10.5005/jp-journals-10068-0002

ORIGINAL ARTICLE

A Clinical and Epidemiological Profile of Seropositive Cases of Leptospirosis in a Tertiary Care Hospital in Ludhiana City, India

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ABSTRACT

Introduction: Leptospirosis, an infectious disease caused by spirochetes *Leptospira*, is the most widespread zoonosis in the world. Humans acquire infection through contact with the urine of infected or carrier animals, either directly or through contaminated water or soil. There are only few reports documenting the serological evidence of leptospirosis in northern India.

Aims and objectives: To determine the seroprevalence of leptospirosis among febrile patients and to study their clinical and laboratory profile.

Materials and methods: It is a prospective study conducted over a period of 1 year from April 2015 to March 2016. Febrile patients with clinical suspicion of leptospirosis admitted in the hospital were included in the study. Leptospira immunoglobulin M (IgM) antibodies in the serum samples were detected by enzyme-linked immunosorbent assay (ELISA) to confirm the diagnosis. Serologically confirmed patients of leptospirosis were studied for their clinical presentation and laboratory parameters.

Results: The seroprevalence of leptospirosis in this study was 4% (147/3,661). Leptospirosis was most prevalent in the age group of 46 to 55 years. Male predominance was seen. Maximum number of cases was seen in the months of August and September. Common clinical manifestations were jaundice (57.1%), abdominal pain (40.1%), abdominal distension (27.2%), and myalgia (28.5%). Hepatomegaly (53%) was the predominant clinical sign observed. Laboratory parameters revealed leukocytosis (68.7%), thrombocytopenia (52.3%), and transaminitis (78.2%). Hepatic failure (20.4%) was the most common complication.

Conclusion: Seroprevalence of leptospirosis among febrile cases was 4%, indicating male predominance and seasonal variation. There is the need to review the importance of adding leptospirosis to differential diagnosis of febrile illness.

Keywords: Clinical profile, Enzyme-linked immunosorbent assay, Leptospirosis, Seroprevalence.

How to cite this article: Chitkara S, Chhina D, Gupta V, Mahajan R. A Clinical and Epidemiological Profile of Seropositive Cases of Leptospirosis in a Tertiary Care Hospital in Ludhiana City, India. J Gastrointest Infect 2017;7(1):5-8.

Source of support: Institutional funds

Conflict of interest: None

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INTRODUCTION

Leptospirosis is a widespread zoonotic infection caused by the spirochete *Leptospira*. Rodents are the major reservoirs of infection. Infection results when water or soil contaminated with the urine of an infected animal comes into contact with human skin or mucous membranes.[1] The global burden of disease is unknown because of the paucity of data, but incidence estimates range from 0.1 to 1/100,000/year in temperate areas, to over 100/100,000/year during epidemics in the tropics. An estimated 300,000 to 500,000 severe cases occur each year, with case fatality of up to 30%.[2]

Natural disasters and poor sanitary conditions have contributed to the multiple epidemics reported. Major outbreaks of the disease in South-East Asia due to flooding were reported in Orissa (1999), Jakarta (2003), and Mumbai (2005). It has been a continuing and significant problem in the densely populated, flood-prone low-lying areas of India with recurrent outbreaks been reported from Kerala, Gujarat, Tamil Nadu, and Karnataka. Sporadic cases have been reported from Goa, Andhra Pradesh, and Assam.[3]

Sethi et al[4] retrospectively reviewed the cases diagnosed with leptospirosis during a 5-year period from 2004 to 2008 and reported a sustained rise of leptospirosis cases from 11.7 to 20.5%. Majority of the patients were from Punjab, Haryana, and Himachal Pradesh. Clinically, the most common syndrome is anicteric leptospirosis, a self-limited illness that occurs in 85 to 90% of the cases. It is characterized by constitutional symptoms like fever, headache, severe myalgia, chills with rigors, and prostration. Icteric leptospirosis or Weil's syndrome is the most severe form of leptospirosis that occurs in 5 to 10% of the cases. It is characterized by symptoms of hepatic, renal, and vascular dysfunction.[5]

Laboratory diagnosis of leptospirosis is based on several methods. Isolation of *Leptospira* in cultures is the

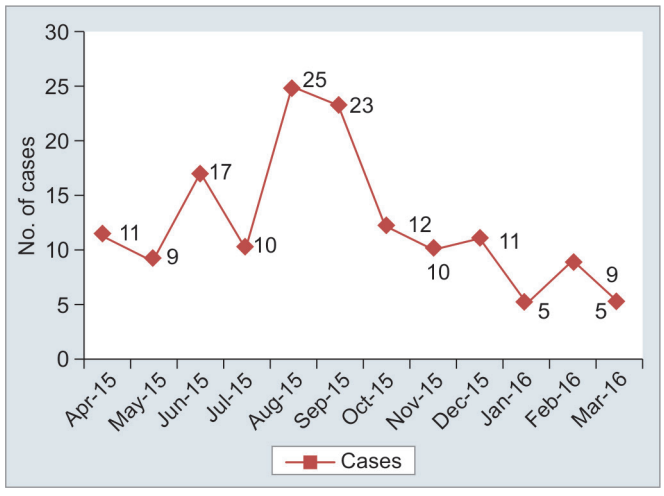
gold standard method for diagnosis. However, culturing the organism is laborious and time-consuming, thus making it unsuitable for rapid diagnosis in the early phase of the disease.[6] Serology is often the most appropriate diagnostic method. Two tests commonly used for the serological diagnosis of leptospirosis are microscopic agglutination test (MAT) and ELISA.[7] The MAT is considered the reference immunological test and has high specificity; its need for facilities to culture and maintain panels of live leptospira makes the test technically demanding, potentially biohazardous and time consuming.[8] Due to complexities of MAT, alternative rapid screening tests for leptospiral antibodies have been developed. The ELISA is a genus-specific test that can detect IgM-class antibody in the early phase of the disease, indicating current or recent leptospirosis.[9]

In general, underreporting of leptospirosis may be due to the difficulty in clinical diagnosis due to its varied clinical manifestation and lack of simple diagnostic tests for early detection. Hence, a study was conducted on prevalence and clinical profile of leptospirosis in patients presenting with an acute febrile illness in the tertiary care hospital.

MATERIALS AND METHODS

This prospective observational study was done over a period of 1 year (April 2015–March 2016). During the study period, blood samples were collected from each febrile patients of age >18 years admitted in the hospital with clinical suspicion of leptospirosis and processed for qualitative detection of leptospiral IgM antibody by ELISA (*Leptospira* IgM ELISA; Panbio Pvt. Ltd., Australia). Serum containing antibodies to *Leptospira* antigen, when present, combine with *Leptospira* antigen attached to the polystyrene surface of the microwells of microtiter plate. After washing the plate, peroxidase-conjugated antihuman IgM was added to the microwells. After a second incubation and washing step, a colorless substrate, tetramethylbenzidine/hydrogen peroxide (TMB chromogen) was added. The substrate was hydrolyzed by the enzyme and the chromogen changed to a blue color. After adding the stop solution, the TMB became yellow. Color development is indicative of the presence of IgM antibodies to *Leptospira* in the test sample. The test procedure was performed according to the protocol provided along with the kit. The results were interpreted according to the manufacturer's instructions, i.e., if values <9 PanBio ELISA units were considered negative; 9 to 11 equivocal, and >11 positive.

Of these, serologically confirmed patients of leptospirosis were evaluated noting their clinical history, presentation, and laboratory parameters on a prestructured proforma. The data obtained were analyzed using descriptive statistics. The chi-square test was used to find out the p-values of the results; p-value <0.05 was considered significant. Approval from institutional ethics committee was taken for this study.



Graph 1: Month-wise positivity of leptospirosis

RESULTS

Of 3,661 serum samples screened for leptospirosis, 147 (4%) were positive. Leptospirosis was more prevalent in the age group of 46 to 55 years (23.1%) and 36 to 45 years (22.4%). Of 147 cases, 117 were males (80%) and 30 were females (20%). The male to female ratio among leptospirosis cases was 4:1. The maximum number of cases was seen in the months of August (17%) and September (15.6%) and the least number of cases (3.4%) in the months of January and March (Graph 1).

Mean duration of fever was 8 days. Clinical symptoms associated with leptospirosis were jaundice (57.1%), abdominal pain (40.1%), headache (34%), myalgia (28.5%), and abdominal distension (27.2%). Common clinical signs observed (Table 1) were hepatomegaly

Table 1: Spectrum of clinical symptoms and signs in leptospirosis (n = 147)

Clinical symptoms	*No. of patients (%)*	*p-value**
Jaundice	84 (57.1)	<0.05*
Abdominal pain	59 (40.1)	>0.05
Headache	50 (34)	<0.05*
Myalgia	42 (28.5)	<0.05*
Abdominal distension	40 (27.2)	<0.05*
Vomiting	37 (25.1)	<0.05*
Decreased urine output	26 (17.6)	>0.05
Altered sensorium	23 (15.6)	<0.05*
Clinical signs		
Hepatomegaly	78 (53)	<0.05*
Ascites	41 (27.8)	<0.05*
Edema	30 (20.4)	<0.05*
Conjunctival suffusion	17 (11.5)	<0.05*

*Significant

Table 2: Lab parameters in leptospirosis (n = 147)

Lab parameters		*No. of patients (%)*	*p-value**
TLC (cells/μL)	Leukopenia (<4,000)	4 (2.7)	<0.05*
	Leukocytosis (>11,000)	101 (68.7)	<0.05*
Platelets (cells/μL)	Thrombocytopenia <100 × 10^3	77 (52.3)	>0.05
	≥100 × 10^3	70 (47.7)	<0.05*
SGOT >50 and SGPT >50 (U/L)		115 (78.2)	>0.05
Total bilirubin > 1.2 (mg/dL)		90 (61.2)	<0.05*
Urea >50 (mg/dL)		43 (29.2)	<0.05*
Creatinine >1.2 (mg/dL)		47 (32)	<0.05*

*Significant; TLC: Total leukocyte count; SGPT: Serum glutamic pyruvic transaminase; SGOT: Serum glutamic oxaloacetic transaminase

(53%), ascites (27.8%), edema (20.4%), and conjunctival suffusion (11.5%). Most patients of leptospirosis had leukocytosis (68.7%), thrombocytopenia (52.3%), and transaminitis (78.2%). Renal dysfunction with raised serum creatinine was present in 23.1% of patients (Table 2). Of 147 patients with leptospirosis, 9 patients had coexisting viral hepatitis (6.1%). Of these 9 patients, 7 tested positive for hepatitis C and 1 each for hepatitis A and B virus. The most common complications (Table 3) seen in patients of leptospirosis was hepatic failure (20.4%) followed by renal failure (11.5%) and shock (8.8%).

DISCUSSION

Although traditionally considered to be a disease of sewage workers, miners, and farmers, leptospirosis is now recognized as one of the common causes of acute febrile illness in the general population. However, as with other developing countries, the infection is largely underreported due to its nonspecific manifestations and limited laboratory capacity, hence undermining the true prevalence of the disease.

In this study, the prevalence of leptospirosis was 4%. Prevalence rates reported by other studies from various parts of the country are highly variable, with a higher prevalence rate from South India of 1.3% by Bawane et al,[10] 11.4% by Sahira et al,[11] and 12% by Prabhakar et al.[12] Maximum number of cases were seen in the months of August and September. Our findings were consistent with those reported by Deodhar and John[13] who observed maximum positivity between the months of July to October, coinciding with the monsoon and postmonsoon season.

Leptospirosis was more prevalent in the age group of 36 to 55 years. Males were predominantly affected and male to female ratio among leptospirosis cases was 4:1. This may be due to the involvement of young male population working in high potential infection areas like agriculture farms, sewage, and mines.

Table 3: Complications in leptospirosis (n = 147)

Complication	*No. of patients (%)*	*p-value**
Hepatic failure	30 (20.4)	<0.05*
Renal failure	17 (11.5)	<0.05*
Shock	13 (8.8)	<0.05*
Encephalopathy	8 (5.4)	>0.05
ARDS	4 (2.7)	<0.05*
Sepsis	2 (1.3)	>0.05

*Significant; ARDS: Acute respiratory distress syndrome

The mean duration of fever in patients of leptospirosis was 8 days, which correlates with the findings of the study by Sambasiva et al[14] which showed that the duration of fever of leptospirosis mostly occurs with a range of 2 to 20 days and lasts for a month. Common clinical symptoms that were statistically significant in patients of leptospirosis in our study were jaundice (57.1%), abdominal pain (40.1%), abdominal distension (27.2%), and myalgia (28.5%). Neurological manifestations in the form of altered sensorium were seen in 15.6% of leptospirosis patients. Such manifestations are varied and often lead to misdiagnosis, unless strongly suspected. Hepatomegaly (53%), ascites (27.8%), edema (20.4%), and conjunctival suffusion (11.5%) were frequent clinical signs seen. This clinical presentation was similar to that reported by Sethi et al.[4] Patil et al[15] also reported fever (100%), jaundice (70%), myalgia (70%), and headache (52.1%) as predominant complaints of patients diagnosed with leptospirosis.

Most cases of leptospirosis had leukocytosis (68.7%), thrombocytopenia (52.3%), and transaminitis (78.2%). Renal function impairment was observed in 32% cases. The above laboratory derangements have been reported in other studies.[4,12] Hepatic failure (20.4%) was the most common complication seen in cases of leptospirosis followed by renal failure (11.5%) and shock (8.8%). Shivakumar and Krishnakumar[16] and Sahira et al[11] also observed hepatic and renal failure as common complications. Of the 147 patients with leptospirosis, 9 patients (6.1%) were found to have coexisting viral hepatitis. Angnani et al[17] reported serological evidence of both leptospirosis and hepatitis in 39.4% of their patients. Leptospirosis and hepatitis B coinfection was reported in 22% of patients by Chandrasekaran.[18]

Our study had a few limitations. Firstly, patients with subclinical or mild infection would not report to a hospital. Therefore, our study would underestimate the community prevalence of leptospirosis because of a referral bias in patients attending a tertiary care center. Secondly, our seroprevalence estimation was limited by the use of a single acute phase serum sample due to noncompliance of patients to report for a repeat serological testing after clinical improvement or loss to follow-up following discharge or death of the patient.

CONCLUSION

Leptospirosis has emerged as a common cause of fever in northern India and all patients presenting with an acute febrile illness, particularly during the monsoon season, should be screened. The presentation may range from a subclinical infection to a severe hepatorenal syndrome. Serodiagnosis in resource-poor settings can be easily done using IgM ELISA. The increased awareness among physicians of common clinical manifestations of leptospirosis and early laboratory diagnosis will help reduce morbidity and mortality associated with the disease.

ACKNOWLEDGEMENT

The authors would like to acknowledge the technical assistance provided by Mr Rajiv Kumar and Mr Sukhwinder Singh.

REFERENCES

1. Levett, PN.; Haake, DA. Leptospira species (leptospirosis). In: Bennett JE, Dolin R, Blaser MJ, editors. Mandell, Douglas, and Bennett's principles and practice of infectious diseases. 8th ed. Philadelphia (PA): Elsevier/Saunders; 2015. pp. 2789-2794.
2. Hartskeer RA. Leptospirosis: current status and future trends. Ind J Med Microbiol 2006 Oct;24(4):309.
3. Himani D, Suman MK, Mane BG. Epidemiology of leptospirosis: an Indian perspective. J Foodborne Zoonotic Dis 2013 Jul-Sep;1(1):6-13.
4. Sethi S, Sharma N, Kakkar N, Taneja J, Chatterjee SS, Banga SS, Sharma SS. Increasing trends of leptospirosis in northern India: a clinico-epidemiological study. PLoS Negl Trop Dis 2010 Jan;4(1):e579.
5. Vaishnavi, C. Leptospirosis. In: Al-Mehtab M, Rahman S, editors. Liver: a complete book on hepato-pancreato-biliary diseases. Mahtab: Elsevier Publishers; 2009. pp. 445-456.
6. Schreier S, Doungchawee G, Chadsuthi S, Triampo D, Triampo W. Leptospirosis: current situation and trends of specific laboratory tests. Expert Rev Clin Immunol 2013 Mar;9(3): 263-280.
7. Ooteman MC, Vago AR, Koury MC. Evaluation of MAT, IgM ELISA and PCR methods for the diagnosis of human leptospirosis. J Microbiol Methods 2006 May;65(2):247-257.
8. Khaki P. Clinical laboratory diagnosis of human leptospirosis. Internat J Enteric Pathogens 2016 Feb;4(1):e31859.
9. Chen HW, Zhang Z, Halsey ES, Guevara C, Canal E, Hall E, Maves R, Tilley DH, Kochel TJ, Ching WM. Detection of Leptospira-specific antibodies using a recombinant antigen-based enzyme-linked immunosorbent assay. Am J Trop Med Hyg 2013 Dec;89(6):1088-1094.
10. Bawane RS, Shiekh N, Ingole KV, Bhise M. Seroprevalence of leptospirosis in tertiary care hospital Solapur: a retrospective study. International J Appl Res 2016 Apr;2(5):183-185.
11. Sahira H, Jyothi R, Ramani Bai JT. Seroprevalence of leptospirosis among febrile patients—a hospital based study. J Academia Industrial Res 2015 Mar;3(10):481-484.
12. Prabhakar PK, Harish BN, Rao RS. Seroprevalence of Leptospirosis among febrile and jaundice patients. Ind J Med Microbiol 1995;13(4):189-191.
13. Deodhar D, John M. Leptospirosis: experience at a tertiary care hospital in northern India. Nat Med J India 2011 Mar-Apr;24(2):78-80.
14. Sambasiva RR, Naveen G, Bhalla P, Agarwal SK. Leptospirosis in India and the rest of the world. Brazilian J Infectious Dis 2003 Jun;7(3):178-193.
15. Patil VC, Patil HV, Agrawal V. Clinical profile and outcome of leptospirosis at tertiary care centre in western Maharashtra. J Acad Med Sci 2012 Dec;2(1):30-37.
16. Shivakumar S, Krishnakumar B. Diagnosis of leptospirosis-role of MAT. J Assoc Physicians India 2006 Apr;54:338-339.
17. Angnani R, Pathak AA, Mishra M. Prevalence of leptospirosis in various risk groups. Indian J Med Microbiol 2003 Oct-Dec;21(4):271-273.
18. Chandrasekaran S. Review on human leptospirosis. Indian J Med Sci 1999 Jul;53(7):291-298.