Epidemic of Leptospirosis: An ICU Experience

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Abstract

Aims: To study the clinical profile and outcome of critically ill patients suffering from leptospirosis with organ dysfunction and correlate mortality with individual risk factors.

Methods: A study of critically ill patients suffering from leptospirosis was carried out in the Medical Intensive Care Unit of a tertiary centre of a metropolitan city between 1st June 2002 and 31st May 2003. All the patients in whom diagnosis was confirmed by ELISA IgM antibody testing underwent thorough clinical examination and necessary biochemical investigations. They received standard antimicrobial therapy and extensive supportive therapy as required. Mortality was correlated with individual risk factors.

Results: Out of 834 total admissions in this period, 60 (7.2%) patients suffered from leptospirosis. There were 48 males and 12 females with age ranging from 12 to 60 years, mean age being 40 years. The clinical manifestations varied from fever (58 patients), jaundice (38), subconjunctival haemorrhages (24), to altered sensorium (22). All the patients had evidence of severe sepsis. Forty six patients had multiple organ dysfunction syndrome (MODS) and 26 required ventilatory support. The total mortality in leptospirosis patients was 52% which was much higher compared to the total MICU mortality (31.4%) in the same period.

Conclusion: Leptospirosis is an important infection associated with high mortality when associated with organ dysfunction. The poor prognostic factors are preponderance of male sex, alcohol dependence, age group > 50 years, MODS, acute respiratory distress syndrome (ARDS), presence of acidosis and need for mechanical ventilation. However, timely intervention and intensive therapy can save many young lives.

INTRODUCTION

Leptospirosis, often considered the most common zoonosis in the world, is caused by Spirochaetes of the genus *Leptospira*, family *Leptospiraceae*. It was first recognized as an occupational disease of sewer workers in 1886, when it was described by Weil (Weil’s disease) in four men with manifestations of severe jaundice, fever and haemorrhage with renal involvement. The disease has a peak occurrence during or immediately following periods of high precipitation. It is most commonly seen in tropical climate and is an important differential diagnosis of patients suffering from febrile jaundice during monsoons.

Leptospires enter the body through cuts, abraded and softened water logged skin, mucous membranes, conjunctivae, aerosol inhalation of microscopic droplets and possibly ingestion. Recreational exposure has also been documented. Epidemics have been frequent in areas of Gujarat, Andaman Islands and Orissa, not to mention the annual outbreaks occurring in Maharashtra during the past few years.

MATERIAL AND METHODS

The study was conducted in the Medical Intensive Care Unit of a tertiary care centre of a metropolitan city over a period of one year. Sixty patients, who had clinical features suggestive of leptospirosis, associated with organ dysfunction according to Acute Physiological and Chronic Health Evaluation (APACHE II) criteria and who tested positive for leptospirosis by Elisa IgM antibody testing were included under the study.

The criteria for inclusion were -

1. Patients presenting with following clinical manifestations suggestive of leptospiral infections.

   * Headache of sudden onset, fever, temperature >39°C, bilateral conjunctival suffusion, meningism, muscle pain, jaundice, albuminuria and history of exposure to infected animals or an environment contaminated with animal
urine.
2. Admission in Medical Intensive Care Unit of patients with SIRS1 and any organ system failure (according to APACHE II)
3. Patients testing positive for leptospirosis by ELISA IgM antibody testing.

The criteria for exclusion from the study —

All patients positive by IgM antibody testing for leptospirosis in whom a concomitant infection like malaria, enteric fever, dengue fever or meningoencephalitis was documented.

All patients underwent a detailed history and physical examination. This was followed by biochemical investigations which included complete haemogram, peripheral blood smear, urine analysis, coagulation profile, random blood glucose, serum creatinine, blood urea nitrogen, liver function tests and serum electrolytes in all the patients.

Arterial blood gas analysis was done in all patients routinely and as and when required. X Ray Chest and ECG were done on all patients.

All patient’s blood and urine samples were sent for analysis for leptospirosis. IgM antibody testing was the diagnostic test used and dark ground microscopy was carried out on all the samples.

CSF study was done in seven patients.

All patients received chemotherapy for leptospirosis in the form of injection crystalline penicillin, the drug of choice12–14 at doses of 15 lakh unit six hourly intravenously. Four patients sensitive to injection crystalline penicillin, were treated with the macrolide azithromycin.

Blood, blood products and supportive therapy in the form of O2 therapy, inotropic support, dialysis, anti-hepatic coma management and ventilatory support was used as and when warranted. The patients were treated in the intensive care unit, and were transferred to general wards once their condition stabilized. Their course was followed up till their discharge from the hospital.

Their clinical profile, investigations, duration of stay, treatment modality and the mortality and morbidity associated with the disease was studied. Mortality was correlated with various risk factors and data was analysed using Chi square test.

RESULTS

The results of our study showed that out of total 834 admissions in MICU during the period 60 patients (7.2%) suffered from leptospirosis.

Out of these, 48 i.e. 80% were males and 12 i.e. 20% were females.

The clinical presentation varied widely (Fig. 1) - 96.6% of the total number of patients had fever, 68.3% had jaundice, 56.67% had oliguria, 40% had subconjunctival haemorrhages, whereas only 6.67% had other haemorrhages.

Out of the total sixty patients, 46 suffered from multiple organ dysfunction syndrome. Five patients had hepatic failure, four had renal failure, three had only respiratory system affected and one each had central nervous system and haematological affection.

Thirty six patients (60%) were alcohol dependent. In 18 (30%), Arterial blood gases reflected acidosis and 26 patients (43.3%) required ventilatory support.

The mortality figures showed that patients with leptospirosis had a mortality of 52% (31/60) compared to the total MICU mortality of 31.4% (263/834) during the same period.

Amongst males mortality was 58.3% and amongst females it was 25%.

Age-wise mortality distribution showed that the 12-30 age group had a mortality of 40% (6), in the age group 30-50 it was 47% (16) and >50 had a mortality of 75% (9 patients).

Patients with ARDS and pulmonary haemorrhages only had the highest mortality of 66.6% followed by those with multiple organ dysfunction syndrome (60.8%). Patients with only hepatic failure had a mortality of 20%.

Table 1 : Mortality relationship with various factors

| Mortality in patients dependent on alcohol | 24/36 (66.6%) |
| Mortality in patients not consuming alcohol | 7/24 (29%) | P < 0.01 |
| Mortality in patients with acidosis on ABG | 14/18 (78%) |
| Mortality in patients without acidosis | 15/42 (35.7%) | P < 0.01 |
| Mortality in patients on ventilatory support | 22/26 (84.6%) |
| Mortality in patients not requiring ventilatory support | 7/34 (20.5%) | P < 0.01 |

Table 1 shows that mortality figures were significantly higher in patients suffering from these complications viz. alcoholism, metabolic acidosis and ventilatory support. Average duration of stay in MICU was 8 days.
DISCUSSION

Leptospirosis is endemic in various parts of India.35-28 In July - August 2000 cases of leptospirosis were reported from Gujarat, Maharashtra, Kerala, and Andaman and Nicobar Islands. A preliminary survey in East Delhi indicated that leptospirosis could be an important cause of febrile illness in patients from urban slums during monsoons and post monsoon season.21 Epidemics have been reported from countries like Nicaragua in the recent past.22

The disease has protean manifestations and as a result is frequently underdiagnosed because of the difficulty of distinguishing it from other undifferentiated febrile illnesses.23-25

In our study, 96.6% patients presented with fever, jaundice (63.3%), oliguria (56.67%), dyspnoea (50%) subconjunctival haemorrhages (40%) altered sensorium (36.6%), myalgia (30%), vomiting and loose motions (20%) and other hemorrhages (6.67%). The duration of symptoms prior to admission ranged from 1 day to 12 days. This correlated well with the usual picture of the acute septicemic phase which begins abruptly with high, remittent fever (38 to 40°C) and headache (> 95%), chills, rigors and myalgias (>80%), conjunctival suffusion with purulent discharge (<30%), abdominal pain (30%), anorexia nausea and vomiting (30 to 60%), diarrhoea (15-30%) cough and pharyngitis (20%) and pretibial maculopapular cutaneous eruption (<10) lasting 3 to 7 days,26-28 as described in other studies. In our study all patients had increased counts ranging from 12000 to 26000/ cumm1. Abnormal creatinine value ranged from 3.5 to 8 mg/dl and total bilirubin ranged from 6 to 24mg/dl. Platelet count was uniformly decreased in patients suffering from haemorrhages. Severe hemorrhagic pneumonitis and acute pulmonary distress syndrome can be prominent manifestations of infection and may occur in absence of hepatic and renal failure22, 28 as was the case in three of our patients. Thrombocytopenia occurred in the absence of disseminated intravascular coagulation (DIC).30

Investigation rests on antibody response or isolation of organism by dark-field microscopy or cultures. By dark-field microscopy false -ve and false +ve are frequent due to low concentration of organism and presence of fibrin and other filamentous cellular extrusions found in most body fluids.31 Blood cultures may be negative if drawn too early or too late. Moreover, cultures should be held for upto 4 months before discarding as negative.32

The reference standard serologic test for detection of leptospiral antibodies is the Microscopic Agglutination test using live organisms.33,34 It is highly sensitive and specific but time consuming and hazardous to perform. New ELISA tests designed to detect IgM antibody are used now with some commercially available IgM ELISA Assays in Australia reporting a sensitivity of 100% and a specificity of 98% and 93% respectively among 59 asymptomatic donors and 233 patients with a variety of viral and bacterial pathogens.34 Our study used this test as the reference.

The results of our study revealed a significant male preponderance with maximum affected in the age group 30-50 years. Maximum percentage of patients (38.3%) suffered from multiple organ dysfunction syndrome. The total mortality in patients with leptospirosis was 60% as compared to the total MICU mortality of 31.4% during the same period. The maximum mortality that of 66.6% was seen in patients having ARDS followed by patients with MODS (61%). This showed that even when treated in an intensive care setup, the severe form of the disease had a poor prognosis. Males showed a higher mortality rate with the older age group being the most affected one (75%). Our study showed that alcohol intake, metabolic acidosis and need for ventilatory support in patients with leptospirosis is associated with a poor prognosis.

In patients with pulmonary involvement treated with steroids two out of three survived. The results were not studied statistically.

Fatality figures for patients developing severe disease have ranged from 5-40%.21 In our study the mortality was fifty percent. Patients who had been admitted to the Intensive Care Unit were critically ill and most of them had at least two systems failure.

Out of patients who presented early and had only one organ system failure, only three succumbed.

Hence early detection of disease and early intervention can reduce mortality.

CONCLUSION

Leptospirosis is more common in men and middle age group. Alcohol dependent patients are more severely affected, because of their low immunity and the additional deleterious effect of alcohol on the liver.

Manifestations vary from person to person and it can affect any system in body. The disease often results in multiple organ dysfunction syndrome.

Mortality rate is higher in patients with ARDS, MODS, acidosis and those requiring ventilatory support.

Timely intervention is needed to decrease mortality.

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