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Typhoid fever outbreak investigation in Ofla Woreda, Southern Zone of Tigray Region, Ethiopia, 2016: An unmatched 1:2 case-control

Zerihun Degebasa Mamo[1*], Aselefech Addisu[2] and Taklu Marama[3]

[1]Department of Public Health Emergency Management, North Shoa Zone, Ethiopia.
[2]Ethiopian Field Epidemiology Training Program, College of Health Sciences, Mekelle University, Ethiopia.
[3]Department of Midwifery, College Health sciences and Medicine, Wolaita Sodo University, Wolaita Sodo, Ethiopia.

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Typhoid fever (TF) is a systemic infection caused by the bacterium, *Salmonella typhi*. Globally, 22 million illnesses and 216,000 deaths occurred annually. The woreda WAS have alerted the outbreak on 27 July, 2016. The objective of this study was to investigate typhoid fever outbreak in Dera Kebele of Ofla woreda, Tigray Region, Ethiopia. Here, a suspected TF case was defined as any person with gradual onset of remittent fever in the first week, headache, arthralgia, anorexia, constipation and or abdominal pain. 45 cases were compared to 90 controls via unmatched case-control study (1:2) using pretested structured questionnaire. Cases were selected randomly. Nine blood and water samples from two sites were collected for microbiological analysis. Data were entered into Epi info 3.5.1 and analyzed using SPSS version 16; multivariate logistic regression was utilized to identify independent factors associated with TF contraction. The significance of association was constructed using odds ratio with its 95% confidence intervals. Results revealed that a total of 98 cases with one death were identified within one week (August 1 to 8, 2016). Overall, 23.2 per 1000 population attack rate with 37 per 1000 population of highest age-specific attack rate in the age group 25-44 were reported. Faecal coliforms were isolated from two water samples and all the nine blood samples were reactive for Salmonella *Typhi H* (*Flagella*) and O (somatic) antigen. Not washing hand after toilet [AOR 4.7; 95% CI (1.75-12.6)] and unhygienic house and environment [AOR 3.09; 95%CI (1.36-7.06)] were risk factors for contracting disease but not storing food for later use [AOR .28; 95 %(0.12, 0.67)] was protective factor. Thus, not washing hand after toilet and unhygienic house and environment were risk factors; hence not storing food for later use was a protective factor. Monitoring environmental sanitation, food hygiene and hand washing practices should be promoted to prevent the disease.

Key words: Typhoid fever, outbreak investigation, Ofla Woreda, Ethiopia.

INTRODUCTION

Globally, typhoid fever remains important public health problems and major causes of morbidity in the

*Corresponding author. E-mail: sagnfuny2015@gmail.com.

developing world (Alberta Health, 2014). It is a systemic infection characterized by fever, malaise, headache, abdominal pain, and other gastrointestinal symptoms caused by Gram-negative bacteria, Salmonella enteric serotype Typhi (S. Typhi) and Paratyphi A, B and C. (Buckle, 2012).

The incubation period is usually 8–14 days but can range from 3 to 60 days depending on the size of infecting dose and host factors. The period of communicability lasts as long as the bacilli are present in the excreta. About 10% of untreated typhoid cases can continue to discharge bacilli for three months (Alberta Health, 2014) and between 2-5% of all cases become chronic carriers (WHO, 2011). About 22 million illnesses and 216,000 deaths occurred annually in the worldwide and the majority seen in resource-poor countries like in South Asia and Sub-Saharan Africa (Blum et al., 2014), where clean water and sanitation is inadequate (Buckle, 2012). In Africa, the burden of typhoid fever is largely unknown mainly because diagnosis of typhoid fever like culture is non-existent in many endemic countries (Samuel, 2008).

In Sub-Saharan Africa, an estimated typhoid fever associated morbidity and mortality (725 cases and 7 deaths per 100,000 person-years) occurred (Slayton, 2013).

More than 8,000 suspected cases of typhoid fever outbreak resulted in last decade in Sub-Saharan African Countries. The outbreak reported in some African countries was associated with high case-fatality rates (Samuel, 2008; Sejvar, 2012; Slayton et al, 2013; Vera von et al., 2016).

In both endemic and large outbreaks areas, most cases of typhoid fever is seen in those aged 3–19 years (WHO, 2011). In a study conducted from suspected patients, 52% of cases are from children younger than 10 years and 40% from 15 to 45 years (Ramani et al., 2012). Even though there is limited scope of studies in Ethiopia, the outbreak in Gondar College of Health Sciences revealed that 79 students had manifested typhoid disease (Tadesse, 2014; Kifelew, 2014). The infection is transmitted via contaminated food or water by fecal or urinary carriers excreting the bacterium. Contaminated water supply, food bought from street vendors, the consumption of raw fruit and vegetables, and a history of contact with other cases or chronic carriers, population density, rainfall, river level, and proximity to water sources were the associated factors of the illness (Parry, 2002; Polonsky et al., 2014; Tadesse, 2014).

Moreover, environmental conditions like lack of access to safe water and sanitation, poor hygiene and poverty, contaminated milk and milk products, poor water and sanitation were associated factors for typhoid fever illness (Blum et al., 2014).

It is estimated that, 62.7% of Ethiopian population relies on unimproved water sources and more than 80% of diseases in Ethiopia are attributed to poor access to clean water and sanitation. The problem is more in the rural area where the people do not have access to the potable water (Tsega, 2013).

Even though certain households have pit latrines, they are poorly constructed and many people practice open defecation. Also, there is no proper damping of animal wastes and disposing of garbage and liquid waste in the surrounding field which lead to contamination of water sources (Tsega, 2013).

In the study area, latrine coverage is 96% of which 87% utilized it, and 76% of latrine had hand washing facility as well as 69% of safe water coverage in the woreda. Therefore, the aims of the investigation were to verify the existence of outbreak, to characterize the outbreak by place, time and person and to identify associated factors of an outbreak

MATERIALS AND METHODS

Study area

The investigation was conducted in Dera “kebele” (small administration in Ethiopia), Ofla woreda (the third-level administrative divisions of Ethiopia) of the southern zone of Tigray Region. It is found 620 km far away from Addis Ababa (Capital city of the country) and 172 km far away from the Mekelle. Ofla woreda has 21 rural kebeles and 6 health centers with 24 health posts (Admasu, 2011).

The total population of the woreda is estimated to be 139,621 of which 70,927 (50.8%) were females which projected from 2007 Central Statistical Agency of Ethiopia (Central Statistical Agency [Ethiopia], August 2013). Under 1 year, less than 5 and less than 15 years constitutes 2.91, 14.59 and 43.7%, respectively (Ofla woreda Health Office, 2016).

Study design and period

An unmatched case-control study was conducted to recruit the study participants from August 11 to 20, 2016.

Sample size determination

The sample size recruited to this study was calculated by using unmatched case-control study formula considering the following assumption like 95% confidence intervals, 80% power with the exposure of 20 and 43% respectively.

$$n_1 = \frac{[Z_{\alpha/2} + Z_{1-\beta}]^2 \bar{p}\bar{q}(r+1)}{r(p_1 - p_2)^2}$$

$n_2 = 2n_1$ in which n_1= number of cases and n_2 is number of controls. Where p = (p1+rp2) / r+1(1.96+0.84)^2 (0.2767+0.7233)*3/2*(0.43-0.2)^2=n_1=45 cases and n_2=2n_1=2(45) = 90 is controls k investigation. For Cases =45 and for controls= 90; total sample size = 135.

Data collection

Data were collected by the principal investigator and co-

investigators including woreda Public Health Emergency Management (PHEM) Officer, Health Centers and Health Extension workers. We have reviewed records of line lists and samples were taken by laboratory technician for confirmation. Cases were selected from the line lists using random sampling by random number methods and active cases search was conducted by house-to-house visits. We interviewed cases and controls using pretested structured questionnaire. The questionnaire was adopted by reviewing different studies related to this investigation (Tadesse, 2014). Controls (person without signs/symptoms of Typhoid fever within one month) were recruited from the family or neighborhood of the cases using WHO standard typhoid fever case definitions.

Operational definition

Fair hygiene: If the compound was free of observable feces and has functional latrine during the study, having no observable feces around squat hole and the footpath was not covered by grass.

Medium hygiene: If the compound was free of observable feces and has functional latrine during the study, but feces is observed around the squat hole.

Poor hygiene: If the feces observed and latrine does not exist in the compound as well as the house is not cleaned during observation.

Standard cases definition and outbreak declaration

Outbreak declaration: Unusual increase of the cases or doubling of cases on subsequent weeks.

Standard cases definition

Suspected case: Any person with gradual onset of steadily increasing and then persistently high fever, chills, malaise, headache, sore throat, cough, and, sometimes, abdominal pain and constipation or diarrhea.

Confirmed case: A suspected case with Widal test, “O” titer of 1/160 and more is very suggestive and done for this investigation.

Inclusion criteria

Cases: Individuals with a disease of interest in the community (similar geographic areas) who meet the standard WHO case definition.

Controls: Those with no signs and symptoms of typhoid fever history within the previous one month were included.

Laboratory investigation

Blood samples from nine cases were collected for a Widal test, which measures agglutinating antibody levels against the O and H antigens was conducted.

Environmental investigation

A team of investigators inspect the hygiene and sanitation of the community, their water supply. Water sample of 200-ml from two sites (river and spring) in Dera kebele was collected using standard Water sampling procedure with the sterilized glass bottle and transported to the regional laboratory for bacteriological analysis in the ice box.

Data quality control

Training for data collectors and woreda experts was given for one day. Completeness of collected data was verified by daily supervision during the investigation period. Additionally, when entering the data into the computer the missing variables and consistency of filling of questionnaires were ensured carefully.

Data management and analysis

Collected data from the questionnaire was checked for completeness, coded and entered into Epi info 3.5.1 and analyzed using SPSS 16. Binary and multivariable logistic regressions were used to identify possible associated factors with the outcome. The results were presented in the form of tables, figures and summary statistics. Adjusted odds ratio (AOR) with its 95% confidence intervals (CI) was used to report statistical significance.

Ethical issue

Permission letter was obtained from the Regional Health Bureau. Before commencement of the investigation, we obtained support and willingness to conduct the study from Woreda Health Office. The objective of the investigation was told to study participants briefly. Afterwards, their oral consent and support were asked to participate in this study and the investigation was commenced with the Woreda Health Office and a verbal consent of interviewees to finish and interrupt the interview was discussed to respect their confidentiality which was assured.

RESULTS

Descriptive epidemiology

A total of 98 cases and one death with 1% case fatality rate of typhoid fever were identified within one week (32-week) by reviewing line list. Trends of an increased number of cases were seen as the following (Figure 1).

The overall attack rate (AR) was 23.2 per 1000 populations. The highest Age Specific Attack Rate (ASAR) was 37 per 1000 populations which were observed between 25 and44 years and 18 per 1000 populations of 15-24 and 45-64 years age group was the lowest AR. From the total Typhoid fever cases, 56(57.1%) were females. The median ages of the cases and controls were 32 (ranges 2- 66 years) and 22 (range 3 - 61 years) respectively (Figure 2).

The major symptoms among cases were fever, abdominal cramp, nausea and weakness. All patients (98) showed fever and weakness (Table 1).

Duration of illness for most cases before visiting the health center was less than three days up to greater than ten days. Only 2 (2%) of them visited the health center within three days of their onset of illness. The median duration of onset of illness before visiting the health

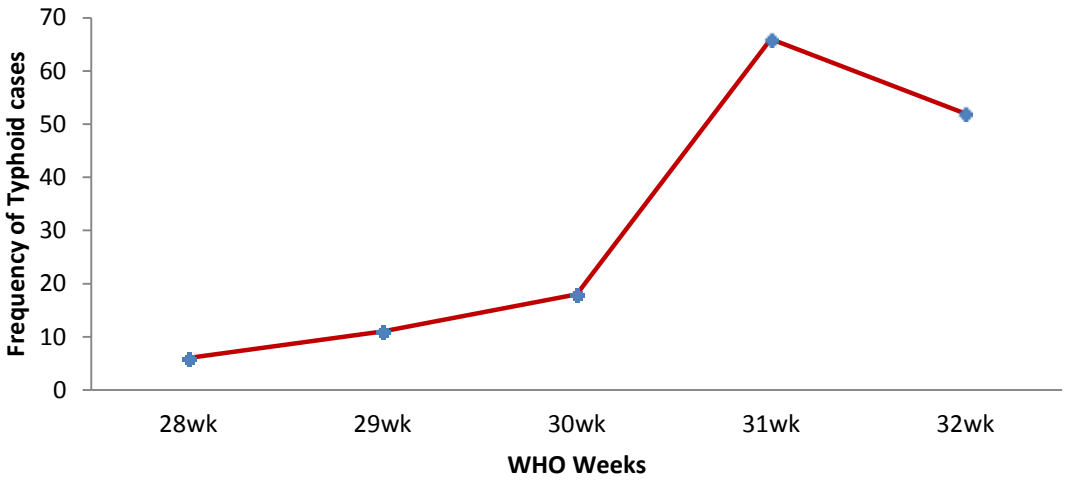

Figure 1. Trend of Typhoid fever via week from Ofla Woreda Health Office, the Southern zone of Tigray, Ethiopian, 2016.

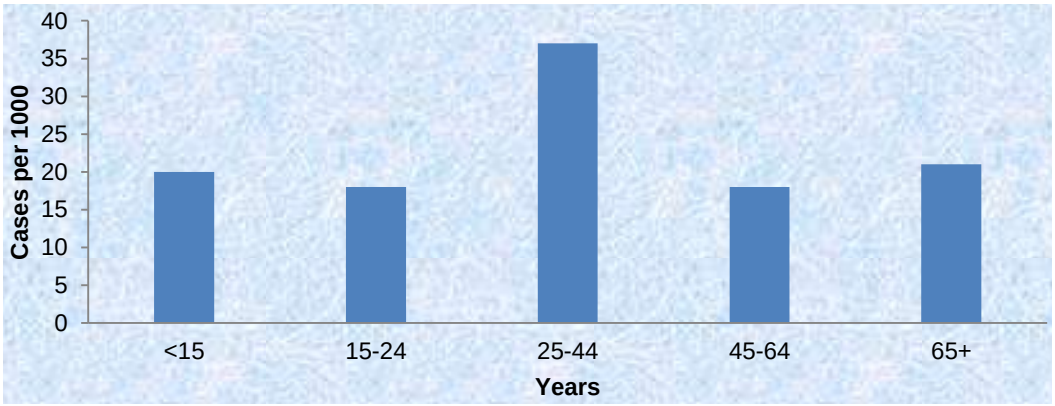

Figure 2. Age specific attack rate (ASAR) per 1000 populations, Ofla woreda, the Southern zone of Tigray, Ethiopian, 2016.

Table 1. Symptoms of Typhoid fever, Ofla woreda, the Southern zone of Tigray, Ethiopian, 2016.

S/N	Signs and symptoms	Frequency	%
1	Fever	98	100
2	Vomiting	28	28.6
3	Abdominal cramp	81	82.6
4	Weakness	98	100
5	Nausea	41	41.8
6	Rash	2	2
7	Diarrhea	41	41.8
8	Headache	68	69.4

facility was 11.8 (ranges 2-28 days) (Table 2).

The onset date of the primary case (index case) was identified at July 29, 2016. The highest cases were registered on August 5, 2016. Date of onset of cases

Table 2. Cases by duration of illness before visiting the health facility, Ofla woreda, the Southern zone of Tigray, Ethiopian, 2016.

Duration of illness before visiting health facility in days	Frequency (%)
<3 days	2 (2)
3-5 days	9 (9.2)
6-10 days	30 (30.6)
>10 days	57 (58.2)
Total	98 (100)

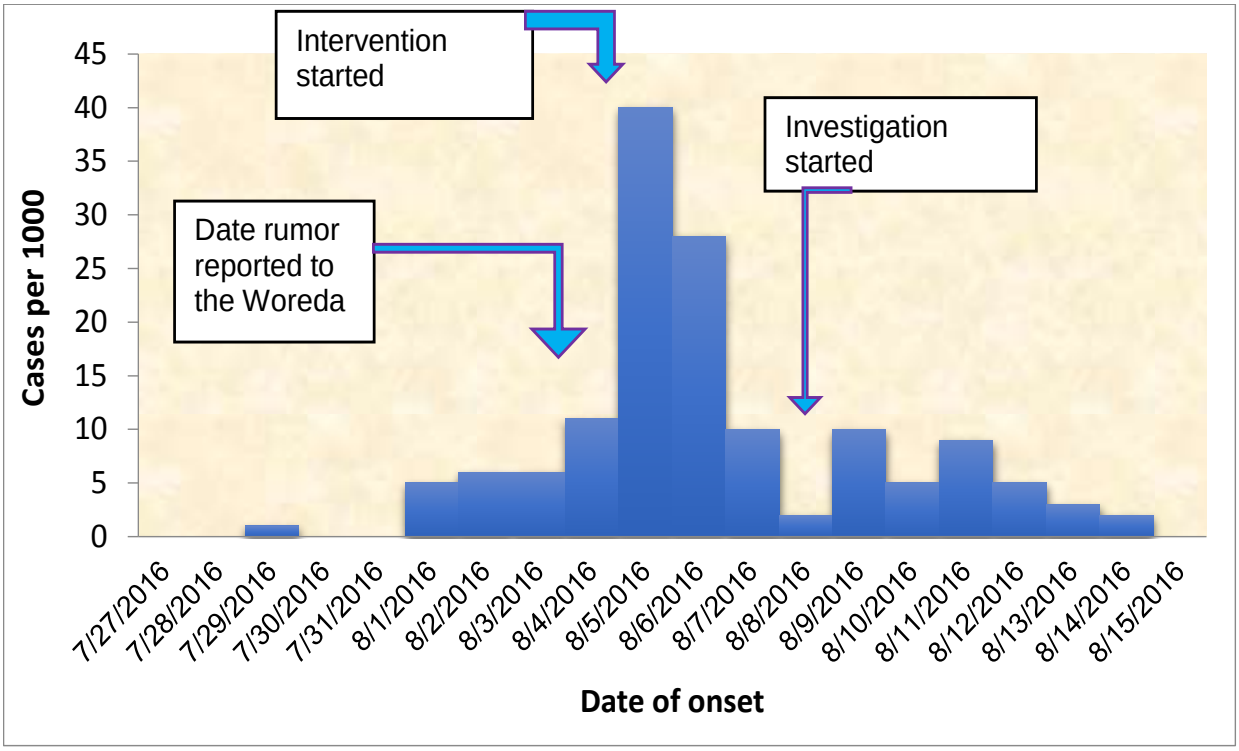

Figure 3. Epidemic curve of Typhoid fever, Ofla woreda, southern zone, Tigray Region, Ethiopian, 2016.

distribution (Figure 3).

Analytic epidemiology

The total of 45 cases and 90 controls were involved in this investigation. The median age of cases and controls were 32 (range 2 – 66 years) and 22 (range 3 – 61 years) years respectively. Among the forty-five patients and ninety controls interviewed, 26 (57.8%) and 48 (53.3%) were females respectively.

We found no statistical significant differences between case patients and controls with respect to time to collect water, the frequency of cleaning water storage, washing hand without soap, prepare food without washing hand.

Even though, 22% of case patients and 38% of controls were reported eating bread.

Educational status of participant [COR 6.87; 95%CI (1.97, 23.99), Hygienic condition in the house and compound [COR 2.58; 95%CI (1.22, 5.49), not washing hand after toilet [COR 4.5; 95%CI (1.78, 11.36) were associated factors and not storing food for later use [COR 0.296; 95% (0.13, 0.66) was a protective factor for typhoid fever outbreak (Table 3).

After controlling the effects of confounding associated factors that statistically significant with disease contraction were not washing hand after toilet [AOR 4.7, 95%CI (1.75, 12.6) and poor hygienic of the house and compound [AOR 3.09, 95%CI (1.36, 7.06) were statistically associated factors and not store food for later use [AOR 0.28, 95%(0.12, 0.67) was a protective factor for this outbreak cases (Table 4).

Table 3. Bivariate analysis of risk factors for typhoid fever, Ofla woreda, southern zone of Tigray, Ethiopia, 2016.

Variable		Frequency		COR(95%CI)
		Cases (%)	Control (%)	
Socio-demographic factors				
Education status	Not read and write	24(53.3)	66(73.3)	6.8(1.97, 23.99)**
	Read write	4(8.9)	12(13.3)	7.5(1.48, 37.9)**
	Elementary	5(11.1)	5(5.6)	2.5(0.46, 13.6)
	Secondary	2(4.4)	3(3.3)	3.75(0.45, 31.6)
	NA	10(22.2)	4(4.4)	1
Marital status	Single	7(15.6)	10(11.1)	3.7(0.9, 15.3)
	Married	21(46.7)	69(76.7)	8.5(2.73, 26.7)**
	Divorced	2(4.4)	1(1.1)	1.3(0.095, 17.7)
	Widowed	2(4.4)	5(5.6)	6.5(0.94, 45.1)
	NA	13(28.9)	5(5.6)	1
Age	≤15	16(35.6)	7(7.8)	1
	16-30	12(26.7)	34(37.7)	6.5(2.14, 1956)**
	31--45	10(22.2)	30(33.3)	6.85(2.19, 21.5)**
	≥46	7(15.6)	19(21.1)	6.2(1.79, 21.46)**
Sex	Male	19(42.2)	42(46.7)	1
	Female	26(57.8)	48(53.3)	1.19(0.58, 2.46)
Risk factors: Water				
Time take to collect water	5-10min	5(11.1)	16(17.8)	1
	10-20min	27(60)	60(66.7)	0.69(0.23, 2.09)
	20-30min	10(22.2)	12(13.3)	0.375(0.1, 1.39)
	>30min	3(6.7)	2(2.2)	0.21(0.027, 1.6)
Frequency of clean water storage	<Week	7(15.6)	24(26.7)	1
	Weekly	21(46.7)	47(52.2)	0.63(0.24, 1.75)
	2 weeks	12(26.7)	14(15.6)	0.34(0.109, 1.07)
	> 2 weeks	5(11.1)	5(5.6)	0.29(0.06, 1.3)
Hygienic status in the house and compound	Fair	1(2.2)	6(6.7)	1
	Medium	21(46.7)	59(65.6)	2.58(1.22, 5.49)**
	Poor	23(51.1)	25(27.8)	5.5(0.6, 49.3)
Use River for drinking	No	2(4.4)	14(15.6)	
	Yes	43(95.6)	76(84.4)	0.25(0.06, 1.16)
Fetch water by deeping	No	18(40)	34(37.8)	1.09(0.53, 2.29)
	Yes	27(60)	56(62.2)	
Animals live in the house	No	36(80)	78(86.7)	0.62(0.24, 1.59)
	Yes	9(20)	12(13.3)	
Wash hand without soap	No	1(2.2)	4(4.4)	0.49(0.05, 4.5)
	Yes	44(97.8)	86(95.6)	
Prepare food without washing hand	No	41(91.1)	89(98.9)	0.12(0.012, 1.06)

Table 3. Contd.

	Yes	4(8.9)	1(1.1)	
Not washing hand after toilet	No	16(35.6)	8(8.9)	4.5(1.78, 11.36)**
	Yes	29(64.4)	82(91.1)	
	Yes	2(4.4)	1(1.1)	
Eat Injera with wot	No	6(13.3)	9(10)	1.38(0.46, 4.16)
	Yes	39(86.7)	81(90)	
Use bread	No	23(51.1)	52(57.8)	0.76(0.37, 1.57)
	Yes	22(48.9)	38(42.2)	
Eat vegetables without thoroughly cooking	no	30(66.7)	65(72.2)	0.77(0.36, 1.67)
	Yes	15(33.3)	25(27.8)	
Use Raw fruit	No	37(82.2)	76(84.4)	0.85(0.33, 2.2)
	Yes	8(17.8)	14(15.6)	
Not store food for later use	No	11(24.4)	47(52.2)	0.296(0.13, 0.66)**
	Yes	34(75.6)	43(47.8)	

Fair: >85%, Medium: 60-85% and Poor: <60%.**-Significant Risk factors, NA-Not Applicable.

Table 4. Multivariable logistic analysis of Typhoid fever associated factors, Southern Zone of Tigray, Ethiopian, 2016.

Variable		Case (%)	Control (%)	AOR(95%CI)
Not washing hand after toilet	No	16(35.6)	8(8.9)	4.7(1.75, 12.6)
	Yes	29(64.4)	82(91.1)	
Not store food for later use	No	11(24.4)	47(52.2)	0.28(0.122, 0.67)
	Yes	34(75.6)	43(47.8)	
Hygienic status of the house and compound	Fair	1(2.2)	6(6.7)	3.09 (1.36, 7.06)
	Medium	21(46.7)	59(65.6)	
	poor	23(51.1)	25(27.8)	

Qualitative analysis

Observed community situation

As we observed different villages of the kebele, most of the local communities existing in the observed villages did not have access to safe drinking water and latrine, and they directly fetched water from the river and spring. Additionally, they were not using soap to wash their hands after using toilet even when washing utensils.

Laboratory investigation

All blood samples (nine) collected from suspected typhoid fever cases were positive for the Widal test. Weil-flex and Rapid Diagnostic Tests (RTDs) were conducted to identify differential diagnosis and were negative. Additionally, fecal coliforms were isolated (100 to 1100 Colony Forming Unit values (CFU) /100 ml) from spring and river water samples which the population uses as drinking water sources and for domestic activities. Based on World Health Organization (WHO) standards, the water is biologically not potable.

Public health action

First, the woreda's health center workers were treated case-patients with antibiotics and Oral Rehydration Salt (ORS) based on their age. Water purification distribution for water treatment, door to door awareness creation on

personal hygiene, environmental sanitation and food quality issues through health education were conducted. We also monitored the antibiotic treatment and improvement of case-patients. Additionally, spring water was cleaned and fenced by the local community.

DISCUSSION

Due to a combination of factors including poor sanitation and food contamination, typhoid fever remains a major public health problem in most resource-poor countries (Samuel, 2008).

The Federal Ministry of Health PHEM guideline sets the threshold for epidemic detection and action as a cluster of Typhoid fever cases in the same settlement in one week. Hence, an unusually increase in the number of the cases or doubling of cases compared to the same weeks were consistent with this outbreak (Katz, 2002; FMOH, 2008).

This outbreak investigation revealed that CFR was 1% which is in line with investigations in Zambia (Hendriksen et al., 2015) which indicates early detection of the outbreak and management of cases. Typhoid fever suspected cases were higher in females than males. This result is consistent with the result from a study in Zimbabwe (Muti et al., 2014; Imanishi et al., 2014; Polonsky et al., 2014) and in Mozambique (Sejvar, 2012). This may be due to females tending to be caregivers of those who are ill at home. Thus, there was the higher likelihood of spreading the disease if appropriate hygiene practices were poorly observed and also exposure through household activities including preparation of food. However, it is in contrast with a study done in Zambia (Hendriksen et al., 2015).

This investigation revealed that the time between the onsets of symptoms of the cases to the first time outbreak cases came to the health facility took the range of 2 to 28 days. The first few cases did not seek health care until they were visited by Health professionals. This may be due to payment fear for health services at the Health Center.

Infections may be acquired from poor environmental sanitation, inappropriate hand washing after toilet and contaminated food. Therefore, the peak of an epidemic curve was seen on August 5, 2016 (WHO week 31) and the curve fell dawn within few days after getting its peak. This sharp increase and decrease of the epidemic curve typical characteristic of common source type of epidemic which is supported by the study in Zimbabwe at 2012 (Polonsky et al., 2014) and at 2014 years (Muti et al., 2014, Imanishi et al., 2014).

Not washing hand after toilet which is consistent with study done in Ethiopia (Getnet, 2014) and poor hygiene of house and compound which is in line with study done in Malawi (Blum et al., 2014), Malaysia (Ramani et al., 2012), Zimbabwe (Muti et al., 2014; Imanishi et al., 2014), Kenya (Akullian, 2015) remains significant factors associated with Typhoid fever contraction. During the investigation of this study, some constraint includes late starting of the investigation leading the cases to take antibiotic therapy which prevented collecting of biological samples for culture confirmation. Also, Widal agglutination test is a non-specific test, so some cases with reactive Widal test may be non-typhoid acute febrile illness cases.

Conclusion

In conclusion, the outbreak of Typhoid fever in Ofla woreda was due to not washing of hands after toilet, as well as poor hygiene of the house and compound. Not storing food for later use was a protective factor for this outcome. Intervention measures to control the outbreak including cases management, water purification distribution for water treatment and door to door health education to the community via health workers and team investigators were conducted. Therefore, it was recommended that health workers should give health education to the community on hand washing practice after toilet and environmental sanitation and promote the community to treat water by boiling because the community faced the shortage of clean water (non-potable).

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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