

Leptospirosis: Experience at a tertiary care hospital in northern India

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ABSTRACT

Background. Leptospirosis is primarily a disease of wild and domestic mammals. Man is infected either directly through contact with an infected animal or indirectly by water or soil contaminated with the urine of an infected animal. We studied the incidence of leptospirosis in patients presenting with an acute febrile illness of more than 7 days to a tertiary care hospital in northern India.

Methods. This study was done over a period of 1 year and included 647 patients who presented with an acute febrile illness for more than 7 days. These patients were screened for leptospirosis using the Dri-Dot test and ELISA.

Results. Using the Dri-Dot screening test, 244 of 647 patients (37.7%) were positive for leptospirosis. Of these 244 patients, 200 (82%) were positive by ELISA.

Conclusion. Leptospirosis is common in northern India and should be considered as a possible differential diagnosis in patients with an acute febrile illness of more than 7 days' duration.

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INTRODUCTION

Leptospirosis is a zoonosis of ubiquitous distribution. The term is used for diseases caused by all leptospira regardless of serotype.¹ Primarily a disease of wild and domestic mammals, man is infected through contact with an infected animal either directly or indirectly by water or soil contaminated with the urine of an infected animal. The spectrum of disease ranges from subclinical infection to a severe syndrome of multiorgan dysfunction characterized by headache, fever, myalgia, jaundice, hepatomegaly and convulsions.² Leptospirosis was first reported from the Andaman Islands in 1929, and has since affected all parts of India.³ Although national incidence data are not available, leptospirosis has been recognized as a major health problem. Natural disasters and poor sanitary conditions have contributed to the multiple epidemics reported,⁴ and several outbreaks of the disease have been reported in recent years.^{5,6} Although studies have highlighted the epidemicity and prevalence of leptospirosis in India,⁷ reports of human leptospirosis from northern India are few. Hence, we studied the incidence of leptospirosis in patients presenting with an acute febrile illness to a tertiary care hospital in northern India.

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METHODS

This prospective study was done at the Department of General Medicine, Christian Medical College and Hospital, Ludhiana, India over a 1-year period. A detailed history was taken and examination done in all adult patients (>12 years of age) presenting to the outpatient clinic or inpatients in our department with an acute febrile illness of >7 days. Complete blood counts, renal and liver function tests, and urinalysis were done. The Lepto Tek Dri-Dot (latex agglutination, Biomerieux) test was used for screening. Those positive by this test were tested for leptospirosis using ELISA. The ELISA-positive patients formed the study cohort. In addition, a blood smear for malarial parasites, dengue IgM ELISA, Widal test and a blood culture were also done in all the patients.

All patients were tested for hepatitis B surface antigen and antibody to hepatitis C virus. Those patients whose symptoms and signs were suggestive of viral hepatitis, such as disappearance of fever with the appearance of jaundice and marked elevation of liver enzymes were tested for hepatitis A and E viruses.

Lepto TeK Dri-Dot (Biomerieux)

The Lepto Tek Dri-Dot assay for rapid screening of leptospirosis detects leptospira-specific antibodies in human serum. The sensitivity ranges from 72.3% to 88.2%, and specificity from 89.9% to 93.9%.⁸

Leptospira ELISA Test (IBM)

Leptospira IgG/IgM ELISA are qualitative and/or quantitative tests for the detection of human antibodies against leptospira in serum or plasma. The ELISA test is reported to have a sensitivity of 100% and a specificity of 93%.⁹

RESULTS

There were 647 patients who presented with an acute febrile illness. Of these, 244 (37.7%) had a positive Lepto TeK Dri-Dot assay. Of these 244 patients, 200 (82%) were positive by ELISA. Hence, the incidence of leptospirosis was 30.9% in this cohort. There were 123 (61.5%) men and 77 (38.5%) women. The majority of them (162; 81%) presented between the months of July to October, coinciding with the monsoon and post-monsoon season in Punjab.

Their mean age was 38 years (range 14–80 years) and 128 patients (64%) were between 31 and 50 years of age. Fifty-three (26.5%) were housewives; 44 (22%) businessmen; 49 (24.5%) office workers; 39 (19.5%) students and 15 (7.5%) labourers.

All patients presented with fever. The other symptoms at the time of presentation included headache in 178 (89%), myalgias in 112 (56%) and jaundice in 107 (53.5%). There was a history of

contact with an animal in 57 (28.5%) patients. On examination, 144 (72%) had jaundice, 131 (65.5%) had conjunctival suffusion and 134 (67%) had hepatomegaly. Ecchymosis and/or petechiae were seen in 57 (28.5%), meningism in 52 (26%) and altered sensorium in 6 patients (3%).

Laboratory investigations showed that 18 patients (9%) had a haemoglobin value <10 g/dl. Fifty-two patients (26%) had leucocytosis. The serum creatinine was >1.5 mg/dl in 17 patients (8.5%). Elevated transaminases were present in 116 patients (81%) and the bilirubin was raised in 120 (60%).

Leptospirosis also occurred as a coinfection. Among the 200 patients, dengue was the commonest coexisting infection (35 patients, 17.5%) followed by malaria (15 patients, 7.5%). Of the 200 patients with leptospirosis, viral markers for hepatitis were done in 165 (82.5%) patients, 30 (15%) of whom were found to have coexisting viral hepatitis. Of these 30 patients, 24 (80%) tested positive for hepatitis E and 2 for hepatitis A virus. Two patients had both hepatitis A and E infection. One patient tested positive for hepatitis B and one had infection with hepatitis B and C.

Three patients died. Two patients had fulminant hepatic failure, of which one had hepatitis B infection while the other had coinfection with hepatitis B and C. One patient died due to acute pancreatitis and multiorgan dysfunction syndrome due to leptospirosis.

DISCUSSION

The seroprevalence of leptospirosis in patients with an acute febrile illness has been studied less often in northern as compared with southern India. The highest positivity rate of 25.6% has been reported from southern India. The reported positivity rates are 8.3%, 3.5%, 3.1% and 3.3% in northern, western, eastern and central India, respectively.¹⁰

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. We found that 200 of 647 (31%) patients had serological evidence of leptospirosis. A seroprevalence of 8.8% and 21.7% has been reported from Chandigarh and Varanasi, respectively, by Sethi *et al.*¹¹

Leptospirosis has a peak during the monsoon and post-monsoon months, and occurs more commonly in people living in urban slums with poor sanitation and low hygienic conditions. However, in the past decade, it has been reported from all parts of urban and rural India.¹² We found the highest prevalence among housewives (26.5%) followed by businessmen (22%).

Leptospirosis has two distinct clinical syndromes—a mild anicteric febrile illness seen in 90% of patients, and a severe variety (10%) with jaundice and other manifestations (Weil disease).¹³ The laboratory investigations in our study were consistent with mild disease; the haematological profile was normal in most patients. Chawla *et al.*¹⁴ encountered leucocytosis in all their patients. Liver, kidney and central nervous system involvement may be present in any combination. We did not encounter any patients with central nervous system manifestations.

We found coinfection with dengue in 35 (17.5%) patients. This was akin to the report by Kaur¹⁵ who detected dual infection with leptospirosis and dengue in 9.4% of patients. Thirty (15%) had serological evidence of coinfection with hepatitis, 26 of whom were positive for hepatitis E. Angnani *et al.*¹⁶ 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.¹⁷

Three of our patients died, two of whom had fulminant hepatic failure due to hepatitis B and/or C infection. The third patient who died had multiorgan dysfunction due to leptospirosis. The reported mortality rates range from 10.8% to 66% among patients with leptospirosis.^{18–20}

Limitations

The majority of infections with leptospires are subclinical or of mild intensity. Such patients would not report to a hospital and the diagnosis would be missed in them. Our study would underestimate the community prevalence of leptospirosis because of a referral bias in patients attending a tertiary level centre.

The Dri-Dot test for leptospirosis has a relatively low sensitivity (72.3%–88.2%). It is possible that some patients with leptospirosis were not diagnosed using this test. However, ease of availability and simple point-of-care use not requiring technical skill dictated the use of this test for the initial screening of patients.

Conclusion

Leptospirosis occurs in northern India and all patients presenting with an acute febrile illness, particularly during the monsoon season, should be screened. It affects anyone irrespective of their age and occupation. The presentation may range from a subclinical infection to a severe syndrome of multiorgan dysfunction.

Serodiagnosis by a microagglutination test (MAT) is the gold standard but is not universally available. Leptospirosis can be easily diagnosed using a latex agglutination test and IgM ELISA. We recommend that all persons with fever for >7 days should be screened for leptospirosis.

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Is the skin sensitivity test required for administering equine rabies immunoglobulin?

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ABSTRACT

Background. Rabies immunoglobulins are life-saving in patients with severe exposure to rabies. Despite the high degree of purification of equine rabies immunoglobulin (ERIG), the product inserts still recommend a skin sensitivity test before administration of this heterologous serum. A recent WHO recommendation states that there are no scientific grounds for performing a skin test before administering ERIG because testing does not predict reactions and it should be given irrespective of the result of the test. In this conflicting situation, we assessed the use of the skin sensitivity test in predicting adverse events to ERIG.

Methods. The data analysed were from the Antirabies Clinic of the Kempegowda Institute of Medical Sciences Hospital, Bengaluru, India. The period of study was 26 months (June 2008–July 2010). The skin sensitivity test was validated by evaluating its sensitivity, specificity, predictability, false-positive and false-negative results.

Results. A total of 51 (2.6%) adverse events were reported in 31 (1.5%) subjects. Most of these were mild to moderate in nature and subsided without medication. There was no serious adverse event. The sensitivity and specificity of the skin sensitivity test to predict an adverse event was 41.9% and 73.9%, respectively.

Conclusion. Our experience with the skin sensitivity test suggests that it may not be required before administering ERIGs, as recommended by WHO.

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INTRODUCTION

Human rabies is endemic in India. According to a recent WHO estimate, 55 000 deaths occur annually due to human rabies globally, 20 000 (36%) of which occur in India.¹ Rabies immunoglobulins (RIGs) are life-saving in patients with severe exposure to rabies. Human RIGs are imported, expensive and scarce. However, equine rabies immunoglobulins (ERIGs) are indigenously produced, less expensive and more widely available. Despite the high degree of purification of ERIGs, the product inserts still recommend a skin sensitivity test (SST) before administration of this heterologous serum.^{2–4} This has brought disrepute to the product and, as a result, healthcare professionals are reluctant to use it. A recent WHO recommendation states that there are no scientific grounds for performing a skin test before administering ERIG, because testing does not predict reactions and it should be given irrespective of the result of the test.⁵ It also suggests that the treating physician should be prepared to manage anaphylaxis which, although rare, could occur during any stage of administration.

Because of this recommendation, we studied the utility of SST in predicting adverse events to ERIG.

METHODS

The data analysed were from the records of the Antirabies Clinic of the Kempegowda Institute of Medical Sciences Hospital, Bengaluru, India. The period of study was 26 months (June 2008–July 2010). A total of 2008 patients had received purified, pepsin-digested ERIGs. The brands used were Equirab (Bharat Serums & Vaccines Limited, Mumbai) in 1560 (77.7%) patients; Abhayrig (Human Biological Institute, Hyderabad) in 404 (20.1%); Zyrig (Zydus Cadila, Ahmedabad) in 40 (2%) and Vinrig (Vins Bioproducts, Andhra Pradesh) in 4 patients (0.2%).

For the SST, 0.1 ml of sterile normal saline was injected intradermally using an insulin syringe (26G needle) into the flexor aspect of the right forearm. This raised a 5–6 mm orange skin-like induration (control injection). Similarly, 0.1 ml of ERIG was