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Original Article

Household and Environmental Risk Factors for Kala-azar: A Case-Control Study in Tertiary Care Hospital of Bangladesh

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Abstract

Background: Visceral Leishmaniasis (VL), commonly known as Kala-azar is a chronic febrile disease occurs widely throughout the world. There are many risk factors which can influence the causation of kala azar in Bangladeshi people. The aim of the present study is to describe the Sociodemographic, household and environmental risk factors of kala-azar among a case series of Bangladeshi patients**. Method:** This case control study was carried out at inpatient department of Community Based Medical College Hospital, Mymensingh from July 2010 to June 2011, for a period of 1(one) year. The study samples were clinically and parasitologically confirmed kala-azar cases. The controls were rK 39 strip test negative hospitalized cases admitted for other reason. **Results:** Univariate analysis showed that nature of wall in the main structure, floor of the house, presence of cracks and crevices in walls, presence of a granary inside houses and presence of bamboo trees near houses, were risk factors for kala-azar. Multivariate analysis showed that Presence of cracks and crevices in walls (OR=3.429, 95%CI=1.037-11.338, *P* =0.043) and presence of bamboo tree around houses (OR=5.652, 95%CI =1.368-23.347, *P* =0.017) in rural areas of study region, were significant risk factors for kala-azar. **Conclusion:** These findings have important practical implications because they suggest that on improving housing and environmental conditions in rural areas, may be particularly effective in reducing the incidence of kala-azar and its transmission of infection by sand fly vectors. [Journal of Science Foundation, 2016;14(2):56-61]

Key words: Kala-azar; visceral leishmaniasis; household and environmental risk factors

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Introduction

Kala-azar is caused by *L. donovani* complex, which includes *L. donovani*, *L. infantum* and *L. chagasi*. It is characterised by prolonged irregular fever, lymphadenopathy, hepato-splenomegaly and progressive anaemia (Agrawal et al., 2005). Leishmaniases are caused by 20 species of *Leishmania* (L) and transmitted by 30 species of sand fly (Desjeux 1992). *Leishmania donovani* is transmitted by the female sand fly and humans are the only reservoir in South Asia (WHO 1990).The disease kills almost all untreated patients (Boelaert et al., 2000). More than 90% of global VL cases occur in six countries: Bangladesh, Brazil,

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Ethiopia, India, South Sudan and Sudan (Alvar et al., 2012).Worldwide there are estimated to be approximately 500,000 cases of visceral leishmaniasis per year and many of them are associated with epidemics particularly in Indian subcontinent and Sudan (Sundar et al., 1999).The large number of endemic countries illustrates the global importance of the problem (WHO 1996). A current study showed that the high prevalence of Kala-azar positive cases were seen in the district of Mymensingh, followed by that of Tangail, Gazipur, Dhaka, Sirajgonj and Manikganj districts of Bangladesh (Begum et al., 2002). The upazilas of Trishal and Fulbaria, within the district of Mymensingh, have 60% of all cases in the country according to the Ministry of Health. An entomological survey shows density of sand flies both vector and non-vector species were significantly higher in endemic areas than non-endemic areas (Alam et al., 2009).

Now-a-days, the disease shows wide spread geographical distribution and is being reported from previously non-endemic areas. Economic and demographic circumstances that contribute to increased prevalence include: new agro-industrial project, large-scale migration of populations, unplanned urbanization, and man-made environmental changes. Sand fly is found to take rest in cattle shades in much greater number than inhuman dwelling. The density of it here is 8-10times higher than human dwelling. In human dwelling they are usually found inside crack sand crevices of the wall, loose bricks, behind furniture, underside the beds, in empty boxes and on hangings in the living room. Outdoor resting places are bushes, rodent's burrow, rat holes in trees and bases of banana clumps (Chowdhury et al., 1993).In common with its neighbors' India and Nepal, VL in Bangladesh is anthroponotic. Living in proximity to a Kala-azar case is the strongest risk factor for the disease (Bern and Chowdhury 2006). Mud walls, palpable dampness in house and peridomestic vegetation may increase infection risk through enhanced density and prolong survival of the sand fly vector. Bed net use, sleeping on a cot and indoor residual spraying are generally associated with decreased risk. Poor micronutrient status increases the risk of progression to Kala azar (Bern et al., 2010).There are a number of studies on risk factors for L. donovani infection and VL in the Indian subcontinent. In these studies VL patients or asymptomatically infected individuals are generally compared to healthy non-infected individuals respectively. Briefly, L. donovani infection, defined as positivity in serology or leishmanin skin test (LST) in a cross-sectional survey, has been associated with age, gender, house structure and socio-economic status as well as previous VL cases in the house or in the proximity (Schenkel et al., 2006; Bern et al., 2007; Singh et al., 2010; Rijal et al., 2010).According to these studies the risk factors for L. donovani infection and VL are not always concordant (Bern et al., 2010).However it is difficult to conclude that they are completely different as the studies conducted so far used different methodology (i.e. different markers for infection, VL case definitions or study designs) and surveyed different populations, usually limited to single or few communities from India, Nepal or Bangladesh with relatively high and recent transmission. To properly compare the risk factors for kala-azar infection on the same population and over the same time frame is required. The aim of this study is to evaluate if individual, household and environmental factors associated with kala-azar in Bangladesh and other subcontinent countries were different. Therefore this case control study will help to determine whether household and environmental characteristics were risk factor for occurrence of Kala-azar.

Methodology

The study was carried out at the Community Based Medical College Hospital, in Mymensingh district from July 2010 to June 2011. The study is designed as a case control study. Patients admitting the inpatient department of Community Based Medical College Hospital, Mymensingh during the study period. The cases were rK 39 strip test positive and parasitologically confirmed cases of Visceral Leishmaniasis and the controls were rK 39 strip test negative hospitalized cases admitted for other reason. Since no prior quantitative information on various risk factors was available, estimated visceral leishmaniasis prevalence in Indian sub-continent (Bangladesh, India and Nepal) was found 21 cases per 10,000 sample population (National guideline on Kala-azar Elimination Program in Bangladesh, 2010). As the available number of cases in the setup are not many, over the study duration we could recruit 60 cases and 120 controls for the present case series. The case control ratio was 1:2. The Study subjects were recruited from the cases enrolled for a Randomized Controlled Trial at the study place. They were primary cases i.e., has never been diagnosed or treated for Kala-azar in past. A separate consent process was followed for the present case-control study. As part of the Randomized Control Trial the cases were rK39 strip test positive and already confirmed by splenic aspiration positive for LD bodies. The controls were approached for written informed consent process to participate in the study and negative rK39 strip test. Inclusion criteria- includes male or female of all ages with rk39 positive at baseline assessments and history of fever, for at least 2 weeks with

Anaemia (5<Hb<10g/dl) and/or Loss of weight and/or Splenomegaly. Exclusion criteria were known Hepatitis or known HIV positive, patients who present with Post Kala-azar Dermal Leishmaniasis, Clinical symptoms of chronic underlying disease such as severe cardiac, renal or hepatic impairment, patient with Positive HRP2/pLDH Combo test for Malaria and patient unwilling to participate. Interview schedule and check list were uses as research tool. The pre-designed semi-structured questionnaires were used for both the cases and controls. A face to face interview with the cases and controls and in case of cases unable to respond for the illness, spouse or the closest attendant were interviewed for filling out the questionnaire. The variables included to record/measure were age, sex, BMI, income, marital status, longest residence in kala azar area, nature of wall in the main structure ,floor ,roof of the house, presence of cracks and crevices in wall, presence of natural light inside living room, presence of granary ,vegetation, banana and bamboo tree close to living house. Data were entered into a computer and data file was constructed. Forms were decoded and scrutinized for accuracy and consistency. Data were analyzed using Epi-Info version 6.2 (Centers for Disease Control and Prevention, Atlanta, GA) and validated by logical and range checks with SPSS version 16.0. For each of the study factors, risk was estimated by calculating the odds ratio (OR) as an approximation of the relative risk with 95% confidence intervals (CIs) using Epi-Info version 6.2. The significance of the OR was analyzed with the Mantel-Haenszel chi-square test. On the basis of the OR in univariate analysis, variables that were statistically significant were included in the multiple logistic regression model. Stepwise multiple logistic regression was then applied for the identification of significant risk factors using SPSS version 16.0.Approval from the Bangladesh Medical Research Council (BMRC) was taken prior to commencement of the study. The study was reviewed and approved by the Scientific Advisory Committee (SAC) and Institutional Ethical Committee. Informed consent was obtained from all cases and controls before including them into study**.**

Results

The unadjusted ORs of risk factors for individual and family characteristics is shown in Table 1. The results showed that Nature of wall in the main structure, floor of the house, presence of cracks and crevices in wall, presence of a granary around the house, presence of bamboo trees near house were significant risk factors by univariate analysis.

Table 1: Household and environmental factors

Factors	**Cases (n = 60)**	**Controls (n = 120)**	***P***
Longest residence in kala azar area			
Yes	53 (88.3%)	108 (90.0%)	0.732
No	7 (11.7%)	12 (10.0%)	
Nature of wall in the main structure			
Kacha	27 (45.0%)	33 (27.5%)	0.019
Not Kacha	33 (55.0%)	87 (72.5%)	
Floor of the house			
Mud	55 (91.7%)	80 (66.7%)	0.001
Not mud	5 (8.3%)	40 (33.3%)	
Roof of the house			
Tin	57 (95.0%)	113 (94.2%)	0.818
Others	3 (5.0%)	7 (5.8%)	
Presence of cracks & crevices in wall			
Yes	27 (45.0%)	13 (10.8%)	0.001
No	33 (55.0%)	107 (89.2%)	
Surrounding environment			
Presence of natural light inside living room	53 (88.3%)	113 (94.2%)	0.168
Presence of granary within 50 meter of living house	55 (91.7%)	95 (79.2%)	0.034

Factors	**Cases (n = 60)**	**Controls (n = 120)**	***P***
Presence of vegetation within 50meter of living house	58 (96.7%)	115 (95.8%)	0.785
Presence of banana tree within 50meter of living house	49 (81.7%)	101 (84.2%)	0.671
Presence of bamboo tree within 50meter of living house	54 (90.0%)	77 (64.2%)	0.001

The results of multiple logistic regression analysis are shown in Table 2. The significant risk factors on the basis of adjusted ORs for kala-azar in multivariate analysis were identified. Some factors, which were significant in univariate analysis, were not significant risk factors in multivariate analysis. The adjusted ORs and 95% CIs for each significant variable are shown in Table 2. Presence of cracks & crevices in walls in houses was a significant risk factor for kala-azar (OR = 3.429, 95% CI = 1.037-11.338, *P* = 0.043). The presence of a bamboo tree in rural areas of study region, around houses was an also significant risk factor (OR = 5.652, 95% CI = 1.368-23.347, *P*= 0.017). The presence of vegetation such as small creepers, herbs, and bushes in the vicinity of houses was a significant risk factor in univariate analysis but, did not show significance in multivariate analysis. However, presence of bamboo trees in the vicinity of houses was significantly associated with kala-azar (OR = 5.652, 95% CI = 1.368-23.347, *P*= 0.017).

Table: 2. Risk factors for Kala-azar by multivariate analysis using a logistic regression model

Variable	**Regression coefficient**	**SE**	**Odds ratio**	**95% CI**	**p value**
Nature of wall	-.317	0.570	.729	.238-2.227	.579
Floor of the house	1.378	0.713	3.967	.980-16.059	.053
Cracks and crevices in wall	1.232	0.610	3.429	1.037-11.338	.043
Presence of granary near living house	.297	0.767	1.345	.299-6.044	.699
Presence of bamboo tree near living house	1.732	0.724	5.652	1.368-23.347	.017

CI = Confidence Interval

Discussion

This study is probably the first attempt to assess the association of various household and environmental factors with occurrence of kala-azar using a case-control design approach.The use of mud for wall construction or for plastering walls was found to be significantly associated with kala-azar, a finding previously reported in other studies (Dhiman and Sen 1991). *Phlebotomus argentipes* sand flies are commonly found in cracks and crevices of mud walls, mud-plastered walls, or unplaster brick walls in rural areas of endemic zone of kala-azar in Bangladesh. These endophagic sand flies usually breed inside cowsheds and human dwellings, especially inside cracks and crevices of walls where optimum temperature and humidity are available (Hati 1983). Mud walls can retain moisture for many months after the rainy season, which further increases favorable conditions for sand fly breeding and resting (Napier 1926). Filling of cracks and crevices in walls with a mixture of lime and mud has been advocated as an ecologic approach for the control of *P. argentipes* inside houses (Kumar et al., 1995). In this study presence of cracks and crevices has significant risk association with kala-azar.

The presence of granaries inside houses was significantly associated with kala-azar in univariate analysis, but not in multivariate analysis. The presence of granaries inside houses was found to be significantly associated with kala-azar because they are usually kept in bedrooms. It is the usual practice in rural areas to frequently clean the outer surface of the granary with water. The mud cracks and crevices on the outer side of granaries retain the moisture and thus provide sufficient dampness for breeding and resting of sand flies. Empty granaries also provide suitable places for breeding of sand flies because of easier access. Immature sand flies (larvae) have also been detected in soil collected inside granaries. The presence of granaries inside houses as a risk factor of kala-azar has also been previously reported. In this study, bamboo trees near houses were found to be a significant risk factor for kala-azar. It has been reported that some plants such as *Amaranthus spinosa* (*Amaranthaceae), Musa sapientum*, and *Croton sparciflorous* are very rich source of fructose and thus attract *P. argentipes*. (Dinesh and Dhiman 1991; Dhiman 1992). Bamboo trees (*Bambusa*

Arundinacea (*Graminede*)) are one of the common peridomestic plants that grow in large numbers and in clusters near houses in several upazillas in Mymensingh districts as well as other endemic kala azar area in Bangladesh. Although they are not a source of fructose for sand flies, they do provide good support for high fructose–containing climber plants such *A. spinosa* (*Amaranthaceae)*. Thus, sand flies get attracted towards bamboo trees. Bamboo trees also provide shade and consequently produce dark and humid surroundings around the vicinity of the houses, creating suitable resting sites for sand flies.

Thus, the household and environmental characteristics identified as risk factors of VL in this study could help strengthen existing control strategies. Better housing and improved environment conditions in disease-areas could reduce the transmission of the disease by eliminating conditions suitable for breeding of sand flies inside the houses. These findings have important practical implications because they suggest that these measures, along with appropriate vector control and improved treatment facilities in rural areas, may be particularly effective in reducing the incidence of kala-azar and its transmission of infection by sand fly vectors.

This is a hospital based unmatched case-control study. The hospital was in the city. So the study could not collect the representative samples. Most of the patients were from the urban or semi urban areas. So the rural patients were lacking. We did not have enough resource and scopes.

Conclusion

This small case control study reveals presence of Bamboo tree near houses, Kacha floor in the house, presence of cracks and crevices in walls of houses were the major household and environmental risk factors for development of kala-azar in Mymensingh region of Bangladesh. Further studies with larger sample size and covering other Kala-azar regions of the country to improve the precision of quantification of risk factors in a country perspective.

References

Agrawal S, Rai M and Sundar S. Management of visceral leishmaniasis: Indian perspective. J Post grad Med. 2005 51; 53-57

Alam MS, Wagatsuma Y, Mondal D, Khanum H, Haque R. Relationship between sand fly fauna and Kala azar endemicity in Bangladesh. Journal Acta Tropica 2009; 112:23-25

Alvar J, Vélez ID, Bern C, Herrero M, Desjeux P, Cano J, Jannin J, Den Boer M: Worldwide and global estimates of its incidence. PLoS One. 2012, 7: e35671-10.1371/journal.pone.0035671

Begum N, Masum MA, Mamoon AB, Begum A. Visceral leishmaniasis among the suspected febrile patients. Bangladesh Journal of Medicine Jan, 2002; 13: 21- 25

Bern C, Courtenay O, Alvar J. Of cattle, sand flies and men: a systemic review of risk factor analysis for South Asian visceral leishmaniasis implication for elimination, Journal PLoS Neglected Tropical Diseases, February 2010; ISSN: 1935-2727

Bern C, Haque R, Chowdhury R, Ali M, Kurkjian KM, et al. (2007) The epidemiology of visceral leishmaniasis and asymptomatic leishmanial infection in a highly endemic Bangladeshi village. Am J Trop Med Hyg 76: 909–914

Boelaert M, Criel B, Leeuwenburg J, Damme van W, Le Ray D and Van der Stuvft P. Visceral leishmaniasis control: A public health perspective. Trans R Soc Trop Med Hyg. 2000. 94; 465–471

Cary Bern & Rajib Chowdhury.The epidemiology of visceral leishmaniasis in Bangladesh: prospects for improved control. Indian J Med. Res123, March 2006; pp.275-288

Chowdhury MS, Ahmed MTU, Hussain AMZ, et al. Visceral leishmaniasis its control.1st ed. Dhaka: IEDCR; 1993; 4 - 28

Desjeux P. (1992). Human leishmaniasis: epidemiology and Public health aspects. Wrld Hlth Stat Q. 45; 267-75

Dhiman RC, Dinesh DS. An experimental study to find out the source of fructose to sand flies. Indian J Parasitol, 1992; 16: 159–160

Dhiman RC, Sen AB. Epidemiology of Kala-azar in rural Bihar (India) using village as a component unit of study. Indian J Med Res, 1991; 93:155–160

Dinesh DS, Dhiman RC. Plant sources of fructose to sand-flies, particularly Phlebotomus argentipes in nature. J Commun Dis, 1991; 23: 160–161

Hati AK. Current status of leishmaniasis—vector biology. Proceedings of the Indo-UK Workshop on Leishmaniasis, 1983; 84–91

Kumar V, Kesari S, Sinha NK, Palit A, Ranjan A, Kishore K. Field trial of an ecological approach for the control of Phlebotomus argentipesusing mud and lime plaster. Indian J Med Res, 1995; 101: 154–156

Napier LE. An epidemiological consideration of the transmission of Kala-azar in India. India Med Res Memoir, 1926; 4: 219–265

National guideline on Kala azar Elimination Program in Bangladesh, 2010

Rijal S, Uranw S, Chappuis F, Picado A, Khanal B, et al. (2010) Epidemiology of Leishmania donovani infection in high-transmission foci in Nepal. Trop Med Int Heal TM IH 15 Suppl 2: 21–28

Schenkel K, Rijal S, Koirala S, Koirala S, Vanlerberghe V, et al. (2006) Visceral leishmaniasis in southeastern Nepal: a cross-sectional survey on Leishmania donovani infection and its risk factors. Trop Med Int Health 11: 1792–1799

Singh SP, Picado A, Boelaert M, Gidwani K, Andersen EW, et al. (2010) The epidemiology of Leishmania donovani infection in high transmission foci in India. Trop Med Int Health 15 Suppl 2: 12–20

Thakur CP. Socio-economies of visceral leishmaniasis in Bihar (India). Trans R Soc Trop Med Hyg , 2000;94: 156–157

TK. Jha, Shayam Sundar, Thakur, Bachmann Peter, Juntra Kabwang, Chris Fisher, Andres Voss et.al .Multefosine, an oral agent for the treatment of Indian Visceral Leishmaniasis. The New England Journal of Medicine. 1999; 341 (24):17995-99

WHO (1996) World Health Report 1996.Report of Director -General WHO

World Health Organization. Control of the leishmaniases. Report of a WHO Expert Committee. World Health Organ Tech Rep Ser. 1990;793:1–158