Leptospirosis presenting to an intensive care unit in provincial New Zealand: a case series and review

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ABSTRACT

Background: Leptospirosis is a disease associated with meat and agricultural workers which is endemic in New Zealand and Australia. During 2003–2005, it resulted in 207 hospitalisations in New Zealand. Hawke's Bay had the highest regional incidence in 2004 and 2005. While admission to intensive care units with leptospirosis is not infrequent, no such cases have been described in the literature from New Zealand, and only five from Australia.

Methods: A chart review of all patients admitted to the intensive care/high dependency unit of a regional hospital in New Zealand with a diagnosis of leptospirosis from June 1999 to May 2005. Admission features, progress and diagnostic tests were collated, and APACHE II score on admission and daily Sequential Organ Failure Assessment (SOFA) score were calculated.

Results: 15 cases were identified; median age was 44 years (range, 27–62), and 13 were men. Myalgia, headache, nausea and vomiting were common; nine had conjunctival suffusion. Ten had hypotension and 14 had renal failure before ICU admission. Eleven received vasoactive support, and three received renal replacement therapy. Median length of ICU stay was 4 days (range, 2–11; mean, 4 days). Median hospital stay was 6 days (range, 2–13; mean, 7.6 days). All patients survived and were discharged free of dialysis.

Conclusion: Leptospirosis presents to the ICU with a variety of signs and symptoms. Renal failure is the most common organ dysfunction requiring intensive care, and its severity is disproportionate to other signs of severe sepsis. Leptospirosis has a good prognosis with early management in an ICU.

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Leptospirosis is a zoonotic disease which is endemic in New Zealand and Australia and is associated with meat and agricultural workers.[1] Patients presenting to hospital with leptospirosis have a variety of symptoms and may present with, or develop, critical illness requiring intensive care admission.

Leptospirosis is caused by the bacterium *Leptospira interrogans*, from the family Leptospiraceae. Human infection may occur through either direct contact with infected animal urine or tissue, or indirect contact with organisms in contaminated soil or water. The animal reservoirs of greatest significance in New Zealand are sheep and cattle, and meat workers and farmers form the majority of patients affected by leptospirosis.

Leptospirosis is a notifiable disease in New Zealand. Notifications numbered several hundred per year two decades ago,[2] but had dropped to 56 per year in 1996, although there was probably considerable under-reporting.[2] The national notification rate in 2005 was 2.3 per 100 000,[3] with an average of 69 hospitalisations annually in 2003–2005.[3-5] Hawke's Bay, on the east coast of New Zealand's North Island had an incidence of 13.1 per 100 000 in 2004 and 8.4 per 100 000 in 2005, the highest rates in the country.[3,5]

Clinical presentation of leptospirosis ranges from a mild, flu-like illness (anicteric leptospirosis) to severe, life-threatening disease with hepatorenal failure (icteric leptospirosis or Weil's disease). It generally affects the hepatic and renal systems, although multiple other organs may be involved. Reported morbidity and mortality rates vary widely between regions, possibly influenced by differences in inclusion criteria for case series (Table 1).[6-20] While admission to intensive care units with leptospirosis is not infrequent, no such cases have been described in the literature from New Zealand, and only five from Australia.[21-22]

Difficulties in culturing the organism and long reporting times for serological and molecular techniques make it extremely difficult to confirm leptospirosis in the acute setting.

Hawke's Bay Hospital provides secondary level services to a population of 150 000 in relative geographical isolation from tertiary services. Hawke's Bay Hospital Intensive Care Services is the sole local provider of intensive care for the Hawke's Bay district, providing seven intensive-care (ICU) and four high-dependency (HDU) beds.

This case series describes patients with leptospirosis requiring admission to the Hawke's Bay ICU/HDU between June 1999 and May 2005.

Methods

We searched the hospital database for patients discharged with a diagnosis of leptospirosis (ICD10 code A27) who had HDU or ICU admission between June 1999 and May 2005. We compared cases with the public health database held by the Medical Officer of Health to determine the proportion notified.

The following information was collected from a systematic review of the medical records:

- demographic characteristics;
- presenting symptoms, signs and investigations in the emergency department (ED);
- time of ED and ICU/HDU referral, and reason for ICU/HDU referral;
- treatment and subsequent investigations;
- further complications during ICU/HDU admission; and
- diagnostic tests performed for leptospirosis.

We also calculated:

- daily Sequential Organ Failure Assessment (SOFA) scores during ICU/HDU admission, using the lowest daily measurements. When data were incomplete, the level of organ dysfunction was scored at zero for that day.
- APACHE II score on admission, with risk of death indices.

We used standard definitions of systemic inflammatory response syndrome (SIRS), sepsis, severe sepsis and septic shock.[23] Suspected sepsis was defined as the presence of two or more SIRS criteria with a clinical suspicion of infection at the time.

Hypotension was defined as systolic blood pressure less than 90 mmHg or mean arterial pressure less than 70 mmHg.

Table 1. Leptospirosis mortality in different areas

Country	Mortality	No. of patients	Case mix
India[9]	52%	60	ICU, leptospirosis
India[18]	7.69%	143	Community outbreak, all patients
Brazil[7]	14.4%	840	In-hospital patients
Brazil[6]	55%	42	Leptospirosis with ARDS requiring ventilation
Netherlands[17]	5%	159	All cases
Turkey[20]	16.6%	12	Patients with Weil's syndrome
Thailand[14]	11.6%	148	Hospital patients in outbreak
Thailand[19]	14.0%	121	Hospital patients
US (Hawaii)[16]	10%	20	All cases
Thailand[8]	18.5%	362	Hospital cases
Barbados[13]	13.8%	398	All "severe" leptospirosis
Barbados[10]	12.7%	138	In-hospital patients

ARDS = acute respiratory distress syndrome. ◆

Table 2. Presenting characteristics and diagnostic tests used in 15 patients with leptospirosis

Patient	Age	Sex	Occupation	Previous medical history	Symptoms	Symptom duration (days)*	Diagnostic tests		
							MAT	PCR	ELISA
1	56	M	Meat inspector	Hypertension	Fever, headache, nausea/vomiting	7	+	–	ND
2	54	M	Meat worker	Hypertension, type 2 diabetes (diet-controlled), gout	Myalgia, sore throat, cough	7	+	–	ND
3	47	M	Meat inspector	Nil	Fever, headache, myalgia	5	+	ND	+
4	62	M	Meat worker	Nil	Fever, headache, myalgia, sore throat, dyspnoea	5	ND	+	ND
5	55	M	Meat worker	Nil	Fever, nausea/vomiting, myalgia	4	ND	+	–
6	41	F	Meat processor	Nil	Headache, nausea/vomiting, myalgia	3	+	ND	ND
7	41	M	Meat worker	Nil	Headache, nausea/vomiting	6	+	+	ND
8	46	M	Offal processor	Nil	Sore throat, cough	4	ND	+	–
9	38	F	Meat worker	Nil	Fevers, nausea/vomiting, myalgia, sore throat, cough	4	+	ND	ND
10	44	M	Cattle farmer	Nil	Fevers, headache, nausea/vomiting, myalgia	3	+	–	ND
11	45	M	Freezing worker	Nil	Fever, myalgia, cough	2	+	ND	ND
12	29	M	Freezing worker	Nil	Fever, nausea/vomiting, myalgia, sore throat	6	–	–	ND
13	27	M	Farmer	Nil	Fever, nausea/vomiting	2	+	ND	ND
14	43	M	Meat worker	Nil	Fever, headache, myalgia	5	+	ND	+
15	41	M	Meat worker	Nil	Fever, nausea/vomiting, myalgia	4	+	ND	ND

* Before presentation. MAT = microscopic agglutination test. PCR = polymerase chain reaction. ELISA = enzyme-linked immunosorbent assay.
+ = positive. – = negative. ND = not done. ◆

As previous measurements of renal function were unavailable, a serum creatinine concentration twice the upper limit of normal (0.22 mmol/L) was used to define acute renal failure.[24] Oliguria was defined as urine output less than 0.5 mL/kg for 2 hours or longer.

Results

Incidence and demographics

Seventeen patients fulfilled the search criteria, but two had been diagnosed with other conditions since their hospital discharge summaries were written, leaving 15 patients in the case series.

Over the 6 years, 114 cases of leptospirosis were notified in Hawke's Bay, an incidence of 12.7 cases per 100 000 annually. The ICU admissions represented 13% of these cases or 1.7 cases per 100 000 population per year. Only eight of the 15 patients had been previously reported to the Medical Officer of Health.

Our 15 patients had median age of 44 years (range, 27–62; mean, 44.6 years), and 13 (87%) were male. All patients had an occupational risk of leptospirosis exposure. Two had comorbid conditions: hypertension in one, and hypertension, diet-controlled type 2 diabetes and gout in another (Table 2).

Presentation

The most common presenting symptoms were myalgia (73%), fever (73%), nausea or vomiting (60%) and headache (47%) (Table 2). Less commonly, patients complained of sore throat (33%) and cough (27%). One patient presented with dyspnoea. The median duration of symptoms before ED presentation was 4 days (range, 2–7 days).

Presenting vital signs are shown in Table 3. Tachycardia and fever were common. Other signs recorded in the clinical notes were conjunctival suffusion (60%) and jaundice (13%). Six patients (40%) had abnormalities on chest auscultation, five with bilateral basal crepitations, and one with unilateral basal crepitations.

At ED presentation, 10 patients (67%) fulfilled criteria for sepsis, and five fulfilled criteria for sepsis cardiovascular organ failure (Table 3). Five patients (33%) displayed fewer than two SIRS criteria at ED presentation.

Initial diagnosis and antibiotic treatment

Fourteen patients (93%) had leptospirosis included in the differential diagnosis on assessment in the ED and were begun on antibiotic therapy at admission. One patient's admission diagnosis was atrial fibrillation, with leptospirosis queried the following day.

The differential diagnoses at admission influenced initial antibiotic selection. Broad-spectrum antibiotics were used in nine patients, and narrow-spectrum antibiotics aimed at leptospirosis in five. The patient with atrial fibrillation received broad-spectrum antibiotics the day after admission, when a septic cause was queried.

Patient disposition

Reasons for patient admission to the ICU/HDU are shown in Table 4. Ten patients (67%) were transferred directly from the

Table 3. Clinical parameters at presentation to the emergency department in 15 patients with leptospirosis

Patient	Meets SIRS criteria	Temperature (°C)	Heart rate (beats per min)	Respiration rate (breaths per min)	White cell count ($\times 10^9$/L)	Lowest BP in ED (mmHG)	Conjunctival suffusion	Bilirubin (μmol/L)
1	No	36.0	82	16	13.9	100/60	Yes	11
2	Yes	36.2	88	32	12.5	80/50	No	46
3	Yes	37.4	116	22	8.4	88/60	Yes	76
4	No	35.7	108	16	10.1	110/68	Yes	24
5	No	36	85	36	6.1	130/80	Yes	8
6	Yes	38.4	115	24	10.5	93/61	No	8
7	Yes	36.5	100	18	15.3	101/50	Yes	59
8	Yes	36.4	160*	22	13.9	92/58	Yes	48
9	Yes	36.8	100	22	11.2	85/46	No	
10	No	35.7	60	26	4.4	95/62	No	70
11	Yes	38	100	18	13.1	130/90	No	46
12	Yes	37.9	127	36	31.5	100/57	Yes	17
13	Yes	38.5	100	20	13.4	130/55	No	18
14	Yes	38.2	108	20	6.5	120/80	Yes	16
15	No	36.2	70	16	8.1	100/60	Yes	64

* Patient was in atrial fibrillation. SIRS = systemic inflammatory response syndrome. BP = blood pressure. ED = emergency department. ◆

Table 4. Organ dysfunction in 15 patients with leptospirosis

	Reason for ICU/HDU admission*	Present during ICU admission†
Renal failure	14/15	13/15
Hypotension	8/15	10/15
CXR abnormality	–	10/15

* As described in the clinical notes.
† Renal failure: oliguria > 2 hours after resuscitation, or serum creatinine level > 0.22 mmol/L.
Hypotension: systolic blood pressure < 90 mmHg or mean arterial pressure < 70 mmHg.
ICU = intensive care unit. HDU = high dependency unit. CXR = chest x-ray. ◆

ED to the ICU/HDU because of: renal failure (five patients), renal failure and hypotension (four patients), and renal failure, respiratory failure, and metabolic acidosis (one patient).

Five patients (33%) were initially transferred from the ED to the general medical ward. Subsequent ICU referral was precipitated by hypotension with worsening renal function (three patients, one of whom had decompensated atrial fibrillation), hypotension (one patient) and hypoxaemia (one patient). Time on the ward was half a day (two patients), and 1, 2 or 3 days (one patient each).

At ICU/HDU admission all patients fulfilled the criteria for severe sepsis. Organ dysfunction included cardiovascular dysfunction (hypotension) in 10, renal dysfunction in 14, and respiratory failure alone with a P/F ratio (arterial oxygen to fraction of inspired oxgen) of 219 mmHg in one (Table 4).

Of the 14 patients referred to the ICU with renal failure, eight had associated oliguria. One patient had persistent oliguria despite fluid resuscitation, without ever having an associated serum creatinine level above the upper limit of normal.

Treatment in the ICU/HDU

All patients received intravenous hydration. In those patients not receiving renal replacement therapy, median fluid intake over the first 24 hours in ICU was 8258 mL (range, 4540–13 135 mL). Vasoactive medications (inotropes and vasopressors) were used in 11 patients (73%): dobutamine in four, noradrenaline in four, adrenaline in four, and vasopressin in one. Three patients receiving pressor agents also received hydrocortisone.

Antibiotics were continued in all cases, but a narrower spectrum antibiotic regimen was introduced when there was confidence in the diagnosis of leptospirosis (Table 5).

Renal replacement therapy, typically continuous venovenous haemodiafiltration at a total of 1000 mL/hour filtration and 1000 mL dialysis, was implemented in three patients. One also received ventilation for respiratory failure, pressor support and a 4-day course of drotrecogin alfa (activated).

APACHE II scores

The median APACHE II score following ICU admission was 16 (range, 8–25; mean, 15.8). The median estimated risk of death was 0.23 (range, 0.14–0.56; mean, 0.26).

Clinical progress in the ICU/HDU

SOFA scores are shown in Figure 1. Eleven patients had scores of 3 or more for an individual organ system: 11, five and two patients for the renal, cardiovascular and respiratory systems, respectively. Four patients developed organ dysfunction scores of 3 or more in two or more organ systems, while 13 patients had scores of 2 or more in two or more organ systems. Typically, SOFA scores peaked on Days 1 or 2 of ICU admission.

Few patients developed new complications after admission to the ICU/HDU. One patient received 12 L of intravenous fluid over 6 hours for hypotension and oliguria, but remained oliguric. Despite receiving 25 L of fluid during the first 24 hours in the ICU and early pressor support, he progressed to acute renal failure. He developed pulmonary oedema, requiring dialysis to remove this fluid.

Two patients had cerebrospinal fluid sampled, both showing culture-negative lymphocytic meningitis.

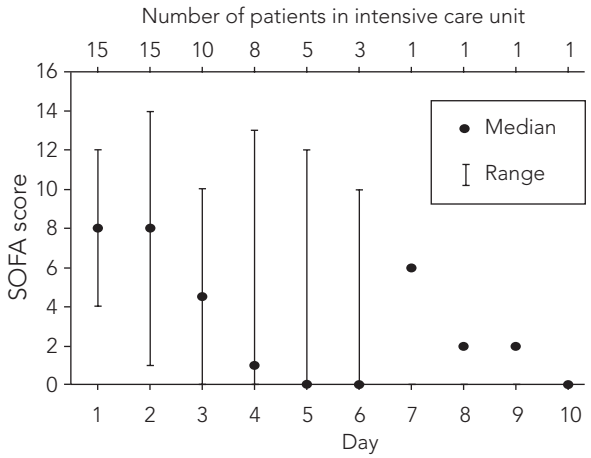
Four patients had cardiovascular complications. One had atrial fibrillation with poor rate control at presentation. Another developed a troponin I rise to 8.2 μg/L, a nodal heart rhythm with frequent premature ventricular contractions persisting for 18 hours, and electrocardiograph changes comprising widespread ST elevation and repolarisation abnormalities, consistent with pericarditis/myocarditis. These signs resolved without specific changes in management. A third patient showed a period of Mobitz type I second-degree heart block, which resolved spontaneously. A fourth patient developed severe septic shock, with complications of cardiac dysfunction, presumed to be a result of sepsis, and ventilatory failure, requiring ventilation, renal replacement therapy and other organ support.

Ten patients were noted to have abnormalities on chest x-ray while in the ICU/HDU, most commonly evidence of alveolar fluid

Table 5. Antibiotic treatment in the ICU/HDU

Antibiotic	Sole antibiotic	In combination
Cefepime	1	3
Ceftriaxone	4	5
Cefuroxime	1	2
Penicillin	2	2
Gentamicin	0	1
Amoxycillin or amoxycillin–clavulanate	1	3
Metronidazole	0	1
Doxycycline	0	1
Erythromycin	0	1

Figure 1. Daily total SOFA score and number of patients remaining in the ICU/HDU



SOFA = Sequential Organ Failure Assessment. ICU = intensive care unit. HDU = high-dependency unit.

(nine patients) and pulmonary congestion in the form of upper lobe diversion/increased vascular markings (six). Less common abnormalities were pleural effusions (two patients), interstitial shadowing (one patient) and perihilar opacities (one patient).

Diagnostic testing

Eleven patients had leptospirosis confirmed by a microscopic agglutination test (MAT) (Table 2). Three patients did not have MAT performed, and, in these, diagnosis was based on a positive result on polymerase chain reaction (PCR) testing. In one patient, both PCR and MAT were negative, but clinical staff believed that the diagnosis of leptospirosis remained clinically the most probable.

Outcomes

All patients survived to discharge. No patient required readmission to the ICU/HDU. Median length of ICU/HDU stay was 4 days (range, 2–11; mean, 4 days). Median hospital length of stay was 6 days (range, 2–13; mean, 7.6 days). All patients were discharged free of renal replacement therapy and other organ support.

Discussion

An epidemiological study in New Zealand reported that "an overwhelming majority of cases of leptospirosis in New Zealand [occur] among livestock farm workers and meat processing workers".[1] A male to female ratio of 10:1 was also noted. National surveillance data of notified cases of leptospirosis show a 13:1 ratio.[3-5] At 13:2, the sex distribution of our case series is similar, probably reflecting the sex distribution of the agricultural and meat processing workforce. Although leptospirosis is a notifiable disease in New Zealand, almost half the patients in our series had not been reported to the Medical Officer of Health before this review. Nationwide, the number of positive laboratory tests is about 25% higher than the notification rate, indicating that reporting compliance is less than ideal.[3] Subclinical cases undoubtedly occur, as do cases which are effectively treated despite misdiagnosis. The incidence of non-diagnosis, along with the poor reporting compliance, means that the true incidence of leptospirosis may be much higher than reported. It is also possible that some cases may be treated in ICU without a diagnosis of leptospirosis being made.

Clinical features: The signs and symptoms of leptospirosis are protean. The most common presenting symptoms in our series were myalgia (73%), fever (73%), nausea or vomiting (58%) and headache (47%). In other studies, myalgia and headache were common presenting symptoms, and fever was almost universal.[8,15,25]

Conjunctival suffusion was recorded in 60% of our patients. Chawla et al describe subconjunctival haemorrhage in 40% of patients admitted to the ICU,[9] but we could find no other reports of the incidence of conjunctival signs in patients with leptospirosis.

Abnormalities on chest auscultation were found in 40% of our patients. It has been suggested that the presence of crepitations on chest auscultation is associated with a higher incidence of haemoptysis and cyanosis.[26] In patients admitted to ICU with leptospirosis, the presence of pulmonary rales was associated with a high mortality.[19] No patients in our series were found to have haemoptysis or cyanosis on admission.

Cardiovascular effects: A range of cardiovascular manifestations occur in leptospirosis, as demonstrated in this series. At ED presentation, 10 patients had two or more signs of SIRS which, combined with leptospirosal infection, fulfils the criteria for sepsis. While 10 (66%) of our patients had hypotension before ICU referral, profound or prolonged hypotension and septic shock were far less common.

Other cardiovascular complications that have been noted in association with leptospirosis are arrhythmias, myocarditis and congestive heart failure.[27,28] In this case series, three patients had episodes of arrhythmia associated with leptospirosis. Any form of sepsis can predispose to atrial fibrillation and other arrhythmias. Overall, 11 patients required support with vasoactive medication.

Renal effects: Acute renal failure is common in leptospirosis and may result from ischaemic tubular damage, possibly secondary to vasculitis.[27,28] Other contributing mechanisms include dehydration, jaundice and rhabdomyolysis.[26,27,29] Renal failure recovered rapidly in our patients with return to normal function, consistent with recovery of patients in other series.[12,29]

In our series, renal complications were prominent, with 11 patients scoring 3 or more on the SOFA scale, and three patients requiring renal replacement therapy. Moderate hypotension was probably a contributory factor in seven patients. However, renal impairment occurred in three patients without documented hypotension and was out of proportion to the degree of shock found in those with hypotension. The mechanisms involve more than the factors that cause renal impairment in severe sepsis and septic shock alone. Oliguria as a result of leptospirosis is associated with an increased risk of death.[19,30] Daher et al found renal failure with associated oliguria in Weil's disease to be the only independent risk factor for death.[15] All nine patients with renal failure and associated oliguria did well. Significantly, 12 of the 13 patients with renal failure had normal serum creatinine level at discharge, as would be expected with acute tubular necrosis. One patient was discharged with a mildly elevated creatinine level, but was lost to follow-up.

Hepatic effects: Hepatic dysfunction is described in icteric leptospirosis but is rarely life-threatening.[26,27] In the series described by Chawla et al, 63% had jaundice,[9] while, in a series by Esen et al, 87% had abnormal liver function tests.[31] Hepatic dysfunction is thought to be caused by a subcellular defect rather than macroscopic hepatocellular injury. Mild hepatic dysfunction in the form of elevated serum bilirubin level was common in our case series and did not appear to influence management or outcome.

Respiratory effects: Significant pulmonary dysfunction occurred in two patients, who developed SOFA scores of 3–4. One required invasive ventilation, and another organ support. This patient had significant opacity in the right middle zone. Possible mechanisms for life-threatening ventilatory failure in leptospirosis include alveolar haemorrhage or acute respiratory distress syndrome.[26] A further six patients developed milder pulmonary dysfunction. Chest x-ray abnormalities were common, occurring in 66% of the patients. The main mechanism proposed for pulmonary dysfunction in leptospirosis is alveolar haemorrhage caused by vasculitis.[15] Daher et al found no association between oliguria and pulmonary rales.[15] Fluid overload due to oliguric renal failure is therefore not thought to be the primary factor causing pulmonary symptoms. The same study found no association between pulmonary involvement and either cardiac failure or myocarditis. The radiographic changes showing alveolar consolidation in our patient series may represent alveolar haemorrhage, but the absence of haemoptysis or other clinical signs makes this unlikely. Alveolar haemorrhage would not explain the other findings of pulmonary congestion, pleural effusion, and interstitial and perihilar opacities. Pulmonary oedema from acute respiratory distress syndrome or fluid overload is a more plausible explanation.

Coagulopathy: Icteric leptospirosis often causes a haemorrhagic diathesis not thought to be related to hepatic dysfunction or thrombocytopenia. The mechanism is thought to be severe vasculitis with endothelial injury.[27] Coagulopathy is ubiquitous in severe sepsis, but overt disseminated intravascular coagulopathy is less common.[32] Although it is possible that alveolar haemorrhage occurred in some of our patients, no overt bleeding problems were noted. Mild thrombocytopenia was found in eight of our patients, contributing to their SOFA scores. Severe sepsis and septic shock cause some form of coagulopathy in the vast majority of patients and commonly increase international normalised ratio (INR).[32] However, overt coagulopathy was not apparent in these patients.

Neurology: Central nervous system involvement in icteric leptospirosis can occur as aseptic meningitis, thought to be due to a host immune response rather than direct meningeal infection.[33] Our two patients who had CSF drawn demonstrated this. Whether the other 13 patients had CSF abnormalities is unknown.

Antibiotic treatment: While there have been few well designed, well controlled antibiotic studies in leptospirosis, early appropriate antibiotic treatment appears to reduce mortality.[34,35] However, the role of antibiotics in management of late-presenting severe leptospirosis remains controversial.[36,37] A randomised placebo-controlled study of patients presenting 4 days after symptom onset demonstrated a non-significant trend towards worse outcomes in those who received penicillin.[36]

Our patients typically presented about 4 days after symptom onset. Once the diagnosis of severe sepsis or leptospirosis was suspected, all received antibiotics. While multiple factors influenced initial antibiotic selection, all patients received a β-lactam antibiotic, either alone or in combination. Penicillin is advocated as specific therapy, while doxycycline or cefotaxime are suitable alternatives in severe leptospirosis.[38] It is likely that third- and fourth-generation cephalosporins would have similar efficacy.

Mortality: The limitations of the APACHE II scoring system, coupled with the small number of patients, make accurate estimates of mortality difficult. APACHE II scores on admission predicted a 25% hospital mortality which, after adjusting for our unit's standardised mortality ratio, predicted two to three deaths. Other studies of patients with leptospirosis have revealed mortality rates ranging from 3% to 19%, while case series of Weil's disease and icteric leptospirosis in Turkey and India have shown mortality rates of 17% and 52%, respectively.[9,20] The co-location of the HDU with the ICU in our hospital may have lowered the severity threshold for admission in our patients. However, despite our patients being relatively young and healthy, the group had median and mean APACHE II scores of 16, reflecting the major physiological abnormalities present.

Diagnostic testing: The laboratory tests performed to confirm leptospirosis varied, and the recent addition of a lept-

ospirosis-specific PCR test has changed the diagnostic algorithm.[39] MAT, a serological test, is regarded as the most sensitive and specific test for leptospirosis, but is complex to perform and limited to reference laboratories.[40,41] Often regarded as the "gold standard" for leptospirosis diagnosis, its sensitivity is estimated at 98.2%, and specificity at 96.4%.[39]

The leptospirosis IgM enzyme-linked immunosorbent assay (ELISA) has a sensitivity of 48.7% on acute serum, 75.0% on convalescent serum, and 86.5% when both samples are tested.[40]

As PCR detects leptospiral DNA rather than patient antibodies, which require time to develop, PCR testing of serum, urine, and CSF is promising as a rapid diagnostic aid.[42,43] The demonstration of leptospiral DNA by molecular methods or isolation of leptospires by culture confirms the diagnosis of leptospirosis, and may help differentiate between current infection and past exposure when the significance of positive serological results is uncertain.[41] However, negative results for direct leptospiral isolation and DNA testing do not rule out active disease.[40] Thus, in our series, one patient with a clinical diagnosis of leptospirosis was included despite negative blood results.

The limitation of all diagnostic tests is that they fail to aid diagnosis in the acute setting. No test is available in the first few hours of admission, and over half the patients in our series had been discharged from ICU before confirmatory laboratory results were available. Delayed confirmation is often a factor in omission of notification. The development of rapid PCR diagnostic tests may aid in early specific management.[39]

Summary

Leptospirosis remains a significant medical problem that may present to the ICU with a variety of signs and symptoms. Conjunctival suffusion is common. Renal failure is the most common organ dysfunction requiring ICU management, and its severity is disproportionate to other signs of severe sepsis. Despite the severity of presenting problems, leptospirosis has a good prognosis with early management in an ICU.

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