

A STUDY OF CLINICAL AND SOCIO-DEMOGRAPHIC PROFILE OF PATIENTS WITH ANTI- LEPTOSPIRA IGM ANTIBODIES ADMITTED TO A TERTIARY CARE HOSPITAL IN ALAPPUZHA, KERALA

Chinnu Sajeev¹, Neethu John², Parvathy V Das³, Greeshma Hareendranath²

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Corresponding Author:

Dr. Neethu John,

Email: neethujohn1980@gmail.com

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¹Assistant Professor, Department of Microbiology, Govt Medical College, Alappuzha, Kerala, India

²Associate Professor (CAP), Department of Microbiology, Govt Medical College, Alappuzha, Kerala, India

³Assistant Professor, Department of Microbiology, Govt Medical College, Alappuzha, Kerala, India.

Abstract

Background: Leptospirosis, a bacterial zoonotic infection, is one of the leading causes of death in Kerala, especially during the monsoon period. The clinical presentation of leptospirosis is usually mild in majority of the patients, but can be severe in 10% of patients. The diagnosis of leptospirosis is a dilemma among clinicians, as the clinical picture varies from person to person and place to place. This study aimed to analyse the varied clinical presentations of patients with ELISA confirmed (serologically confirmed) leptospirosis and also the epidemiological features associated with these patients in this area. **Materials and Methods:** This is a retrospective study of six-month duration conducted in a tertiary care hospital in Alappuzha, Kerala. The clinical and socio-demographic profile of serologically positive leptospirosis patients were studied in detail. Information was entered in excel and analysed using SPSS software. **Result:** A total of 667 serum samples from clinically suspected leptospirosis cases were received in Microbiology Laboratory, of which 83 samples were tested IgM Leptospira antibody ELISA positive. The mean age of the study population was found to be 46.19 ± 4.10 . Fever of acute onset was seen in 43%, acute kidney injury in 38%, respiratory symptoms in 8% of seropositive leptospirosis patients. Leucocytosis, elevated liver enzymes and altered renal function were noted in 81%, 27% and 22% patients respectively. Thrombocytopenia, a feature more commonly associated with dengue fever, was noted in 30% patients. Two patients showed leptospira and dengue virus co-infection. **Conclusion:** Large scale studies are to be carried out to analyse the varied clinical presentations as well as to find out the most prevalent serovars in the region. Measures to improve the availability of molecular tests like PCR in all the tertiary care centres (in addition to serological tests like ELISA) will definitely make an earlier detection of leptospirosis possible.

INTRODUCTION

Leptospirosis is a zoonotic disease caused by the bacteria Spirochetes of the genus *Leptospira*.^[1] Leptospirosis is caused by various pathogenic species of *Leptospira*, of which *Leptospira interrogans* is the most common worldwide.^[2] *Leptospira* sp. infect both wild and domestic animals. Humans acquire the infection either through direct contact with infected animals or through environment contaminated with their urine. Cattle, rodents and other domestic animals act as reservoirs for *Leptospira* and shed them in their urine.^[3]

According to World Health Organization, 10-100 people per 100,000 are affected with leptospirosis in tropical countries. In India, human leptospirosis was first reported from Delhi in 1966.^[3,16] Presently, the disease is found in most of the states in India.^[4] The serovars commonly isolated from India include *L. hebdomadis*, *L. canicola*, *L. icterohaemorrhagiae*, *L. pomona*, *L. australis* and *L. autumnalis*.^[16] The disease has variable manifestations ranging from subclinical infection to multiple organ involvement and death.^[5] It can manifest with initial symptoms of fever, myalgia, headache and jaundice.^[6] Ten percent of individuals infected with *Leptospira* sp. can progress to severe disease with sepsis and multiple-organ failure.^[7] Severe disease can affect

the lungs, liver, kidney, peripheral nerves, eyes, muscles and heart. The underlying pathology of severe disease is an uncontrolled cytokine storm followed by immune paralysis.^[8] The most severe form of the disease is called Weil's disease.^[9] Milder cases are treated with doxycycline. Severe disease requires intravenous penicillin G or third generation cephalosporins.^[10,11]

The occurrence of the disease has a clear association with poor sanitation, natural disasters and floods. Agriculture-based rural population is at highest risk for leptospirosis. As the organisms can be transmitted through food and water, food safety and sanitation also play a vital role in preventing large scale outbreaks. Outbreaks follow floods or heavy rainfalls in tropical regions. Frequent outbreaks have been reported from several states in India.^[12-14,24]

Serological assays such as IgM *Leptospira* antibody detection (ELISA) are the most commonly used tests for diagnosis of leptospirosis in a patient with clinical symptoms. Serovars can be differentiated by MAT. Direct demonstration of the spirochetes in clinical samples with microscopy and culture is often cumbersome. Molecular diagnosis is expensive.

The provisional diagnosis of leptospirosis is a challenge among the clinicians, as the clinical picture varies from person to person and time to time. Therefore, a study was conducted to note the clinical and socio-demographic features of serologically confirmed leptospirosis cases admitted in our institution.

MATERIALS AND METHODS

The study was conducted in Department of Microbiology in a tertiary care centre in Alappuzha, Kerala. The study population included all serologically confirmed (IgM *Leptospira* ELISA positive) leptospirosis patients admitted in our institution during a period of six months. IgM *Leptospira* ELISA was carried out using TRUSTWELL ELISA kit and IgM dengue capture ELISA was carried out using NIV ELISA kit. It was done as a retrospective study by analysing case records of the patients included in the study. Variables like age, sex, occupation, clinical features like fever, respiratory symptoms, gastro-intestinal symptoms, acute kidney injury, laboratory parameters like liver function test (LFT), renal function test (RFT), platelet count, presence of co-infection with dengue virus (IgM Dengue Capture ELISA positivity) were analysed. Descriptive statistics in the form of mean, standard deviation (SD), and percentages was used for formulating the results of this study. The study protocol was reviewed and approved by the Institutional Research Committee and Institutional Ethics Committee.

RESULTS

During the six-month study period, a total of 667 serum samples were received from patients with

clinically suspected Leptospirosis. Out of these 667 serum samples, 83 were positive for IgM *Leptospira* antibodies. The clinical records of these 83 serologically confirmed leptospirosis patients were obtained from medical records library and their socio-demographic data, clinical features, antibiotics used and prognosis were analysed. Among the 83 sero-positive leptospirosis patients, 66.3% (n=55) were males and 33.7% (n=28) were females [Figure 1]. The mean age of the study population was found to be 46.19 ± 4.10 (Range 7 to 89 years). The age distribution of the study population is shown in [Figure 2]. Majority of the study population were manual labourers by occupation (n=27, 33%). The occupational distribution of the study population is shown in [Figure 3].

The most common presentation was fever of acute onset (43%), mostly associated with chills and myalgia. Gastro-intestinal symptoms like abdominal pain and diarrhoea were present in 11% (n=15) of the study population. Features of acute kidney injury were present in 38% of the patients (n=52). Respiratory symptoms like breathlessness were present in 8% (n=11) of the patients. Symptom-wise distribution of the study group is depicted in [Figure 4].

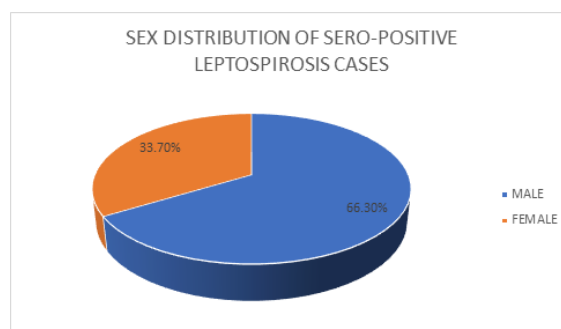


Figure 1: sex distribution of positive leptospirosis cases

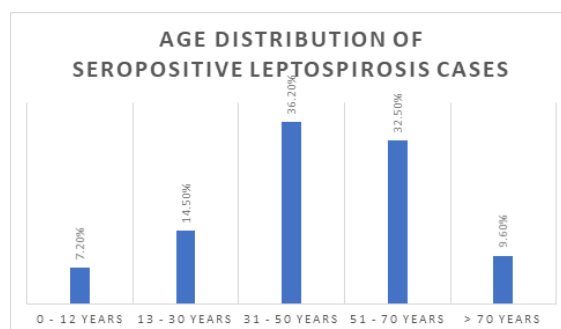


Figure 2: age distribution of seropositive leptospirosis cases

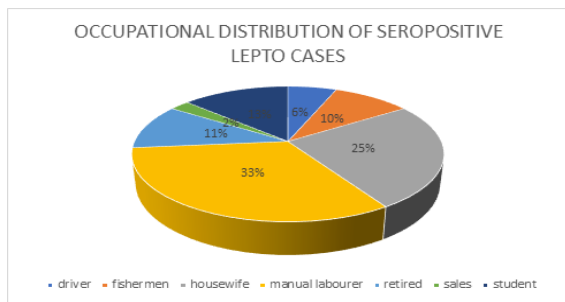


Figure 3: occupational distribution of seropositive leptospirosis cases

Laboratory parameters like total leukocyte count (TLC), liver function test (LFT), renal function test (RFT) and platelet count were also analysed. The presence of leucocytosis (elevated TLC) was noted in 81% of the patients. Only two patients had leukopenia, while others had a normal TLC. Elevated liver enzymes were present in 27% patients and raised blood urea and serum creatinine levels were noted in 22% patients. Thrombocytopenia, a feature more commonly associated with Dengue fever, was noted in 30% patients. The distribution of laboratory parameters is shown in [Figure 5].

Out of the 83 patients who were IgM *Leptospira* ELISA positive, two were positive for IgM Dengue Capture ELISA as well. Therefore, two patients had laboratory confirmed dengue co-infection. The patients were treated either with doxycycline, clarithromycin, ceftriaxone or crystalline penicillin. Majority of the patients recovered with these drugs (81/83), and only two patients expired.

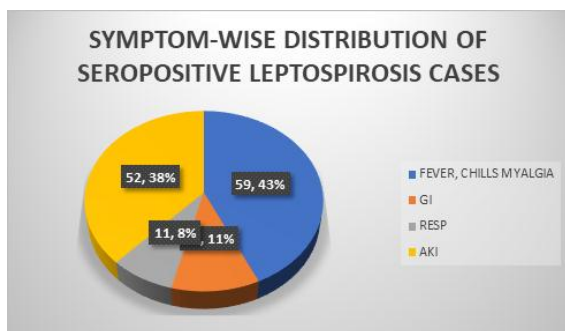


Figure 4: symptom-wise distribution of seropositive leptospirosis cases

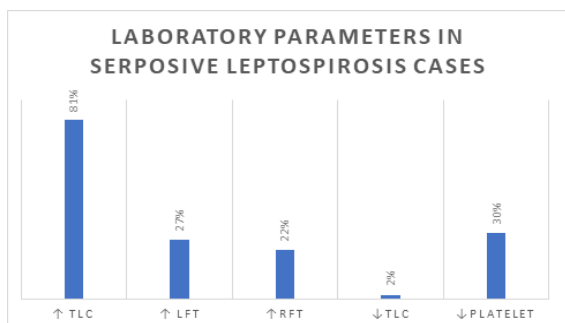


Figure 5: laboratory parameters in seropositive leptospirosis cases

DISCUSSION

Leptospirosis is a zoonotic disease common in tropical countries like India due to favourable conditions for transmission like abundance of rainfall, rice fields and reservoir animal hosts.^[15] The seroprevalence of leptospirosis in India is high, ranging from 7% to 30% depending on the location.^[16] The seropositivity rate in our study was 12.4% (83/667). This study is carried out in Alappuzha, a coastal district in Kerala, with backwaters and canals and is also famous for recreational water sports. Hence, leptospirosis is endemic in this district with spikes occurring in the number of cases during the monsoon season or after rainfall related floods. Due to climate change and global warming, unpredictable rains and floods have become very common in this area over the last 5 years.^[17] Even-though awareness campaigns and prophylactic measures are undertaken every year to reduce the number of cases, the number of leptospirosis cases and associated mortality are still alarming.

Early diagnosis and management of leptospirosis is very crucial in preventing complications and mortality. But early clinical diagnosis of leptospirosis has been challenging for the clinicians because of the varied and non-specific presentations as well as the non-availability of molecular tests like PCR in resource poor settings. The clinical picture can vary from person to person, place to place and time to time. Most patients in our study presented with acute febrile illness which is also the presentation in conditions like dengue fever, malaria, influenza and scrub typhus.^[18]

Most of the cases occurred in young males and the most common occupation in the study population was manual labour work like farming. Most patients in our study presented with acute febrile illness which is also the presentation in conditions like dengue fever, malaria, influenza and scrub typhus.^[18] Acute kidney injury was present in 38% patients, which is more suggestive of leptospirosis rather than malaria or dengue or influenza. Gastro-intestinal symptoms like abdominal pain and diarrhoea were present in 11% and respiratory symptoms like breathlessness was present in 8% of the patients. Various studies have shown GI symptoms in the range of 4 to 40% and respiratory symptoms in the range of 6 to 71%.^[15] Leucocytosis, a feature that helps to rule out viral infections was present in majority of the study population. Leukopenia was noted in 2 patients. Altered liver function tests (raised serum bilirubin and transaminases) were found in 27% patients. Elevated blood urea and serum creatinine levels were present in 22% of the patients. Alterations in both LFT and RFT were found in 15.7% (n=13) patients. Thrombocytopenia, a feature more commonly associated with dengue fever, was present in 30% of the patients. In a systematic review and meta-analysis of leptospirosis in India by N. Gupta et al, they have

noted thrombocytopenia in 50% of the patients. According to their study, average bilirubin, AST, ALT were 2.7-14.6 grams/dl, 58-524 IU/l, 58-503IU/l respectively and average creatinine at presentation ranged from 1.8 -5.4 mg/dl in adult leptospirosis patients.

The antibiotics used for treatment in the study population included doxycycline, clarithromycin, ceftriaxone, crystalline penicillin or a combination of these drugs. Out of the 83 seropositive leptospirosis cases, 81 patients got better with treatment and was discharged, but two patients expired. These two expired patients had elevated liver enzymes, elevated serum creatinine and low platelet count. Platelet count was less than 30,000 in these two patients. They also had elevated serum amylase and lipase levels. According to Philip N et al,^[19] the independent predictors of severity included Acute Kidney Injury, ALT > 50 IU and platelet < 150 × 10⁹/L. A study by Esen S et al,^[20] showed that mortality in leptospirosis, was not associated with the presence of thrombocytopenia. But contrary to that, a study by Spichler et al,^[21] showed that thrombocytopenia was an independent risk factor for mortality in leptospirosis.

In a case series reported by Herath NJ et al,^[22] it was found that significantly elevated amylase (> five times the upper normal value) were present in severe leptospirosis cases. They also emphasized the importance of identification of acute pancreatitis as a common complication of Leptospirosis, in order to reduce mortality and morbidity.

Co-infection with dengue virus can occur, which can lead to challenges in diagnosis as well as management of the patients. In our study, two patients had dengue and leptospira co-infection (serologically confirmed- both were positive for IgM Leptospira ELISA as well as IgM dengue capture ELISA) and both the patients got better with treatment. A study by Sachu A et al,^[23] have noted serologically confirmed leptospirosis and dengue co-infection in 3.4 % of their patients and there was 3% mortality in the co-infected patients. As both leptospirosis and dengue infections are very common in this area, particularly in monsoon season, possibility of co-infection should be kept in mind by the clinicians.

CONCLUSION

The number of leptospirosis cases that occur every year in the state and the associated morbidity and mortality are alarming. Extensive awareness campaigns about the disease and prophylactic measures (both general and chemoprophylaxis) are being undertaken by the public health sector in the state, which has to be reinforced further. Early detection is very important in successful management of the patients. Large scale studies comprising tertiary care centres in all districts of the state have to be planned and implemented to study the varied

clinical presentations as well as to find out the most prevalent serovars in the region. Also, measures are to be initiated to improve the availability of molecular tests like PCR in all the tertiary care centres (in addition to serological tests like ELISA) which will definitely make an earlier detection of leptospirosis possible.

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