Original Article

Clinico Epidemiological Study of Human Leptospirosis in Hilly Area of South India-A Population Based Case Control Study

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Abstract

Background: Leptospirosis is the most common zoonotic disease in the world affecting both animals and humans. Environmental, occupational, and sociocultural practices which vary from region to region favors the disease transmission in addition to lacunas in prompt diagnosis and treatment of cases. There are limited data on the seroprevalence of this neglected tropical disease in India. To assess the risk factors associated with Lepospirosis disease. **Materials and Methods:** A population-based case control study was conducted in Kodagu district of southern India from January 2022 to March 2022. Of the 74 confirmed cases during the year 2021, 70 cases and 140 age group and gender-matched controls participated in the study. Data were collected by using semi-structured questionnaire containing details of sociodemographic, occupational, and environmental factors. The collected data were coded and exported to STATA (16.1) and analyzed by univariate and multivaiariate logistic regression to identify significant risk factors. **Results:** Environmental factors such as flooding or collection of water near the house (adjusted Odds Ratio [aOR] = 4.9, confidence interval [CI]: 1.4-17.0), proximity to an open sewer (aOR = 4.9, CI: 1.2-19.1) and occupational factors such as presence of skin cuts or abrasion during work (aOR = 4, CI: 1.4-11.6), direct contact with mud or water during work (aOR = 9.7, CI: 3.3-27.7), animal farming (aOR = 3.4, CI: 1.0-11.6), presence of rodents in the house (aOR = 4, CI: 1.2-12.6), and presence of rodent habitats like grain storage area (aOR = 3.5, CI: 1.1-11.0) were significantly associated with leptospirosis. **Conclusion:** Leptospirosis poses a potential public health problem in the district. Interventions like prompt diagnosis and treatment, sensitization programs, and rodent control measures will significantly control this neglected tropical disease.

Keywords: Case-control study, India, leptospirosis, risk factors

Introduction

Leptospirosis is considered as the most common zoonotic disease in the world affecting both animals and humans resulting in more than 10 lakh cases and around 50,000 deaths worldwide.[1-3] Owing to the little information available about the true incidence of leptospirosis in India due to the factors such as misdiagnosis, undiagnosis due to lack of lack diagnostic facilities, and lack of awareness among healthcare personnel it is estimated that the positivity rate in south India is around 25.6%, whereas it is 8.3% in northern part of India and ranges from 3.5% to 3.3% in other parts of the country.[4]

People living in tropical and subtropical countries are most affected with human leptospirosis where factors like environmental conditions, social, and cultural practices favors its transmission in addition to scarcity of resources for prompt diagnosis and treatment of cases.[5]

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With more than 14 infectious species containing 250 serotypes,[6] Leptospira can be transmitted by domestic, wild, and peridomestic animals.[7] Environmental conditions like warm wet soil and water sources will enable the organism to survive weeks together leading to direct human contact in urban and rural settings.[8,9]

Once it enters into the human body, the leptospira spreads to major organs and after an incubation period ranging from 2 to 30 days the disease manifests with clinical features like

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muscle ache, headache, fever and chills, vomiting, nausea, and abdominal pain for around 4 to 7 days. Antileptospira-specific antibodies mainly of IgM type are produced as part of humoral immunity which can be detected by diagnostic tests like Microscopic Agglutination Test and Enzyme-Linked Immunosorbant Assay (ELISA).[10]

Exposure to contaminated urine of animal carriers or contact with contaminated soil or water either directly or indirectly results in disease transmission.[11] Various studies have reported predominant risk factors for transmission of leptospirosis especially in tropical countries include people living in proximity cattle farms, farming job which involves walking and working with barefooted in paddy fields, sewers, and contact with flood waters.[12,13]

Although many descriptive studies done across various geographical areas have reported the common basic determinants of the disease, but the nature and magnitude of these factors might vary from region to region with specific factors for the specific community which necessitates analytical study designs to identify and understand the risk factors responsible for disease transmission so that effective strategies can be planned for prevention and control of the disease in the community. Hence, this population-based case control study was done to assess the risk factors associated with lepospirosis disease in this hilly area of southern India.

Materials and Methods

Kodagu is a hilly district in southern part of Karnataka state in India and not being an endemic area for leptospirosis, this study was conducted as part of epidemic investigation. It has a population of 5.5 lakhs with majority (85.4%) of them living in rural areas. One of the major river Cauvery originates here and the district receives an average annual rainfall of 3,000 to 3,800 mm and temperature of 11°C to 28°C and this area is prone for seasonal floods which occurred predominantly during 2018-2021.[14] The main occupation of people in this region is agriculture involving paddy cultivation and coffee plantations with many warehouses for storage of agriculture produce.[15]

A total of 486 suspected cases of leptospirosis presenting with symptoms of fever and jaundice were reported by District Surveillance Unit during the period from September 2021 to January 2022. Blood samples were collected from all the suspected cases and were tested by IgM ELISA technique and of which 74 samples were confirmed for the disease through IgM ELISA test which is having sensitivity and specificity of 85% and 90%, respectively, and can be compared to other tests like Microscopic Agglutination Test.[16-18]

Case definition and exclusion criteria: Of 74 laboratory confirmed cases, 70 were included in the study. Persons who had migrated within one month of disease and those who were having history of viral diseases like Dengue or Japanese encephalitis were excluded from the study.

Control definition: Those who were negative for the disease and residing in the same area without the history of migration during disease appearance in cases were included as controls. Any person who was diagnosed with leptospirosis in the past or at the time of the study was excluded from the control group.

Study procedure: After preparing the line list of all the confirmed cases with their home addresses, the study was initiated with the approval of institutional ethics committee (KoIMS/IEC/27/2021-22). All the cases were matched with controls in terms of factors such as gender and place of residence (within 50 m radius) and age group with interval of 10 years.

Data were collected by interview method using a prevalidated semi-structured questionnaire used in the previous study done in India with consistent reliability having Cronbach's alpha 0.8[19] containing details of informed consent and information regarding sociodemographic, their occupation, exposure history such as contact with contaminated water, skin injury, presence of animals such as rodents at residence or work place, garbage and drainage facility in and around the house, details of animal farming, etc.

Persons residing within 50 m radius of the confirmed case who met above criteria were contacted and details were collected after they agreed to participate in the study as first and second controls.

Statistical analysis

Collected data were coded and entered into the STATA (16.1) for analysis. Univariate logistic regression was performed to calculate the odds ratio (OR) with 95% confidence interval (CI) for potential risk factors and significant factors (P <.05) were included in multiple logistic regression to find out the independent risk factors and P value less than. 05 was considered as statistically significant.

Results

A total of 70 confirmed leptospirosis cases and 140 controls from neighborhood were matched for the place of residence, age group, and gender. Among the cases, majority of them were in 18-30 age group (34.3%) followed by 31-45 years (30%) and 41-60 years (25.7%). More than 80% of them were living in rural areas and nearly 47% were farmers by occupation followed by house wife (24.3%) and doing daily wage works (8.6%) such as construction, coffee plantations, etc., [Table 1]. 85.7% of cases and 83.8% of controls were Hindu by religion. The mean age of the study subjects was 39.6 years and more than half (51.4%) of them were males [Table 2]. Univariate and multivaiate analysis to determine the various potential risk factors was performed as depicted in Table 3.

Environmental factors

Individuals who were exposed to flood water or collection of water in and around the house had Crude Odds Ratio (COR) of 6.7 (95% CI: 3.0-15.2) when compared to those who were not. Similarly, presence of open sewer within the vicinity of

the house [COR 11.6 (95% CI: 1.8-14.0)] and garbage in open area [COR 5.7 (95% CI: 1.0-5.5)] were found to be other risk factors. It also showed there was a significant association between leptospirosis and possible environmental factors like open water source as a cause of contamination and absence of waste disposal facility around the house [Table 3].

Exposure to rodents and animals

In our study, animal farming was identified as an important risk factor for leptospirosis [COR 8.4 (95% CI: 3.9-18)]. Similarly, places with signs of rodents in the work places [COR 5.5 (95% CI: 2.4-12.6)], presence of grain storage or godown in and around house [COR 5.2 (95% CI: 2.4-11.3)], and presence of rodents in the house [COR 8.7 (95% CI: 4.0-19.1)] were found to be independent risk factors which were significantly associated with leptospirosis [Table 3].

Table 1: Baseline characteristics of leptospirosis cases (*n*=70)

Variables	Frequency	Percentage
Age group (years)		
18-30	24	34.3
31-45	21	30.0
46-60	18	25.7
61-75	7	10.0
Gender		
Male	36	51.4
Female	34	48.6
Place of residence		
Rural	57	81.4
Urban	13	18.6
Occupation		
Daily Wage Worker	6	8.6
Farmer	33	47.1
House Wife	17	24.3
Professional	4	5.7
Student	10	14.3
Clinical features		
Fever	63	90.0
Myalgia	49	70.0
Vomiting	23	32.9
Oliguria	21	30.0
Jaundice	11	15.7
Abdominal pain	11	15.7
Cough	20	28.6
Dyspnoea	5	7.1
Pallor	6	8.6
Hepatomegaly	4	5.7

Table 2: Characteristics of the study subjects

Variables	Category	Cases (total=70)	Control (total=140)
		Number (%) or mean (SD) Number	Number (%) or mean (SD) Number
Age	Female	38.24 (±14.251)	41.85 (±13.691)
	Male	41.03 (±14.897)	37.61 (±15.023)
Gender	Female	34 (48.6%)	68 (48.6%)
	Male	36 (51.4%)	72 (51.4%)

Occupational risk factors

Outdoor activity factors like predominant occupation of farming [COR 7.5 (95% CI: 3.6-15.6)], presence of skin cuts or abrasion during work [COR 7.1 (95% CI: 3.6-14.1)], and direct contact with mud or water during work [COR 10 (95% CI: 4.7-21.4)] were found to be significant risk factors. However, univariate analysis showed that other factors like contact with river or stream or pond or reservoir and wearing open footwear did not put individuals at risk of leptospirosis infection.

Multivariate conditional logistic regression analysis was performed to find out the likely risk factors after confounding factor adjustment. Variables with P <.05 were included in multivariate analysis [Table 3].

Presence of flooding or collection of water near house and proximity to an open sewer (within 15 m) are the two environmental factors which were found to be significantly associated with leptospirosis with an adjusted Odds Ratio (aOR) of 4.9 (95% CI: 1.4-17.0) and 4.9 (95% CI: 1.2-19.1), respectively.

Factors like involving in animal farming with [aOR 3.4 (95% CI: 1.0-11.6)], presence of rodents in the house [aOR 4 (95% CI: 1.2-12.6)], and presence of rodent habitats like grain storage or godown [aOR 3.5 (95% CI: 1.1-11.0)] were reported as potential risk factors.

With regard to occupational risk factors like presence of skin cuts or abrasion during work [aOR 4 (95% CI: 1.4-11.6)] and direct contact with mud or water during work [aOR 9.7 (95% CI: 3.3-27.7)] were significantly associated with leptospirosis.

Discussion

Our study is the first of its kind to investigate the outbreak of leptospirosis in this region of southern part of India. This district receives rainfall for a period of 4 to 5 months starting from June to October in almost every year.

In our study, majority of the patients belonged to the age group of 18-45 years indicating potential risk of occupational exposure among these working age group which is in concurrence with study findings by Patil DY[20] in Mumbai, wherein the majority of cases were in the age group of 25-50 years and studies done in northern and coastal part of India[21-23] and also in different parts of the world.[18,19] The gender-wise distribution of cases was almost equal in our study which is contrast to studies by Holla R *et al.*,[21] Kembhavi RS,[24] and by DebMandal M[25] reported prevalence was high among males. This might be due to factors like migration of male working population for better employment opportunities and female member of the family looking after the agricultural activities.

It was observed in various studies that there are vide geographical variations in leptospirosis risk factors across the

Table 3: Association of potential/suspected and independent risk factors with leptospirosis

Variables	Cases (*n*=70)	Controls (*n*=140)	COR* (95% CI)	*P*	AOR** (95%CI)	*P*
Presence of flooding or collection of water near house	24 (34.3%)	10 (7.1%)	6.7 (3.0-15.2)	0.001	4.9 (1.4-17.0)	0.01
Proximity to an open sewer (15 m)	24 (34.3%)	6 (4.3%)	11.6 (4.3-30.2)	0.002	4.9 (1.2-19.1)	0.02
Presence of garbage in and around the house	26 (37.1%)	13 (9.3%)	5.7 (2.7-12.2)	0.001	2.8 (0.8-9.9)	0.1
Use of open water source	8 (11.4%)	65 (46.4%)	0.1 (0.54-1.7)	0.92		
Absence of waste disposal facility around the house	32 (45.7%)	25 (17.8%)	0.9 (1.1-3.3)	0.7		
Presence of skin cuts or abrasion during work	36 (51.4%)	18 (12.8%)	7.1 (3.6-14.1)	0.001	4 (1.4-11.6)	0.009*
Farmer	32 (45.7%)	14 (10.0%)	7.5 (3.6-15.6)	0.02	2.7 (0.9-8.3)	0.06
Open footwear use	38 (54.3%)	77 (55.0%)	1 (0.57-1.83)	0.92		
Contact with river or stream or pond or reservoir	16 (22.8%)	38 (27.1%)	0.7 (0.4-1.5)	0.50		
Direct contact with mud or water during work	34 (48.6%)	12 (8.6%)	10 (4.7-21.4)	0.001	9.7 (3.3-27.7)	0.001*
Involved in animal farming	31 (44.3%)	12 (8.6%)	8.4 (3.9-18)	0.04	3.4 (1.0-11.6)	0.04
Presence of grain storage/godown in and around house	23 (32.8%)	12 (8.6%)	5.2 (2.4-11.3)	0.001	3.5 (1.1-11.0)	0.03
Place with signs of rodents in the work place	21 (30.0%)	10 (7.1%)	5.5 (2.4-12.6)	0.001	2.8 (0.7-10.8)	0.12
Presence of rodents in the house	30 (42.8%)	11 (7.8%)	8.7 (4.0-19.1)	0.001	4 (1.2-12.6)	0.01

*Crude Odds Ratio,**Adjusted Odds Ratio

globe. Our study reported presence of skin cuts or abrasion during work, contact with water or mud during work, and agricultural activities as the strongest occupational risk factors responsible for leptospirosis which is in congruence with the findings in south Gujarat[26] and middle Andaman.[27] Studies done by Sahneh E[9] in north Iran and by Dewi PS in Indonesia[28] reported similar findings with regard to exposure of injured skin to contact with stagnant water or mud during work. This might be probably due to practice of traditional way of cultivation by using animals or machines in India without wearing any kind of protective devices resulting in high chances of injuries and coming in contact with contaminated water and mud. Farming poses a significant risk factor for leptospirosis as observed in our study which is in concurrence with study findings by Patil DY[20] in Maharashtra, Desai KT[26] in southern Gujarat, and studies by Esfandiari B *et al.*,[29] Sahneh E,[9] Schønning M. H[30] in Sri Lanka, and by Vanasco NB[31] in Argentina where majority of the cases were noticed in those involved in rural occupations. However, factors like contact with river or stream or pond or reservoir and wearing open footwear were not significantly associated with leptospirosis. This might be due to inconsistency in behavioural and occupational practices among the study subjects.

Our study documented that environmental risk factors such as presence of flooding or collection of water in and around the house and proximity to sewer had the highest risk of leptospirosis. Overflow of sewer drainage and collection of water is common during rainy season mainly because of many tributaries of the river present in this area resulting in frequent flooding and landslides leading to disruption of health services might be the reason for water contamination during monsoon season. Studies done in Uttar Pradesh part of northern India,[32] Indonesia,[28] and Fiji[33] reported similar findings with OR of 2.73, 2.2, and 1.9, respectively. These factors increase chances of rodent inhabitation in addition to daily living factors resulting in stimulation of disease life cycle.

The risk of leptospirosis was three times higher in relation to involvement in animal farming as per our study findings. This temporal association could be due to animal and poultry waste which attracts rodents resulting in frequent transmission of the disease through contamination of soil with urine. These findings are in line with studies done in Maharashtra,[24] Middle Andaman,[27] and by Regmi L,[18] Esfandiari B *et al.,*[29] Suwanpakdee S,[34] and by Mwachui MA.[35] Our study also noted that rodent exposure factors like presence of rodents in the house and at the workplace and also presence of grain storage areas like godown had a higher risk for leptospirosis. There is a high chance of soil contamination by infected urine of rodents which are present in the house and at the workplace resulting in disease transmission and these findings are in concurrence with studies by Kembhavi RS,[24] Desai KT,[26] Maze MJ,[10] Sahneh E,[9] and Dewi PS.[28]

Given the nature of retrospective study, the first and foremost limitation in our study was recall and selection bias for which we put maximum effort to minimize it by relying on accurate definitions of exposure in the study protocol and probing questions by trained data collector. We also tried to minimize the impact of interviewer's bias by taking measures like standardizing the data collection method, adhering to study protocol, training for data collectors, and applying an interviewer blinding technique.

Conclusion

Our study concludes that leptospirosis is a potential public health problem affecting mainly population in productive age groups. Human behavioral factors are significant components in leptospirosis prevention. Measures like using protective devices like gum boots and gloves would reduce the chances of getting exposed to contaminated stagnant water which requires health education and sensitization programs focusing mainly on social and cultural aspects of the risk groups. In addition to above interventions such as integrated rodent control

measures and also identification of high-risk zones followed by emphasize on target population through surveillance activities by healthcare workers would be significantly beneficial in bringing the burden of this neglected tropical disease.

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Conflicts of interest

There are no conflicts of interest.

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