during epidemiological weeks 5 to week 24 [12]. The reduction in the number of cases may partly have

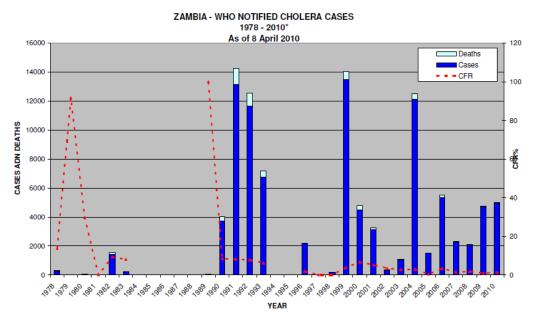


Figure 1 Distributions of number of cholera cases and case fatality rates by year: 1978-2010. Source: WHO. Global Task Force on Cholera Control. Cholera country profile: Zambia. URL: http://www.who.int/cholera/countries/ZambiaCountryProfile2011.pdf

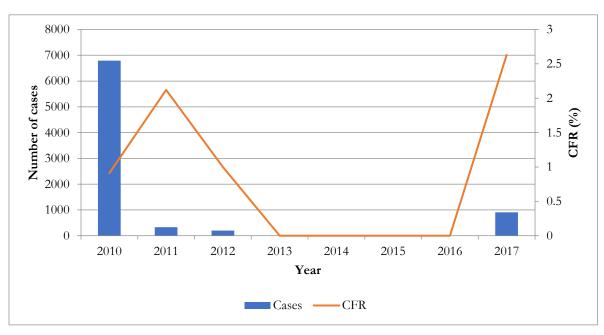


Figure 2 Distributions of number of cholera cases and case fatality rates by year: 2010-2017

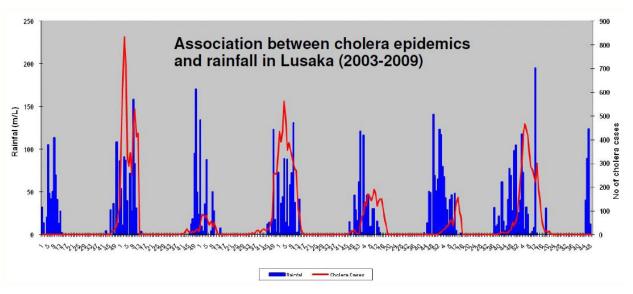


Figure 3 Distributions of number of cholera cases and rainfall patterns: 2003-2009. Source: WHO. Global Task Force on Cholera Control. Cholera country profile: Zambia. URL: http://www.who.int/cholera/countries/ZambiaCountryProfile2011.pdf

been due to different t periods. It is surprising that WHO did not document the epidemic that occurred in 2016 given that WHO partly supported provision of cholera vaccine to curb the 2016 epidemic in its early stage in April 2016 [12]. It is likely that although no cholera cases were reported by WHO in the other years (2013-2015), there could have been epidemics in these years as well. In 2011, out of 330 cases, 7 died (CFR = 2.12%) and in 2012, 2 out of 198 cases died (CFR = 1.0%) [13]. Case fatality rate of <1% may indicate good management of cases [14]. Cholera deaths result from severe dehydration and can usually be prevented by administration of large amounts of fluid that can be administered orally. Differences in case fatality rates in Zambia may partly be due to differences in amounts of fluids given to patients and how quickly patients had access to this treatment.

The current outbreak in Lusaka district was reported on 6 October 2017 to the WHO [15]. Initially, between 28 September and 7 December 2017, 547 cases including 15 deaths (CFR = 1.8%) were reported. By 18 December 2017, a total of 908 cases were reported with a CFR of 2.6%

[16]. This rise in number of cases and CFR, prompted the Ministry of Health to institute a quick response to contain the outbreak at an early stage by forming a response coordination team comprising senior members of staff in line ministries (political will and leadership), Lusaka Water and Sewerage Company, Lusaka City Council, Disaster Management and Mitigation Unit, Defence Forces, WASH and health promotion teams, National Epidemic Preparedness, Prevention, Control and Management committee and the Zambia National Public Health Institute; resource mobilisation through partners and private organizations, surveillance and case management; strengthening laboratory facilities; health promotion and communication and instituting an oral cholera vaccine campaign. This action is in line with the three strategic axes for The Global Roadmap to 2030 which are Axis 1: Early detection and quick response to contain outbreaks at an early stage; Axis 2: A multisectoral approach to prevent cholera in hotspots in endemic countries; and, Axis 3: An effective mechanism of coordination for technical support, resource mobilisation, and partnership at the local and global level [17]. To reduce CFR by maximizing supplies, equipment and human resource, the Heroes National Stadium was converted into a cholera treatment hospital with 500 bed capacity with room for expansion. Case fatality rates seen in Figure 1 of as high as 100% were based on small numbers of reported cases. Yearly case fatality rates since 2010 have been around 1%, except in 2011 when a CFR of 2.1% was reported (Figure 2). Between 1996 and 2004, 69 strains of V. cholerae serogroup O1 were isolated in Zambia [18]. These different strains may respond differently to treatment. Mwansa et al [19] reported V. cholerae serogroup O1 to have had a low level of resistance to tetracycline during 1990-1991 (2-3%) that increased to 95% in subsequent epidemics in which resistance patterns of over 70% were reported for chloramphenicol (78%), doxycycline (70%) and trimethoprim-sulphamethoxazole (co-trimoxazole) (97%).Geographically, occurred in peri-urban areas of Lusaka, Luapula, Southern and Copperbelt provinces between epidemiological weeks 40-45 of the year and weeks 20-25 of the following year [20]. WHO observed a very strong association between rainfall and cholera cases [4] as shown in Figure 3 and also noted that outbreaks usually started during the month of October and ended between mid-May/beginning of June of the following year. Luque Fernández et al [21] found that an increase in temperature 6 weeks prior to the beginning of the rain season followed by an increase in rainfall 3 weeks later beyond expected levels, led to an increase in the number of cases of cholera within the following 3 weeks. Phiri et al [22] also reported an association between cholera cases and rainfall patterns. Factors that increase the risk of getting cholera included consumption of raw vegetables [23], contact with cholera case [24], absence of latrine [25], unsafe main source of drinking water [22] and increased number of people in a household [22]. Protective factors for cholera were consumption of kapenta [23], presence of drainage systems surrounding houses [25], treatment of drinking water [24-26] and hand washing with soap [3,24-26].

A new vaccine produced by (Shantha Biotechnics, Hyderabad, India) as a single dose rather than a two-dose was administered to 576,043 people over the age of 1 year living in 9 townships of Lusaka at greatest risk for cholera in April 2016. Epidemics call for desperate measure and as such, although the vaccine was not registered in Zambia, the Ministry of Health approved its emergency use. The administrative coverage was 73.4%. After the vaccination campaign, few cholera cases were reported and there was no evidence of the disease spreading within the vaccinated areas [12]. However, the outcomes of the intervention were unclear.

In response to the current epidemic of 2017-2018, a cholera vaccination campaign using Euvichol (EuBiologics Co., Ltd, South Korea) oral cholera vaccine was launched on 10 January 2018 in the hot spots of Lusaka, namely: Chipata and Kanyama sub-divisions [27]. Although the vaccine is supposed to be given as two doses two weeks apart, only one dose was given. It remains to be seen what impact this vaccination campaign will have on the epidemic. However, in a modelling study, the single dose was found to avert more cases and deaths than a standard two-dose campaign in Zimbabwe, Haiti and Guinea [28].

Among the enteric diseases (cholera, dysentery and typhoid fever), cholera has been well documented. It is important that interventions to prevent cholera should be evidence based. The new Zambia National Public Health Institute (ZNPHI) should have a strong research team to provide such evidence and an effective information system to provide information timely to stakeholders for prevention purposes. ZNPHI should coordinate research on cholera during epidemics. However, some important, countryrelevant information has been obtained uncoordinated research that could be used in controlling or preventing cholera. Given limited resources, targeted interventions to prevent cholera epidemics should consider these factors that have been shown to be associated with cholera in Zambia, in particular covering peri-urban areas of Lusaka, Luapula, Southern and Copperbelt provinces and fishing camps. These findings suggest that cholera may be effectively controlled using a multidisciplinary integrated approach that may include provision of clean water, adequate sanitation, health promotion covering personal and environmental hygiene, passive and active surveillance of cholera cases, and the treatment of cases. Provision of clean water and sanitation are vital in the prevention of cholera which could be done by partly avoiding contamination of drinking water by laying the drinking water and waste water systems far apart and partly by avoiding sinking of boreholes in an area with many septic tanks. Provision of piped water from a source far away from the septic tanks is a cheaper option to providing safe drinking water in the long run than treating water at household level

Bacteria dysentery

There is little documentation of dysentery epidemics in Zambia. In June 1990, an outbreak of *Shigella dysenteriae* Type 1 dysentery was reported in a prison in western Zambia and by December 1991 a total of 24,774 cases had been recorded with a case fatality rate of 10.2% [29]. There are no other documented epidemics.

Factors associated with dysentery included: recent contact with a person with dysentery, a family member with preceding dysentery, households sharing their latrine with other households, obtaining drinking water only by hand-dipping and eating cooked relish (a cooked meat or vegetable dish) purchased from a vendor [30].

Among the *Shigella* species, *S. flexneri* was resistant to ampicillin and co-trimoxazole (both 100%), followed by chloramphenicol and streptomycin (both 83.8%). *S. dysenteriae* was resistant (100%) to both ampicillin and co-trimoxazole. *S. bodii* was 100% resistant to ampicillin, co-trimoxazole and chloramphenicol [31]. The importance of

monitoring antibiotic sensitivity patterns cannot be overemphasised for better management of cases.

Clearly, there is scanty information on dysentery. Outbreaks of dysentery can only be efficiently prevented or curtailed if information to design interventions is available. As a notifiable disease, it must be correctly and timely reported.

Typhoid fever

Few typhoid fever epidemics have been documented in Zambia. Bisseru [32] reported an outbreak of typhoid fever in a girls' camp in Zambia. A more recent outbreak of typhoid fever was reported in 2010-2012 that affected 2,040 patients, with a fatality rate of 0.5% [33].

Piped water supply was associated with a reduction in the incidence of typhoid fever in Lusaka, Zambia [34]. Provision of safe piped water is critical in the prevention of typhoid fever as well as curtailing the epidemic.

Regular monitoring of antibiotic sensitivity patterns is vital in good management of cases. Hendriksen et al [33] reported that most (83.0%) isolates were multidrug resistant (MDR). In another study conducted by Kalonda et al [35], all the fifty *Salmonella* Typhi were resistant to sulphamethoxazole, ampicillin, trimethoprim and cotrimoxazole, and concluded that multidrug resistant *Salmonella* Typhi was emerging in Lusaka.

Tracking typhoid fever epidemics would provide information on its prevention and further studies should be conducted on risk factors for typhoid fever to guide targeted interventions in Zambia.

Conclusion and recommendation

Tracking of cholera epidemics and establishment of its risk factors have been satisfactory. At the national level, the health information system should be improved to document typhoid fever and dysentery epidemics. ZNPHI should establish a strong research department to determine risk factors for typhoid fever and dysentery that can be used

in designing interventions to prevent or curtail typhoid fever and dysentery epidemics

References

- 1.Ministry of Health [Zambia], World Health Organization, Centers for Disease Control and Prevention. Technical guidelines for integrated disease surveillance and response in Zambia. Adapted from the 2010 2nd edition. Technical guidelines for integrated disease surveillance and response in the African region developed by WHO AFRO and CDC. August 2011, version 1.3. Lusaka, Zambia.
- 2.CDC. Division of Foodborne, Waterborne, and Environmental Diseases (DFWED). CDC's lead epidemiology and surveillance group for tracking pathogens and identifying sources for bacterial enteric (intestinal) infections transmitted by food and other routes. URL: https://www.cdc.gov/ncezid/dfwed/edeb/index.html.
- Centers for Disease Control and Prevention (CDC). Cholera epidemic associated with raw vegetables--Lusaka, Zambia, 2003-2004. MMWR Morb Mortal Wkly Rep. 2004;53(34):783-6.
- WHO. Global Task Force on Cholera Control. Cholera country profile: Zambia. URL: http://www.who.int/cholera/countries/ZambiaCountryProfile2011. pdf.
- 5. WHO. Wkly Epidemiol Rec 2014;89(31):345-56.
- 6. WHO. Wkly Epidemiol Rec 2015;91(40):517-44.
- 7. WHO. Wkly Epidemiol Rec 2016;91 (38):433-40
- 8. WHO. Wkly Epidemiol Rec 2017;92(36):521-36...
- Chirambo RM, Mufunda J, Songolo1 P, Kachimba JS, Vwalika B. Epidemiology of the 2016 cholera outbreak of Chibombo district, central Zambia. Med J Zambia 2016;43(2):61-3.
- 10.Murebwa-Chirambo R, Mwanza R, Mwinuna C, Mazaba ML, Mweene-Ndumba I, Mufunda J. Occurrence of cholera in Lukanga fishing camp, Kapiri-mposhi district, Zambia. Health Press Zambia Bull 2017;1(1): 55-61.
- 11.Kabwe P, Moonde L, Gama A, Hadunka F, Sinyangwe N, Kateule E, et al. Descriptive characterization of the cholera outbreak In Lusaka District, 2016. Health Press Zambia Bull. 2017;1(2):35-44.
- 12.Poncin M, Zulu G, Voute C, Ferreras E, Mbwili-Muleya C, Malama K, et al. Implementation research: reactive mass vaccination with single-dose oral cholera vaccine, Zambia. Bulletin of the World Health Organization. URL:
- http://www.who.int/bulletin/online_first/en/.
- 13.WHO. URL: www.who.int/wer/2013/wer8831.pdf?ua=1.
- 14.WHO. WHO Report on Global Surveillance of Epidemic-prone Infectious Diseases. WHO/CDS/CSR/ISR/2000.1. Geneva, WHO.
- 15.WHO. Emergencies preparedness, response. Cholera Zambia. Disease Outbreak News 11 December 2017. URL: http://www.who.int/csr/don/11-december-2017-cholera-zambia/en/.
- 16.Hamoonga R, Mukonka VM, Kapata N, Sinyange N, Kapaya F, Moraes A. A summary report of cholera outbreak in Lusaka district as of 18th December 2017. Health Press Zambia Bull 2017;1(12):8-10
- 17.Global Task Force on Cholera Control. Ending cholera: a global roadmap to 2030. URL:
- http://www.who.int/cholera/publications/global-roadmap.pdf?ua=1.
- 18.Bhuiyan NA, Nusrin S, Ansaruzzaman M, Islam A, Sultana M, Alam M, et al. Genetic characterization of Vibrio cholerae O1 strains isolated in Zambia during 1996–2004 possessing the unique VSP-II region of El Tor variant. Epidemiol Infect 2011;140(3):510-8.
- 19.Mwansa JC, Mwaba J, Lukwesa C, Bhuiyan NA, Ansaruzzaman M, Ramamurthy T, et al. Multiply antibiotic-resistant Vibrio cholerae O1 biotype El Tor strains emerge during cholera outbreaks in Zambia. Epidemiol Infect 2007;135(5):847-53.

- 20.Olu O, Babaniyi O, Songolo P, Matapo B, Chizema E, Kapin'a-Kanyanga M, et al. Cholera epidemiology in Zambia from 2000 to 2010: implications for improving cholera prevention and control strategies in the country. East Afr Med J 2013;90(10):324-31.
- 21.Luque Fernández MA, Bauernfeind A, Jiménez JD, Gil CL, El Omeiri N, Guibert DH. Influence of temperature and rainfall on the evolution of cholera epidemics in Lusaka, Zambia, 2003-2006: analysis of a time series. Trans R Soc Trop Med Hyg 2009;103(2):137-43.
- 22.Phiri P, Nzala SH, Baboo KS. Number of people in household and source of drinking water: Factors associated with the recurring cholera outbreaks in Sinazongwe district of southern Zambia. Med J Zambia 2015;42(4):184-92.
- 23.Dubois AE, Sinkala M, Kalluri P, Makasa-Chikoya M, Quick RE. Epidemic cholera in urban Zambia: hand soap and dried fish as protective factors. Epidemiol. Infect 2006;134:1226–1230; Centers for Disease Control and Prevention (CDC). Cholera epidemic associated with raw vegetables--Lusaka, Zambia, 2003-2004. MMWR Morb Mortal Wkly Rep. 2004;53(34):783-6.
- 24.Matapo B, Chizema E, Hangombe BM, Chishimba K, Mwiinde AM, Mwanamwalye I, et al. Successful multi-partner response to a cholera outbreak in Lusaka, Zambia 2016: A case control study. Med J Zambia 2016;43(3):116 22.
- 25.Sasaki S, Suzuki H, Igarashi K, Tambatamba B, Mulenga P. Spatial analysis of risk factor of cholera outbreak for 2003–2004 in a periurban area of Lusaka, Zambia. Am. J. Trop. Med. Hyg 2008;79(3):414–21.
- 26.Dubois AE, Sinkala M, Kalluri P, Makasa-Chikoya M, Quick RE. Epidemic cholera in urban Zambia: hand soap and dried fish as protective factors. Epidemiol Infect 2006;134:1226–30.
- 27.WHO. Africa region. WHO supports the immunization of 1 million people against cholera in Zambia. URL: http://afro.who.int/news/who-supports-immunization-1-million-people-against-cholera-zambia.
- 28.Azman AS, Luquero FJ, Ciglenecki I, Grais RF, Sack DA, Lessler J. The impact of a one-dose versus two-dose oral cholera vaccine regimen in outbreak settings: A modeling study. PLoS Med 2015;12(8):e1001867.
- 29.van der Hoek W, van Oosterhout JJ, Ngoma, M. Outbreak of dysentery in Zambia. S Afr Med J 1996;86:93-4.
- 30. Tuttle J, Ries AA, Chimba RM, Perera CU, Bean NH, Griffin PM. Antimicrobial-resistant epidemic Shigella dysenteriae type 1 in Zambia: modes of transmission. J Infect Dis 1995;171(2):371-5.
- 31.Chiyangi H, Muma JB, Malama S, Manyahi J, Abade A, Kwenda G, et al. Identification and antimicrobial resistance patterns of bacterial enteropathogens from children aged 0–59 months at the University Teaching Hospital, Lusaka, Zambia: a prospective cross sectional study. BMC Infect Dis 2017;17:117.
- 32.Bisseru B. Typhoid (enteric) fever--an outbreak in a girls camp in Zambia. Med J Zambia 1984;18(3):36-8.
- 33.Hendriksen RS, Leekitcharoenphon P, Lukjancenko O, Lukwesa-Musyani C, Tambatamba B, Mwaba J, et al. Genomic signature of multidrug-resistant Salmonella enterica serovar Typhi isolates related to a massive outbreak in Zambia between 2010 and 2012. J Clin Microbiol 2015;53:262–72.
- 34.Bahl MR. Impact of piped water supply on the incidence of typhoid fever and diarrhoeal diseases in Lusaka. Med J Zambia 1976;10(4):98-9
- 35.Kalonda A, Kwenda G, Musyani CL, Samutela MT, Mumbula M, Kaile T, et al. Characterization of antimicrobial resistance in Salmonella enterica Serovars Typhi and paratyphi B in Zambia. J Med Sci Tech 2015;4(1):3-12

OUTBREAK REPORT

Cholera Outbreak in Chienge and Nchelenge Fishing Camps, Zambia, 2017

A Gama^{1, 2, 3}, P Kabwe ^{1,2}, F Nanzaluka ^{1,2}, N Langa^{1,2}, LS Mutale ^{1,2}, L Mwanamoonga^{2,4,5}, G Moonga⁵, G Chongwe⁵, N Sinyange^{1, 2,3}

- 1. Field Epidemiology Training Programme, Lusaka, Zambia
- 2. Ministry of Health, Government of the Republic of Zambia, Lusaka, Zambia
- 3. Zambia National Public Health Institute, Lusaka, Zambia
- 4. University Teaching Hospital, Lusaka, Zambia
- 5. University of Zambia, Lusaka, Zambia

Correspondence: Angela Gama (angelagama13@yahoo.com)

Citation style for this article:

Gama A, Kabwe P, Nanzaluka F et al. Cholera Outbreak in Chienge and Nchelenge Fishing Camps, Zambia, 2017. Health Press Zambia Bull. 2017;2(1), pp12-19.

On the 15th of February, 2017, the first case of suspected cholera was reported from Chienge district which has fishing camps with its neighbor district Nchelenge. We investigated the extent, the serotype of the *Vibrio cholera* and possible sources of exposure of the outbreak.

A suspected cholera case was defined as any resident from Chienge or Nichelenge who presented with acute watery diarrhea from February 14th through April 4th 2017. A Confirmed cholera case was defined as a suspected cholera case in which *Vibrio cholerae* O1 or O139 was isolated through culture. Rectal swabs from three case-patients were collected for culture. We interviewed suspected case-patients using a semi structured questionnaire. Twelve water samples were tested for fecal contamination.

A total of 73 suspected cases and 3 confirmed cases were identified. Majority (76%) of the cases were from Chienge district. The mean age was 24 years. *Vibrio cholera 01*, serotype Inaba was isolated. Of the 76 case-patients, 60 were interviewed. 27 percent of the suspected cases interviewed did not use soap for hand washing while 75% used stagnant water for hand washing. 7 of the 12 water points were contaminated with fecal coliforms. There is need to provide access to safe water and sanitation and effect social behavior change interventions on hygiene practices in Chienge and Nchelenge districts.

Background

Each year, there are 1.3 to 4.0 million cases of cholera, and 21, 000 to 143, 000 deaths worldwide [1]. The Sub-Saharan Africa accounts for 60% of the cases [2]. In southern Africa, 4 countries in 2010 reported 16, 330 cholera cases of which 41.6% were from Zambia [3]. Cholera has continued to be a public health problem in Zambia, in 2016 there were a total of 1,179 cumulative cases of cholera reported [4]. Most (73%) of the cholera outbreaks in

Zambia have been reported in Lusaka province followed by Luapula province (7%) [3].

Nchelenge had recorded a total of 1, 155 cumulative cases of cholera from 2002 to 2007 [5]. Chienge district reported the last outbreak of cholera in 2013, with 217 case-patients and seven deaths. Since 2013, there have been no record of cholera outbreak in Nchelenge and Chienge districts, however, on the 15th of February, 2017 an acute diarrhea and vomiting illness, suspected to be cholera and the index case, was reported at Kabwe Rural Health Centre in Chienge district. The index case was a female 24-year-old who tested positive for Cholera using a Rapid Diagnostic Test (RDT). By 27th March, 2017, a total of 68 patients were admitted for suspected cholera in Chienge and Nchelenge districts. The Zambia Field Epidemiology Training Program was called by Ministry of Health to support the provincial office to control the cholera outbreak. We investigated the extent of the outbreak, the serotype and antibiotic susceptibility of the Vibrio cholerae, and possible sources of exposure.

Methods

Luapula province is located in the northern part of Zambia bordering the Democratic Republic of Congo. Chienge and Nchelenge are neighboring districts in Luapula province located in the valley along Luapula River and Lake Mweru. These districts are relatively rural and the main occupation for the population is subsistence farming and fishing. People usually move to fishing camps during the fishing period [5]. There is an influx of traders into these districts coming from all over the country and neighboring countries to buy fish and other farming produce. Kefulwa fishing camp boarders between Chienge and Nchelenge districts. Kafulwe Rural Health Centre is located in Kafulwe village on Lake Mweru about three kilometers west of Chienge-Nchelenge road.

We reviewed medical records from Kafulwe and Kabwe Rural Health Centres for suspected and confirmed cases. Information regarding date of onset of symptoms, signs, symptoms and outcome was collected and used to update the line list. We defined a suspected cholera case as any resident from Chienge or Nchelenge presenting with acute watery diarrhea from February 14th through April 4th, 2017. A Confirmed cholera case was defined as a suspected cholera case in which *Vibrio cholerae* O1 or O139 was isolated through culture. We interviewed all the casepatients that we could locate using a semi-structured questionnaire. The questionnaire included questions on demographics, cholera risk factors, sources of drinking water and knowledge about cholera.

Oral consent was obtained from the participants before administering the questionnaire. We explained the purpose of the interview to the participants and that participation was voluntary. Confidentiality was guaranteed by ensuring that data collected was anonymous and not identifying participant's information by use of codes. Permission was sought to review the records from the Provincial health

officer and district health officer. Ethical approval was obtained post investigation prior to publishing, from the University of Zambia Biomedical Research Ethics Committee (UNZABREC)

We collected three rectal swabs from three suspected cholera patients (before the patients were given antibiotics) who were admitted to Kafulwe Rural Health Centre at the time of the outbreak (2nd April 2017) investigation. The three rectal swabs were transported to the University Teaching Hospital Laboratory in Lusaka, just over a thousand kilometers away. The samples were cultured and serological tests were done using using polyvalent O1 and mono-specific Ogawa and Inaba antisera. Susceptibility to antimicrobial agents namely ampicillin, *salbactam* and septrin was determined by the Kirby–Bauer disk diffusion method and interpreted as recommended by the National Committee for Clinical Laboratory Standards with commercial antimicrobial discs (Oxoid, Basingstoke, UK) [6].

Immediately after the interviews, water samples were collected from water points where the case-patients usually fetched drinking water. The water samples were tested using Hydrogen Sulphide test kit (Visio Technologies, Karnataka, India) to check for possible fecal contamination. Details of the water points, date, and time of sample collection and the name of the collector were indicated on each Hydrogen Sulphide test bottle for identification.

We worked together with the Luapula provincial health team to respond to the outbreak by giving health education and conducting contact tracing for the cholera case-patients that came during the time of the investigation. The health education involved discussions on cholera prevention with the case-patient's family and neighbors. Prophylaxis and health education on personal hygiene was given to contacts of case patients.

Table 1 Demographic Characteristics of Cholera Case-patients From Chienge and Nchelenge Districts, February to April 2017

CHARACTERISTIC	Number (%)		A. A. D. D.	
		Population by Age	Attack Rate Per 100,000 People	
A (V) (v = 70)				
Age (Years) (n=76)				
≥9	12 (16)	119,589	10	
10- 19	18 (24)	73,368	25	
20 – 29	23 (30)	53,582	43	
30-39	12 (16)	44,019		
≥40	11(14)		27	
SEX (N=76)		50,295	22	
Males	51 (67)	167,975	30	
Females	25 (33)	165,106	15	
SYMPTOMS (n =50*)	, ,		10	
Watery Diarrhoea	50 (100)			
Vomiting	32 (64)			
Abdominal Pains	20 (40)			
Fever	8 (16)			
Headache	1 (2)			
EMPLOYMENT STATUS (n =60**)				
Fishermen	36 (60)			
Farmer	14 (23)			
Traders	6 (10)			
Unemployed	4 (7)			
Formal Employment	0 (0)			
EDUCATION (n=60**)				
No Education	19 (32)			
Primary	34 (57)			
Secondary	7 (12)			
Tertiary	0 (0)			
RESIDENCE (n =60**)				
Temporal	5 (87)			
Permanent	53 (91)			
Missing	2 (3)			

Table 2 Attack and Fatality Rate of cholera in Chienge and Nichelenge Districts of Luapula province February - April 2017 (n=76

District	n (%)		Number Fatalities	of	Population	Attack Rate Per 100,000 People	Case Fatality Rate (%)
Chienge	58 (76)		1		141988	41	2
Nchelenge	17 (24)	0	191092		9	0	

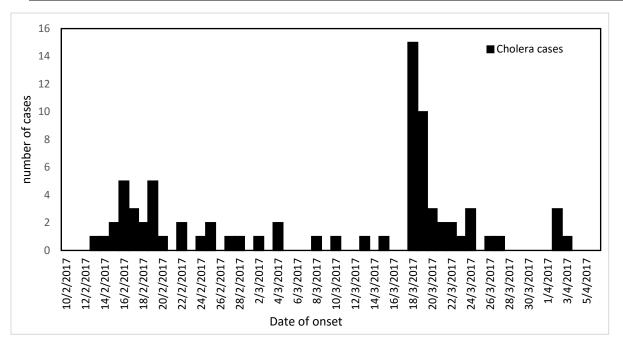


Figure 1 Cholera cases by date of symptom onset in Chienge and Nchelenge district, February – April, 2017 (n=76).

The data were entered and analyzed using Epi Info, Version 7 (CDC, Atlanta, USA). Descriptive statistics were carried out to measure relative frequencies, and percentages of the variables. The Central Statistics Office population projections [7] were used to calculate the attack rate per 100, 000 population. We described the outbreak by time, place and person

Results

Table 3 Knowledge, Attitudes and Practices of the Suspected Cholera cases towards Cholera from Chienge and Nchelenge District of Luapula Province of Zambia, February-April, 2017 (n=60)

Characteristic	Number
	(%)
Ever heard about cholera	
Yes	38 (63)
No	5 (8)
Don't know	12 (20)
Data Missing	5 (8)
How is cholera transmitted*	
By mosquito bites	3 (5)
Drinking contaminated water	26 (43)
Eating contaminated food	34 (57)
Close contact with a cholera	7 (12)
patient	
Airborne	10 (17)
Don't know	17 (28)
Knowledge on prevention*	
Cleaning surroundings	35 (58)
Treatment of water for drinking	28 (47)
Washing hands before eating	40 (67)
Washing hands after using toilets	30 (50)
Washing fruits before eating	11 (18)
Don't know	6 (10)

Table 1 shows attack rate of males (30/100, 000) was twice that of females (15/100, 000). The majority of the casepatients were from Chienge district (76%) which had an attack rate of 4 per 10, 000 population (Table 2). 3 casepatients were confirmed by culture. There was one death recorded in Chienge (case fatality of 2 %). The epi curve showed a propagated cholera outbreak (Figure 2). Table 4 shows Risk factors for the Suspected Cholera cases, of note is that 80% of the respondents reported consuming unsafe water. Health education on prevention of cholera was given to 845 contacts, 55 bottles of chlorine were also distributed.

Laboratory results confirmed *Vibrio cholera 01* isolates, serotype Inaba (from all the 3 samples cultured) sensitive to ciprofloxacin, ampicillin and salbactam and resistant to septrin. Of the 12 samples collected from the water points (shallow wells, boreholes, and a stream) within the affected communities and tested, five boreholes and two wells were contaminated with fecal coliforms

Discussion

The cholera outbreak in Chienge and Nchelenge districts was caused by Vibrio cholera 01, serotype Inaba. Chienge was the most affected than Nchelenge which might have been due to its densely populated fishing camps and trading area on the shores of Lake Mweru. Vibrio cholera 01, Ogawa was reported in the cholera outbreaks in Lusaka in the year 2003, 2004, 2015 and 2016 [8] which was different from what was isolated in Chienge and Nchelenge districts of Luapula province of Zambia. However, Vibrio cholera 01, serotype Inaba is the most common cause of cholera epidemics in other parts of Africa such as Democratic Republic of Congo (DRC), Kenya and Namibia [9, 10, 11]. These findings suggest that the index is likely to have acquired it from the neighboring areas along Lake Mweru in DRC. Among the tested antibiotics, Vibrio cholerae was only resistant to septrin. Complete resistance to septrin has continued in Zambia from the year 2004 to date which

might be due to its continued use for therapy and

Table 4 Risk factors for the Suspected Cholera cases from Chienge and Nchelenge District of Luapula Province of Zambia, February-April, 2017

	Number
	(%)
Where do you buy your food	
Markets	13 (22)
Streets	15 (25)
Do not buy food	32 (53)
Treatment of water*	
Chlorination	11 (18)
Boiling	7 (12)
Do not treat	42 (70)
Residence	
Temporal	5 (8)
Permanent	53 (88)
Missing	2 (3)
Availability of toilets (pit latrines) in their	
homes	
Yes	56 (93)
No	4 (7)
Sources of drinking water for the	
households *	
Stream	21 (35)
Borehole	14 (23)
Shallow well	15 (25)
Lake	10 (18)
Spring	8 (13)
Rain water	2 (3)
Do you wash your hands with soap/ash?*	
With soap	34 (57)
With ash	14 (23)
With nothing	16 (27)
Do you use running water or stagnant	
water?* With running water	13 (22)
With stagnant water	45 (75)
Missing data prophylaxis in other conditions [12].	2 (3)

The results revealed that the attack rate for men was twice that of women which might have been because most of the case-patients were fishermen. Scarcity of toilets and proper sanitation in the fishing camps might have contributed to the fishermen acquiring cholera. This finding was consistent with a study done in Uganda, where Cholera outbreaks were reported as the main cause of morbidity and death in the fishing villages [13]. Studies in Burundi, the DRC and Tanzania have also shown that Cholera outbreaks have been reported in areas and villages on the lakeshores [14]. Cholera outbreaks are common in communities around the lake shores because aquatic environment like lakes are reservoirs for cholera [15]. In addition, studies have also shown that the predisposing factors of cholera outbreaks along the lakeshores include poor sanitation and hygiene, illiteracy and using contaminated lake water [16].

The findings showed that there were knowledge gaps about cholera transmission among the residents of Chienge and Nchelenge districts. Studies have also shown that people who have knowledge and understanding of a risk are likely to adopt preventive measures [18, 19]. Most case-patients did not observe water treatment procedures and proper personal hygiene prior the outbreak which might have contributed to the transmission of cholera from one person to another thus resulting in a propagated outbreak. A study conducted in in 2010 in Nchelenge district also revealed that most (52%) of the respondents did not observe

personal hygiene such as washing hands after using the toilet [5]. A study assessing knowledge, attitudes and practices regarding cholera in South Africa Limpopo area, reported that most people (86%) had knowledge on cholera transmission however, most hygiene practices such as washing hands was not followed [17]

Some water points were found to be contaminated; this may be attributed to the fact that the water sources in this

area were groundwater sources such as shallow wells, springs, streams and wells which are easily contaminated by fecal material [20]. Most outbreaks resulting from contamination of ground water sources such as wells and boreholes with *V. cholera* have been reported in other countries [11, 21]. In most of these outbreaks, an epidemiological link to a contaminated ground water sources has been established [13, 21, 22]. An outbreak of cholera reported among participants at a wedding ceremony in a village in Qazvin, Iran was associated to well water [21]. Approximately 95,531 suspected cases of cholera reported in Zimbabwe in 2008 were linked to drinking contaminated water from boreholes and wells [23].

There were two limitations identified in the investigations. Firstly, only a few specimens were confirmed by culture because the microbiology laboratory in Luapula province was closed for renovations. Therefore, confirmation of the etiology of the outbreak was delayed because specimens had to be transported to the University Teaching Hospital Laboratory in Lusaka for culture which is over a thousand kilometers away from Chienge and Nchelenge. Secondly, an analytical study to determine risk factors for the outbreak was not done. In spite of only confirming 3 out of 76 cases, this report is a record of the serotype and the antimicrobial susceptibility pattern of Vibrio cholera isolated in Luapula province. Additionally, the antimicrobial susceptibility pattern of Vibrio cholera recorded is essential to guide the selection of antibiotics and monitor changing trends in the local isolates of Vibrio cholera. Despite these limitations, this report provides important epidemiological information about the outbreak that happened in this area in 2017, and this information can be used to institute control measures and serve as a reference point for future outbreaks if any.

Providing safe water and proper management of excreta to avoid contamination of other water sources are significant measures to decrease cholera transmission in Chienge and Nchelenge districts. We recommend a health education intervention program to educate people on transmission, prevention and control of cholera with a lot of emphasis on the use of water-treatment procedures. As a short-term measure, introduction of cholera vaccination among the population at risk would be an important step to prevent and control cholera in Chienge and Nchelenge districts as some of the social determinants may take long to be addressed. Finally, joint cross boarder surveillance and response programs between Zambia and the DRC would be essential to decrease cholera transmission in communities along Lake Mweru.

The outbreak of cholera in Chienge and Nchelenge from February 14th through 4th April 2017 was caused by Vibrio cholera 01, serotype Inaba. Poor sanitation and personal hygiene, drinking unsafe water from the shallow wells and boreholes might have been the possible sources of exposure for developing cholera in both Chienge and Nchelenge. We recommend further research on factors associated with cholera outbreaks in Chienge and Nchelenge. The findings suggest the need of continuous sensitization of cholera for the population at risk such as the fishing camps even in the absence of outbreaks. It is strongly recommended that providing safe water and social behavior change communication for the population at risk to improve appropriate hygienic practices and sanitation are important measures that should be taken to reduce cholera transmission in Chienge and Nchelenge district of Zambia.

Competing Interests

The authors declare that they have no competing interests.

Acknowledgements

We thank the Zambia Ministry of Health, National Public Health Institute and the Field Epidemiology coordinators for their support in our investigation. This outbreak was supported in part by funding through the President's Emergency Plan for AIDS Relief (PEPFAR). We thank the provincial health management team, Luapula Province and district health management teams of Chienge and Nchelenge districts for their cooperation.

References

- 1.Ali M, Nelson AR, Lopez AL, Sack DA. Updated Global Burden of Cholera in Endemic Countries. Remais JV, ed. PLoS Neglected Tropical Diseases. 2015;9(6):e0003832. doi:10.1371/journal.pntd.0003832
- 2.World Health Organization. Cholera surveillance and number of cases. Geneva: 2016
- 3.Olu O, Babaniyi O, Songolo P, Matapo B, Chizema E, Kapin'a-Kanyanga M, et al. Cholera Epidemiology in Zambia From 2000 To 2010: Implications for Improving Cholera Prevention and Control Strategies in the Country. East Afr Med J. 2013;90(10):324–31
- 4.UNICEF. Zambia Cholera Outbreak Report. 2016
- Kabita, K., Knowledge, Attitude And Practice Of cholera Outbreaks in Nchelenga District,
- 2010:http://dspace.unza.zm:8080/xmlui/bitstream/handle/12345678 9/3333/kabitakabita0001.PDF?sequence=1
- 6.National Committee for Clinical Laboratory Standards. Performance standards for antimicrobial disk susceptibility tests. NCCLS document M100-S10. Wayne, PA. 2000.
- 7. Sasaki, S., Suzuki, H., Igarashi, K., Tambatamba, B. and Mulenga, P. (2008) 'Spatial Analysis of Risk Factor of Cholera Outbreak for 2003 2004 in a Peri-urban Area of Lusaka, Zambia', 79; 414–421
- 8.Zambia Central statistics office, "2010 census of population and Housing, Population and Demographic projections 2011-2035" Lusaka, 2013
- 9.Miwanda, B., Moore, S., Muyembe, J., Nguefack-tsague, G., Kabangwa, I. K., Ndjakani, D. Y., Mutreja, A., Thomson, N., Thefenne, H., Garnotel, E., Tshapenda, G., Kakongo, D. K., Kalambayi, G. and Piarroux, R. 'Democratic Republic of the Congo'. 2015); 21(5).
- 10.Onyango, D., Karambu, S., Abade, A., Amwayi, S. and Omolo, J. 'High case fatality cholera outbreak in Western Kenya, August 2010', Pan African Medical Journal. 2013; 1–7.
- 11.Smith AM, Keddy KH, De Wee L. Characterization of cholera outbreak isolates from Namibia, December 2006 to February

- 12.Mwansa JCL, Mwaba J, Lukwesa C, Bhuiyan Na, Ansaruzzaman M, Ramamurthy T, et al. Multiply antibiotic-resistant Vibrio cholerae O1 biotype El Tor strains emerge during cholera outbreaks in Zambia. Epidemiol Infect [Internet]. 2007;135(5):847.
- 13.Bwire G, Munier A, Ouedraogo I, et al. Epidemiology of cholera outbreaks and socio-economic characteristics of the communities in the fishing villages of Uganda: 2011-2015. Ryan ET, ed. PLoS Neglected Tropical Diseases. 2017;11(3):e0005407. doi:10.1371/journal.pntd.0005407.
- 14.Nkoko DB, Giraudoux P, Plisnier P, et al. Dynamics of Cholera Outbreaks in Great Lakes Region of Africa, 1978–2008. Emerging Infectious Diseases. 2011;17(11):2026-2034. doi:10.3201/eid1711.110170.
- Smith AM, Keddy KH, De Wee L Characterization of cholera outbreak isolates from Namibia, December 2006 to February 2007. Epidemiology and Infection. 2008;136(9):1207-1209. doi:10.1017/S0950268807009685.
- 16.Lutz C, Erken M, Noorian P, Sun S and Diane McDougald D. Environmental reservoirs and mechanisms of persistence of Vibrio cholera, Frontiers in Microbiology, 2013 doi: 10.3389/fmicb.2013.00375
- 17. Sasaki, S., Suzuki, H., Igarashi, K., Tambatamba, B. and Mulenga, P. (2008) 'Spatial Analysis of Risk Factor of Cholera Outbreak for 2003 2004 in a Peri-urban Area of Lusaka, Zambia', 79; 414–421
- 18.Ncube, A., Jordaan, A., Mabela, B. Assessing the knowledge, attitudes and practices regarding cholera preparedness and prevention in Ga-Mampuru village, Limpopo, South Africa. Jàmbá: Journal of Disaster Risk Studies, 8, jan. 2016.
- 19.Adams, Robert John. "Improving Health Outcomes with Better Patient Understanding and Education." Risk Management and Healthcare Policy 3 (2010): PMC. Web. Dec. 2017, pp. 61–72. 2.
- 20.Tierney, K.J., Lindell, M.K. & Perry, R.W., Facing the unexpected: Disaster preparedness and response in the United States, John Henry Press, Washington, DC. 2001,
- 21. Ranjbar, R., Rahbar, M., Naghoni, A., Farshad, S., Davari, A. and Shahcheraghi, F 'A cholera outbreak associated with drinking contaminated well water', Archives of Iranian Medicine, 2011 14(5), pp. 339–340. doi: 0010.
- 22. Ahmed, S., Bardhan, P. K., Iqbal, A., Mazumder, R. N., Khan, A. I., Islam, M. S., Siddique, A. K. and Cravioto, A. (2011) 'The 2008 cholera epidemic in Zimbabwe: Experience of the icddr,b team in the field', Journal of Health, Population and Nutrition, 29(5), pp. 541–546. doi: 10.3329/jhpn.v29i5.8909.
- 23. Mason PR. Zimbabwe experiences the worst epidemic of cholera in Africa. J Infect Dev Ctries. 2009;3(2):148–51.

19

OUTBREAK REPORT

Typhoid fever outbreak investigation in a malaria endemic community, Solwezi, North-Western province, Zambia, 2017

FD Mwansa^{1,2,3}, A Gama^{1,2,3}, F Kapaya^{1,2,3}, E Yard^{1,4}, R Kumar^{1,4}, G Chongwe^{1,3}, N Sinyange^{1,2}

- 1. Field Epidemiology Training Programme, Lusaka, Zambia
- 2. Ministry of Health, Government of the Republic of Zambia.
- 3. School of Public Health, Lusaka, University of Zambia.
- 4. U.S. Centers for Disease Control and Prevention (CDC) Zambia.

Correspondence: Francis Dien Mwansa (<u>DrFrancis.Mwansa@MOH.gov.zm</u>)

Citation style for this article:

Mwansa FD, Gama A, Kapaya F et al. Typhoid fever outbreak investigation in a malaria endemic community, Solwezi, North-Western province, Zambia, 2017. Health Press Zambia Bull. 2017;2(1); pp20-28.

On 10th March 2017, the Zambia Ministry of Health received media reports of a suspected typhoid outbreak in North-western Province, including two deaths. We investigated to confirm the outbreak, aetiology, and mode of transmission, and to devise control measures.

We reviewed patient and laboratory records and interviewed suspected casepatients using a structured questionnaire. A suspected case was anyone presenting with fever and either a headache or abdominal pains for at least three days, and may be associated with one or more of the following: diarrhoea, vomiting, constipation, and weakness from 20th December 2016 to March 17th 2017 in Luamala Area of Solwezi District in North-Western province. Stool samples (n=11) were collected for culture, and malaria rapid diagnostic tests were done on all patients. The five water wells in the area were subjected to total and faecal coliform analyses. Data were cleaned using Epi-Info version 7, and analysed descriptively using Stata 13.

We identified 28 suspected case-patients (Median age(IQR): 13 years, Interquartile range (8-15 years). Fever (100%), headache (89%), and abdominal pain (71%) were most common; 86% tested positive for malaria. Six cases (including two deaths) came from a single household. The epidemic curve suggested a continuous source. Most suspected case-patients (70%) collected water from a single well. Residents practiced open defecation. Most wells (80%) had faecal and total coliform contamination. Two patients' stool sample cultures yielded Salmonella Typhi and Salmonella Paratyphi.

The results suggest a typhoid outbreak. Water contamination might have contributed. In response, local health authorities were urged to continue implementation of health education, and decontamination of the toilets and wells. Malaria is endemic in this region (as in most parts of Zambia), and because early symptoms between the two diseases are similar, typhoid diagnosis was delayed. During a typhoid outbreak, patients from the affected area presenting with fever should be tested for typhoid.

Introduction

Typhoid fever is an epidemic-prone disease caused by a gram-negative bacterium called Salmonella Typhi and Salmonella Paratyphi. Typhoid is a resultant disease that ranges clinically from the common Salmonella gastroenteritis (diarrhoea, abdominal cramps, and fever) to enteric fevers (including typhoid fever) which are lifethreatening febrile systemic illnesses requiring prompt antibiotic therapy, and at times surgery, particularly when a bowel perforation occurs [8]. The disease in sub-Saharan African is complicated by the endemic nature of malaria [16]. Patients presenting with fever may initially be presumed to have malaria. Interpretation of the symptomatology, therefore, needs a high index of suspicion.

On 10th March 2017 the media reported an outbreak of diarrhoea and headache with high-grade fever in the Luamala area of Solwezi district with two deaths. The district health office (DHO) within a week set up a medical camp in Luamala area to provide treatment and sent severe

cases to Solwezi General Hospital. Like most parts of the country, malaria is endemic in the area, and the 2016 malaria prevalence in Northwestern Province was 22.6%. All but five of the reported cases, at that time, had received antibiotics for the fever. Five of them did not respond to the antibiotics and antimalarials.

Luamala is a remote area situated 45 kilometres south-east of the municipal town of Solwezi. The area is not well connected to the town due to a untarred road and poor mobile network connectivity. Approximately 4,800 people, mostly adults between the age of 20-45 years, and children under 12 years of age reside in this area with very limited facilities of water, food, electricity, health care, and other social amenities [4].

Three Zambia Field Epidemiology Training Programme (ZFETP) residents and a Public Health Specialist from the Ministry of Health joined the provincial rapid response team on 12th March 2017 to conduct an outbreak investigation together with the DHO. By this date, 19 reported cases of typhoid were reported in Solwezi.

Our objectives were to investigate the extent of the outbreak, confirm the aetiology of the outbreak, describe the outbreak in time, person and place, hypothesise on the possible sources of exposure, and to devise appropriate control measures.

Methods

We reviewed line lists of patients diagnosed with suspected typhoid fever at Solwezi General Hospital as well as Luamala Health Centre, and cases of typhoid fever reported to health workers to retrospectively identify suspected cases. From March 12, 2017, suspected cases were identified prospectively through patient interviews and implementation of an active surveillance system. Active surveillance was conducted from March 12, 2017 to April 30, 2017 using a structured case surveillance form. Health Centre staff were asked to complete a surveillance form on

patients meeting the suspected case definition, and to then update the line list and epidemic curve accordingly.

We defined a suspected case as any person presenting with fever (38°C and above) and either a headache or abdominal pains for at least three days, and may be associated with any of the following; diarrhoea, vomiting, constipation, and weakness from 20th December 2016 to 21st March 2017 in Luamala Health Centre Catchment Area. A period three times the incubation period was chosen to determine the baseline incidence prior to the outbreak. A confirmed case had S. Typhi or paratyphi isolated from their blood or stool. We conducted hypothesis-generating interviews, then interviewed suspected case-patients with a standard typhoid fever questionnaire which captured demographics, clinical history, contacts, and possible risk factors (foods eaten, participation in traditional practices, source of drinking water, contact with others suspected to have had the same illness, and attendance at community events).

We used a checklist (which captured toilet information presence, use and proximity to water points, presence/absence of open defecation and disposal methods where no toilets existed, et cetera) to assess the environment and homes of the participants and to assess the risks and outbreak preparedness of the community. Records of patient notes were also reviewed to obtain information on symptoms at presentation, as well as on case management.

Portalab was used to analyse water chemically for faecal coliforms and total coliforms. Water samples were collected from all the five sources available in the area in the morning on the same day as interviews in clean one litre container bottles. No water samples were sent for culture as testing could only be done in Lusaka, and samples could not be transported within the recommended time of within 72 hours.

We collected five diarrheal stool samples at first contact with the patient, transported in a cold box and were analysed microscopically for the presence of ova and parasite(s). Bacteriological analysis was performed for the detection of Salmonella, Shigella, E. coli O157: H7, Yersinia, and Vibrio cholerae using MacConkey's agar, SS agar, TCBS agar and Sorbitol MacConkey's agar (Oxoid). About, half pea-sized samples were inoculated on culture media plates, and incubated aerobically at 37°C for 48 hours. Samples collected with transport swabs were used to inoculate Campylobacter-selective medium supplemented with 5% Sheep Blood, followed by incubation under a microaerophilic environment at 42°C for 48 to 72 hours. Transport swabs were further immersed in Selenite F broth (Oxoid).

Bacterial isolates from clinical samples were processed for identification using standard biochemical reactions such as oxidase, triple sugar iron, indole, sulfide, motility, citrate and urea hydrolysis. API20E strips (bioMerieux, Inc.) were used for further confirmation. Serotyping was performed to identify Salmonella strains using Specific antisera (BD). Data were entered into Epi Info version 7 and cleaned then analysed using Stata version 13. Data were reported as frequencies and proportions. We calculated attack rates by obtaining Census information from the CSO census projections (Central Statistical Office Zambia 2012).

Results

We identified 26 suspected case-patients, and 2 confirmed case-patients. The median age of case-patients was 13 years (range: 2–69 years) (Table 1). Over 90% of illnesses occurred in persons 1–19 years old. Overall, half (54%) of case-patients were male.

In unstructured interviews, three of the suspected casepatients mentioned contact with people who were suspected to have died of the same disease during the same period in the same village.

All the case-patients interviewed (n=28) except for one (who was referred directly to Solwezi General Hospital) were once admitted at Luamala Health Centre before being

discharged then subsequently referred to the General Hospital. Fever (100%), headache (89%), abdominal pain (71%) and body weakness (61%) were the commonest symptoms case-patients presented with. Other symptoms included diarrhoea (46%), vomiting (21%) and constipation (15%). Most (86%) suspected case-patients were also positive (by rapid diagnostic test) for malaria and were treated. Clinic records showed that fever persisted even after completion of treatment but subsided within 72 hours of treatment with Ciprofloxacin and Paracetamol orally. Most (75%) case-patients reported to the clinic for help within 12 to 36 hours of the onset of symptoms.

Most (96.3%) of the cases drew their drinking water from shallow wells (water table no deeper than 7m from the surface) owned by members of Luamala area as shown in table 3. Most (70.4%) drew water from well 'A' due to its central location. Majority (79%) of the cases reported consistently washing their hands after using the toilet, but only 32% and nine percent reported washing hands before handling food and water respectively.

All water points (except one borehole at the clinic) which included four shallow wells and the nearby river, were contaminated with faecal coliforms. The residents did not share any other common exposure or activity such as food and travel other than well-water as indicated in table 1.

The outbreak had a 0.6% attack rate and 7% case fatality rate from a catchment population of 4,800 people. These were the proportions of those who died from the casepatients and the case-patients from the catchment population respectively.

Of the five who had stool samples taken for culture prior to their initiation of antibiotics, two had their samples grow *Salmonella typhi* and *Salmonella paratyphi*.

As shown in Figure 1, most of the cases were seen in early March 2017 although there was an increase in early February 2017 compared to early January 2017.

Table 1 Demographic characteristics of suspected cases of typhoid fever, Luamala Health Centre, North-western province, 20th December 2016-21st March 2017(n=28)

Category	Number (%)
Median age (range), in years	13 (2-69)
Age group, in years	
1-9	12 (44)
10-19	13 (46)
20-29 >/= 30	0(0)
,	3 (11)
Sex	15 (54)
Male	15 (54)
Female	13 (46)
Symptoms	20 (4.00)
Fever	28 (100)
Headache	25 (89)
Abdominal Pain	20 (71)
Body Weakness	17 (61)
Diarrhoea	13 (46)
Vomiting	6 (21)
Constipation	4 (15)
Malaria Positivity	24 (86)
Time To Treatment From Disease Onset	
Within 12 hours	5 (18)
Between 13 and 24 hours	10 (36)
Between 25 and 36hours	11 (39)
Over 36 hours	2 (7)
Water Source	
Shallow Well	20 (74)
Stream	4 (14)
Borehole	9 (32)
Hand Washing	
After Toilet	22 (78.6)
Before Handling Food	9 (32.1)
Before Handling Water	2 (7.1)
School Going	
Yes	22 (79)
No	4 (14)
Not Applicable*	2 (7)
* For adults who were not school going	

^{*} For adults who were not school going

Table 2 Attack and Case Fatality Rates For the suspected case-patients of typhoid fever, Luamala Health Centre, North-western province, 20th December 2016-21st March 2017 (n=28)

Category	Number/percentage
Number of cases	28 people
Catchment population (CSO)	4800 people
Attack rate	0.6%
Deaths	2 people
Case Fatality Rate	7%

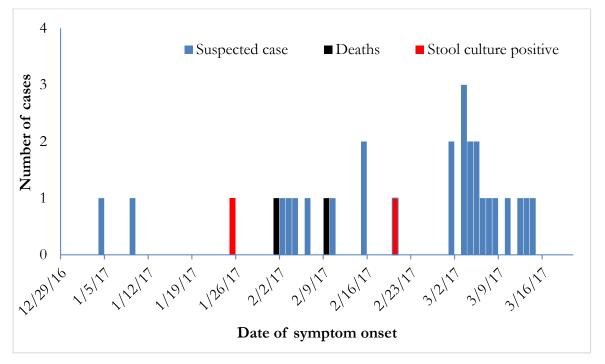


Figure 1 Suspected cases, deaths, and lab results for typhoid fever by date of symptom onset at Luamala Health Centre, North-western province, January -March 2017 (N=28)

Table 3 Water sources by village for Suspected cases of typhoid fever at Luamala Health Centre, North-western province, January - March 2017 (N=27)

Villages	Water source	Number sick (%)
Kabambanya	Well 'A'	19 (70.4)
Longolo	Well 'B'	3 (11.1)
Mili	Well 'C'	3 (11.1)
Malitela	Scoop wells	2 (7.4)
Masheka	Unknown	1 (3.7)

Table 2 shows the attack and case fatality rates of suspected cases of typhoid fever in Luamala Health Centre of Northwestern province from 20th December 2016-21st to March 2017 amongst the 28 case-patients.

Table 3 shows the number of those who drunk water from specific wells and got sick. All the water points listed were shallow wells, except for the one labelled unknown for whom the interviewee was not certain about the source of household water.

Discussion

The investigation suggested S. Typhi and paratyphi typhoid outbreak, which affected mostly children and teenagers, who were diagnosed late, and associated with a high malaria positivity in a malaria endemic region. Because most of the patients waited more than 24 hours after symptom onset to seek clinical care, the association of every fever with Malaria contributed to the delay in confirming the diagnosis [1]. All these factors may have led to deaths of two case-patients.

Even after finishing the prescribed course of antimalarials, those who were found with malaria continued running high sustained fevers, but were kept at the health facility because clinicians believed they would respond to the treatment. A number of those whose malaria tests were negative still received anti-malarials as the health workers considered, against the prescribed guidelines, that the patients were false negatives. Eventually, the numbers of non-responders raised an alarm. Malaria, in an area like this, can therefore be said to impact when a patient gets treatment for typhid and ultimately the outcome. Therefore, the true magnitude of typhoid is difficult to quantify given that the clinical picture is often confused with many other febrile illnesses. Patients with malaria are also said to be more susceptible to getting typhoid infection [16].

Twenty- patients met the case definition. All the cases were at one point admitted at either Luamala Health Centre and/or Solwezi General Hospital. We found most cases to be young and school-going; thus, this suggested a greater risk of exposure in places where school-going pupils met. Slightly more males were affected, but given the small sample size, the conclusion could not be made as to whether this represented a higher risk in males. The two deaths were all older than 20 (aged 22 and 39) but given the small sample size, we could not conclude as to whether the risk of mortality was higher in those who were older or not. This gave a mortality rate of 4/10,000 population.

Once patients given empirical antibiotics (penicillin), and fluoroquinolones (Ciprofloxacin) started responding, all who complained of fever at the health centers were subsequently put on the same treatment plan immediately. This made it impossible difficult for investigators to collect samples from patients at the time of investigation, because they had already started antibiotic treatment. The two patients who died, having not received fluoroquinolones and had stayed with high fevers over two weeks raised the suspicion. For subsequent casepatients, samples had to be collected before commencing the patients on antibiotics leading to the growth of *Salmonella typhi* and *paratyphi* in two of the five samples. Widal's test was positive in two cases up to 1/160 dilution.

Early commencement of antibiotics often leads to a delay in confirming the diagnosis. Additionally, with the nearest laboratory over 45km away on an untarred and often flooded road, poor mobile network connectivity, and no public transport in addition to limited alternatives, confirming the diagnosis in a laboratory proved difficult. Hence, infectious disease outbreaks of that nature would go on, particularly if the clinicians were not very observant, and claim lives.

Luamala was declared an open-defecation-free zone in 2014, and most people reported washing their hands after using the toilet. However, none of the cases reported washing their hands with soap. This ought to be addressed beyond the outbreak for a meaningful response to the problem possibly by ensuring water safety practices are maintained in this community. None of the cases treated water before drinking prior to health education during the outbreak.

The provincial and district team who set up camp earlier were using generic instruments like a generic line list and standard integrated disease surveillance and response (IDSR) case definitions. As a result, most of the important information such as symptoms were missed on the line list, and traditional sample handling techniques enabled the delay in making the diagnosis. Working together with both the district and provincial teams, we updated the line list guided by a tailored case definition which specified the location and time period of interest.

As demonstrated by the information obtained from the provincial and district health offices' administrative reports checked only for the preceding two years, typhoid-like illness were very common in the whole province and district. In Luamala, the epidemic curve showed isolated, but consistent cases that fit the suspected typhoid case definition. A month prior to the February 2017 peak, the area received the reported heaviest rainfall in the recent past which damaged most of the toilets. The environmental health officers had since advised the community to practice the cat-method of burying soon after defecation, and the faeces may have washed into the shallow wells after the rains. Human faecal matter was evident almost everywhere.

In the southern African region, there is no coordinated typhoid surveillance [5]. Individual countries however do record investigation of typhoid cases, and publish reports as seen in Zimbabwe were quite a number of such outbreaks have been recorded [10,14] in Tanzania, Malawi and Mozambique equally similar investigations have been recorded as demonstrated by [3,7,9,11,13,16]. We could not find much-published work on Typhoid outbreak investigation in Zambia. Like many African countries, limited and often lack of laboratory services hampers confirmation let alone publications about disease outbreaks like typhoid [15]. This outbreak investigation paper provides a look into an outbreak investigation in the challenging environment of rural Zambia, where malaria is endemic.

One of the principal limitations of this investigation was that we were not able to establish associations with key risk factors other than age, gender and location. Due to limited resources and time, the investigation did not include control selection, because more focus was on controlling the outbreak. In particular, it would have been useful to demonstrate a direct epidemiological link between the epidemic and the drinking water sources suspected of being the source of contamination. Much as it was clear that most of the cases drunk from one identified well, there were equally a lot more that drunk from the same well but did not get sick. Almost all the water samples taken during the epidemic from Luamala community's water sources contained evidence of faecal contamination. However, the bacteria could not be isolated or cultured, as S. typhi is said to be very difficult to culture from water samples [6,17]. This is why high levels of faecal contamination in areas of elevated risk for typhoid fever infection is frequently taken as a proxy for S. typhi contamination. For a more precise method, polymerase chain reaction would have been more specific and sensitive [18]. While Widal's tests were done, they could not be used to make conclusions as the guidelines which ensure more specificity [2] was not followed. It was however a useful in strengthening the indices of suspicion amongst both the clinicians and the investigating team. Participants' knowledge on typhoid was not assessed. This would have supplemented the information obtained. We were unable to collect bone marrow samples for culture, which is very useful as it may remain positive even after 5 days of antibiotic treatment. Schools were not included in the investigation despite a huge proportion of the affected being school-going. Lack of this information limited the team's ability to devise appropriate and more specific control measures for the school in the region.

Conclusion

This investigation suggests a typhoid outbreak, despite delays in confirming two of the five samples. Our hypothesis was that feacal contamination of drinking water sources following heavy rains might have contributed to the outbreak. The local health authorities were urged to continue implementation of health education on typhoid and general water safety, and decontamination of the toilets and wells. Given the endemicity of typhoid and malaria, clinicians should be reminded that patients from the affected area presenting with fever but testing negative for Malaria, should be investigated for typhoid. As it may not be possible to test every fever patient for typhoid, a criterion is needed to guide on who and/or when typhoid testing should be done for every malaria suspected case.

Acknowledgements

This investigation was funded in part by the U.S. Presidents Emergency Plan for AIDS Relief (PEPFAR). We would also like to thank the Ministry of Health leadership at all levels who were supportive in facilitating and taking part in this investigation. The findings and conclusions in this manuscript are those of the authors and do not necessarily represent the official views of the U.S. Centers for Disease Control and Prevention.

References

- 1.Agwu, E. et al., 2009. High incidence of co-infection with Malaria and Typhoid in febrile HIV infected and AIDS patients in Ekpoma, Edo State, Nigeria. Brazilian Journal of Microbiology, 40(2), pp.329–332. Available at:
- http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1517-83822009000200022&lng=en&nrm=iso&tlng=en [Accessed June 18, 2017].
- 2.Bakr, W.M. et al., 2011. The dilemma of widal test which brand to use? a study of four different widal brands: a cross sectional comparative study. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3050682/pdf/1476
 - https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3050682/pdf/14-0711-10-7.pdf [Accessed June 23, 2017].
- 3.Breiman, R.F. et al., 2012. Population-based incidence of typhoid fever in an urban informal settlement and a rural area in Kenya: Implications for typhoid vaccine use in Africa R. D. Gosling, ed. PLoS ONE, 7(1), p.e29119. Available at:
 - http://dx.plos.org/10.1371/journal.pone.0029119 [Accessed April 23, 2017].
- 4.Central Statistical Office Zambia, 2012. Population and Demographic Projections 2011 2035, Available at: https://www.google.co.zm/url?sa=t&rct=j&q=&esrc=s&source=we b&cd=1&cad=rja&uact=8&ved=0ahUKEwj-q5T0zMnSAhUC0hoKHVdvCgQQFggYMAA&url=http%3A%2F%2Fwww.zamstats.gov.zm%2Freport%2FCensus%2F2010%2FNational%2FZambia%2520Census%2520Projection%25202011%2520-
- 5.Crump, J.A., Luby, S.P. & Mintz, E.D., 2004. The Global Burden of Typhoid Fever. Bulletin of the World Health Organization, (82), pp.346–353. Available at: http://www.who.int/rpc/TFDisBurden.pdf [Accessed April 23, 2017].
- 6.Luby, S.P. et al., 1998. Risk factors for typhoid fever in an endemic setting, Karachi, Pakistan. Epidemiology and Infection, 120(2), p.S0950268897008558. Available at: http://www.journals.cambridge.org/abstract_S0950268897008558 [Accessed March 20, 2017].
- 7.Malisa, A. & Nyaki, H., 2010. Prevalence and constraints of typhoid fever and its control in an endemic area of Singida region in Tanzania: lessons for effective control of the disease. Journal of Public Health and Epidemiology, 2(5), pp.93–99. Available at: http://www.academicjournals.org/jphe [Accessed April 23, 2017].
- 8.Moradi, B. & Huang, Y.-P., 2008. Objectification Theory and Psychology of Women: a Decade of Advances and Future Directions. Psychology of Women Quarterly, 32(2008), pp.377–398. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21413334 [Accessed April 23, 2017].
- 9.Morpeth, S.C., Ramadhani, H.O. & Crump, J.A., 2009. Invasive non-Typhi Salmonella disease in Africa. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America, 49(4), pp.606–11. Available at: https://academic.oup.com/cid/article-lookup/doi/10.1086/603553 [Accessed April 23, 2017].
- 10.Muti, M. et al., 2014. Typhoid outbreak investigation in Dzivaresekwa, suburb of Harare City, Zimbabwe, 2011. Pan African Medical Journal, 18. Available at: http://www.panafrican-medjournal.com/content/article/18/309/pdf/309.pdf [Accessed April 18, 2017]
- 11.Mweu, E. & English, M., 2008. Typhoid fever in children in Africa. Tropical medicine & international health: TM & IH, 13(4), pp.532–40. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18312473 [Accessed April 23, 2017].
- 12.Neil, K.P. et al., 2012. A large outbreak of typhoid fever associated with a high rate of intestinal perforation in Kasese district, Uganda, 2008-2009. Clinical Infectious Diseases, 54(8), pp.1091–1099. Available at: https://academic.oup.com/cid/article-lookup/doi/10.1093/cid/cis025 [Accessed April 23, 2017].

- 13.Pitzer, V.E. et al., 2015. Mathematical modeling to assess the drivers of the recent emergence of typhoid fever in Blantyre, Malawi. Clinical Infectious Diseases, 61(suppl 4), pp.S251–S258. Available at: https://academic.oup.com/cid/article-
- $lookup/doi/10.1093/cid/civ710\ [Accessed\ April\ 23,\ 2017].$
- 14.Polonsky, J.A. et al., 2014. Descriptive epidemiology of typhoid fever during an epidemic in Harare, Zimbabwe, 2012 M. Kirk, ed. PLoS ONE, 9(12), p.e114702. Available at:
 - http://dx.plos.org/10.1371/journal.pone.0114702 [Accessed April 18, 2017].
- Slayton, R., Date, K. & Mintz, E., 2013. Vaccination for typhoid fever in Sub-Saharan Africa. Human Vaccines & Immunotherapeutics, 9(4), pp.903–906. Available at:
- http://www.ncbi.nlm.nih.gov/pubmed/23563513 [Accessed April 23, 2017].
- 16.Takem, E., Roca, A. & Cunnington, A., 2014. The association between malaria and non-typhoid Salmonella bacteraemia in children

- in sub-Saharan Africa: a literature review. Malaria Journal, 13(1), p.400. Available at:
- http://malariajournal.biomedcentral.com/articles/10.1186/1475-2875-13-400 [Accessed April 23, 2017].
- 17.Tran, H.H. et al., 2005. Risk factors associated with typhoid fever in Son La province, northern Vietnam. Transactions of the Royal Society of Tropical Medicine and Hygiene, 99(11), pp.819–826. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16099488 [Accessed May 5, 2017].
- 18. Wilkes, G. et al., 2011. Associations among pathogenic bacteria, parasites, and environmental and land use factors in multiple mixed-use watersheds. Water Research, 45(18), pp.5807–5825. Available at: http://linkinghub.elsevier.com/retrieve/pii/S0043135411003563 [Accessed May 5, 2017].