

**CLINICAL PROFILE OF LEPTOSPIROSIS IN A TERTIARY CARE CENTRE IN NORTH KERALA**Sreejith R<sup>1</sup>, Thulasidharan N. K<sup>2</sup><sup>1</sup>Assistant Professor, Department of General Medicine, Government Medical College, Kozhikode, Kerala.<sup>2</sup>Professor and HOD, Department of General Medicine, Government Medical College, Kozhikode, Kerala.**ABSTRACT****BACKGROUND**

Leptospirosis is one of the most common zoonotic diseases prevalent in the world and very common in India. It is caused by the spirochaete *Leptospira* spp. It is endemic in Kerala with frequent epidemics during rainy seasons. Severe leptospirosis or the Weil's syndrome is characterized by fever with myalgia, icterus, acute kidney injury, thrombocytopenia with high mortality. Other organs like heart, pancreas and lungs are involved rarely. This study was conducted to assess the clinical profile and to detect the trends in clinical presentation and complications of Leptospirosis.

**MATERIALS AND METHODS**

This was a retrospective study conducted at Government Medical College, Kozhikode, a tertiary care centre in North Kerala, India, involving 150 cases of IgM ELISA positive cases of Leptospirosis from inpatients of medical wards and ICU. All the patients were investigated and assessed for the complications and outcome.

**RESULTS**

150 clinically and serologically confirmed cases of leptospirosis were included in this study of which 109 (72.7%) were males and 103 (68.7%) were manual labourers. Of the 150 cases, 22 (14.7%) patients expired. Fever was present in all patients with myalgia being the most common associated symptom followed by headache and vomiting. Most common sign was conjunctival congestion (127, 84%) followed by calf muscle tenderness (95, 63.3%). Most common complication encountered was hepatorenal syndrome (103, 68.7%). There was a high incidence of myocarditis (43, 28.7%), ARDS (27, 18%) and pancreatitis (26, 17.3%).

**CONCLUSION**

Leptospirosis is very common in Kerala and occurs throughout the year with an increasing incidence from the months of August to October. Manual labourers, especially males were the most common group affected. Most common complication encountered was hepatorenal syndrome with relatively early onset i.e. by the end of first week. There was a relatively increased incidence of complications like myocarditis, ARDS and pancreatitis in our study suggesting an increased incidence of sepsis like presentation with MODS.

**KEYWORDS**

Leptospirosis, Hepatorenal Syndrome, Myocarditis, ARDS, Pancreatitis.

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**BACKGROUND**

Leptospirosis is one of the most important zoonotic diseases worldwide caused by spirochete *Leptospira* genus with more than 200 serovars, having approximate incidence of >10 cases per 100,000 population per year.<sup>1</sup> This disease affects large population of humans, especially in the tropical countries. This disease, though age old, remains as one that produces a major impact and health concern due to its morbidity and mortality. Lack of a proper reporting system, delay in diagnosis and increasing incidence of complications

add on to the predicament. The evolving clinical picture has not been studied in detail, even though the disease is endemic with outbreaks following every rainy season or floods. Even with proper treatment mortality ranges from 5-20%.<sup>2</sup>

Leptospirosis remains one of the most common zoonotic disease in Kerala, where it is considered to be endemic and is transmitted by rodents especially rats, even though it may be transmitted from other primary reservoirs like cattle, pigs or dogs. It is transmitted to humans by exposure to urine of primary hosts which contaminates water or soil and when infected water or soil comes in contact with skin abrasions or mucous membranes.<sup>3</sup> Heavy seasonal rainfall, floods and waterlogging, with high population density and abundant rodents make it ideal for the organism to spread disease in humans in this part of the country.

Leptospirosis presents with fever along with myalgia and majority will be asymptomatic. Among the symptomatic, initial leptospiremic phase is associated with high grade fever with chills, myalgia, conjunctival congestion, headache

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and rash. Immune phase is characterised by fever with organ dysfunction in form of hepatorenal syndrome, myocarditis and acute respiratory distress syndrome. This syndrome was described by Adolph Weil and it is known as Weil's disease now. Even though the organ involvement described in classical Weil's disease is mainly hepatic and renal involvement, any other organ may be involved. In this background, we planned to conduct a retrospective analysis of the clinical profile of Leptospirosis. There are several studies identifying the mortality predictors of Leptospirosis in which increasing age,<sup>4</sup> severity of presentation, organ involvement in form of ARDS,<sup>5</sup> acute renal failure<sup>6</sup> or neurological involvement.<sup>7</sup> The study aims at identifying the changing pattern of leptospirosis over time and the varied clinical presentations.

## MATERIALS AND METHODS

This retrospective cross-sectional study was conducted on 150 cases of Leptospirosis confirmed with IgM *Leptospira* antibody from a period of January 2017 to December 2017 admitted in medical wards and intensive care unit of department of Medicine, Government Medical College Kozhikode. Information regarding clinical profile, investigations and complications were recorded in a proforma, from the case records. Data was analysed using SPSS statistical software and results were expressed as using proportional percentage.

### Diagnostic Criteria for Organ Dysfunction

1. Acute renal failure was defined by the presence of the serum creatinine level of >1.5 mg/dl.
2. Oliguria was defined by the presence of a first 24-h urine volume of <400 mL.
3. Acute respiratory distress syndrome was defined by the presence of all of the following criteria: no clinical signs of congestive heart failure; arterial gas exchange index of partial pressure of oxygen/fraction of inspired oxygen of <200; a chest radiograph revealing diffuse alveolar process with normal cardiothoracic ratio.
4. Myocarditis was defined by presence of ECG findings with elevation of cardiac biomarkers and/or echocardiographic findings in absence of pre-existing cardiac disease.
5. Pancreatitis was defined as patients with abdominal pain and elevated serum amylase and lipase with or without ultrasound evidence of pancreatitis.

## RESULTS

Total number of patients included in the study was 150 and mean age of study population was 44 years. Majority of the patients (109;72.7%) were males with a male to female ratio of 2.65. 103 patients (68.7%) were manual labourers which included farming, construction workers or cleaning workers. 78% of the cases occurred during the time period from August to December. In our study, 22 patients expired, and the overall mortality percentage was 14.7%. All the study subjects had fever (100%) with a mean duration of 7 days before presentation into our institution. Myalgia was a

significant symptom seen in 148 patients (98.7%). 93 patients (62%) had headache and 81 patients (54%) had vomiting associated with the fever. 114 patients (76%) had high coloured urine on admission and 90 patients (60%) had jaundice. 87 patients (58%) had complaints of oliguria and 33 patients (22%) had dyspnoea on presentation. Other minor symptoms were abdominal pain in 23 patients (15.3%), arthralgia in 22 patients (14.7%), upper gastrointestinal bleed in 17 patients (11.3%), chest pain in 13 patients (8.7%), hematuria in 10 patients (6.7%) and haemoptysis in 4 patients (2.7%).

On analysis of the comorbid illness 22 patients (14%) was Diabetic. 34 patients (22.7%) were alcoholic and 40 patients (26.7%) were smokers. 23 patients (15.3%) give history of prior NSAID intake.

On general examination, conjunctival congestion was present in 127 patients (84%), followed by calf muscle tenderness in 95 patients (63.3%). Pallor was identified in 29 patients (19.3%) and subconjunctival haemorrhage in 19 patients (12.7%). Other minor features were oedema in 17 patients (11.3%) and clubbing in 6 patients (4%). Mean pulse rate among the patients at time of admission was 90/minute and mean systolic and diastolic BP was 108- and 70-mm Hg respectively. Mean respiratory rate was 19/minute. Systemic examination showed positive gastrointestinal findings in 46 patients (30.7%), majority being mild to moderate hepatomegaly in 32 patients (21.3%) and abdominal tenderness in 10 patients (6.7%). This was followed by respiratory system findings in 30 patients (20%), 28 patients (18.7%) having bilateral crepitations. Neurologic findings were obtained in 7 patients (4.7%), majority being neck stiffness.

Blood investigations at the time of admission showed a mean haemoglobin of 11.7 g% and a mean total leucocyte count of 13300/mm<sup>3</sup> at the time of admission. Mean platelet count was 69600/mm<sup>3</sup> with a minimum value of 5000/mm<sup>3</sup> and mean ESR was 84 mm /first hour. Mean blood urea value was 94 mg% and showed an increase to 104 mg% at the end of three days of hospitalisation. The mean serum creatinine value was 3.8 mg% at the time of admission. The mean sodium was 131 and mean potassium was 3.4 meq/l on admission. Liver function tests showed conjugated hyperbilirubinemia with a mean total bilirubin of 8.7 mg% up on hospitalisation. Mean ALT and AST values were 112 and 80 mg% respectively. Mean value of serum albumin was 2.7 g% with a mean total protein of 5.4 g% on the day of admission.

Investigation results showed albuminuria in 96 patients (64%), presence of pus cells in 84 patients (56%) and hematuria in 50 patients (33.3%). Abnormal ECG findings were seen in 47 patients (31.3%), most important being sinus tachycardia. Chest X-Ray showed positive findings in 22 patients (14.7%). Ultrasound abdomen showed liver involvement in 40 patients (26.7%), renal involvement in 49 patients (32.7%), pancreatic involvement in 5 patients (3.3%) and ascites in 4 patients (2.7%). Echocardiogram was abnormal in 14 patients (9.3%) and Troponin I was positive in 45 patients (30%).

The most common complication encountered was Hepatorenal involvement in 103 patients (68.7%) followed by myocarditis in 43 patients (28.7%). ARDS, pancreatitis and AKI without hepatic involvement was encountered in 27 (18%), 26 (17.3%) and 21 (14%) respectively. The least common complications were isolated hepatic involvement in 9 patients (6%), meningoencephalitis in 3 patients (2%) and Pulmonary alveolar haemorrhage in 2 patients (1.3%).

## DISCUSSION

Leptospirosis is a zoonotic disease with versatile clinical manifestations. Most of the cases of leptospirosis is anicteric while the severe form of leptospirosis called the Weil's syndrome presents with multiorgan dysfunction especially the liver and kidney and is often described as the pseudo hepatorenal syndrome. It can involve many other organs like lung causing ARDS and pulmonary alveolar haemorrhage, heart resulting in myocarditis, nervous system as meningoencephalitis and pancreatitis. Most of the other system involvement other than liver and kidney are less frequently reported. Leptospirosis is increasing in incidence and severity in our part of the country evidenced by the increase in number of cases encountered each year. Similar studies have shown increase in incidence of cases from various parts of North India as well.<sup>8,9</sup> In our study of 150 patients with IgM leptospira antibody positivity, we observed an increase in the number of complications as well comparing with published literature.

Mean age of patients in our study was 44.5 years in our study comparable to study done by Patil et al in Maharashtra where the mean age was 42 years.<sup>10</sup> Majority of our patients were males and 68.7% of the study subjects (both males and females) were manual labourers with exposure to contaminated water or soil. This included farming, building construction and waste cleaning which has got high risk of exposure to contaminated environment. 57% of the cases occurred from the month of August to October, which coincided with the post-monsoon season in this part of the country. Interestingly the cases were relatively less compared in June and July, where heavy rainfall occurred.

In our study, high grade intermittent fever with chills was present in all patients with significant myalgia in most, followed by headache and vomiting. The mean duration of onset of illness was one week prior to admission to our institution. This could be owing to the fact that it is a tertiary care centre, but a delay in referral or over the counter treatment may have also played a role. Major systems involved were renal and hepatic with jaundice, high coloured urine and oliguria. Renal involvement is classically described in the immune phase that is, from the second week of illness, but our patients had early onset of renal dysfunction as evidenced by symptoms like high coloured urine, oliguria and rise in blood urea and serum creatinine on admission itself. The mean value of serum creatinine was 3.8 mg% which comes in the usual described range of 3-8 mg%. Sambasiva et al described abnormal urinalysis findings in 70-80% and in our study 50-64% showed albuminuria, pyuria or hematuria or its combination.<sup>11</sup> Hepatic involvement was

characterised by jaundice and conjugated hyperbilirubinemia with moderate elevation in AST and ALT which was consistent with pattern described classically in Leptospirosis.<sup>12</sup> Respiratory involvement was noted by presence of dyspnoea, tachypnoea, haemoptysis or respiratory findings like crepitations or by desaturation or abnormal Chest X-Ray or arterial blood gases. Haemoptysis was reported to have an incidence of 17-50% in some series but our study showed only 2.7%.<sup>13</sup> Other atypical symptoms could also be noted in our study like abdominal pain, hematuria and upper gastrointestinal bleed.

Most common comorbidity observed was Diabetes Mellitus and smoking was the most common addiction observed in the patients. Many patients had history of NSAID intake, probably due to over the counter prescription for fever and myalgia, but lack of proper history or documentation might have underestimated the data.

Most significant examination findings were conjunctival congestion and calf muscle tenderness. These are the most important clues to an early diagnosis. Subconjunctival haemorrhage, one of the classically described finding was seen in only a minority of patients in our study. Oedema was seen in a small sub group only. Most of the patients were having features of dehydration characterised by low mean systolic and diastolic BP, with absence of tachycardia. Systemic examination showed majority of positive findings in gastrointestinal findings, hepatomegaly being the commonest finding. This was followed by respiratory involvement with crepitations being the most common finding. Cardiovascular and neurologic findings were elicited in a minority only.

General laboratory profile showed neutrophilic leucocytosis with thrombocytopenia and an elevated ESR. Most patients had acute kidney injury with elevated blood urea and serum creatinine levels, which increased on the third day of admission. The pattern of renal involvement with predominant rise in blood urea levels and mild rise in creatinine suggested majority was having a pre-renal type of renal failure. Most patients had hyponatremia and mild hypokalaemia on admission. Liver function tests showed conjugated hyperbilirubinemia with mild elevation in AST and ALT which is the characteristic pattern described.<sup>14</sup> The patients also had hypoalbuminemia with little evidence of coagulopathy. Urine microscopy showed albuminuria, with microscopic hematuria suggesting glomerular involvement. ECG findings were seen in 31.3% of patients, most important being sinus tachycardia but 28.7% among total patients had evidence of myocarditis characterised by ST, T changes in ECG with elevated Troponin I or by Echocardiogram findings or both. CXR showed findings like infiltrates in a minority and 5 patients with ARDS had a normal Chest X-Ray initially and were diagnosed by ABG criteria.

Most common complication encountered in our study was renal failure. Various studies done in Maharashtra, Chennai and other parts of India also showed that renal failure is the most common complication encountered in Leptospirosis.<sup>15,16</sup> Together, hepatic and renal involvement

was the most common presentation evident from the study. Another important observation in our study was the significant number of study subjects who had myocarditis and pancreatitis. As reported in literature, incidence of myocarditis in Leptospirosis is as low as 8-10%<sup>17</sup> and one series showed an incidence of severe pancreatitis in 24%,<sup>18</sup> ARDS was observed in increased incidence and was present in 48% of the patients who expired. In A Spanish study, Martines et al described ARDS in 11% of the cases. The least common complications were isolated hepatic involvement in 9 patients (6%), meningoencephalitis in 3 patients (2%) and Pulmonary alveolar haemorrhage in 2 patients (1.3%). Even though pulmonary alveolar haemorrhage was rare it was fatal in both cases.

## CONCLUSION

Leptospirosis is very common in Kerala and occurs throughout the year with an increasing incidence from the months of August to October corresponding with the monsoon and post rainy season. Manual labourers, especially males were the most common group affected highlighting the fact of having increased likelihood of contact with contaminated environment. High grade fever with myalgia was the most important symptom observed in the study followed by headache and vomiting. Most common complication encountered was hepatorenal involvement with relatively early onset by the end of first week. Most important examination findings were conjunctival congestion with calf muscle tenderness and were the early clues to the clinical diagnosis. Subconjunctival haemorrhage and haemoptysis occurred in less number of cases compared with existing literature. Neutrophilic leucocytosis with thrombocytopenia with conjugated hyperbilirubinemia and mild elevation of liver enzymes was the commonest pattern of laboratory findings. Renal function tests with elevated blood urea and mild elevation in serum creatinine with hyponatremia and hypokalaemia was observed in most study subjects suggesting a pre-renal failure in majority. There was a relatively increased incidence of complications like myocarditis, ARDS and pancreatitis in our study suggesting an increased incidence of sepsis like presentation with MODS. Even though pulmonary alveolar haemorrhage was low in incidence it was a fatal complication.

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