ORIGINAL ARTICLE

RELAPSING FEVER OUTBREAK INVESTIGATION IN BEYEDA DISTRICT, NORTHWEST ETHIOPIA: CASE CONTROL STUDY

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ABSTRACT

Background: *Ethiopia is the main endemic focus of louse borne relapsing fever (LBRF). It usually occurs in form of outbreaks under conditions of poor socioeconomic status, overcrowding, drought and famine.*

Objective: *The aim of the study was to investigate the occurrence of an outbreak of relapsing fever in Beyeda district in 2020, and identify risk factors for infection.*

Method: *A community based unmatched case control study was conducted in Beyeda district. All patients from 19 May to 28 June 2020 were included based on clinical onset of illness and laboratory results. Seventy-eight patients with 78 controls were included in the study. Data was entered to Epi Info Version 7.1.1 and analyzed by SPSS version 26.*

Result: *A total of 78 confirmed relapsing fever cases that had attack rate of 83/100,000 with no deaths were reported. Among all patients 50% (39) were male and 31 (39.7%) were under 15 years old. The mean age of participants was 26.57 and standard deviation was 15.67. Mass sleeping (AOR = 7.05, 95% CI (1.75 – 28.47), having contact a patient with RF (AOR= 10.5, 95% CI (2.9 – 38.6), washing clothes at least weekly (AOR = 0.019, 95% CI (0.004 – 0.10), low frequency of body bath (more than a week) (AOR = 6.64, 95%CI (1.56 – 28.18) and low frequency of grooming hair(more than a month) (AOR = 4.6, 95%CI (1.01 – 21.4) showed a statistically significant association.*

Conclusion: *Mass sleeping and poor personal hygiene contributed to the outbreak. Participants less than 15 years age were more affected in this outbreak. The outbreak was contained due to prompt interventions taken. Strong preventive measures were recommended to prevent emergence of future outbreak of relapsing fever. Health education should be delivered towards relapsing fever prevention in the district.*

Key words: *Outbreak, Relapsing Fever, Beyeda district, Ethiopia*

INTRODUCTION

Relapsing fever is a recurrent febrile infection caused by various Borrellia spirochetes, a motile spirochete that measures 5 to 40 µm in length that are transmitted either by lice (epidemic relapsing fever) or by ticks (endemic relapsing fever)(1).Borrellia recurrentis is the etiologic agent for louse-borne relapsing fever (LBRF) and humans are the only known reservoirs. It is transmitted from human to human by the body louse, Pediculus humanus(2).

The incubation period of LBRF ranges from 4 to 18 (average 7) days. The attack starts abruptly with a fever that increases to nearly 40˚C in a few days, accompanied by rigors. Early symptoms include headache, dizziness, generalized aches and pains (affecting

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especially the lower back, knees, and elbows), anorexia, nausea, vomiting, and diarrhea. Upper abdominal pain, cough, and epistaxis develop later(3). A petechial or ecchymotic rash, particularly involving the trunk, is seen in 2% to 8% of patients, and 7% to >70% of patients develop jaundice (4). Sub- conjunctival hemorrhages and epistaxis are common (25%), hemoptysis, gastrointestinal bleeding, and retinal hemorrhages less so(3). In severe cases, neurological involvement, myocarditis, acute respiratory distress syndrome, hepatic failure, spleen rupture and disseminated intravascular coagulation leading to intracranial, massive gastrointestinal, pulmonary or peripartum hemorrhage may occur (3).

The febrile period lasting 2–7 days, alternates with afebrile periods of 4–14 days and the number of relapses varies from 1 to 10 without treatment(5).The disease can be severe and death may occur in 10–40% of symptomatic cases in the absence of appropriate treatment, and in 2–5% of treated patients(3).
Relapsing fever is diagnosed by identification of spirochetes on a peripheral blood smear (either by dark field microscopy or microscopic examination of a stained thick or thin blood film) during febrile episodes, and polymerase chain reaction (PCR) targeting the 16S rRNA gene may be used for confirmation(6).
Treatment of choice is a single dose of procaine penicillin, tetracycline or doxycycline, and patients should be closely monitored for a potentially severe Jarisch-Herxheimer reaction (JHR)(7). A variety of antibiotic drugs, including erythromycin, chloramphenicol, and penicillin are effective as single-dose treatment (given orally or parenterally) in LBRF(8). A meta-analysis of antibiotic treatment of LBRF published by Guerrier and Doherty in 2011 found no significant difference between tetracycline and penicillin with regard to mortality rate. Tetracycline use was found to be associated with faster resolution of fever and a lower risk of relapse compared to penicillin treatment. However, tetracycline use appears to be associated with a higher risk for JHR compared to penicillin treatment(7).

Relapsing fever occurs as epidemic under conditions of overcrowding, poverty, draught and famine, homeless people in crowded shelters in unhygienic conditions are also at risk of louse born relapsing fever especially in high land areas and during the cool rainy season, when it is more difficult to change and wash clothing(9).

Large outbreaks usually occur following man-made break downs in public health, as typified by the epidemic following world war II that involved about 10 million cases and one million deaths(2).

Even though LBRF cases declined significantly worldwide due to the highly-decreased incidence of body louse infestations after the 1940s, it still remains the major public health problem and a common cause of hospitalization and death in East African countries, particularly in Ethiopia(10).

Ethiopia is main endemic focus of LBRF. Several large epidemics have been recorded in the country, usually following war and famine. Localized epidemics continue to occur when circumferences become favorable. The latest epidemic occurred in 1991/92, at the end of the civil war in Ethiopia. It occurred among military recruits returning to their residence areas, and later spread to different sections of the community, including schools. During this epidemics among 389 patients from Arsi, in southern Ethiopia, the case fatality rate was 3.5 % (11).

Infestation is more frequent in the high lands where people bath and wash clothes less frequently, and use more bedding. In 2002/03 LBRF was reported as seventh of the top ten leading causes of admission and death among adults in the country. More than 9000 cases were reported to the ministry of health in the same year. However, lack of diagnostic facilities

in rural health clinics and incomplete reporting made it difficult to estimate the total number of cases(12).

In Ethiopia, different reports show there have been continuous LBRF out breaks in different regions. Among them, in 2010 in Southern Ethiopia (Hosanna hospital), LBRF admissions accounted for 27% of total admissions and 6% of the mortality rate in Jimma hospital in South Western Ethiopia(13).

A more recent study of prevalence of lice infestation among school children showed that 66.8% of the students harbored body lice. The prevalence was significantly higher in Debre-Berhan, 76.4%, at an altitude of 2850 meters, compared to Gambella, 60.3%, located at an altitude of 485 meters above sea level. In urban areas, the disease occurs mainly among jobless migrants, daily laborers, prisoners and the poor(14) .

In 2012 there were LBRF out breaks in Bahir Dar Amhara region with an overall attack rate of 0.26 per 1000 individuals with zero deaths. An unmatched community based case control and descriptive cross-sectional outbreak investigation was conducted in Bahir Dar that suggests poor personal hygiene, overcrowding and lack of clean clothes are the major risk factors for relapsing fever among affected individuals(15).

In the Beyeda district, north Gondar zone in Amhara region, there is high frequency of relapsing fever outbreaks due to the prevailing poverty, community living overcrowding and cold weather. Because of the existence of different risk factors that favors the occurrence of epidemic relapsing fever such as poor economic status community way of life and overcrowding due cold weather. The aim of this investigation was to investigate the occurrence of louse born relapsing fever**,** identify the primary risk factors and suggest practical control measures to alleviate the disease burden in this community.

METHOD

Study area: Beyeda district has a total population of 97,492 with a one to one male female ratio. Based on 2007 Ethiopian national census, 3.38% are urban inhabitants. At that time Beyeda had a population density of 100.19. This was greater than the zone average of 63.76 persons per square kilometer and the national average of 4.48 persons per house hold. The altitude of the district is 2700-4620 meters above the sea level. The climate condition includes four climate zones that are 43.1% Dega, 40% Weyina Dega, 11.09% Wurchi and 5.81% Kola. It is one of the highland districts in Ethiopia and includes the Semien Mountains (Ras Dejen). The Amhara regional government classified this district as one of its 47 drought prone and food insecure districts due to its inaccessibility and lack of basic infrastructure in 1999(16).

Study period: This study was undertaken from 19 May 2020 to 28 June 2020 in Melba Kara Kebele of Beyeda district, northwest Ethiopia.

Study Design: Unmatched case control study, conducted in 78 cases with 78 controls.

Population:

Target Population: The populations of Beyeda district

Study population: Populations consistently residing in Melba Kara kebele both for cases and controls.

Study unit:

Cases: Patients with clinical features of louse born relapsing fever who visited health facilities and both tested positive for Borrella and were epidemiologically linked to a confirmed case between May1–June 28, 2020.

Control: Apparently healthy individuals in similar kebeles for selected cases were interviewed during the study period.

Sample size determination and sampling method: In our study area we proposed to enroll all relapsing fever cases that fulfilled our study inclusion criteria. Finally, 78 relapsing fever cases were interviewed for investigation. For each positive case one controls was randomly interviewed among healthy individuals in the same kebele.

All relapsing fever cases presented during the period of investigation were enrolled to the study. One control (an individual who was not complaining relapsing fever or showing clinical manifestations and apparently healthy) was selected randomly for each selected cases on the same day in the community.

Selection of cases and controls:

Inclusion criteria: All relapsing fever cases came with in the study period.

Exclusion criteria: Individuals that had any sign and symptoms of disease were excluded from the control group.

Data Collection Tools and Procedures: Cases and controls were interviewed face to face using a structured questionnaire that requested participant's socio-demographic data, knowledge about the disease and exposure to risk factors. The questionnaire was adapted from several similar studies. Cases were registered and followed daily within the study period. Their sleeping spaces were observed and data regarding possible risk factors for relapsing fever was collected.

Data Quality Assurance: The questionnaire was checked for validity before starting data collection. To monitor and improve the data collection system and quality, each completed questionnaire was daily reviewed by the principal investigators.

Data processing and statistical analysis: Collected data were checked for completeness and inconsistencies. Then the data was coded and entered to Epi Info version 7.1.1 and exported to excel. Some variables were grouped and recoded using SPSS version 26 software. The entered data were cleaned and edited before subsequent analysis. Finally, analysis was done by using SPSS version 26. Measures of central locations (Mean, Median) and measures of dispersions (standard deviation) were calculated for cases and controls. Bivariable and multivariable logistic regression analyses were done to identify the relationship between the independent and dependent variables. Independent variables that have p-value equal to or less than 0.2 in the bivariable logistic regression analysis were entered in multivariable logistic regression analysis. All statistical tests were two sided and significant associations were declared at p-value less than 0.05 in multivariable analysis.

Ethical Considerations: A formal letter was written by North Gondar zone health department (N/G/H/2027) to Beyeda District administration health office epidemic response task force and Dilyibza health center to get permission and facilitate the investigation process. Informed consent was obtained from the study units and their families (if children) and any information related with personal identification was not used in the report. Confidentiality and benefit for the study participants (treatment and health education for cases and health education for controls) were maintained throughout the process.

Operational Definition :

Mass sleeping*:* Sleeping in one place by 6 or more individuals(17).

Knowledge: about Relapsing fever(18)

- *Good Knowledge:* Among respondents those scores 60% and above (scores nine and above among 15 knowledge questions)
- *Poor knowledge:* Among respondents those scores less than 60% (scores eight and below among 15 knowledge questions)

RESULT

Descriptive epidemiology: A total of 78 confirmed relapsing fever cases (AR: 83/100,000 Pop) with no deaths were reported on May 1, 2020. During the investigation the index case was a 28 year old male reported from Melba Kara kebele of Dilyibza cluster on March 15, 2020. He is farmer in the rainy season and day laborer in the winter season. He had traveled to the neighboring Tekezie River for work where one of his friends developed acute febrile symptoms. In order to avoid contracting the disease of his friend he returned home. After one week he developed similar symptom including recurrent fever, headache, chills and myalgia. All total reported cases were from Dilyibza cluster health center. The relapsing fever case report reaches the maximum at the 21th epidemic week in May and ended in June (27th epidemic week) (Figure 1).

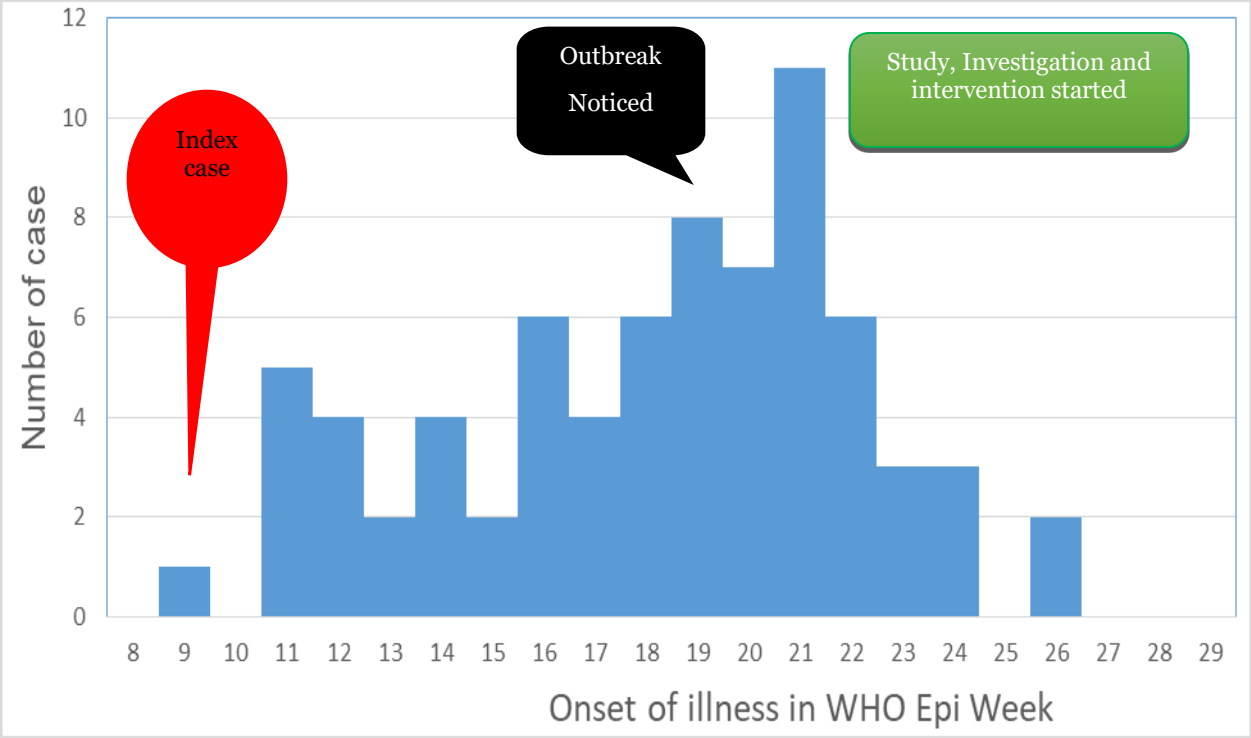

Figure 1:- Epi curve of Relapsing Fever outbreak in Beyeda district, northwest, Ethiopia, 2020.

Descriptions of Relapsing fever cases by person: Among 78 relapsing fever cases reported in 2020, from Beyeda district 31 (39.7%) were under 15 years old. The mean age of the participant was 26.57 and standard deviation was 15.67. Males were almost equally affected with Females that each accounts for about 39 cases (50%).

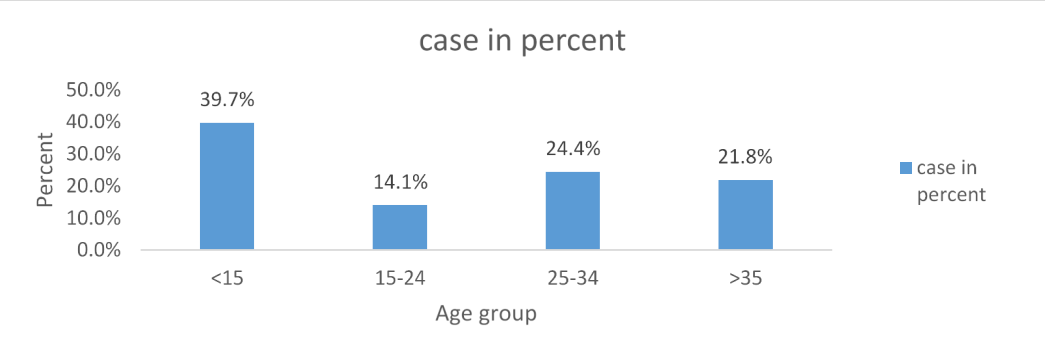

Figure 2: *distribution of relapsing fever by Age group in Melba Kara kebele of Beyeda district Northwest, Ethiopia 2020.*

Clinical Sign and symptoms: Among 78 investigated cases (100%) cases developed symptoms of fever, 71 developed headache (91%), 64 had malaise (82.1%), 25 had joint pain (32.1%) and 76 had nose bleeding (97.4%). Most cases had four or more combined systems. All cases were treated with antibiotics and intra- venous fluid. All cases recovered from their illness completely.

Analytic Epidemiology: During this case-control study, 78 relapsing fever cases and 78 controls were interviewed. Selected controls were unmatched by age and sex with case-patients. With regard to age distribution, 30 (38.5%) of the cases and 45(57.7%) of the controls were 15-34 years old. Regarding sex, 39(50%) of the cases and 47(60.3%) of the controls were male. In education, 46(59%) of cases and 45(57.7%) of controls were illiterate. All cases and control are Orthodox religion followers, of the Amhara ethnic group, and lived at home.

Bi-variate logistic regression analysis shows the statistical difference observed among the age of cases and controls under age 15 is four times greater than for those over age 35, (COR=4.86, 95% CI 1.85 – 12.5 at 0.001 of p Value). Males are at 66% higher risk for infection than females (COR = 0.66 (0.35-1.24), p value 0.199) (Table 1).

In bivariate analysis, all personal and environmental factors were significantly associated with the occurrence of RF disease except knowledge status and travel history (Table 2).

Multivariable analysis of mass sleeping (AOR = 7.05, 95% CI (1.75 – 28.47)), having contact with RF ill patient (AOR= 10.5, 95% CI (2.9 – 38.6)), washing clothes at least weekly (AOR = 0.019,95% CI (0.004–0.10)), frequency of body bath (AOR = 6.64, 95%CI (1.56 – 28.18)) and frequency of grooming hair (AOR = 4.6, 95%CI (1.01 – 21.4)) showed a statistically significant association with infection. The odds of acquiring relapsing fever for those who sleep in a mass was 7 times and having contact with RF ill patient was 10 times higher than in compared with sleeping in a member of less than six and no contact with RF ill patient respectively. The odds of having disease in individuals who had not groomed their hair in more than a month was 4 times and those who had not taken a body bath in over a week was 6 times higher than those who groomed their hair monthly and washed weekly respectively. In addition, People who had washed their clothes at least weekly were at 98.1% lower risk than those not washing clothes weekly. No statistical differences were found on occupation, age, sex, knowledge status and time taken to gain water when comparing cases &controls.

Action taken: An epidemic response task force that organized in the district level participated in active case detection. Action plan

Table 1: Bivariate and multivariable analysis of socio demographic variables of RF outbreak, in Beyeda district Northwest Ethiopia, 2020.

Variable	Category	Case N (%)	Control N (%)	COR (95% CI)	AOR (95% CI)
Age group	<15 years	31(39.7)	9(11.5)	4.86(1.85–12.5)	17.90 (2.4- 133.4)
	15-24	11(14.1)	24(30.8)	0.647 (0.25 – 1.67)	1.12 (0.20-6.93)
	25-34	19(24.4)	21(26.9)	1.27(0.53 – 3.07)	2.30(0.40–13.12)
	>35 years	17(21.8)	24(30.8)	1	1
Sex	Male	39(50)	47(60.3)	0.66 (0.35 – 1.24)	0.36 (0.11–1.62)
	Female	39(50)	31(39.7)	1	1
Educational status	Illiterate	46(59)	45(57.7)	2.56(0.747– 8.7)	NI
	Primary	28(35.9)	23(29.5)	3.04(0.843 – 10.9)	NI
	Secondary & above	4(5.1)	10(12.8)	1	NI
Marital Status	Married	34(43.6)	48(61.5)	1.702(0.58– 5.028)	NI
	Single	35(44.9)	28(35.9)	0.955(0.32– 2.9)	NI
	Other	9(11.5)	9(2.6)	1	NI
Occupational status	Farmer	32(41)	35(44.9)	0.851(0.418– 1.73)	NI
	House wife	17(21.8)	16(20.5)	0.989(0.418– 2.34)	NI
	No Occupation	29(37.2)	27(34.6)	1	NI
Monthly in-come	<1000ETB	21(26.9)	18(23.1)	1.6(0.655 – 4.07)	NI
	1000-2000ETB	42(53.8)	39(50)	1.5(0.68 – 3.33)	NI
	>2000ETB	15(19.2)	21(26.9)	1	NI

NI *- Not included*

Table 2: Bivariate and multivariable analysis of personal and environmental factors associated with RF outbreak, in Beyeda district Northwest Ethiopia, 2020.

Variable	Category	Case N (%)	Control N (%)	COR (95% CI)	AOR (95% CI)
Knowledge status	Good	59(75.6)	67(85.9)	0.51(0.224– 1.16)	0.242 (0.33–1.78)
	Poor	19(24.4)	11(14.1)	1	1
Mass sleeping	Yes	50(64.9)	27(35.1)	3.37(1.75– 6.5)	7.05 (1.75– 28.47)*
	No	28(35.4)	51(64.6)	1	1
Change cloth at night	Yes	50(64.1)	67(85.9)	3.411(1.55 – 7.5)	2.4 (0.63–9.34)
	No	28(35.9)	11(14.1)	1	1
Washing clothes at least weekly	Yes	30(38.5)	70(89.7)	0.42 (0.017 – 0.102)	10.5 (2.9–38.6)*
	No	48(61.5)	8 (10.3)	1	1
Contact With LBRF ill patient	Yes	75(96.2)	11(14.1)	14.42(6.37-32.62)	10.5 (2.9–38.6)*
	No	3(3.8)	67(85.9)	1	1
Having travel history	Yes	24(30.8)	19(24.4)	1.38(0.68- 2.80)	NI
	No	54(69.2)	59(75.6)	1	NI
Frequency of grooming hair	>A month	36(46.2)	13(16.7)	4.29(2.04 – 9.01)	4.6 (1.01 – 21.4)*
	At least monthly	42(53.8)	65(83.3)	1	1
Frequency of body bath	>A week	56(71.8)	35(44.9)	3.13(1.6 – 6.1)	6.64 (1.56 – 28.18)*
	At least weekly	22(28.2)	43(55.1)	1	1
Time taken to gain water	>15 minute	54(69.3)	41(52.6)	2.03(1.06– 3.9)	0.69 (0.197 – 2.41)
	<15 minute	24(30.8)	37(47.4)	1	1

** Significant association* ***NI*** *- not included*

on how to manage the outbreak was developed by task force. Contact tracing was done and house to house health education was given for all visited. The task force engaged in mass screening. Supportive supervision was provided by zonal team in the case management and epidemiological linkage. Delousing (soaking clothes in boiled water and shaving scalp hair) was done. Those mass sleeping in households were advised to reduce number of persons who sleep together and to maintain their personal hygiene and environmental sanitation. Post outbreak surveillance was done.

DISCUSSION

As Ethiopian public health emergency management guidelines recommend, an unusual increase of relapsing cases or doubling of relapsing fever cases on subsequent weeks is considered as outbreak. Beginning from May19, 2020, relapsing fever cases were reported and up to the end of our investigation 27 June 2020 about 78 cases were registered in Dilyibza Health center of Beyeda district. During our investigation, we reveal and examine the presence of relapsing fever outbreak in Beyeda district(19).

In this study area males and females were equally affected. Persons under 15 years old were more affected (39.7% of the total case) than other age groups followed by 15 up to 34 (38.5%) and greater than 35 years (21.8%) sequentially. These results differ from a study conducted in Bahir- Dar in 2012 (91.2% were males and 97.1% were age group of 15-34yrs). This may be because our study was conducted in rural setting, with home residency and a stable way of life in compared to the Bahir Dar study that was urban, where most participants lived on the streets and were daily laborers(15).

However, the infection rate was 83 per 100,000 which was greater than similar study done in Bahir Dar, in which the infection rate was 26 out of 100,000. In our study, the death rate from relapsing fever was zero. This could be due to good treatment and case management and follow up in the treatment sites. This zero death rate was similar in Bahir Dar [15] and lower than in (1.9% in Asella hospital, 3.6% in Hosanna hospital and 4.6% Gondar, Ethiopia)(11-13).

Mass sleeping, contact history with relapsing fever ill patients, infrequent clothes washing, body baths, and hair grooming were significantly associated with relapsing fever outbreak in our study area. The odds of acquiring relapsing fever for those sleeping in masses (more than six people) (AOR=7.05, 95% CI (1.75-28.47)) was seven times greater than for those who sleep in groups of less than six. This result is consistent with a study done in Mekele (AOR= 15.9, 95% CI (4.79-60.15)) and in a study conducted in Addis Ababa (AOR=5.5, 95% CI (1.1-28.0))(20, 21). The odds of contracting LBRF disease was 4 times greater in individuals who groomed their hair less than once a month (AOR = 4.6, 95%CI (1.01 – 21.4)) and 6 times greater for those who had taken body bath less than once a week (AOR = 6.64, 95%CI (1.56 – 28.18)) These data are consistent with a study conducted in Bahir Dar (AOR =8.01, CI (3.51-18.29)) (15).

Those who had contact with a patient with LBRF were 10 times more likely to be infected than those who had no contact with an ill patient (AOR= 10.5, 95% CI (2.9 – 38.6)). This was dissimilar with a study in Bahir Dar (15). This difference might be due to the practices of mass sleeping and sharing clothes in our rural study area vs urban areas where most participants lived less closely, on the streets.

In addition, Peoples who washed their clothes at least

weekly were at 98.1% lower risk than those who did not wash clothes weekly (AOR = 0.019, 95% CI (0.004–0.10). This result is not concurrent with a study done in Addis Ababa (AOR= 0.2, 95% C I (0.02, 2.0))(21). The difference may be due to the sampling method which is hospital-based in Addis Ababa and community-based in our study. It may also be due to the possible difference between the lifestyles of the study participants.

Similar to Bahir Dar and Addis Ababa studies, no statistical differences were found due to sex and changing cloths at nigh compared both cases and control(15, 21).

Limitation: Study design effect (possible bias due to unmatched case control study design)

There may be missed or hidden cases.

CONCLUSION

There was confirmed relapsing fever outbreak in Beyeda district, 2020. Individuals less than 15 year's old age were more number of people affected in this outbreak. Mass sleeping, contact history with relapsing fever ill patient, frequency of washing clothes, hair grooming, and body baths were attributed to the relapsing fever outbreak. Males and females were almost equally affected.

Based on our observations and study results the following were recommended. Mass sleeping should be reduced as far as possible and personal hygiene maintained, especially for those under age 15. Continuous educational programs on louse-borne relapsing fever health should be provided for area communities (including discussion of causes, transmission and prevention). Active surveillance should strive to identify cases and intervene early. Health facilities may need support in materials and laboratory equipment for better diagnosis and training for health care workers provided. The district task force and the public health emergency management should actively follow and conduct surveillance for public health important diseases.

Competing interest: The authors declare that they have no competing interests.

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