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Factors associated with visceral leishmaniasis infection in North Gondar zone, Amhara region, North West Ethiopia, case control study

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Abstract: Background: Leishmaniasis is becoming a major public health problem both in terms of geographical spread and incidence. Visceral leishmaniasis, the worst form among its clinical forms, is the second largest cause of parasite related death responsible for 500,000 new cases each year. No or few risk factor data is available in North Gondar zone on this deadly disease. Objective: To assess determinants of visceral leishmaniasis in North Gondar Zone, North West Ethiopia. Methods: Facility based unmatched case-control study was employed from September 1-30, 2013. Samples of 545 case control pairs were included using consecutive sampling technique. Data was collected using pretested structured questionnaire; entered into EpiData version 3.1 and exported to SPSS version 16.0 for analysis. Crude and adjusted odds ratio with 95% CI was calculated to determine the strength of association between response and predictor variables. P-value less than 0.05 were considered as a level of significance. Result: Male sex (OR=4.64; 95%CI=2.29, 9.39) and age below 15 years (OR=3.26; 95%CI=1.54, 6.92) were positively associated with visceral leishmaniasis infection. Mud wall (OR= 2.49; 95%CI=1.12, 5.58), presences of dog (OR=4.41; 95%CI= 2.25, 8.62), termite hills (OR=3.04; 95%CI=1.59, 5.81) and acacia trees (OR=3.19; 95%CI=1.70, 5.99) increased the risk of infection. Outdoor sleeping (OR=6.28; 95%CI= 3.41, 11.55) was also associated with higher risk of infection. HIV infection (OR=3.28; 95%CI=1.45, 7.39) and malnutrition (OR=2.92; 95%CI=1.55, 5.51) were associated with higher risk of infection. Conclusion: Male gender and being below 15 years of age were positive socio-demographic determinants of visceral leishmaniasis. House made with mud wall was among the associated factors. Presence of dog, termite hills and acacia trees were also important risk factors. Outdoor sleeping was positively associated with visceral leishmaniasis. HIV and malnutrition were also important predictors of the disease. Therefore, the risk of infection can be reduced by improving housing condition, sleeping indoor above ground, making residential area free and far from termite hills and acacia tree. The role of peridomestic animals should also be investigated.

Keywords: Visceral Leishmaniasis, Infection, Ethiopia

1. Introduction

As recognized in a resolution of the sixtieth World Health Assembly in 2007, leishmaniasis is among the most neglected tropical diseases. More than 12 million people are currently infected throughout the world with 2 million new infections each year (a number that is rising), and 350 million people are estimated to be at risk. It affects the poorest populations in 88 countries [1]. Visceral leishmaniasis (VL) is an old, an elapsed, mysterious and neglected disease yet is a major public health problem. It is a debilitating disease with estimated 500,000 new cases every year, and a tenth of them will die. Since 1993, Kala-azar endemic foci have expanded drastically, accompanied by a sharp rise in the number of cases [2]. Eastern Africa is the world's second largest VL foci next to South-East Asian region with an estimated 30,000 cases per year. It occurs in numerous parts in Ethiopia, Eritrea, Kenya, Somalia, Sudan and Uganda causing an estimated 4,000 deaths annually [3]. A case control study done in Brazil reported that highest proportion of cases

were males (OR=2.3) [4]. Similarly, an epidemiological systematic review and meta analysis conducted in America to assess factors associated with VL revealed that the male sex was significantly associated with the infection, with ORs of 1.30 (1.17-1.44) and 2.38 (1.65-3.45) [5].

According to S. Akter, et al. [6], VL infection was associated with age. Another study done in Nepal revealed age ≥15 years (OR 5.5, 95% CI: 1.2–25.0) is associated with increased risk of infection [7]. Human VL infection is also linked with family size of the household. A study from Addis Zemen, Ethiopia revealed presence of association between number of family members in a household and risk of VL infection (AOR=3.54, 95%CI=1.9, 6.6) [8]. The work of S. P. Singh et al. showed that low socioeconomic status was associated with increased risk of VL infection (OR=2; 95%CI=1.05, 3.83) [9]. Another study from India also reported that higher socio economic status was associated with reduced risk of infection (OR=0.5; 95%CI=0.3-1) [10]. Similarly a study done in Nepal showed that poverty incidence is associated with the KA incidence rate [11].

A case control study done in India demonstrated that living in a house of thatched wall was high risk for the disease (OR=2.92; 95%CI=1.71-4.97) [9]. Similarly, another study from India also showed that house made of mud wall was associated with VL infection (AOR=1.71; 95%CI=1.33-2.20) [12]. A case-control study from southern Ethiopia also indicated that proximity of termite hills to home was associated with the disease [13, 14]. Presence of acacia tree and sleeping under it at night was also associated with increased risk of infection [15, 8]. A case-control study conducted in Urban Residents in Dharan, Town of Eastern Nepal to investigate factors for VL reported that sleeping on bed (OR 0.31, 95% CI 0.13-0.78) and ownership of cattle (OR=0.11 95% CI 0.01- 0.92) were protective for VL infection [16]. Another similar study done in Kenya and Uganda borders also indicated that place of sleeping was highly associated with VL infection (OR=4.38, 95%CI=1.24, 15.49) [17].

A case control study conducted in Addis Zemen to assess risk factors for VL in a New Epidemic Site in Amhara region, Ethiopia, 2009, indicated that habitual outdoor sleeping was associated with increased risk of VL infection (OR=2.27, 95%CI=1.1-4.7) [8]. A case control study conducted in Fangak, South Sudan revealed that regular use of a bed net during the rainy seasons provides a degree of protection from kala-azar [18]. A finding from India also highlighted that a bed net ownership and its consistent usage was protective but not statistically significant at the 5% level (OR=0.62; 95%CI=o.37-1.03 for bed net ownership and OR=0.79; 95%CI=0.60-1.02 for its use) [9]

Visceral leishmaniasis has been claimed to be 5th opportunistic infection considered as one of AIDS defining illness [19]. The study done in Tigray, showed that being infected with HIV was the most important predictor of death among VL patients (AOR=4.5) [20].

In northern Ethiopia, the prevalence of visceral leishmaniasis is steadily rising posing an increasing public health issue. To develop effective prevention and control strategies, it is important to create understanding on the epidemiological determinants of the disease [21]. Risk factor data are essential to design the appropriate public health response. Based on these contexts, the present study was conducted with regard to factors associated with visceral leishmaniasis infection in North Gondar Zone, Amhara region, Ethiopia.

2. Participants and Methods

2.1. Study Design, Period and Area

Institutional based unmatched case-control study was employed. The study was conducted in North Gondar zone, North West Ethiopia from September 1-30/2013. Gondar town is the capital of the zone located at 742 Kms from Addis Ababa and 180 Kms from the regional capital city Bahir Dar to the North West Ethiopia. There were three Kala azar treatment centers (Gondar University and Metema hospitals and Abderafi health center) in the zone that provides comprehensive kala azar treatment, prevention and control and other research activities.

2.2. Population

2.2.1. Source Population

Cases: All patients in the three Kala azar treatment centers, namely Metema and Gondar University hospitals and Abderafi health center.

Controls: All apparently healthy patients registered at outpatient department of the selected health institutions for any other illnesses than leishmaniasis who tested negative for VL with a serological test (rK39) diagnostic modality which most of the facilities used for diagnostic purpose.

2.2.2. Study Population

The study population was all confirmed leishmaniasis patients who were on treatment and patients registered in the corresponding health facility at outpatient unit for any ill health condition than leishmaniasis tested negative for VL.

2.3. Variables

Dependent Variable: Visceral leishmaniasis infection.

Independent variables: Age, sex, occupation, monthly family income, family size ,sleeping habit, ownership of a mosquito net & pattern of use, knowledge on VL symptoms, transmission, prevention methods, knowledge about resting and breeding site of sand fly, termite mounds near house, acacia trees near house, domestic animals ownership, sleeping area, HIV/AIDS, malnutrition, tuberculosis, and malaria.

2.4. Sample Size Determination and Sampling Procedures

Sample Size was determined by two population proportion formula for unmatched case control study design using Epi-Info 7 statistical software by considering that the proportion of usual sleeping on ground near cattle (main exposure variable) 20.9 % among controls and 34.57%, among cases, which is estimated from other similar study [8].

Ninety five percent confidence level, 80% power and case to control ratio of 1:4 to detect an odds ratio of 2.0 was used. Accordingly, 109 cases and 436 controls were included in the study. To calculate sample size dog ownership, usually sleeping outside the house and usually sleeping near cattle on ground were considered to be main exposure variables. But to get maximum sample size usual sleeping near cattle on ground was taken as the main exposure variable. Each study subject (case) was selected from all study areas consecutively until the total sample size was achieved. Similarly, for the controls every eligible patient registered at outpatient unit for any illness than VL tested negative for VL was included. Accordingly, the maximum sample was obtained from Abderafi health center (49 cases and 196 controls) followed by Metema hospital (43 cases and 172 controls) and the rest (17 cases and 68 controls) from Gondar University hospital.

2.5. Data Collection

Interviewer administered pretested structured questionnaires adopted from different literatures was employed to collect data. The questionnaire was first prepared in English and then translated in to Amharic and back translated to English by principal investigator and language teachers to check for its consistency. Exposure status histories about sleeping area, sleeping habit, presence of any family member in the house with VL infection and any travel history to kala azar endemic areas was asked and documented retrospectively for the past one year. Nutritional status of study subjects was determined by Weight for Height (Wt/Ht) estimated by Z-score as WHO per standard. Four health professionals, three nurse data collectors and a BSc Nurse Supervisor working in selected health institution were assigned.

2.6. Data Quality Assurance

Before conducting the main study, pre test was carried out on 6 cases and 22 controls at Addis Zemen health center. One day training was given for data collectors and Supervisor. The supervisor was checked filled questionnaires for its completeness on daily basis. The principal investigator and supervisor were made a day to day on site supervision during the whole period of data collection. At the end of each day, the questionnaires were reviewed and checked for completeness and consistency. Data entry was made by EpiData statistical soft ware to ensure double entry verification so as to minimize error.

2.7. Data Management and Analysis

After checking for completeness, data were coded and entered into EpiData version 3.1 databases and then exported to SPSS for Windows version 16.0 for analysis. Descriptive and summary statistics was employed. Crude and adjusted odds ratio with 95% CI was calculated to determine the strength of association between response variable and predictor variables. P value less than 0.05 was considered as a level of significance. All explanatory variables having p - value of less than or equals to 0.2 in univariate analysis were fitted to multiple logistic regression analysis so as to identify independent factors and to evaluate the relative influence of the different co-variates

2.8. Ethical Consideration

The study was ethically approved by research ethical committee review board of Jimma University. Before commencing data collection legal permission with letter of support was obtained from Amhara regional health bureau and North Gondar Zone Health Department. In addition, each treatment center was fully and clearly informed about the aim of the study. After thoroughly discussing the ultimate purpose of the study, an informed verbal consent was received from each study subjects. For young children who were not capable to respond for questions that explore exposure status and knowledge level, parents or guardians were provided consent and responded to the questionnaire. Strict confidentiality was also maintained through coding of questionnaire anonymously.

3. Results

3.1. Socio Demographic Characteristics

Table 1. *Socio economic & demographic characteristics of study participants in North Gondar zone, Sep.2013*

Number of Respondents			
Cases (n= 109) Controls (n=436)			
Characteristics	**N (%)**	**N (%)**	**P-value**
Sex			
Male	89 (81.7)	246 (56.4)	<0.01
Female	20 (18.3)	190 (43.6)	1.00
Age in years			
< 15	26 (23.9)	48 (11.0)	<0.01
≥ 15	83 (76.1)	388 (89.0)	1.00
Level of education			
Illiterates	34 (12.8)	127 (29.1)	0.67
Formal education	75 (68.8)	309 (70.9)	1.00
Marital status			
Married	54 (49.5)	207 (47.5)	0.70
Others[a*]	55 (50.5)	229 (52.5)	1.00
Ethnicity			
Amhara	99 (90.8)	408 (93.6)	1.00
Others[b]*	10 (9.2)	28 (6.4)	0.32
Religion			
Orthodox Christian	101 (92.73)	392 (89.9)	1.00
Others[c]*	8 (7.3)	44 (10.1)	0.38
Family size			
1-5	69 (63.3)	332 (76.1)	1.00
>5	40 (36.7)	104 (23.9)	<0.01
Occupation			
Farmer	44 (40.4)	145 (33.3)	0.24
Daily laborer	21 (19.2)	98 (22.4)	0.23
Others[d]*	44 (40.4)	193 (44.3)	1.00
Monthly income			
<1100 ETB	66 (60.6)	136 (31.2)	<0.01
≥ 1100 ETB	43 (39.4)	300 (68.8)	1.00

Others[a]* =Single, divorced, widowed; Others[b]*=Tigre, Oromo; Others[c]*=Muslim, Protestant; Others[d]*=Merchant, House wife, Student

A total of 545 subjects, 109 (20%) cases and 436 (80%) controls were enrolled and interviewed. Eighty nine (81.7%) of cases and 246 (56.4%) of controls were males. Twenty six (23.9%) of cases and 48 (11%) of controls were below the age

of 15 years. The mean (±SD) and median age of cases was 24.5 ± 9.5 and 23 years respectively. The mean age of controls was 6.6 years greater than that of cases and their median age was 29 years. Thirty four (12.8%) of cases and 127 (29.1%) of controls were illiterates. Nearly one half of cases (49.5%) and (47.5%) of controls were married. There was no significant difference in mean family size (±SD) between cases and controls (4.6±2.3 Vs 4.2±2.2 SD). Maximum family size of cases was 9 while that of controls was 13. Majority, (60.6%) of cases earned monthly family income of less than the median (Table 1).

Table 2. *House hold and environmental variables of cases and controls, North Gondar zone, Sep. 2013*

Number of Respondents			
Cases (109) Controls (436)			
Variables	**N (%)**	**N (%)**	**P-value**
Housing condition:			
Type of roof			
Corrugated iron	62 (56.9)	257 (58.9)	1.00
Thatched roof	47 (43.1)	179 (41.1)	0.69
Type of floor			
Earthen floor	76 (69.7)	128 (29.4)	1.00
Cemented	33 (30.3)	308 (70.6)	0.85
Type of wall			
Mud	84 (77.1)	361 (82.8)	0.17
Cemented	25 (22.9)	75 (17.2)	1.00
Presence of domestic animals in the home:			
Dog available in the house			
Yes	76 (69.7)	150 (34.4)	<0.01
No	33 (30.3)	286 (65.6)	1.00
Cat available in the house			
Yes	42 (38.5)	100 (22.9)	<0.01
No	67 (61.5)	336 (77.1)	1.00
Cattle available in the house			
Yes	60 (55.0)	127 (29.1)	<0.01
No	49 (45.0)	309 (70.9)	1.00
Presence of termite hill around home			
Yes	72 (66.1)	159 (36.5)	<0.01
No	37 (33.9)	277 (63.5)	1.00
Presence of acacia tree around home			
Yes	71 (65.1)	167 (38.3)	<0.01
No	38 (34.9)	269 (61.7)	1.00
Sleeping place			
Bed	35 (32.1)	253 (58.0)	1.00
Experience sleeping on ground	74 (67.9)	183 (42.0)	<0.01
Ever sleep near domestic animals during night			
Yes	35 (32.1)	73 (16.7)	<0.01
No	74 (67.9)	363 (83.3)	1.00

Eighty four (77.1%) of cases and 361 (82.8%) of controls possessed houses made with mud walls. Of total respondents, 76 (69.7%) of cases and 150 (34.4%) of controls had at least one dog in their home during study period. Respondents were also asked about ownership of cattle and other domestic animals. Accordingly, 60 (55%) of cases and 127 (29.1%) of controls reported that they possessed cattle (Table 2).

About presence of termite hills, 72 (66.1%) of cases and 159 (36.5%) of controls reported the presence of termite hills around their residential area. With respect to the presence of an acacia tree, 71 (65.1%) of the cases and 167 (38.3%) of the controls reported the presence of the tree around home. Study participants were also asked where to sleep at home. Seventy four (67.9%) of cases and 183 (42%) of controls reported that they had experience of sleeping on ground during the past one year (Table 2).

Majority (69.7%) of cases and 142 (32.6%) of controls had experience of outdoor sleeping habit at least during some seasons in the past one year. Nearly half (49.5%) of cases and 33.5% of the controls do not possessed mosquito nets. Three hundred and eighty, (69.7%) of participants ever heard about the word kalaazar. Only 170 (31.2%) of study subjects knew ways of transmission of VL. Vast majority, (92.3%) of cases and 94.7% of controls knew that VL can be transmitted through sand fly bite. But only 28 (25.7%) of cases and 96 (22.0%) of controls knew resting and breading site of sand fly. Concerning awareness on symptoms, 79 (72.5%) of the cases and 302 (69.3%) of the controls had awareness on the common symptoms of VL. Majority of cases (71.6%) and controls (73.2%) reported that they could identify at least one prevention method of VL (Table 3).

Table 3. *Individual behavioral variables of cases and controls in North Gondar zone, Sep. 2013*

Number of Respondents			
Cases (n= 109) Controls (n=436)			
Variables	**N (%)**	**N (%)**	**P-value**
Sleeping habit			
Never sleep outside	33 (30.3)	294 (67.4)	1.00
Experience sleep outside	76 (69.7)	142 (32.6)	<0.01
Mosquito net possession			
Yes	55 (50.5)	290 (66.5)	1.00
No	54 (49.5)	146 (33.5)	<0.01
Pattern of use			
Always	24 (43.6)	204 (70.3)	1.00
Some times	30 (54.5)	82 (28.3)	0.51
Never used	1 (1.8)	4 (1.4)	0.74
Ever heard of kalaazar			
Yes	78 (71.6)	302 (69.3)	1.00
No	31 (28.4)	134 (30.7)	0.64
Know how VL transmitted			
Yes	39 (35.8)	131 (30.0)	0.25
No	70 (64.2)	305 (70.0)	1.00
Know place where sand fly can rest and bread			
Yes	28 (25.7)	96 (22.0)	0.41
No	81 (74.3)	340 (78.0)	1.00
Know VL symptoms			
Yes	79 (72.5)	302 (69.3)	1.00
No	30 (27.5)	134 (30.7)	0.51
Know prevention of VL			
Yes	78 (71.6)	319 (73.2)	1.00
No	31 (28.4)	117 (26.8)	0.74
Had family member with VL			
Yes	26 (23.9)	59 (13.5)	<0.01
No	83 (76.1)	377 (86.5)	1.00
Travel history			
Yes	14 (12.8)	52 (11.9)	0.79
No	95 (87.2)	384 (88.1)	1.00

Less than one half (30.3%) of cases and (10.3%) of controls were tested positive for HIV. Forty eight (44.0%) of cases' and

71 (16.3%) of controls' nutritional status was found to be less than the standard (Table 4).

Table 4. *Co-morbid variables of cases and controls in North Gondar zone, Sep. 2013*

Number of Respondents			
Cases (n= 109) Controls (n=436)			
Variables	**N (%)**	**N (%)**	**P-value**
HIV status			
Positive	33 (30.3)	45 (10.3)	<0.01
Negative	76 (69.7)	391 (89.7)	1.00
Nutritional status			
Normal	61 (56.0)	365 (83.7)	1.00
Malnourished	48 (44.0)	71 (16.3)	<0.01
Tuberculosis			
Yes	2 (1.8)	6 (1.4)	0.72
No	107(98.2)	430 (98.6)	1.00
Malaria			
Yes	6 (5.5)	19 (4.4)	0.61
No	103(94.5)	417 (95.6)	1.00

Logistic regression analysis was carried out to determine the most important variables predicting VL among the study participants. All the variables which show significant association during the bivariate logistic regression analysis were entered to multivariate back ward conditional logistic regression model to control for confounders.

During the bivariate analysis sex, age, family size and monthly family income show significant association with outcome variable. On the other hand marital status, level of education, ethnicity, religion and occupation do not show statistically significant association. The finding from this study demonstrated a significant association between sex and VL infection. Males were about 4.6 times more likely to be affected with VL than females (AOR=4.64; 95%CI=2.29, 9.39). As to the finding, age was also significantly associated with increased risk of VL infection. Children less than 15 years were 3.3 times more likely to be infected with VL than adults who are aged 15 years and above (AOR=3.26; 95%CI=1.54, 56.92) (Table 5).

Table 5. *Associated factors with VL infection in North Gondar, Amhara, North West Ethiopia, Sep 2013*

Number of Respondents				
Cases (n= 109) Controls (n=436)				
Factors	**N (%)**	**N (%)**	**COR (95%CI)**	**AOR (95%CI)**
Sex				
Male	89 (81.7)	246 (56.4)	3.44 (2.04, 5.79)	4.64 (2.29, 9.39)**
Female	20 (18.3)	190 (43.6)	1.00	1.00
Age in years				
< 15	26 (23.9)	48 (11.0)	2.53 (1.49, 4.31)	3.26 (1.54, 6.92)**
≥ 15	83 (76.1)	388 (89.0)	1.00	1.00
Monthly income				
<1100 ETB	66 (60.6)	136 (31.2)	3.39 (2.19, 5.23)	2.77 (1.52, 5.04)**
≥ 1100 ETB	43 (39.4)	300 (68.8)	1.00	1.00
Type of wall				
Mud	84 (77.1)	361 (82.8)	0.69 (0.42, 1.16)	2.49 (1.12, 5.58)*
Cemented	25 (22.9)	75 (17.2)	1.00	1.00
Dog presence in the house				
Yes	76 (69.7)	150 (34.4)	4.39 (2.79, 6.91)	4.41 (2.25, 8.62)**
No	33 (30.3)	86 (65.6)	1.00	1.00
Cattle present in the house				
Yes	60 (55.0)	127 (29.1)	2.98 (1.94, 4.58)	2.58 (1.38, 4.83)**
No	49 (45.0)	309 (70.9)	1.00	1.00
Presence of termite hill around home				
Yes	72 (66.1)	159 (36.5)	3.39 (2.18, 5.27)	3.04 (1.59, 5.81)**
No	37 (33.9)	277 (63.5)	1.00	1.00
Presence of acacia tree around home				
Yes	71 (65.1)	167 (38.3)	3.01 (1.94, 4.67)	3.19 (1.70, 5.99)**
No	38 (34.9)	269 (61.7)	1.00	1.00
Sleeping place				
Bed	35 (32.1)	253 (58.0)	1.00	1.00
Experience sleep on ground	74 (67.9)	183 (42.0)	2.92 (1.87, 4.56)	2.88 (1.57, 5.31)**
Sleeping habit				
Never sleep outside	33 (30.3)	294 (67.4)	1.00	1.00
Experience sleep outside	76 (69.7)	142 (32.6)	4.77 (3.03, 7.52)	6.28 (3.41, 11.55)**
HIV status				
Positive	33 (30.3)	45 (10.3)	3.77 (2.26, 6.29)	3.28 (1.45, 7.39)**
Negative	76 (69.7)	391 (89.7)	1.00	1.00
Nutritional status				
Normal	61 (56.0)	365 (83.7)	1.00	1.00
Malnourished	48 (44.0)	71 (16.3)	4.05 (2.57, 6.38)	2.92 (1.55, 5.51)**

*P<0.05, **P<0.01

The study demonstrated that family size has statistically significant association with VL infection in bivariate analysis. But family size does not show statistically significant association when entered to multivariate logistic regression analysis. According to this study, monthly family income is an important predictor for VL infection. Those getting monthly family income of below the median had nearly 3 times more chance of getting VL infection than those who earned above (AOR= 2.77; 95%CI=1.52, 5.04) . All, but sleeping near domestic animals during night, factors in this block show significant association with VL infection both in bivariate and multivariate logistic regression. But sleeping near domestic animals during night does not reach level of significance in multivariate logistic regression analysis (Table 5).

Living in a house made from mud wall increases the odds of getting VL infection by 2.5 times (AOR=2.49; 95%CI=1.12, 5.58). Respondents who owned dog (AOR= 4.41; 95%CI=2.25, 8.62) and cattle (AOR=2.58; 95%CI=1.38, 4.83) are 4.4 & 2.6 times more likely to be at risk of acquiring VL infection than those who had no respectively. Presence of termite hills around the house increases the risk of infection by 3 times (AOR= 3.04; 95%CI=1.59, 5.81). Presence of acacia tree also increases the risk of getting VL infection by about 3.2 folds (AOR=3.19; 95%CI=1.70, 5.99). A person who had experience of sleeping on the ground is 3 times more likely to be at risk of getting VL infection (AOR= 2.88; 95%CI=1.57, 5.31).

During the bivariate analysis, sleeping habit (outdoor Vs indoor), mosquito net ownership, and presence of a family member with history of VL infection in the past one year showed significant association. On the other hand pattern of mosquito net usage, having information about kala azar, number of family members with previous VL infection history and travel to kala azar endemic area in the past one year do not show statistically significant association with VL infection. However, only sleeping habit showed statistically significant association with VL infection when entered to multivariate back ward logistic regression analysis. Subjects who had experience of outdoor sleeping were about 6.3 times more likely of getting VL infection than those who never sleep outside (AOR=6.28; 95%CI=3.41, 11.55)

Statistically significant association was demonstrated between co-morbid conditions and VL infection in present study. Being infected with HIV and presence of malnutrition were statistically significantly associated with VL infection during bivariate and multivariate logistic regression analysis. Individuals infected with HIV were about 3.3 times more affected than those who tested negative for HIV (AOR=3.28; 95%CI=1.45, 7.39). Malnourished individuals were about 3 times more likely to be infected with VL (AOR=2.92; 95%CI=1.55, 5.51) (Table 5).

4. Discussion

This study was conducted to assess risk factors for VL infection in North Gondar, North West Ethiopia. Since analytical method was employed in this study, it can provide better insight of the determinants of VL infection in the area.

This study demonstrated significant association between gender and VL infection. This result is supported by a result from case control study done in Brazil which reported that highest proportion of cases were males (OR=2.3) [4]. Similarly, a case control study from Bihar, India reported that 75.93% of cases were males with male to female ratio of 3:1 [12]. Another epidemiological systematic review and meta analysis done in America to assess factors associated with VL also revealed that the male sex was significantly associated with the infection, with ORs of 1.30 and 2.38 [5]. The male gender predominance of the infection could be due to the reason that males are mostly engaged in outdoor activities and stay out door from dawn to dusk that might increase their contact with sand fly and in most rural parts of our country men mostly forced to sleep outside to keep their cattle and farm from theft.

Current study demonstrated that age has a significant association with VL infection. In line with this finding, a study done in Trishal Upazila, Bangladesh demonstrated a significant association between VL and different age groups [6]. Another study done in Nepal also indicated that age is associated with increased risk of infection [7]. Similarly, a study done in south Sudan indicated that the peak age group for VL infection was under five children of which 89% were under the age of three years old [18]. The possible justification for this age based predominance is it could be due to the reason that children whose age is below 15 years are with less developed immune system and most of them would not have previous attack with VL which could make them partially immured after getting infected with the disease commonly observed in areas with sustained transmission of the disease.

Monthly family income was an important predictor of VL infection in present study. Consistent with this finding, S. P. Singh et al. reported that low socioeconomic status was found to be associated with VL [9]. Another study done in India also showed that higher socio economic status was associated with reduced risk of VL infection compared to lower ones [10]. Similarly, a study done in Kenya and Uganda demonstrated that highest socio economic status was protective to VL infection [17]. A report from systematic review and meta analysis that assessed subjects' income directly showed that an increase in income was associated with a decrease in the occurrence of the disease [5]. The probable justification for this could be that low income can affect over all status of household and individuals in many aspects. Low income can be associated with poor housing conditions, poor environmental hygienic conditions, poor nutritional status and increased risk of infections including HIV/AIDS.

According to this study type of wall from which house was made (cement Vs mud) showed statistically significant association with VL infection. This finding is consistent with findings from other studies which indicated that housing condition is one of the most important factors for VL. A case control study done in India demonstrated that thatched wall of housing condition is high risk for the disease [9]. Similar study

from India also showed that house made of mud wall was statistically significantly associated with VL infection [12]. The possible reason for this could be due to the fact that thatched and mud walls are most likely to be cracked and favorable for entrance and breeding of the vector.

Presence of dog was an important predictor for VL in present study. Consistent with this finding a study done in Addis Zemen, Ethiopia indicated dog ownership was associated with VL [8]. The finding of epidemiological survey and meta analysis in the combined data also demonstrated pattern of increasing likelihood of infection for subjects with dogs in the household. The possible justification could be that dogs are reservoir hosts for canine VL and they attract sand flies for search of blood meal.

Subjects who owned cattle were 2.6 times more likely of getting VL infection than their counterparts. Against this study, a case-control study conducted in Urban Residents in Dharan Town of Eastern Nepal to investigate factors for VL and a study from rural Bihar, India reported the negative association between cattle ownership and risk of VL infection [10, 16]. This could be due to the reason that cattle in India and Nepal might be kept away from human beings in a separate room unlike our case in which most of rural residents keep cattle and other domestic animals inside house with close proximity to human beings especially during cold season due to fear of theft.

According to current study, presence of termite hills and acacia trees around the house was associated with VL infection. In line with this finding, the case-control study conducted in southern Ethiopia reported proximity to termite hills was significantly associated with the disease [13, 14]. Consistent with our finding, a study from Addis Zemen reported association between risk of VL and presence of acacia trees near the house [8]. The probable reason could be that termite hills and acacia tree with barks are highly favorable sites for breeding and resting of sand flies.

Like in other studies, sleeping area (bed Vs ground) was among the most important predictors of VL infection in present study. A case-control study conducted in Urban Residents in Dharan Town of Eastern Nepal to investigate factors for VL showed that sleeping on bed was protective [16]. The result of this finding indicated presence of statistically significant association between sleeping habit and VL infection. Experience of outdoor sleeping was found to be major risk factor for VL infection according to current study. This finding is consistent with findings from other different areas. A study from Addis Zemen indicated that habitually sleeping outside was associated with increased risk of VL [8]. This could be due to the reason that sleeping outside increases the likely hood of being bitten by the vector.

As findings from other different countries current study highlights a significant association between bed net ownership and risk of VL infection. Bivariate logistic regression of this study revealed that having not mosquito net is a risk factor for VL infection though it did not reach significance level when other variables were added to the model. A case control study conducted in Fangak, South Sudan revealed that regular use of a bed net during the rainy seasons provides a degree of protection from kala-azar [18]. A similar finding from India also highlighted that a bed net ownership and its consistent usage was protective but not statistically significant at the 5% level.

Positive serostatus for HIV was among the most important predictors of VL in current study. In line with present result, findings all over the world highlighted the importance of HIV as risk factor for VL infection [19, 22]. A study conducted in Tigray, Ethiopia showed that HIV positive serostatus was the most important predictor of death among patients with VL [20]. The possible reason for this could be that both diseases attack the immune system of human beings and VL affects the already weaken immune system on top of HIV.

Individuals whose BMI is less than the standard (-1Z score) were about 3 times more likely to be at risk of getting VL infection than their counter parts in this study. In line with this finding, a finding from recent randomized trial study conducted in Gondar University Hospital, reported that majority of cases had BMI below 18.5 and out of 25 patients, 11 were malnourished (BMI<18.5) and 12 were severely malnourished (BMI<16) while the BMI of all controls was found to be above 18.5 [23]. Another study conducted in Kenya and Uganda also indicated that nutritional status of cases was extremely poor [17]. The probable justification for this could be due to the reason that malnutrition affects the immune system and reduce the immune response, hence increase the likelihood of infections.

5. Limitations of the Study

The study was conducted in selected VL treatment centers with high disease burden; therefore, this may affect generalizability of findings. Co-morbid factors did not exhaustively include other co-morbid conditions except for some commonest ones and as to the VL-HIV co-infection, which comes first (chicken–egg dilemma) could not be clearly differentiated that may reverse which is the factor.

6. Conclusions

This study identified factors associated with VL infection and highlighted the devastating effect of co-morbid conditions with visceral leishmaniasis. The conclusions to be drawn from this study are aimed at the implementation of intervention measures, prevention, and control of the disease. The socio-economic and demographic factors that were more strongly associated with the infection, regardless of all other variables were age (being below 15 years), sex and income. Males and persons with low monthly family income were at increased risk of the disease. Poor wall of housing is the single most important risk factor among housing condition characteristics. Ownership of domestic animals, especially dog and cattle and presence of termite hills and acacia trees near the house are important environmental risk factors. Sleeping on the ground, and any experience of outdoor sleeping were important predictors of VL infection. Not having mosquito net and presence of family member with VL

in the past year were associated with increased risk of VL only in bivariate analysis. Co-morbid conditions, specifically being infected with HIV and malnutrition were also strongly associated with higher risk of infection. The prevention of VL should be given emphasis or the risk of infection can be reduced by improving household income and avoiding domestic animals and clearing residential area from termite hills and making far from acacia tree.

Having mosquito nets, as well as individual protective measure such as avoid sleeping on the floor, avoiding sleeping outdoors, reducing HIV prevalence in the general community and improving nutritional status greatly lowers the risk of infection from VL. The complex role of dogs and other domestic animals in the transmission cycle should be further investigated and well documented.

Authors' Contribution

KB: Conceptualized the research problem, designed the study, prepared the proposal, conducted field work, and analyzed the data, manuscript writing.

FT: Revised the proposal, participated in data analysis and the report revision

DM: Revised the proposal, participated in data analysis and the report revision

YT: Participated in preparing the manuscript for publication

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