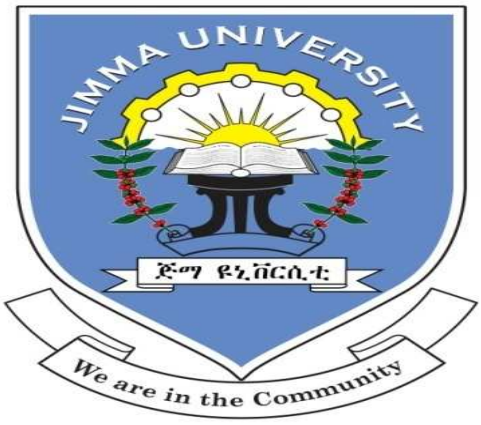
FACTORS ASSOCIATED WITH VISCERAL LEISHMANIASIS INFECTION IN NORTH GONDAR ZONE, AMHARA REGION, NORTH WEST ETHIOPIA



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A thesis submitted to Jimma University, College Of Public Health and Medical Sciences, Department of Epidemiology in Partial Fulfillment of the Requirements for the Degree of Master of Public Health in Epidemiology

Feb. 2014
Jimma University

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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 was 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 genders 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.

Acknowledgement

My deepest appreciation and heartfelt gratitude goes to my advisors Mr. Fasil Tessema and Mr. Desalegn Massa for their unreserved help in reviewing my work and giving me constructive advice and guidance from the development of proposal till the write up that helped me materialize my work which otherwise this thesis could not have been fruitful. Supervisors and all data collectors are highly acknowledged for the effort they put to the quality of this thesis. Above all my heartfelt thanks go to study participants who spent their time in responding my questionnaire. Last but not least, I would like to extend my heartfelt thank to all staffs and administrators in all study sites for their unreserved provision with necessary information and materials.

Table of content

Content **page**

List of Tables

List of figure

Acronym

AIDS	Acquired Immunodeficiency Syndrome
ART	Anti Retroviral Therapy
BMI	Body Mass Index
CI	Confidence Interval
CL	Cutaneous Leishmaniasis
HIV	Human Immunodeficiency Virus
ICASA	International Conference on AIDS and Sexually Transmitted Infections in Africa
KA	Kala Azar
KAP	Knowledge, Attitude & Practice
LST	Leihmanin Skin Test
MCL	Mucocutaneous Leishmaniasis
MOH	Ministry Of Health
MSF	Médecins Sans Frontières
MSF-H	Médecins Sans Frontières-Holland
NID	Neglected Infectious Diseases
PKDL	Post-kala-azar Dermal Leishmaniasis
RDT	Rapid Diagnostic Test
SPSS	Statistical Package for Social Study
TDR	Research and Training in Tropical Diseases
VL	Visceral Leishmaniasis
WHO	World Health Organization

CHAPTER 1:- Introduction

1.1. Background

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 (mostly developing) countries (1). It is transmitted through the bite of infected vector, sand fly. Of 500 known phlebotomine sand fly species, only some 30 of them have been identified as vectors of the disease. Only the female sand fly transmits the disease (2).

The main clinical forms of the disease are: visceral leishmaniasis (VL), whose animal reservoir is dog for its zoonotic form, cutaneous leishmaniasis (CL), for which rodents served as main animal reservoirs in rural foci and mucocutaneous leishmaniasis (MCL) whose animal reservoirs are sylvatic mammals (3). An extremely diverse array of disease manifestations which vary from simple cutaneous lesions, to severely debilitating, serious mucous lesions, or fatal visceral disease is produced by these various leishmania species. Some infections are self healing, but others are relentlessly progressive and resistant to all known drugs (4).

Visceral leishmaniasis, also known as kala azar, is caused by species of the L. donovani complex. VL is the most severe form of the disease with almost 100% mortality rate if not treated; characterized by irregular attacks of fever, progressive weight loss, hepatosplenomegaly, skin damage and hair loss, and anemia (5). VL is an old, a forgotten, largely unknown 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. The actual figure of death from the disease may be higher than this estimate considering the existence of its unidentified foci. Since 1993, Kala-azar endemic foci have expanded significantly, accompanied by a sharp rise in the number of cases (6).

Except Australia and Antarctica, leishmaniases are recently prevalent on all continents, and are endemic in 88 (72 are developing) countries worldwide (7); predominantly in tropical and sub-tropical regions. Africa, parts of Asia, Middle East, Latin America and the Mediterranean regions took the lion share of the burden (8).

Leishmaniasis currently threatens 350 million men, women and children around the world (9). The disease is most prominent in East Africa, Southeast Asia and South America. There is an estimated incidence of 1 to 1.5 million cases of CL and 500,000 cases of VL each year, primarily in South America, East Africa and the Indian Subcontinent (10, 11). The largest focus of VL is in the South-East Asian region, with an estimated 300,000 cases. East Africa has approximately 30,000 cases per year, and the third largest focus is in the Americas with 4,000 cases reported in 2006 (1).

In Africa, VL is transmitted mainly in rural areas either from a zoonotic source (in sporadic endemic areas) or human to human in secondarily anthroponotic foci (12). It is found in parts of Sudan, Kenya, Somalia, Eritrea and Ethiopia (13).

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 (9). New foci are appearing at an alarming rate, and incidence in East Africa is on the increase (1).

The first case of VL in Ethiopia was documented in 1942 in the southern parts of the country. Now, there are about 2,000 to 4,500 cases every year from over 40 localities in different parts of the country, with endemic areas in the lowlands of the central, northwest, south and southwestern parts of the country. Most infections are acquired in north-west Ethiopia in the lowlands of Metema and Humera, south-west Ethiopia in the Segen, Woitu and Omo river basins, and in other isolated foci in the rift valley (14).

Sporadic cases of VL have been identified from Wolkayit Tsegede (Gondar), Gibdo, Raya, and Kobo (Wello), Kijawa (Gambella) and Gelana (Sidamo) and Genale (Bale) river basins (15). The disease is particularly prevalent in the lowlands of northern Ethiopia. Here, hundreds of thousands of migrant workers arrive every year to work the agricultural season (13).

The disease is spreading to a number of previously non-endemic highland areas, as exemplified by the recent outbreak in Libo and Fogera, Amhara regional State, a highland area (1, 13, and 16). A national kala-azar task force was established in 2008 with the aim of eliminating kala-azar from the country by 2015 (17).

1.2. Statement of the Problem

Leishmaniasis ranks the third in disease burden in disability-adjusted life years caused by neglected tropical diseases and is the second cause of parasite-related deaths after malaria; but due to different reasons, it is not given attention and emphasis that would be justified seeing its health importance (18).

Visceral leishmaniasis kills more than 50, 000 people worldwide; among parasitic diseases, only malaria is more deadly (19). It remains a public health problem all over the world. This disease was included by the World Health Organization in the list of neglected tropical diseases targeted for elimination by 2015 (16).

The north-western Metema-Humera focus (which extends northwards to Eritrea and westwards into eastern Sudan) is a major VL focus which presently accounts for approximately 60% of the total disease burden in Ethiopia (16). Recurrent epidemics of visceral leishmaniasis have occurred in Metema and Humera; recently a devastating epidemic occurred in Humera with an estimated annual incidence of 1,500-2,000 cases (15).

In northern Ethiopia, the prevalence of visceral leishmaniasis is steadily rising posing an increasing public health issue. To develop effective prevention and control strategies on the transmission of the disease it is important to generate knowledge on the epidemiological determinants of the infection (20).

Risk factors for VL are comparatively scarce in North Gondar. Therefore, the aim of this study was to fill this gap in describing factors that pose people at risk of acquiring this deadly disease in North Gondar Zone, Amhara region, new endemic area with high disease burden.

CHAPTER 2:- Literature Review

2.1. Risk factors for VL

Specific risk factors include age and genetic background and the presence of dog and other domestic animals. Behaviors such as sleeping outside under acacia trees and living in houses constructed of grassy material appear to increase risk of infection. Proximity of human dwellings to termite mounds increases the risk. Although L. donovani infection has been demonstrated in dogs in several foci, their importance in the transmission cycle is uncertain. Keeping dogs and other domestic animals inside the house is thought to promote human infection. Dogs served as reservoir hosts for the L. infantum and attract sand flies (21).

2.1.1. Socio-demographic and socio-economic factors

The association between VL and socio-economic and socio demographic characteristics have been cited by different studies. These studies have shown that VL infection was associated with gender, age, marital status, family size and economical status (22, 23). Poverty and lower educational status were associated with increased risk of VL. Poverty increases the risk of infection in many ways related to poor housing and peridomestic sanitary conditions like lack of waste management and appropriate sleeping facilities, open sewerages may serve as vector breeding and resting sites and increase access to human beings and other domestic animals.

An epidemiologic and parasitologic assessment done in Addis Zemen, Amhara region, Ethiopia in may 2005 showed that male gender is associated with VL infection in the study area in which the prevalence of positive LST (Leishmanin Skin Test) was higher among men (34%) than women (26%; P=0.06) and rose significantly with age among men (X^2 for trend 28.5, P < 0.00001) but not in women (X^2 for trend 2.9, P =0.09) (24). Another case control study done in Brazil also reported that highest proportion of cases were males (OR=2.3) (25). 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) (26). However, a case control study done in Addis Zemen, Ethiopia, 2009, did not show the presence of association between VL infection and gender (27). Similarly, a study conducted in Bangladesh, 2012, demonstrated absence of association between gender and VL infection in which 44.6% of respondents were females and 43.2% males (28).

According to S. Akter, et al. (28), VL infection was associated with age. Similarly, a study done in Bihar, India also indicated that VL is associated with age of respondents in which majority (64.67%) of cases were aged between 15 to 45 years (29). 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 (30).

Human VL infection is also linked with family size of the household. A study from Addis Zemen 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) (27). Similarly, a cross-sectional survey conducted in Nepal on Leishmania donovani infection and its risk factors also indicated that large family size was associated with increased risk of VL infection (OR 4.4, 95% CI: 1.6–12.6) (30).

Different studies in various parts of the world documented that household income level is significantly associated with human VL infection. These studies showed that low socio economic status is major risk factor for VL infection (31, 32). 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) (33). 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) (34). A systematic review and meta analysis that assessed subjects' income directly also showed that an increase in income was associated with a decrease in the occurrence of VL infection (26). Similarly a study done in Nepal showed that poverty incidence is associated with the KA incidence rate (35).

2.1.2. Household and environmental risk factors

The risk of acquiring the disease is mediated through poor housing conditions, lack of personal protective measures against the vector. Living in a house with thatch walls constructed of grassy material and sleeping on the ground increased risk of VL infection. 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) (33). 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) (36). A cross sectional study conducted in Nepal to assess risk factors for VL also reported that house constructed in mud (OR 3.0, 95% CI: 1.1–7.6) was among the risk factors for VL infection (30).

The habit of keeping dogs and other domestic animals inside the house and sleeping near dogs were associated with increased risk of infection as dogs are the L. infantum reservoir hosts and also attract sand flies (21, 23). A case control study done in Addis Zemen, Ethiopia, 2009, on 171 case-control pairs showed that, dog ownership was associated with VL (OR=2.76; 95%CI=1.5-5.1) with an increased trend of infection with number of dogs, ORs of 2.46 (95%CI= 1.5–4.0) for those having one dog, and 2.88 (95% CI, 1.0–8.2) for those with two or more dogs (27). A finding of epidemiological survey and meta analysis also demonstrated that a pattern of increasing likelihood of infection with dog ownership (OR = 1.23; 1.07–1.42) (26).

In the northern part of Ethiopia, the vector of VL is associated with acacia trees and in the south with termite hills (9, 14). Termite mounds are important vector breeding and resting sites. Proximity of human dwellings to termite mounds & practice of sitting on termite mounds increases the risk of infection (37). Finding from a study done in Kenya showed that presence of large number of termite mounds (P=0.001, df=8, x^2=39.821) and resting or sitting near termite mounds (P=0.001, df=2, x^2=17.67) was associated with increased risk of VL infection (6). A case-control study from southern Ethiopia also indicated that proximity of termite hills to home was associated with the disease (38, 39). Presence of acacia tree and sleeping under it at night was also associated with increased

risk of infection (21, 27). 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 (40). 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) (41).

2.1.3. Individual behavioral factors

In addition to socio-economic and household and environmental factors, risk of kala-azar will also be determined by individual behavioral factors such as nomadic behavior, associations with livestock, sleeping outdoors. Man-fly contact is increased by sleeping out of doors habitually (42). Sleeping on the ground increased risk of VL infection (21).
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) (27). Another case control study done in Argentina also showed the presence of marked dose-response effect with the number of months per year spent sleeping outdoors (OR=10.0; 95%CI=3.4-29.6) (43).

In a case control study conducted in Kenya and Uganda, it was found that having a mosquito net was associated with a decreased risk of VL infection (OR=0.39; 95%CI=0.16, 0.95) (41). 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 (44). 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) (33). Similarly, it was evidenced from the work of Seife Bashaye, et al. (27) that insecticide-treated nets may only protect a portion of those at risk of infection.

2.1.4. Co-morbid factors

Malnutrition: Poor nutritional status in general and protein-energy malnutrition in particular increase the risk that an infection will progress to clinically manifests full blown disease of visceral leishmaniasis (22).

A randomized trial study conducted in Gondar University Hospital, Ethiopia, revealed that majority of kalaazar patients had BMI below 18.5 (median $\pm$ SEM: 16.5 $\pm$ 0.3); 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 (21.5 $\pm$0.8) (45). A study conducted in Kenya and Uganda also indicated that malnutrition was among the main determinants of the disease in which nutritional status of cases was extremely poor; 51.6% of all cases were severely anaemic and 48.4% were moderately anaemic (41).

HIV co-infection: The first case of leishmaniasis associated with HIV infection was reported in 1985, and the number of reported cases in southern Europe subsequently increased rapidly. Since that time, 35 countries have reported cases of coinfection. HIV infection increases the risk of developing VL by a factor of between 100 and 1000 in endemic areas, reduces the likelihood of response for treatment, and highly increases the probability of relapse (1).

Different studies all over the world highlighted the importance of HIV infection as risk factor for VL. A study done in Humera, Ethiopia, reported that 31% of VL patients were tested positive for HIV. Concomitant occurrence of HIV with VL not only hastens the progress of VL infection to clinical VL but also troubles the VL treatment by increasing risk of non responsiveness to commonly available drugs and repeated relapse of the disease after treatment. VL has been claimed to be 5th opportunistic infection considered as one of AIDS defining illness by World Health Organization (WHO) (46). The study done in Tigray, showed that being infected with HIV was the most important predictor of death among VL patients (AOR=4.5) (47). A case control study from Teresina, northeastern Brazil, reported that HIV co-infection was the most important factor of death among patients suffering from VL infection (OR = 19.0; CI= 1.7, 211.3) (48).

2.2. Significance of the study

Since resources in the context of NID and zoonoses research are extremely limited, especially when compared to HIV/AIDS, malaria and tuberculosis, there is a strong need for identifying key research priorities in terms of disease control (49).

Risk factor data are essential to design the appropriate public health response. The results of this study will be used to determine which and where target interventions and control strategies should be delivered, and will guide researchers towards the development of future studies of better methodological quality.

The study will serve to identify and characterize main determinants relatively rapid and cheap to collect, and complements other sources of risk factor information that are more specific; and it will ultimately help in the successful implementation of appropriate and locally adapted prevention and control strategies. It will also help health planers and donors working in the area to provide with recent insight of the problem to revise their program and design appropriate prevention and control tools.

CONCEPTUAL FRAME WORK

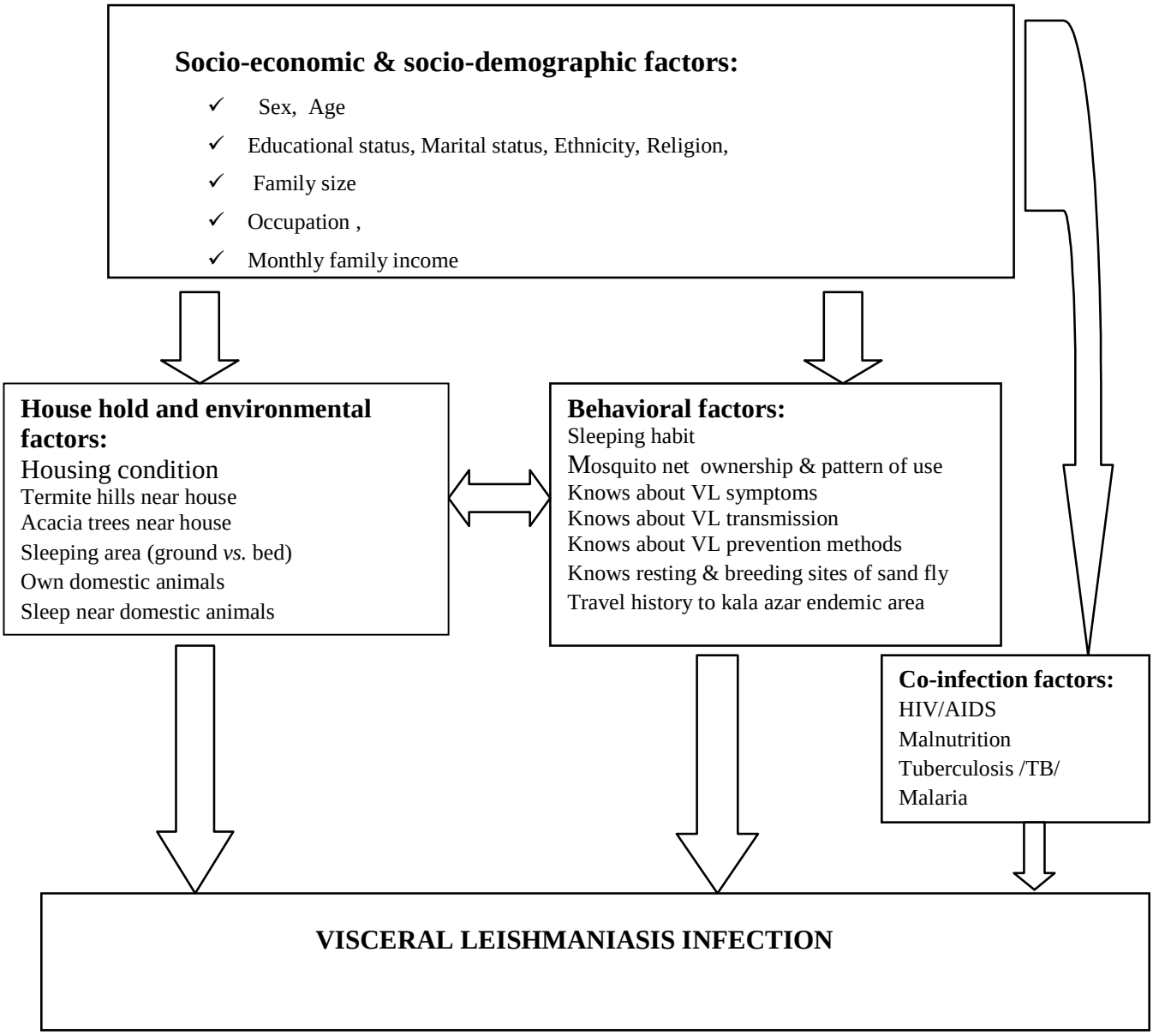

Fig. 1: Conceptual frame work

CHAPTER 3:- Objective of the study

3.1. General Objective

- To determine factors associated with visceral leishmaniasis in North Gondar Zone, North West Ethiopia.

3.2. Specific Objective

- To identify factors associated with human VL infection in north Gondar zone.

CHAPTER 4:- Materials and methods

4.1. Study setting

North Gondar is one of the 11 zones in Amhara region with an estimated population of 2,929,628 (forecasted for 2005 E.C. by zonal statistical department) of which 207,044 are urban dwellers and the rest in the rural areas. 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.

4.2. Study period

The study was conducted from Sep. 1 to 30, 2013.

4.3. Study design

Study design: Institutional based unmatched case-control study.

4.4. Population

4.4.1. 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.

4.4.2. 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.

4.4.3. Study Unit: The study unit of cases was confirmed leishmanises patient receiving treatment, and apparently healthy individual counterpart controls tested negative for VL.

4.4.4. Inclusion criteria: Kala azar patients and apparently healthy kala azar free patients and voluntary for interview.

4.4.5. Exclusion criteria: Patients who were seriously ill and with mental disorders and those who were not willing to be interviewed.

4.5. Sampling procedures and sample size determination

4.5.1. Sample Size Determination: Sample Size was determined by two population proportion formula for unmatched case control study design as shown below 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 (27). 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. The formula to calculate the required sample size manually is as follows:

$$\frac{\left[Z\alpha/2\sqrt{(1+1/r)\,p\,(1-p)} + Z\beta\sqrt{p_1(1-p_1) + p_2\frac{(1-p_2)}{r}}\right]^2}{(p_1 - p_2)^2}$$

Where:-

α= The level of significance= 0.05

β = The power of the test = 80 %

r = Ratio of Controls to Cases = 4

p_1= Hypothetical proportion of controls with exposure = 20.9%

P_2 = Hypothetical proportion of cases with exposure = 34.57%

P= pooled estimate of P_1 & P_2 = $\frac{P_1+rP_2}{1+r}$

4.5.2. Sampling Procedures: 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.

4.6. Study variables

- ***Independent variables****:*
  - Socio-economic and demographic variables (Age, sex, occupation, monthly family income, family size)
  - Behavioral variables (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)
  - Environmental and house hold variables (termite mounds near house, acacia trees near house, domestic animals ownership, sleeping area.
  - Co-infection (HIV/AIDS, malnutrition, tuberculosis, malaria) factors
- ***Dependent Variable:*** Visceral leishmaniasis infection.

4.7. Data Collection Process

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.

4.8. Data processing 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.

4.9. Ethical considerations

Ethical clearance and approval was obtained from Ethical clearance board of public health and medical science college of Jimma University. Official support letter was given from Jimma University to Amhara Regional Health Bureau and Gondar University hospital. Support letter was also sought from the regional health bureau to Zonal 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.

4.10. Plan for dissemination and utilization of findings

The result of this study will be presented at defense at Jimma University and will also be submitted to the College of Public Health and Medical Sciences department of Epidemiology. The findings will be reported to Amhara Regional Health Bureau, North Gondar Zonal Health Department, and MSF-Holland Abderafi to enable them take recommendations in to consideration during their planning process. Attempts will also be made to get the thesis published on peer reviewed journals for wider communication.

4.11. 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.

4.12. Operational definitions

Visceral leishmaniasis or Kala azar (KA): A case of visceral leishmaniasis is a person showing clinical signs (mainly prolonged irregular fever > two weeks, splenomegaly and weight loss) with serological and/or parasitological confirmation of the diagnosis.

Co-infection: VL patients suffering from one or more of (HIV, malnutrition, tuberculosis or malaria) at admission

Direct agglutination test (DAT): the aqueous antigen which has to be kept refrigerated and/or the freeze-dried antigen which is stable at ambient temperature useful for the serologic diagnosis of VL.

Termite hills: Raised soil structures with several ventilation shafts built over underground nest of the termites.

Apparently healthy: An individual who is free from WHO case definition signs and symptoms of visceral leishmaniasis.

Exposure status history: participants were asked about some exposures (experience of sleeping on the ground, experience of outdoor sleeping, previous history of VL, presence of a member in the family with history of VL, travel history to kala azar endemic areas) in the past one year.

Presence of termite hills and acacia trees around: The presence of termite hills and acacia tree near house was an estimated distance less or equals to 100 meters.

Nutritional status: Normal $\geq$ -1Z-score

: Malnourished < -1Z-score

CHAPTER 5:- Result

A total of 545 subjects, 109 (20%) cases and 436 (80%) controls were enrolled and interviewed.

I. Socio economic & demographic characteristics

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 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

II. House hold and environmental variables

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).

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

III. Individual behavioral variables

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

IV. Co-morbid variables

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

Risk factors for VL

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).

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) (Table 5).

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) (Table 5).

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 kalaazar (being aware of its symptoms and transmission methods, knowing where vector of VL can rest and breed and knowing prevention methods of VL), 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) (Table 5).

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).

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**

Chapter 6:- 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 predictors and determinants of VL infection in the area. In addition, this study tried to assess and measure sero-status for HIV, nutritional status and other most common inter-current infection status of study subjects.

This study demonstrated significant association between gender and VL infection. This result is supported by a result from a case control study done in Brazil which reported that highest proportion of cases were males (OR=2.3) (25). Similarly, a case control study from Bihar, India reported that 75.93% of cases were males with male to female ratio of 3:1 (36). 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 (26). 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.

However, a case control study done in Addis Zemen, Ethiopia, 2009 did not show statistically significant difference in sex among cases and controls (27). The possible justification for this variation could be seasonal variation in which the study was conducted; the Addis Zemen study was conducted in January which is post harvest season in which there might not be significant activity difference between men and women and all family members sleep outside their house due to fear of hot weather condition. Similarly, unmatched case control study done in Fangak, South Sudan, 2011, to assess Risk factors for the transmission of kala-azar also indicated that more than half (56%) of cases were females (44). The probable explanation for this discrepancy could be cultural difference in our society and the Sudan in which Sudanese women are highly engaged in outdoor activities than men that could increase their exposure to sand fly bite.

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 (28). Another study done in Nepal also indicated that age is associated with increased risk of infection (30). 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 (44). 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. And children in this age group in most of the third world countries including Ethiopia and Sudan are forced to engage in outdoor activities like herding cattle and other domestic animals that increase likelihood of their exposure to sand fly bite.

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 (33). Another study done in India also showed that higher socio economic status was associated with reduced risk of VL infection compared to lower ones (34). Similarly, a study done in Kenya and Uganda demonstrated that highest socio economic status was protective to VL infection (41). 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 (26). Similarly a study done in Nepal showed that poverty incidence is associated with the KA incidence rate. One percent reduction in poverty incidence could reduce KA incidence by about 1.6%, implying that poverty reduction will be a very effective mechanism of reducing KA (35). 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 (33). Similar study from India also showed that house made of mud wall was statistically significantly associated with VL infection (36). Another study from Nepal reported that house constructed in mud was risk factor for VL infection (30). 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 his finding a study done in Addis Zemen, Ethiopia indicated dog ownership was associated with VL (27). 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 (34, 40). 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 (38, 39). Similarly, a finding from Kenya reported that

presence of large number of termite mounds (P=0.001) and resting or sitting near termite mounds (P=0.001) was associated with increased risk of getting VL infection (6). Consistent with our finding, a study from Addis Zemen reported association between risk of VL and presence of acacia trees near the house (27). The probable reason could be that termite hills and acacia tree with barks are highly favorable sites for breeding and resting of sand flies.

However, a case control study done in Kenya and Uganda did not support the finding of current study in which proximity of termite mounds and acacia trees were not associated with increased risk of VL (41). The possible explanation for this difference could be due to the reason that termite hills and acacia tree would probably extremely common throughout the affected communities in Kenya and Uganda that would not be differ in exposure among cases and controls.

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 (40). Another similar finding from Kenya and Uganda also indicated that people who change sleeping area between bed and ground were at higher risk of getting VL infection (41). The possible justification for this could be that sleeping on ground may be related with increased moisture which may attract sand fly and favorable for it.

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 (27). Another similar study from Argentina showed the presence of marked dose-response effect with the number of months per year spent sleeping outdoors (43). 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. Similar to this finding a result from the work of Seife Bashaye, et al highlighted that ownership of a treated bed net appeared to lower risk of infection, but it did not reach statistical level of significance (27). 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 (44). 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 (46, 50). A study conducted in Tigray, Ethiopia showed that HIV positive serostatus was the most important predictor of death among patients with VL (47). Similarly, a case control study conducted in Teresina, northeastern Brazil, reported that HIV co-infection was the most important factor of death among patients suffering from VL infection (48). 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 (45). Another study conducted in Kenya and Uganda also indicated that nutritional status of cases was extremely poor (41). 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.

Contrary to current finding, house-to-house demographic and immunological surveys conducted in 10 selected clusters in Nepal demonstrated that no clear association was found between nutritional status and DAT result positivity and malnutrition had no association with the infection rate (51). The possible explanation for this difference could be due to difference in study design and Nepal might be in a better economical stand than Ethiopia so that malnutrition state in a general community may be lower than here.

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.

Chapter 7:- Conclusion and Recommendations

7.1. Conclusion

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.

7.2. Recommendations

The findings of this study provide a useful and potentially valuable tool for leishmaniasis control. Policy makers and health planners need to understand possible determinant factors which increase risk of infection within the community.

Policy makers

- Development and distribution of canine anti-leishmanial vaccine for dogs should be commenced.
- Integrated disease surveillance response including passive case detection shall be strengthened to early predict the incidence and prevalence of the disease so as to take prompt intervention measures in such endemic areas.

Health bureaus, Agriculture bureaus and NGOs working on leishmaniasis

- Strengthen the collaboration and integration of the leishmaniasis prevention and control activities with other disease control programs aimed against vector borne diseases.
- Insecticide treated bed net supply should be strengthened and sustainable.
- Dog culling activities targeting non-owned or stray dogs should be advocated.

General community

- Sleeping above the ground on bed prepared from any locally available material is highly advisable and avoiding outdoor sleeping as much as possible.
- Keeping domestic animals away from human beings in a separate room.
- Constructing houses at least 100 meters away from acacia trees with cement wall (if possible) or making mud walls well plastered and clearing residential area from termite hills.

Researchers

- The role of dog in the transmission cycle should be well investigated.
- Study should be conducted to further investigate the controversial association between domestic animal ownership and VL infection.

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ANNEXS

Annex I: Consent form

INTRODUCTION AND CONSENT:

My name is ----------. I am working with Mr. Kindie Bantie doing a research as partial fulfillment for the requirement of Masters Degree in Public Health at Jimma University, Department of Epidemiology. I am intended to interview patients in this health institution to assess risk factors of visceral leishmaniasis (kala azar) disease. I am going to ask you some questions that are very important for the programmers in health care services to plan improved intervention of this ugly disease. Your name will not be written in this form and the information you give is kept confidential. If you do not want to answer all or some of the questions, you do have the right to do so. However, your willingness to answer all of the questions would be appreciated. Would you participate in responding to the questions in this questionnaire?

Yes_____ No_____ (Thank him/her and pass to next interviewee)

Name and signature of the interviewer who sought the consent_____

Interviewer name _____ Supervisor name _____ Date of interview

Annex 2: Questionnaire English version

Questionnaire for the assessment of factors for VL in North Gondar Zone, Amhara region, North West Ethiopia, September 2013

VL status, 1= Present 2= Absent

Part I: Socio economic & demographic data

1. Sex 1= Male 2= Female
2. Age in years……
3. Educational status, 1=Illiterate 2= Formal education (highest grade achieved)
4. Marital status 1= single 2= Married 3=Divorced 4= widowed
5. Ethnicity 1= Amhara 2= Tigre 3= Oromo 4= others, specify……
6. Religion 1= Orthodox Christians 2= Muslims 3= Protestant 4= others, specify……..
7. Family size (in number) ----------
8. What is your occupation? 1= Government employee 2= Merchant 3= House wife 4= Daily laborer 5= farmer 6= student
9. How much the family earn monthly?

Part II. House hold and environmental variables

1. *Type of roof? 1= Corrugated iron sheet* 2= Thatched roof 3= Other (specify)
2. Type of floor? 1= Cemented 2= Earthen floor
3. Type of wall? 1= Cemented 2= Mud
4. Is there dog in your home? 1=Yes 2= No
5. Is there cat in your home? 1= Yes 2= No
6. Do you possess cattle in your home? 1= Yes 2= No
7. Is there termite hill near your house at a 100 meter distance? 1= Yes 2= No
8. Is there acacia tree near your home at a 100 meter distance? 1= Yes 2= No
9. Where do you sleep at home in the past one year? 1= On the bed 2= On ground 3= Mixed
10. Do you sleep near domestic animals? 1= Yes 2= No
11. Have you had family member with VL in the past one year? 1= Yes 2= No
12. If yes to Q. 11, how many members?

Part III: Individual behavioral variables

1. Specify your sleeping habit 1= Never sleeps outside 2= Sleeps outside during some months 3= Sleeps outside all of the year
2. Do you have mosquito net? 1= Yes 2= No
3. If yes to Q. 2, pattern of use? 1= Always 2= some times 3. Never use
4. Have you ever heard of kala azar? 1= Yes 2= No
5. If yes to above question, how (where) did you heard of it? 1. Mass media 2. Health facility (health professionals) 3. Friends
6. Do you know how VL is transmitted? 1= Yes 2= No
7. If yes to Q. 6, how? 1= through sand fly bite 2= through sharing of contaminated sharps 3= through respiratory droplets 4= others (specify)……
8. Do you know where vector of VL rest and breed? 1= Yes 2= No
9. If yes to Q. 8, list them, 1= termite hills 2= Acacia trees 3= Cracks 4= Others (spe
10. Do you know symptoms of VL? 1= Yes 2= No
11. If yes to Q. 10, ask respondent to list at least 3. 1= fever 2= weight loss 3= abdominal swelling 4= epistaxis (nasal bleeding) 5= gum bleeding 6= loss of appetite
12. Do you know how this disease can be prevented? 1= Yes 2= No
13. If yes to Q. 12, list the methods. 1= Mosquito net 2= Not sleeping habitually outside the door 3= Constructing houses away from termite hills 4= Constructing houses away from acacia trees 5= Constructing houses from cements, plastering walls and making free of cracks. 6= Dog culling 7= Smokes to repel vectors
14. Have you had this illness previously? 1=Yes 2= No
15. If yes to above question, have you been treated for it? 1= yes 2= no
16. If yes to Q. 15, where did you seek treatment? 1= Health institution 2=Pharmacy (self prescription) 3= Traditional healers 4= Elsewhere, specify--------
17. Any history of travel to kala azar endemic area (Humera, Metema, etc) in the past one year 1= yes 2= no
18. Visceral leishmaniasis type identified 1 = Primary 2 = Relapse 3 = Other
19. Duration of illness 1 = 0-1 month 2 = 2-3 months 3 = 4-5 months 4 = More than 5 months

Part IV. Co-morbid factors

1. HIV status 1 = Positive 2 = Negative 3= Unknown
2. Nutritional status 1 = Normal 2 = Malnourished 3= Unknown
3. Tuberculosis present? 1 = Yes 2 = No 3= Unknown
4. Malaria present? 1 = Yes 2 = Unknown

Annex III: Questionare Amharic version

በጅማ ዩኒቨርሲቲ የማህበረሰብ ጤና እና ህክምና ሳይንስ ኮሌጅ ሌሽማኒያ/ካላአዛር/ በሽታ ወሳኝ አብዥዎችን ለማጥናት የተዘጋጀ መጠይቅ ነዉ::

በፈቃደኝነት ላይ የተመሰረተ ቃለ መጠይቅ ለማካሄድ የጋራ ሰምምነት ቅጽ

መግቢያ

ጤና ይስጥልኝ፤ ስሜ ----------ይባላል፡፡ የምሰራው በጅማ ዩኒቨርሲቲ ኢፒዲሞሎጅ የትምህርት ክፍል የማስትሬት ዲግሪ ተማሪ ከሆኑት አቶ ክንዴ ባንቴ ጋር ሲሆን አቶ ክንዴ በጅማ ዩኒቨርሲቲ በህብረተሰብ ጤና ዘርፍ በኢፒዲሞሎጂ ትምህርት ክፍል ለሁለተኛ ዲግሪው ማሟያ ጥናት በማካሄድ ላይ ይገኛል፡፡ የጥናቱ ዓላማ የሌሽማኒያ/ካላአዛር/ በሽታን ወሳኝ አብዥዎች በመለየት የበሽታውን ሥርጭት ለመግታት ለማገዝ ነው፡፡ ስለሆነም፤ ከበሽታው ጋር ተዛማጅነት ያላቸው ወሳኝና ዋና ዋና አብዥዎችን ለመዳሰስ የሚረዱ ጥቂት ጥያቄዎችን አቀርብልዎታለሁ፡፡ የሚሰጡኝ ማናቸውም መረጃ ከጥናቱ ዓላማ ውጭ ለሌላ አገልግሎት አይውልም፤ ለሦስተኛ ወገንም ተላልፎ አይሰጥም፡፡ ሥምዎ በመጠይቁ ላይ አይጠቀስም፡፡ ስለዚህ የእርሶ ምላሽ የበሽታውን ሥርጭት ለመግታት ወሳኝ ሚና እንዳለው ተረድተው በተቻለ መጠን ተዓማኒ መልስ እንዲሰጡኝ በአክብሮት እጠይቅዎታለሁ፡፡ በሙሉም ሆነ በከፊል ላለመመለስ የሚፈለጉት ጥያቄ ካለ እንዲመልሱ አይገደዱም፡፡

በጥናቱ ለመሳተፍ ፈቃደኛ ነዎት? አዎ---------- አይደለሁም----------

ምስጋና

ቃለ መጠይቁን የሞላው ሰው ሥም---------- ፊርማ---------- ቀን----------

የተቆጣጣሪ ሥም---------- ፊርማ----------

የሌይሽማኒያሲስ ሁኔታ፣ 1. አለ 2. የለም

ክፍል ፩፡ የተጠያቂዋ/ዉ አጠቃላይ ማህበራዊ እና ኢኮኖሚያዊ ሁኔታ

1. ፆታ 1.ወንድ 2.ሴት
2. እድሜ ----------
3. የትምህርት ደረጃ 1. ማንበብ ና መጻፍ የማይችል 2. መደበኛ ት/ት (ያጠናቀቁት ከፍተኛ ክፍል)
4. የጋብቻ ሁኔታ 1. ያላገባ/ች 2. ያገባ/ች 3. የፈታ/ች 4. የሞተባት/በት
5. ብሄር 1.አማራ 2.ትግሬ 3. ኦሮሞ 4. ሌላ (ይገለጽ)
6. ኃይማኖት 1. ፖርቶዶክስ 2. ሙስሊም 3. ፕሮቴስታንት 4. ሌላ (ይገለጽ)
7. የቤተሰብ ቁጥር----------
8. ስራ 1. የመንግስት ሰራተኛ 2. ነጋዴ 3. የቤት እመቤት 4. የቀን ሠራተኛ 5 ሌላ (ይገለጽ) -------
9. የወር ገቢ (የቤተሰቡ አጠቃላይ ገቢ) በብር----------

ክፍል ፪፡ የተጠያቂ/ዋ/ዉ ቤተሰባዊ እና አባቢያዊ ሁኔታ

1. የቤትዎ ጣራ የተገነባው ከምን ነው? ነ. የቆርቆሮ ክዳን 2. የሣር ክዳን 3. ከሌላ (ይገለጽ)

2. የቤትዎ ወለል የተገነባው ከምን ነው? ነ. ከሲሚንቶ /ሊሾ/ 2. አፈር 3. ከሌላ (ይገለጽ)
3. የቤትዎ ግድግዳ የተገነባው ከምን ነው? ነ. ከብሉኬት 2. ከጭቃ /የተለሰነ/ 3. ከሌላ (ይገለጽ)
4. ከሚከተሉት አንድ ወይም በላይ የቤት እንስሳት በቤትዎ ይገኛሉን?

   ሀ. ውሻ? ነ. አዎ 2. የለም፣ ካለ ስንት/በቁጥር----------

   ለ. ድመት ነ. አዎ 2. የለም፣ ካለ ስንት/በቁጥር-----

   ሐ. የቀንድ ከብቶች ነ. አዎ 2. የለም፣ ካለ ስንት/በቁጥር-----

   መ. ሌላ (ይገለጽ) ነ. አዎ 2. የለም፣ ካለ ስንት/በቁጥር-----
5. በቤትዎ አቅራቢያ የምሥጥ ኩይሳ አለን? ነ. አዎ 2. የለም
6. ከዚህ በላይ በተራ ቁጥር 5 ለቀረበው ጥያቄ መልስዎ አዎ ከሆነ፤ በግምት ምን ያህል ሜትር የርቃል ሜትር
7. በቤትዎ አቅራቢያ የግራር ዛፍ አለን? ነ. አዎ 2. የለም
8. ከዚህ በላይ በተራ ቁጥር 7 ለቀረበው ጥያቄ መልስዎ አዎ ከሆነ፤ በግምት ምን ያህል ሜትር የርቃል
9. ዘወትር የሚተኙት ምን ላይ ነው? ነ. አልጋ ላይ 2. ከመሬት 3. ሁለቱም
10. የቤት እንስሳት በሚያድሩበት አካባቢ ይተኛሉን? ነ. አዎ 2. የለም

ክፍል ፫፡ የተጠያቂ/ዋ/ዉ ግላዊ ባህሪ ሁኔታ

1. የምኝታ ልምድዎ ምን ይመስላል? ነ. ከቤት ውጪ ተኝቼ አላውቅም 2. የተወሰኑ ወራት ከውጪ እተኛለሁ 3. ዓመቱን ሙሉ ከውጪ እተኛለሁ
2. የትንኝ መከላከያ አጎበር አለዎትን? ነ. አዎ 2. የለም
3. ከላይ በተራ ቁጥር 3 ለቀረበው ጥያቄ መልስዎ አዎ ከሆነ፤ የአጎበር አጠቃቀምዎ ምን ይመስላል? ነ. ሁልጊዜ እጠቀማለሁ 2. አልፎ አልፎ ብቻ እጠቀማለሁ 3. ፈጽሞ አልጠቀምም
4. ስለ ካላአዛር በሽታ ሰምተው ዬውቃሉን? ነ. አዎ 2. የለም
5. ከላይ በተራ ቁጥር 5 ለቀረበው ጥያቄ መልስዎ አዎ ከሆነ፤ ከማን ሰሙ? ነ. በሬዲዮ 2. ከጤና ድርጅት /ጤና ባለሙያ/ 3. ከጓደኛ /ከጎረቤት 4. ከሌላ (ይገለጽ)
6. የሌሽማኒያሲስ በሽታ መተላለፊያ መንገዶችን ያውቃሉን? ነ. አዎ 2. የለም
7. ከላይ በተራ ቁጥር 7 ለቀረበው ጥያቄ መልስዎ አዎ ከሆነ፤ እንዴት? ነ. በውሻ ንክሻ 2. በትንኝ ንክሻ 3. ስለታማ ነገሮችን በጋራ መጠቀም 4. በትንፋሽ 5. ሌላ (ይገለጽ)
8. የሌሽማኒያሲስ በሽታ አስተላላፊ ትንኝ ማረፊያና መራቢያ ቦታ ያውቃሉን?
9. ከላይ በተራ ቁጥር 9 ለቀረበው ጥያቄ መልስዎ አዎ ከሆነ፤ ይግለጹ ነ. የምስጥ ኩይሳ 2. የግራር ዛፍ 3. የመሬትና የግድግዳ ስንጥቆች ውስጥ 4. ሌላ (ይገለጽ)
10. የሌሽማኒያሲስ በሽታ ምልክቶች ምን ምን እንደሆኑ ያውቃሉ? ነ. አዎ 2. አላውቅም

11. ከላይ በተራ ቁጥር 10 ለቀረበው ጥያቄ መልስዎ አዎ ከሆነ፤ ምልክቶቹን ይጥቀሱ 1. ትኩሳት 2. የሰውነት ክብደት መቀነስ /መክሳት/ 3. የጉበትና የጣፊያ እበጠት 4. ነስር 5. የድድ መድማት 6. የምግብ ፍላጎት መቀነስ
12. የዚህን በሽታ መከላከያ መንገዶች ያውቃሉን? 1. አዎ 2. አላውቅም
13. ከላይ በተራ ቁጥር 12 ለቀረበው ጥያቄ መልስዎ አዎ ከሆነ፤ መንገዶቹን ይጥቀሱ 1. የትንኝ መከላከያ አጎበር መጠቀም 2. ከቤት ውጪ አዘውትሮ አለመተኛት 3. መኖሪያ ቤትን ከምስጥ ኩይሳ አርቆ መገንበት 4. መኖሪያ ቤትን ከግራር ዛፎች አካባቢ አርቆ መገንበት 5. መኖሪያ ቤትን በሲሚንቶ መገንበት፤ የቤቱን ግድግዳ በደንብ መለሰንና ስንጥቅ እንዳይኖረው ማድረግ 6. ውሾችን ማጥፋት 7. ቤት ውስጥ ጭስ ማጨስ
14. ከዚህ በፊት ይህ በሽታ ይዞዎት ያውቃልን? 1. አዎ 2. የለም
15. ከላይ በተራ ቁጥር 14 ለቀረበው ጥያቄ መልስዎ አዎ ከሆነ፤ ታክመው ነበር? 1. አዎ 2. የለም
16. ከላይ በተራ ቁጥር 15 ለቀረበው ጥያቄ መልስዎ አዎ ከሆነ፤ ህክምናውን ያገኙት የት ነበር? 1. ከጤና ተቋም 2. መድኃኒት ቤት በራሴ ትዛዝ ገዝቼ 3. ከባህል ህክምና መስጫ 4. ሌላ (ይገለጽ)
17. ከቤተሰብዎ አባላት ውስጥ ባለፈው አንድ ዓመት በዚህ በሽታ የተያዘ ነበርን? 1. አዎ 2. የለም
18. ከላይ በተራ ቁጥር 17 ለቀረበው ጥያቄ መልስዎ አዎ ከሆነ፤ ስንት የበተሰብ አባላት፣ ቁጥራቸው ይገለጽ------

ክፍል፬ ፡ የተጓዳኝ በሽታዎች ሁኔታ

1.	የኤች.አይ.ቪ. ሁኔታ	ሀ. አለ	ለ. የለም	ሐ. አይታወቅም
2.	የምግብ እጥረት	ሀ. የለም	ለ. የለም	ሐ. አይታወቅም
3.	የሳንባ ነቀርሳ በሽታ	ሀ. አለ	ለ. የለም	ሐ. አይታወቅም
4.	የወባ በሽታ	ሀ. አለ	ለ. የለም	ሐ. አይታወቅም