Research and Reports in Tropical Medicine

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ORIGINAL RESEARCH

Clinical and laboratory findings in patients with leptospirosis at a tertiary teaching hospital in Jamaica

This article was published in the following Dove Press journal:
Research and Reports in Tropical Medicine
11 November 2010
Number of times this article has been viewed

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Background: Leptospirosis is a zoonotic disease that is endemic in most Caribbean countries. This study examined the clinical presentations and laboratory findings in serologically confirmed cases of leptospirosis.

Patients and methods: The medical records of all hospitalized patients with presumptive and confirmed leptospirosis between June 2005 and May 2006 at the University Hospital of the West Indies were retrospectively reviewed.

Results: There were five serologically confirmed cases of leptospirosis. The mean age of patients with leptospirosis was 57.33 ± 8.21 years (range 41–67 years); all were men exposed to contaminated water or soil, and most cases were diagnosed in November. The most common symptoms were fever, myalgia, nausea, vomiting, headache, abdominal pain, and arthralgia. Increase in the mean serum creatinine concentration in patients with leptospirosis (439.40 ± 129.18 µmol/L) was significant when compared with that in the controls (87.86 ± 4.72 µmol/L; $P = 0.005$). Four of the five patients with leptospirosis showed evidence of hematuria. All patients with leptospirosis showed evidence of hyperbilirubinemia, which was mostly direct hyperbilirubinemia. The mean concentration of total bilirubin was 291.40 ± 52.33 µmol/L in patients with leptospirosis when compared with 9.83 ± 1.28 µmol/L in controls ($P < 0.001$). Thrombocytopenia (platelet count <150,000 cells/mm^3) was observed in 80% of the patients with leptospirosis.

Conclusion: The study indicates the variable clinical manifestations of leptospirosis and emphasizes the importance of continued vigilance of physicians and primary health care workers in increasing the awareness of the seasonal distribution and the need for early diagnosis of leptospirosis.

Keywords: leptospirosis, serological, clinical manifestations, Jamaica, laboratory findings

Introduction

Leptospirosis is a zoonotic bacterial infection caused by spirochetes belonging to the genus *Leptospira*, which comprises about 250 serovars.[1] The disease occurs worldwide, but the incidence is higher in the tropics than in temperate countries,[2,3] mainly because of the longer survival of leptospires in warm and humid environments.

In both developing and developed countries, leptospirosis is an important public health problem. Leptospirosis is seasonal, with a peak incidence occurring during summer or fall in temperate regions and during rainy seasons in tropical regions.[4] Extensive flooding and seasonal rainfall are significant risk factors for acquiring the infection. Transmission of leptospirosis in humans occurs by direct or indirect contact with urine, blood, or tissue from an infected animal containing virulent leptospires.[5] Infection may also arise from bathing or accidental immersion in the fresh water of lakes, rivers, or canals contaminated with the urine of the infected livestock.[5]

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Dovepress
DOI: 10.2147/RRTM.S14118

The early clinical presentation is often nonspecific, with fever, headache, chills, myalgia, and abdominal pain. Two common forms of leptospirosis have been described: the anicteric (most common and mildest) and the icteric (Weil syndrome), which causes severe renal, hepatic, and vascular dysfunction.[6]

Leptospirosis has a high incidence in tropical regions and has been studied extensively in several Caribbean countries. Leptospirosis in the Caribbean area was first reported in 1918 in Puerto Rico by Guiliani, who diagnosed a case on the basis of clinical findings.[7] Leptospirosis is endemic in Guadeloupe, an island in the French West Indies, where it was responsible for 8.8 deaths per million inhabitants from 1991 to 1999, with an incidence rate of 13.7 cases per 100,000 population in 1999.[8] Most information on leptospirosis in the English-speaking Caribbean countries comes from Barbados, Trinidad, and Jamaica. The leptospiral epidemiology of Barbados is apparently the simplest of these, where three serovars of *Leptospira* species (Bin, Copenhaggeni, and Arborea) cause 97% of severe cases in humans.[2] The most complex leptospiral epidemiology is probably that of Trinidad, where 17 serovars have been isolated from humans and 11 animal species; six of these serovars were first found on the island.[2] Leptospirosis was noted in Jamaica in 1942;[9] however, the first proven human case was described in 1953.[10] Between 1960 and 1978, Urquhart et al[11] serodiagnosed 651 infections (12.9%) in 5,021 Jamaicans, some of whom showed clinical signs similar to those of leptospirosis. Of the positive individuals, 57% had been exposed to the serogroup Icterohemorrhagiae, 31% to Hebdomadis (Jules), and 8% to Canicola.[11] From a nonrandom series of livestock sera, Agba et al[12] demonstrated seroconversions to Jules (51.9%), Icterohemorrhagiae (28.1%), Autumnalis (8.3%), Canicola (6.1%), Pomona (5.2%), and Abramis (0.4%).

Many cases of leptospirosis remain unrecognized because of the lack of specificity of signs and symptoms.[13] Confirmation of the diagnosis is also difficult because of problems associated with isolating the organism and serological testing.[14] A better understanding of the clinical and paraclinical findings of leptospirosis is required to enhance its recognition and appropriate treatment. This study was performed to examine the clinical presentations and laboratory findings of serologically confirmed cases of leptospirosis admitted to the University Hospital of the West Indies, Kingston, Jamaica.

Patients and methods

Data collection

The medical records of all hospitalized patients with presumptive and serologically confirmed leptospirosis between June 2005 and May 2006 at the University Hospital of the West Indies were retrospectively reviewed. Sera from 41 patients, suspected of having leptospirosis on the basis of screening tests or clinical findings, were sent for a confirmatory microscopic agglutination test (MAT) at the Veterinary Diagnostic Laboratory, Hope Gardens, Kingston, Jamaica. The MAT was performed by standard method[15] using a battery of 15 serovars, which included reference serovars supplied by the Leptospira Reference Laboratory in Barbados and Centers for Disease Control and Prevention.[16] Laboratory criteria for confirming the diagnosis are as follows: 1) the isolation of *Leptospira* from a clinical specimen or a single titer of 1:100 or greater was considered seropositive and indicative of exposure to leptospirosis and 2) a single titer of 1:800 or greater by the MAT was indicative of acute leptospirosis.[17]

Demographic data (age, sex, and profession), epidemiological data (type of contact, duration between onset of symptoms and admission to hospital, and place of residence), possible symptoms and findings related to the disease (fever, nausea, vomiting, diarrhea, headache, abdominal pain, muscle pain, jaundice, oliguria, hypotension, tachypnea, cough, disturbance of consciousness, and neck stiffness), hepatomegaly, splenomegaly, cephalgia meningism, and disturbed consciousness were recorded. Hematological investigations included complete blood count, leukocyte and platelet counts, and coagulation parameters. Serum biochemical tests included the assessment of serum potassium, aspartate aminotransferase (AST), creatinine, urea, creatine phosphokinase (CPK), bilirubin (total and direct), alkaline phosphatase (ALP), gamma glutamyl transferase (GGT), and proteinuria (24-hour collection) levels. Ten healthy men of similar ages formed the control group.

Statistical analysis

Categorical clinical and laboratory findings of presumptive and serologically confirmed cases were entered into SPSS software (11.5 for Windows; SPSS Inc., Chicago, IL) and assessed by Student's *t*-test, with $P < 0.01$ defined as statistically significant. The results are given as mean ± SE. In addition, analysis of variance, chi-square test, Fisher's exact test, and multivariate analysis were performed.

Results

Review of the medical records revealed 41 patients who were suspected of having leptospirosis on the basis of screening tests or clinical findings. Of these 41 patients, five were serologically confirmed based on *Leptospira* isolation and MAT. All five patients had a single titer greater than 1:100 and were considered seropositive. Furthermore, the MAT

results showed a single titer greater than 1:800, which was indicative of acute leptospirosis.

The infecting serovars for the five serologically confirmed leptospirosis patients were Icterohemorrhagiae, Canicola, Autumnalis, Pomona, Bataviae, Hebdomadis, Jules, and Abramis. All were infected with Icterohemorrhagiae and Canicola.

The mean age of patients with leptospirosis was 57.33 ± 8.21 years (range, 41–67 years); all were men who resided in the parishes of Kingston and St. Andrew (Table 1). The mean duration of symptoms before hospital admission was 6.8 days (range 4–11 days); three were farmers, and another patient was a construction worker. All patients reported exposure to contaminated water or soil, having worked in fields or areas infected by rats. The percentage of males (63.8%) affected in the presumptive group of patients was higher than that of females (36.2%), with a male/female ratio of approximately 2:1. The mean age of these patients was 40.96 ± 3.24 years (range, 15–72 years). Four of the five patients were diagnosed in the first week of November and the other in January. The mean rainfall for the period from June 2005 to May 2006 was highest in October (578 mm) followed by July (488 mm), June (234 mm), and May (224 mm). The mean rainfall for December and January was 77 and 73.4 mm, respectively.

Table 1 Biochemistry findings of controls and confirmed patients with leptospirosis

	Controls (mean ± SE)	Confirmed patients (mean ± SE)	*P* value
Age	55.96 ± 3.34	57.33 ± 8.21	0.786
Sodium (mmol/L)	139.00 ± 3.58	134.20 ± 0.80	0.003
Potassium (mmol/L)	4.29 ± 0.16	3.94 ± 0.47	0.762
Bicarbonate (mmol/L)	24.71 ± 1.27	17.00 ± 1.10	0.023
Chloride (mmol/L)	105.29 ± 1.08	102.00 ± 4.06	0.308
Urea (mmol/L)	4.23 ± 0.31	31.60 ± 10.63	0.063
Creatinine (μmol/L)	87.86 ± 4.72	439.40 ± 129.18	0.005
Total bilirubin (μmol/L)	9.83 ± 1.28	291.40 ± 52.33	<0.001
Direct bilirubin (μmol/L)	3.83 ± 0.60	1165.12 ± 36.68	0.002
Aspartate aminotransferase (U/L)	25.86 ± 0.77	119.60 ± 56.57	<0.001
Alkaline phosphatase (U/L)	56.29 ± 8.66	89.20 ± 23.16	<0.001
Gamma glutamyl transferase (U/L)	24.14 ± 2.82	109.60 ± 33.90	0.005
Creatinine kinase (U/L)	186.40 ± 28.93	269.20 ± 19.73	0.004
Lactate dehydrogenase (U/L)	192.80 ± 27.42	341.75 ± 82.49	0.029
Total protein (g/L)	72.40 ± 0.40	68.80 ± 4.03	0.380
Albumin (g/L)	43.00 ± 1.22	28.80 ± 1.20	<0.001
Globulins (g/L)	29.60 ± 1.12	40.00 ± 4.18	0.130
Hemoglobin (g/dL)	15.43 ± 0.84	11.50 ± 1.29	0.060

Clinical features are summarized in Table 2 and laboratory findings in Table 1. Fever, myalgia, nausea, vomiting, headache, abdominal pain, and arthralgia were the most common symptoms in patients with leptospirosis. Conjunctival suffusion and hepatosplenomegaly were observed in 60% of cases. Respiratory symptoms included cough, hemoptysis, and dyspnea (Table 2). In the presumptive group of patients, the most common symptoms were abdominal pains, nausea, fever, vomiting, myalgia, diarrhea, and headache.

Among these patients, there was clear evidence of renal abnormalities, hepatic dysfunction, elevated CPK levels, and hematological abnormalities (Table 1), and 25% of patients had hyponatremia and hyperkalemia. Elevated serum creatinine concentration was found in patients with leptospirosis (439.40 ± 129.18 μmol/L). This value was significantly different from that of the presumptive patients (170.62 ± 46.80 μmol/L; $P = 0.044$) and controls (87.86 ± 4.72 μmol/L; $P = 0.005$). Further, there was no significant difference between the mean serum urea concentration in patients with leptospirosis (31.60 ± 10.63 mmol/L)

Table 2 Clinical presentations of patients with confirmed leptospirosis

Clinical findings	Confirmed patients, n (%)
Jaundice	5 (100)
Muscle pain	5 (100)
Nausea	5 (100)
Vomiting	5 (100)
Fever (38°C)	5 (100)
Tachycardia	5 (100)
Headache	5 (100)
Cough	5 (100)
Hypotension	5 (100)
Dehydration	5 (100)
Abdominal pain	4 (80)
Neck stiffness	4 (80)
Anorexia	4 (80)
Arthralgia	4 (80)
Hemoptysis	4 (80)
Urine discoloration	4 (80)
Malaise	4 (80)
Conjunctival suffusion	3 (60)
Hepatosplenomegaly	3 (60)
Diarrhea	3 (60)
Backache	2 (40)
Blurred vision	2 (40)
Lymphedenopathy	2 (40)
Retroorbital pain	2 (40)
Chest pain	2 (40)
Dyspnea	2 (40)
Bleeding	1 (20)
Oliguria	1 (20)
Altered mental state	1 (20)
Rash	1 (20)

and that in the control group (4.23 ± 0.31 mmol/L; $P = 0.63$) (Table 1). In four of the five patients with leptospirosis, microscopic evaluation of urine samples showed the presence of red blood cells (>3 red blood cells per high-power field). There was evidence of proteinuria (>0.15 g/24 h) in 60% of patients with leptospirosis (Table 3).

One patient with leptospirosis had elevated CPK levels, which rose to more than sixfold above the normal upper limit (NUL), whereas in others, the CPK levels were within the normal range. The AST levels were above the NUL in 80% of patients with leptospirosis (mean concentration of 119.60 ± 65.57 U/L) (Table 1). All patients with leptospirosis showed evidence of hyperbilirubinemia, which was mostly direct hyperbilirubinemia. The mean total bilirubin concentration was 291.40 ± 52.33 μmol/L in patients with leptospirosis compared with 11.19 ± 40.65 μmol/L in presumptive patients ($P = 0.0342$) and 9.83 ± 1.28 μmol/L in controls ($P < 0.001$; Table 1).

Thrombocytopenia (platelet count <150,000 cells/mm^3) was observed in 80% of serologically confirmed patients with leptospirosis. Anemia was also observed as an obvious finding in all five patients (11.50 ± 1.29 g/dL). One of these patients had leukopenia (<4,000 cells/mm^3), and the other four had leukocytosis (>12,000 cells/mm^3) (Table 3).

Discussion

Although leptospirosis is endemic in Jamaica, there is a relatively low incidence of the disease (six cases/100,000 population/year); hence, most of the population is not routinely exposed to the causative agent. However, in Jamaica, like many other Caribbean countries, the risk of leptospirosis infection increases during rainy seasons, during which localized flooding occurs and individuals become exposed to the leptospire-contaminated waters.[18] Jamaica's bimodal rainfall pattern consists of two peak periods with higher values of rainfall and corresponding periods of lower rainfall amounts.

Table 3 Laboratory results of patients with confirmed leptospirosis

Laboratory parameters	Confirmed patients, n (%)
Hematuria (>3 RBCs/HPF)	3 (60)
Proteinuria (1+)	1 (20)
Proteinuria (2+)	2 (40)
White blood cell count >12,000 cells/mm^3	4 (80)
White blood cell count <400 cells/mm^3	1 (20)
Platelet count <150,000 cells/mm^3	4 (80)
Hemoglobin (<13 g/dL in male and <12 g/dL in female)	4 (80)

Abbreviation: RBCs/HPF, red blood cells per high-power field.

The primary peak occurs in September/October and the secondary in May. The lowest amounts of rainfall occur during the period of February to March and the month of July. This is based on long-term reports, and deviations from this pattern do occur.[19] However, during the period June 2005 to May 2006, the mean rainfall was highest in October followed by July, June, and May. The relatively high rainfall in October could have increased the risk of leptospirosis by enhancing the survival of leptospires in the soil and water. This could have contributed to the diagnosis of leptospirosis in four of the five patients during the first week of November. In a study by Douglin et al[20] of leptospirosis in St. Andrew, Barbados, the incidence of leptospirosis in St. Andrew showed a close association with the mean monthly rainfall, the highest incidence occurring in October and November.

All patients with leptospirosis had a history of rat infestation in their house and of rearing or contact with animals. Similar findings were found in the studies performed in Madras[21] and Port Blair[22] in India. Leptospirosis in humans is acquired by contact with urine or tissues of an infected animal or through contaminated water and soil.[4] Rodents are recognized as the most important sources in the transmission of leptospirosis,[1,4] especially of more severe forms. Leptospirosis is most common among adult males, probably resulting from occupational and recreational exposures.[4,23] In general, farmers, veterinarians, and butchers have a higher risk of acquiring leptospirosis.[24] Furthermore, all patients except one were middle aged. Also in other countries, middle-aged people are the most highly infected.[8] There were two people younger than 20 years in the presumptive group. As in other studies, leptospirosis is rarely recorded in children despite their higher exposure to surface water and animals perhaps because of asymptomatic forms.[25,26]

Fever, nausea, vomiting, and headache were the most common symptoms on admission in this study, like other reports.[27,28] Myalgia and elevated CPK levels are important indicators in differentiating leptospirosis from other icteric diseases. All the patients diagnosed with leptospirosis reported muscle pain on admission. In other large series, myalgia rates were reported between 20% and 100%.[29,30] Jaundice was common in our study, which plays a major role in the leptospirosis of liver involvement[31,32] and often suggests a severe infection.[33] Conjunctival suffusion can be a major and important tool in the confirmation of leptospirosis[34] and occurred in 60% of patients with leptospirosis in this study.

Renal pathology appears to vary during the course of the disease. Urinalysis may reveal sterile pyuria, hematuria,

proteinuria, and granular casts. Acute tubular necrosis (ATN) and interstitial nephritis are the two common renal lesions associated with leptospirosis. Direct leptospiral injury may cause ATN, whereas interstitial nephritis occurs later and is probably related to antigen–antibody complexes of the immune phase.[35,36] Urinalysis findings in this study were frequently abnormal, with proteinuria and hematuria being observed in more than half of the patients with leptospirosis, a finding consistent with other reports.[25,27] Abnormal serum creatinine level was seen in this study (60%), similar to other reports,[34,37] and three patients diagnosed with leptospirosis showed a more than threefold increase in the NUL. An elevated serum creatinine level appears to be one of the best diagnostic signs, as this is rather uncommon for most of the differential diagnoses (influenza-like illness, viral hepatitis, gastroenteritis, or meningitis). Renal failure is frequently reported in patients with leptospirosis (16%–69%).[4,6,38] A previous case-control study in Taiwan found a higher acute renal failure rate.[39] In our study, 60% of patients had renal insufficiency, two required renal replacement therapy, and all of them recovered completely. These findings can lead to the prompt diagnosis of leptospirosis in addition to suspicious clinical features.

Thrombocytopenia is a frequently seen complication in leptospirosis cases[37] and might cause bleeding, leading to death. Thrombocytopenia can be found in up to 50% of patients with leptospirosis having renal failure and is a poor prognostic factor.[40] In a study in Hawaii, thrombocytopenia was found in 58% and leukocytosis in 39% of patients with leptospirosis.[27] In our study, thrombocytopenia was found in 80% of patients, while 20% had leukopenia and 80% had leukocytosis. Patients with leptospirosis may present with afebrile neutropenia without classical signs.[41] Anemia was very common in this investigation as in others.[42]

Bilirubin concentration can exceed 30 mg/dL in patients with severe disease (Weil syndrome). Brief elevations of AST and GGT levels are found with relatively mild disease. In our study, the total bilirubin concentration of patients with Weil disease was greater than 30 mg/dL, and the AST, GGT, and ALP levels were above the NUL.[43] Furthermore, uremia, oliguria, and anuria may occur with the onset of kidney failure in Weil syndrome unless supportive treatment (ie, dialysis) is provided. Fatalities caused by icteric leptospirosis are typically due to renal failure, cardiopulmonary failure, and fatal hemorrhages and are typically associated with the presence of jaundice.[44] Three patients developed Weil syndrome, of which two required renal dialysis. All these patients recovered fully.

Conclusion

The patients with leptospirosis were all male. Highest incidences were in early November after peak rainfall in October. Fever, myalgia, nausea, vomiting, headache, and abdominal pain were more frequent in patients diagnosed with leptospirosis. With the variable manifestations of leptospirosis, clinicians must maintain a high index of suspicion in order to make the correct diagnosis. We emphasize the importance of public education regarding the relative risks, as a means of preventing exposure, and continuing education of medical practitioners and primary health care workers to increase their awareness of the seasonal distribution and early symptoms of leptospirosis.

Disclosure

The authors report no conflicts of interest in this work.

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