OUTBREAK REPORT

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

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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 case-patients 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 life-threatening 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 (38ºC 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 case-patients 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 case-patients 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	0(0)
>/= 30	3 (11)
Sex	
Male	15 (54)
Female	13 (46)
Symptoms	
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

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%

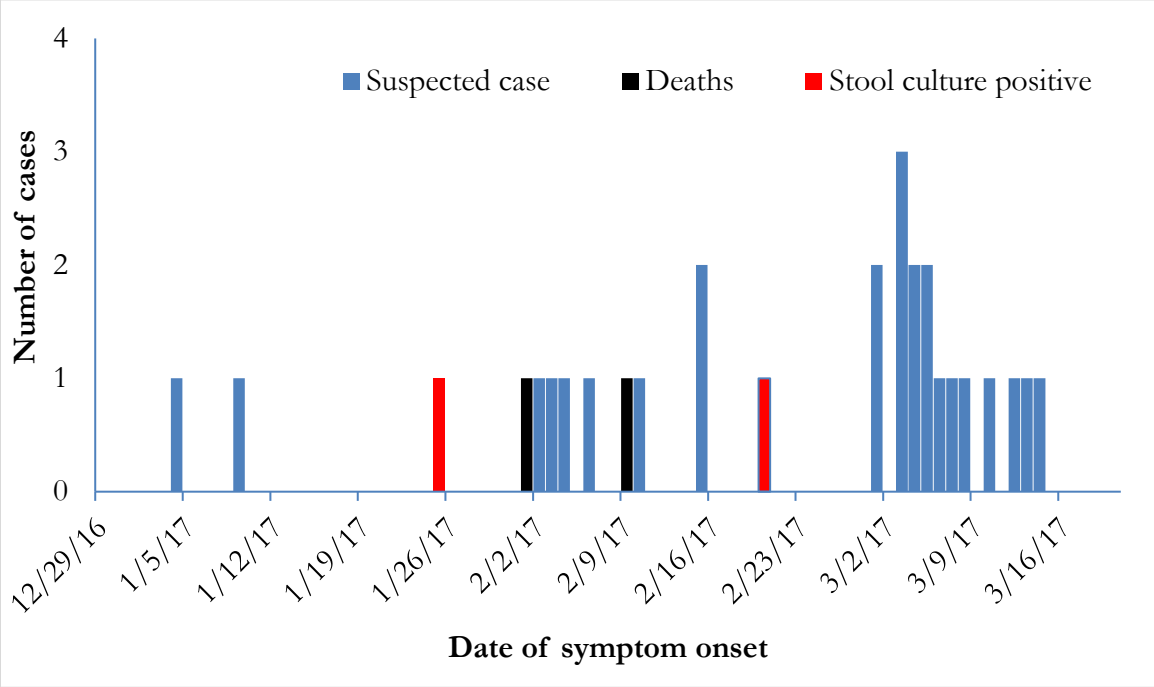

Figure 1 Suspected cases, deaths, and lab results for typhoid fever by date of symptom onset at Luamala Health Centre, North-western province, January -March 2017 (N=28)

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 North-western 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 anti-malarials, 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 case-patients, 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.

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