

Leptospirosis: An Emerging Cause of Hepato-Renal Dysfunction in Young Age Groups

Mayuri Gogoi¹, Lahari Saikia², Vaishali Sarma³, Supriya Sona⁴

ABSTRACT

Leptospirosis is an emerging zoonoses which can present with varied clinical manifestations ranging from mild self-limiting illness to severe disease with multi-organ involvement. Objective: The present study was undertaken to determine the seroprevalence of leptospirosis among patients presenting with febrile illness and to determine the involvement of hepato-renal system in the sero-positive cases with respect to the age groups. Methods: A retrospective study was carried out in patients with febrile illness attending Gauhati Medical College and Hospital over a period of three years from Jan 2019 to Dec 2022. The laboratory data relating to the testing for leptospira IgM ELISA were collected. From all the leptospira IgM ELISA positive cases, the information on demographic, clinical and laboratory parameters were recorded. Results: Sero-prevalence of leptospirosis was found to be 27.9% (151/541). The seropositivity was higher in males as compared to females which was statistically significant. Majority of the patients i.e., 58.9% (89/151) were in the age group of 15-40 years followed by 40-60 years age group (48/151, 31.7%). Fever was the most common presentation seen in 65/71 (91.5%) cases followed by jaundice in 51 /71 (71.8%). Hepato-renal dysfunction was seen in 64.2% (97/151) of the sero-positive patients, majority being in the 15-40 years age group (32.4%) followed by 40-60 years group (24.5%). Conclusion: Leptospirosis along with hepato-renal dysfunction is more common in the working age group with a predominance toward male. Hence the laboratory parameters need to be monitored, and timely intervention should be taken to reduce the mortality and morbidity.

KEY WORDS: Leptospirosis, IgM ELISA, Hepato-renal dysfunction

Introduction

Leptospirosis is emerging as an important public health problem in India^[1, 2]. It is a direct zoonotic disease caused by different pathogenic species of the genus *Leptospira*. Different animals may act as carriers or vectors. Human infection occurs due to accidental contact with carrier animals or environment contaminated with leptospire. The primary source of leptospire is the excreta of animals whose renal tubules excrete the leptospire into the environment with the urine^[3]. Humans are infected by contact with rat urine, especially during paddy cultivation. Increasing numbers

of cases are however being reported in the recent times from urban and semi-urban areas as well due to overcrowding, flooding, and poor sanitation issues which provide an environment favorable for the transmission of leptospirosis^[4].

Leptospirosis presents with a wide spectrum of clinical presentations. While most patients present only with mild fever and recover without complications, a small proportion of them may develop various complications due to involvement of multiple organ systems^[5].

Incidence of leptospirosis ranges between 10-100/1,00,000 cases per year in developing countries. As per the estimates, India should report 0.1-1.0 million cases per year. However, cases reported is considerably less, which are around 10,000 cases per year^[6]. Leptospirosis is a diagnostic challenge because of its protean manifestations and elusive features. It is a disease easily treatable by antibiotic therapy but if left untreated, may prove to be fatal^[7].

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Hepatic involvement in leptospirosis is not an uncommon feature and can vary from asymptomatic rise in transaminases to severe icteric hepatitis. However, detailed studies on the frequency, degree and type of hepatic involvement in leptospirosis are limited^[8].

Though anicteric leptospirosis is the most common form of the disease affecting nearly 90 percent of the patients, severe form of leptospirosis involving kidney and liver known as Weil's disease is also seen in some patients which has a very high mortality^[9].

In India, where an eco-system with inter dependence of humans and animals sharing the same source of food, water and shelter exists, there is abundant opportunity for cross-infection from animals to humans^[10]. Some important predisposing factors for this infection include heavy rainfall, animal rearing practices, unplanned urbanization and agrarian way of life^[5]. This study was therefore undertaken to determine the sero-prevalence of leptospirosis and the hepato-renal involvement among the seropositive leptospirosis cases with respect to the age groups.

Materials And Methods

The present study was a retrospective observational study period of three years between January 2019, and December 2021 carried out in the department of Microbiology, GMCH. The registries of the leptospirosis patients were reviewed and the information on demographic, clinical profile and laboratory parameters of the leptospirosis patients was recorded in a well-structured proforma.

Approval to conduct this study was obtained from the Institutional Ethics Committee bearing No MC/190/2007/Pt-II/Oct-2022/3 dated 27/01/2023. Informed written consent was taken from all the study subjects (format enclosed).

During this period, the microbiology laboratory received serum samples from suspected cases with febrile illness for leptospira serology. Serum samples were tested for qualitative determination of specific anti-leptospira IgM antibody using the PanBio IgM ELISA (Panbio diagnostics, Brisbane, Australia) and J.Mitra IgM ELISA. Initially PanBio IgM kits were used but later due to unavailability of this kit, J.Mitra IgM Kits were used. Both the kits use Indirect ELISA technique. The test procedure was performed according to manufacturer's instructions. With the Panbio IgM kit results were interpreted as Panbio Units. If Panbio units >11 it was considered positive. Sensitivity and Specificity of Panbio IgM kit is 96.5% and 98.5% respectively. Similarly for the J. Mitra IgM kits, Lepto IgM units are calculated and if it is >11 it is considered positive. Sensitivity and Specificity of J.Mitra IgM kit is 99.62% and 99.92% respectively.

Negative controls, positive controls and calibrators were kept with each test run.

Statistical analysis:

Data generated from the present study have been presented in the form of tables and all descriptive analyses have been shown in percentages. *P* value has been calculated to analyze statistical significance.

Results

A total of 541 patients were included in the present study. Of these 541 patients, 27.9% (151/541) were seropositive for anti-leptospira specific immunoglobulin (IgM) antibodies. Among these 151 patients, 76.8% (116/151) were males and 23.1% (35/151) were females and the male to female ratio was 3.3:1 [Table. 2]. The age ranged from 4 to 80 years with a mean age of 37.4 years and median value of 35 years. Of the total 151, 143 (95.3%) were adults and 7 (4.6%) were children ≤15 years of age. Only 6 (3.9%) cases were seen in children less than 15 years old [Table. 1]. The district wise distribution from Kamrup (Rural) 30/151 followed by Kamrup (Metro) 26/151 [Fig. 1].

Table 1: Age wise distribution of the leptospira seropositive cases along with their status of hepato-renal dysfunction

Age	Total number of samples tested for Leptospira IgM ELISA	Total number of leptospira seropositive cases	Leptospira seropositive cases with hepato-renal dysfunction	Leptospira seropositive cases without hepato-renal dysfunction
<15 years	26	6	3	1
15-40 years	296	89	49	3
40-60 years	163	48	37	0
>60 years	56	8	8	0
TOTAL	541	151	97	4

Table 2: Sex wise distribution of the leptospira seropositive cases

Sex of the patient	Total number of samples tested for Leptospira IgM ELISA	Total number of leptospira seropositive cases	Total number of leptospira seropositive cases with hepato-renal dysfunction
Male	354	116	82
Female	187	35	15
TOTAL	541	151	97

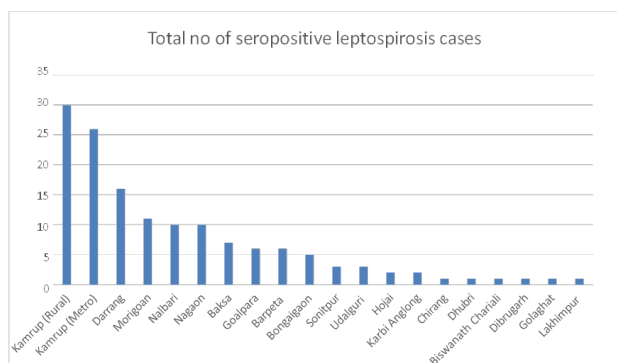


Fig. 1: District-wise distribution of case

Table 3: Clinical features of the leptospirosis sero-positive cases

Clinical feature	Total number of patients showing the symptom
Fever	65
Jaundice	51
Oliguria, difficulty in passing urine	28
Headache	2
Abdominal pain	2
Abdominal swelling	3
Generalised weakness	2
Cough	4
Haematemesis	2
Seizures	2
Loss of consciousness	1

History of exposure to risk factors like exposure to pets and people living in flood affected areas were taken via telephonic conversation with the patients. History could be elicited from 65 patients. In 43/65 (66.1%) cases history of exposure to risk factors was present and in 22/65 (33.8%) no such history was found.

Occupation history was available from 62 patients. Out of the 62 patients, 19 (30.6%) were farmers followed by house-wife (10/62) and students (9/62).

Data on clinical presentation were available from 71 patients. Fever was the most common presentation seen in 65/71 (91.5%) cases followed by jaundice in 51/71 (71.8%) and features of renal involvement 28/71(39.4%). Other less common features were headache, myalgia, cough, abdominal pain and abdominal swelling. The duration of fever was less than 7 days in 47/65 cases and more than 7 days in 18/65 cases [Table. 3]. However, scoring on the basis of the Modified Faine’s criteria was not done in this study.

Laboratory parameters of the leptospira sero-positive cases were also studied. Hyperbilirubinemia was noted in 103 sero-positive patients, out of which 80 patients had Grade IV hyperbilirubinemia. Direct bilirubin (>0.2mg/dl) was elevated in 90 sero-positive cases. The mean values of liver enzymes AST and ALT were found to be 197.25U/L and 159.85U/L respectively. Liver enzymes (AST, ALT) were elevated in 108 patients. The mean Blood urea and creatinine levels were 183mg/dl and 4.4mg/dl respectively. Blood urea was elevated (>40mg/dl) in 98 sero-positive patients. The creatinine levels were elevated (>1.3mg/dl) in 104 patients, out of which 45 patients had creatinine levels more than 5mg/dl. The mean leucocyte count was 1.5×10^3 cells/mm³, leucocytosis was seen in 85 patients. Hepato-renal dysfunction was seen in 64.2% (97/151) of the leptospira sero-positive cases. Mean haemoglobin and platelet count were 10.41g/dl and $125 \times 1000/\text{mm}^3$ respectively. Anaemia and thrombocytopenia were seen in 118 and 97 sero-positive patients respectively. The C-Reactive Protein was elevated in 57/59 cases. Pancreatic involvement in the form of elevated amylase in 6 patients and elevated lipase in 9 patients was also seen [Table. 4].

On enquiring about the patient outcome, information could be obtained from 57 patients. 15/57 patients expired; 35 patients recovered. However, 7 patients had developed renal impairment following leptospirosis and had to undergo dialysis.

Discussion

Leptospirosis is a frequently under-diagnosed infection because of its varied manifestations and difficulty in distinguishing it from other febrile illnesses. Failure to provide timely diagnosis of leptospirosis cases may lead to unnoticed cases developing acute fatal illness^[11]. Our study describes the seroprevalence along the detailed analysis of the abnormalities in the hepatic, renal function parameters in patients with leptospirosis.

The seroprevalence of leptospirosis was found to be 27.9%. In a study done by Kalita *et al* from Northeast India in the year 2008, the prevalence was found to be 22.57%^[12]. From these findings it is evident that there has been an increase in the seroprevalence of leptospirosis in our part of the country which may be due to the better availability of diagnostic tests and also because of episodes of floods in the monsoon season along with urban waterlogging. In a 10- year study done by Chaudhury *et al.* from northern India, the seroprevalence of leptospirosis was reported to be 26.90 %^[13]. The sero-positivity rate of leptospirosis as per studies conducted from other parts of the country ranges from 17.8–40.5%^[14].

Table 4: Abnormalities in laboratory parameters among the leptospira sero-positive cases

Liver Function test parameter	Abnormality	Total number of leptospira sero-positive cases	Total number of sero-positive cases with records available
	Hyperbilirubinaemia		
Total bilirubin	Grade I	6	n=115
	Grade II	5	
	Grade III	12	
	Grade IV	80	
Direct Bilirubin	Normal range	12	n=109
	Elevated (>0.2mg/dl)	90	
Aspartate aminotransferase	Normal range	19	n=108
	Elevated (>40U/L)		
	Mild	54	
Alanine aminotransferase	Moderate	40	n=108
	Severe	5	
	Elevated (>40U/L)		
	Mild	48	
Alkaline Phosphatase	Moderate	8	n=66
	Severe	4	
	Elevated (>130U/L)	39	
Renal Function test	Normal range	27	n=117
	Elevated (>40mg/dl)	98	
Blood urea	Normal range	19	n=124
	Elevated (>1.3mg/dl)	104	
	>1.3 to 5mg/dl	59	
	5 to 9 mg/dl	36	
Creatinine	>10mg/dl	9	n=131
	Leucocytosis (>11000/mm ³)	85	
	Leucopenia (<3500/mm ³)	6	
White Blood Cell count	Normal range	40	n=35
	Haemoglobin		
Female	Anaemia (<12g/dl)	32	n=35
	Normal range	3	

Liver Function test parameter	Abnormality	Total number of leptospira sero-positive cases	Total number of sero-positive cases with records available
Male	Anaemia (<13g/dl)	86	n=116
	Normal range	30	
	Thrombocytopenia (<1,50,000)	97	
Platelet count	Thrombocytosis (>4,50,000)	3	n=130
	Normal range	30	
	Elevated (>140U/L)	6	
Serum Amylase	Normal range	4	n=10
	Elevated (>160U/L)	9	
Serum Lipase	Normal range	1	n=10

In the present study, hepato-renal dysfunction was seen in 64.2% (97/151) of the leptospira sero-positive cases, majority of which belonged to the 15-40 years age group (32.4%) i.e. in the young population followed by 40-60 years group (24.5%). A significant correlation was found between age of the patients and hepatorenal dysfunction (p value is 0.028). The higher number of hepato-renal dysfunction in the 15-40 years age group could be due to the fact that majority of leptospira sero-positive cases were detected in this age group in this study i.e., 58.9% (89/151) were in the age group of 15-40 years. Such clustering of the cases in the age group of 20-40 years has been observed by many other studies^[5, 12, 15-19]. The reason for the higher seropositivity in this age group can be explained by the fact that they contribute the majority of the outdoor working population. And since this disease affects the productive age group, this has lot of economic burden both on the family and society^[20].

In a study done by Goyal *et al.*, hepatic dysfunction was present in 72.5% patients^[8]. Various other studies are shown varying degrees of hepatic and renal involvement in leptospirosis patients^[5, 21-23]. The mean serum bilirubin in the present study was 14.6 mg/dl, which is similar to that reported in previous studies^[5, 8, 24]. The mean serum transaminases values in our study were similar to that reported by Sethi *et al.* but higher than those reported by Clerke *et al.* [40-50 U/L]^[5, 24]. The creatinine levels were elevated in 104 patients, out of which 45 patients had creatinine levels more than 5mg/dl. Seven patients developed renal failure and had to undergo dialysis. Pancreatic involvement was seen in nine patients with elevated amylase/lipase levels.

The male to female ratio was found to be 3.3:1. Males were found to be at higher risk of being seroreactive than females (*P value* = .00053). This finding is consistent with various other studies where the prevalence was found to be higher in males^[12, 13, 15, 16, 25]. This may be generally attributed to men being more involved in agricultural and animal husbandry related activities, as animals are the major sources of infection for humans.

Majority of the leptospirosis patients were farmers (30.6%) and history of exposure to risk factors like animal exposure, living in flood affected areas could be elicited from 66.1% patients. Also, the sero-prevalence of leptospirosis was found to be more the rural districts. Similar findings were reported by some studies where the prevalence of leptospirosis was found to be more in rural areas^[5, 8, 25]. However, the prevalence of leptospirosis was found to be more in urban areas as reported by Shukla *et al.*^[26]

Fever was the most common presentation seen in 65/71 (91.5%) cases followed by jaundice in 51/71 (71.8%). These findings are similar to studies done by Kanan *et al.*, Agarwal *et al.* and Mandal *et al.*^[14, 27, 28]

On analyzing the haematological parameters, leucocytosis was seen in 64.8% (85/131) of the patients. Leptospirosis being a bacterial infection, leukocytosis with neutrophilia is seen^[29]. Anaemia and thrombocytopenia were seen 78.1% (118/151) and 74.6% (97/130) of the sero-positive patients respectively. The thrombocytopenia was significant in patients with leptospirosis in this study, which is observed in various Indian studies as well^[23, 30].

Conclusion

Leptospirosis is an emerging zoonosis. It affects mainly the working-age group with a predominance toward male thus having a major economic impact on the family and the country. Hepato-renal dysfunction in leptospirosis is common and especially more so in the younger age groups leading to long term complications. The increased awareness among physicians of protean clinical manifestations of leptospirosis, effective monitoring of the laboratory parameters along with timely intervention can reduce the mortality and morbidity associated with the disease.

Limitations of the study: Paired sera were not used for Leptospira IgM ELISA testing which could have given better results. Also scoring as per the Modified Faine's Criteria was not done as the detailed clinical history was not available from all sero-positive cases.

Disclosure

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee.

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