LIVER FUNCTION TEST ABNORMALITIES IN LEPTOSPIROSIS

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ABSTRACT

BACKGROUND

Leptospirosis is an emerging infectious disease of global importance with clinical manifestations varying from inapparent infection to fulminant fatal disease. Leptospirosis is endemic in many areas of Kerala. Liver involvement is common in leptospirosis.

MATERIALS AND METHODS

130 cases with confirmed leptospirosis were studied. Clinical features and liver function abnormalities were checked on admission 3 weeks and again at 6 weeks. Follow up data was analysed with SPSS version 21. The type of study conducted was descriptive study (longitudinal) and duration of the study was continues for 11 months.

RESULTS

Fever and myalgia were present in all patients. On admission, 68.46% patients had raised total bilirubin, 67.69% patients had raised direct bilirubin, 93% patients had raised SGOT and SGPT was raised in 93% patients and 36.92% patients had raised ALP. On 3-week and 6-week follow up, only a limited percentage of patients showed persistence of mild elevation of transaminase level and bilirubin level. Prolongation of INR was in 26.92% of patients. The death rate was 6.15%.

CONCLUSION

Liver involvement in leptospirosis was mainly in the form of raised levels of transaminases and bilirubin. High SGOT, SGPT and bilirubin levels were more in patients who died than survived patients. There was significant reduction in SGOT, SGPT and bilirubin levels among survivors at 3 weeks and 6 weeks when compared to admission. Patients with high SGOT, SGPT and total bilirubin levels had prolonged hospital stay.

KEYWORDS

LFT, SGOT Level, SGPT Level, Leptospirosis, Duration of Hospital Stay.

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BACKGROUND

Leptospirosis is a zoonotic disease caused by pathogenic spirochetes of genus leptospira. Leptospirosis is a globally important disease with apparent re-emergence's illustrated by recent outbreaks on virtually all countries. Leptospirosis has worldwide distribution, but occurs most widely in the tropics and subtropics because of the climate and poor hygienic conditions. In many parts of the world and in Indian states, epidemics are closely linked to heavy rainfall and floods (as in Mumbai, Tamil Nadu, Andhra Pradesh and Kerala).[1] Leptospirosis is endemic in many areas of Kerala.[2]

The word Leptospira is derived from Greek word 'leptos' meaning 'thin' and a Latin word 'spira' meaning 'coiled'. It is the most ancient spirochete that live both in the animals and free in the environment.

Leptospira species are spirochetes belonging to the order Spirochaetales and the family Leptospiraceae. The organism was first visualised from autopsy specimens of a patient thought to have yellow fever.[3] Leptospires require special media and conditions for growth. It may take weeks to months for cultures to become positive.[4] Classifications based on serologic differences better serves clinical, diagnostic and epidemiologic purposes.

The unavailability of diagnostic facilities and the lack of awareness about the disease was the major reasons for overlooking the possibility of leptospiral infection as a cause of febrile illness. Consequently, the incidence of the disease has been grossly underestimated.

Prevention and Control- The risk of leptospirosis can be greatly reduced by not swimming or wading in water that might be contaminated with animal urine or eliminating contact with potentially infected animals. Protective clothing or footwear should be worn by these exposed to contaminated water or soil because of their job or recreational activities. Due to large number of serovars and

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infection sources and wide differences in transmission conditions, the control of leptospirosis will depend on local conditions. Control can be active by controlling the reservoir or reducing infection in animal reservoir population such as dogs or livestock. It is important to establish what animal species are the infection sources in a particular area and control measures should be targeted to them.[5]

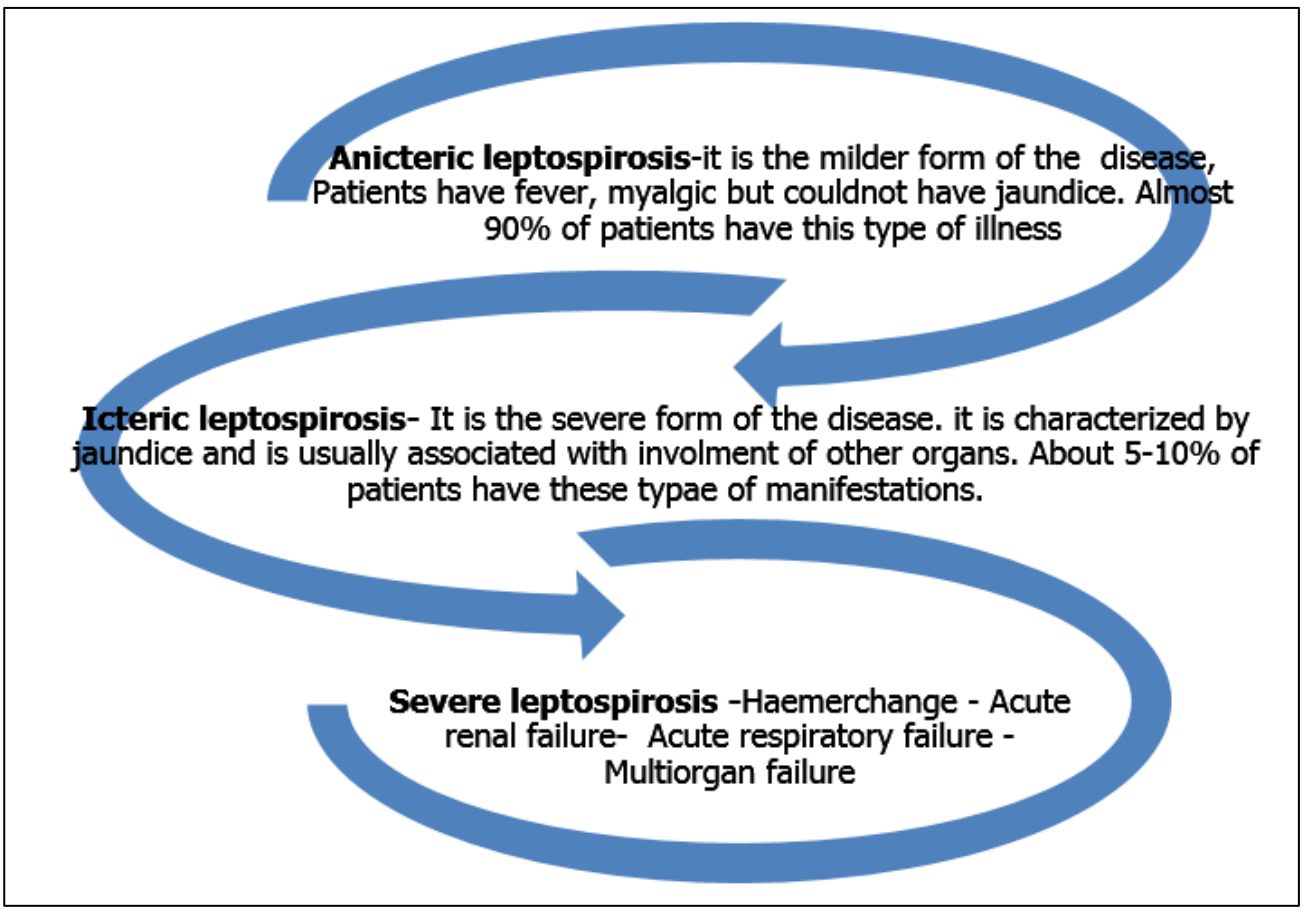

Figure 1. Clinical Type of Leptospirosis

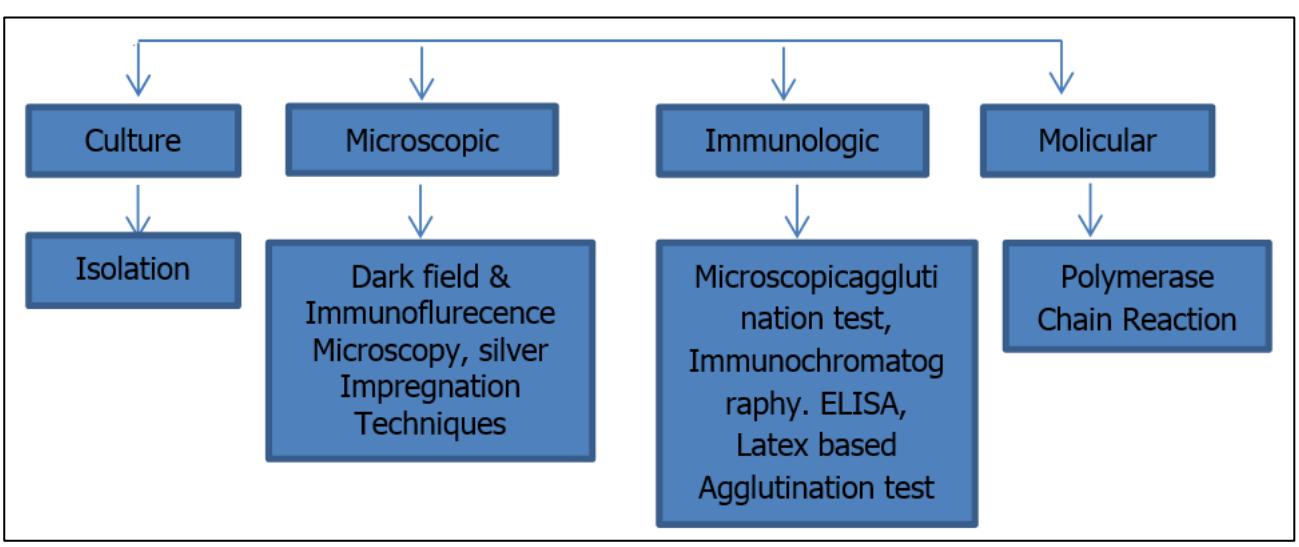

Figure 2. There are Different Laboratory Approaches

Significance of the Study- Adifwell (1886) described the clinical hark of this disease. In India, Kerala, Tamil Nadu and Andaman are endemic for leptospirosis. Now, disease is being reported almost in all parts of India. Kerala has witnessed post-monsoon epidemics of leptospirosis in recent years. Most cases seemed to occur by cutaneous exposure of legs, while walking in stagnant water or moist soil. This implies that leptospira multiplies in the walking paths where water remained undrained for a period of 2-3 days after rains. Rapid urbanisation and construction activities in the past two decades resulting in blocking of natural drainage of rain water and consequent water lodging near human habitats also contributes to this.

Clinical manifestations maybe in the mild form such as influenza-like illness with headache and myalgia or in severe form characterised by jaundice, hepatic dysfunction, renal dysfunction and haemorrhagic diathesis. Jaundice is the most important clinical feature. It may be mild-to-severe. It starts after 4 to 7 days of illness. Hepatic encephalopathy or death due to hepatic failure is rare. Hepatomegaly and tenderness in right hypochondrium is usually seen. Liver function test abnormalities is common in leptospirosis. Serum bilirubin, mostly direct bilirubin can be markedly elevated as compared with other liver enzymes.

Icteric patients with mild increase in transaminase should always raise suspicion of leptospirosis. Serum AST is only mildly or moderately elevated unlike in viral hepatitis. In deteriorated situations, the systematic parenchymal cellular dysfunction in leptospirosis could evolve into extensive cellular necrosis, severe and extensive destructions of cells in various organs, not only in muscle and liver leads to unusual AST elevation. A delayed and disproportionate AST elevation in leptospirosis hints in fulminant disease course with high mortality. Thus, in addition to clinical symptoms, serial follow up of transaminase could provide some evidence to predict prognosis and severity in leptospirosis.

Objectives

1. To study the distribution of patients with leptospirosis based on signs and symptoms.
2. To find out the association of clinical variables at the time of admission among survivors and expired of patients with leptospirosis.
3. To find out the association of clinical variables with periods of observation among survivors of patients with leptospirosis.

MATERIALS AND METHODS

In the present study, survey cum longitudinal experimental technique were used. The one group design were selected. Duration of the study continues 11 months in a year. The sample comprised of 130 adult patients with leptospirosis. The patient's age ranged 19-79 years. The sample were selected on the basis of inclusion and exclusion criteria. After the initial phase with admission time, the survivors is 122 and were subject to further phases.

A detailed history, physical examination and baseline investigations noted using a structural formula. The tools such as clinical profile and case history were used. The laboratory investigations routinely during the evaluation of the patients, which included LFT- Bilirubin, SGOT, SGPT, ALP, total protein, serum albumin, platelet count and routine blood investigations.

After the inpatient treatment, the patients were subjected to follow up 3 weeks and at 6 weeks with liver function tests.

Inclusion Criteria

- All the patients with IgM lepto-antibody positive patients with a/c symptoms.
- Age ranged 19-79 years form both gender.
- Inpatients under Medicine Department, Government Medical College, Kottayam, Kerala.
- Patients have no previous history of long-term medication and chronic illness.

Exclusion Criteria- The patients with history of confounding risk factors for elevation of LFT such as-

- Patients with chronic liver disease.
- Alcoholics.

RESULTS

Distribution of patients with leptospirosis based on sign and symptoms.

The total patients were subjected to percentage analysis based on sign and symptoms and tabulated as shown below.

Sign	Number and Percentage	Symptoms	Number and Percentage
Tachycardia (pulse rate >100)	90 (69.25%)	Fever	130 (100%)
Icterus	86 (66.15%)	Myalgia	130 (100%)
Conjunctival congestion	83 (63.85%)	Headache	100 (76.92%)
Oliguria	37 (28.46%)	Vomiting	85 (65.38%)
Hypotension (SBP <90 mmHg)	36 (27.69%)	Abdominal pain	53 (40.76%)
Hepatomegaly	32 (24.61%)	Rash	49 (37.69)
Subconjunctival haemorrhage	24 (18.46%)	Arthralgia	24 (18.49%)

Table 1. Number and Percentage of Patients with Leptospirosis Based on Sign and Symptoms

Most of the patients with leptospirosis belonged to the first signs and symptoms category.

Association of clinical variables at the time of admission among survivors and expired of patients with leptospirosis. The SGOT, SGPT, alkaline phosphate, total bilirubin, total protein, serum albumin, CPR and INR values at the time of admission of patients with leptospirosis between survivors and expired were subjected to test of significance and tabulated as shown below.

Category	Survivors, N1=8		Expired, N2=122		't' Value	P Value
	Mean	SD	Mean	SD		
SGOT	639.75	106.25	109.70	71.80	19.6*	<0.0001
SGPT	334.00	70.09	59.7	59.7	11.01*	<0.0001

Alkaline phosphate	356.13	53.73	133.69	71.32	11.086*	<0.0001
Total bilirubin	17.88	2.90	5.53	5.77	10.732*	<0.0001
Total protein	5.90	6.13	6.0	0.27	0.188*	<0.0001
Serum albumin	3.52	0.68	3.75	0.26	2.11*	<0.0001
CPK	1028.75	145.85	347.80	280.00	11.8*	<0.0001
INR	1028.75	145.85	347.80	280.00	11.85*	<0.0001

Table 2. Result of Test of Significance of the Association of Clinical Variables at Admission between Survivors and Expired Patients

The 't' values with respect to SGOT, SGPT, alkaline phosphate, total bilirubin, total protein, serum albumin, CPR and INR are 19.6, 11.01, 11.086, 10.732, 0.188, 2.11, 11.8 and 11.85. It is inferred that all the 't' values are significant and there existed a significant difference between survivors and expired patients with leptospirosis in their clinical variables at the time of admission.

Association of Clinical Variables with Periods of Observation among Survivors of Patients with Leptospirosis- Among the survivors (N=122) of patients with leptospirosis, the association of clinical categories- SGOT, SGPT, total bilirubin, direct bilirubin, ALP, total protein and albumin with observed periods- admission (D1), three weeks (D2) and six weeks (D3) were subjected to paired t-test and analysed the significant difference and tabulated as shown below.

Category	Period						Association		P Value
	D1		D2		D3		D1 and D2	D1 and D3	
	Mean	SD	Mean	SD	Mean	SD			
SGOT	109.7	71.8	48.77	24.57	35.8	6.03	12.26*	11.74*	<0.0001
SGPT	59.07	27.41	33.11	15.4	25.74	37.49	9.12*	7.91*	<0.0001
Total bilirubin	5.00	4.20	1.51	0.82	1.29	3.0	9.00*	7.92*	<0.0001
Direct bilirubin	2.44	2.65	0.81	1.26	0.39	0.21	9.02*	8.89*	<0.0001
ALP	133.69	71.32	106.67	65.67	94.75	20.75	3.87*	5.89*	<0.0001
Total protein	6.13	0.27	6.25	0.36	6.43	0.47	2.945*	5.369*	<0.0001
Albumin	3.75	0.26	3.91	0.28	3.99	0.46	4.625*	5.069*	<0.0001

Table 3. Result of Significance of Association between Clinical Categories with Observed Time Periods of Survivors, N=122

*- significant.

The paired 't' value in the association between time of admission, D1, and 3 weeks, D2 and that of admission D1, and 6 weeks, D3 with respect to SGOT, SGPT, total bilirubin, direct bilirubin and ALPT. Protein and albumin are 12.26 and 11.74, 9.12 and 7.91, 9.0 and 7.92, 9.02 and 8.89, 3.87 and 5.89, 2.95 and 5.369 and 4.625 and 5.069. It is inferred that the association between period of observation were significant in all the clinical categories among survivor patients with leptospirosis.

RESULTS

- Most of the patients aged between 20 to 49 years (62.30%).
- Out of 130 patients studied, 84 were males and 46 females.
- In the study, 55.38% were farmers by occupation.
- 8 patients died during the inpatient period.
- Fever and myalgia were present in all patients (100%).
- Icterus was seen in 66.15% and subconjunctival haemorrhage in 18.4% patients.
- 68.46% patients had raised total bilirubin on admission. At the end of 6 weeks follow up, 8.19% patients has raised levels.
- 67.69% patients had raised direct bilirubin on admission. At the end of 3 weeks follow up, 37.70% had raised levels, and at the end of 6 weeks follow up, 7.38% patients had raised levels.
- SGOT was raised in 93% patients on admission. By 3 weeks, 36.89% patients, and at the end of 6 weeks, 6.15% had raised SGOT levels.
- SGPT was raised in 93% patients on admission. By 3 weeks, 33.61% patients, and at the end of 6 weeks, 17.21% had raised SGPT levels.
- 36:92% patients had raised ALP on admission by 3 weeks 19.67% patients, and at end of 6 weeks, 4.10% patients had raised ALP levels.
- Prolongation of INR was in 26.92% of patients. In this study, 36.15% patients had raised CPK on admission.
- Most of the cases of leptospirosis occurred during months of August (24.61%), September (20%) and October (14.61%).

DISCUSSION

Majority of study population were in the age group 20-49 years accounting 62.30% (81). This was comparable to studies earlier done by Singh SS, Vijayachari P, Sinha, et al.[6]

In present study, 55.38% (72) were farmers. Occupation of patients in this study revealed occurrence of the disease to be more common in people engaged in outdoor activities like agriculture. This is comparable to study done by MA Muthusethupathi et al.

In this study, 24.61% (32) occurred in month of August and 20% (26) in September. Leptospirosis has a peak during the monsoon and post-monsoon months. Study by H. Sahira, R. Jyothi and J.T. Ramani Bai et al conducted in

Kerala, India, showed that leptospira positive cases were more at the time of heavy rain fall (July and August). This association also correlates with the study done by Mathur M. et al.[7]

Icterus was seen in 66.15% of patients. Hepatomegaly was seen in 24.61% of patients. This is comparable to study done by Dwijen Das and Kallol Bhattacharjee, et al.[8]

68.46% had raised total bilirubin. 67.69% had raised direct bilirubin. This was comparable to study done by Tantitanawat and Tanjatham et al.[9]

In this study, there was 6.15% mortality (8) comparable to study by Dwijen Das, Kallol Bhattacharjee and Amit Kr Kalwar, et al. All patients who died had hepatic, renal involvement and thrombocytopaenia.

In this study, 93% had raised SGOT and 93% had raised SGPT. The elevated SGOT and SGPT were encountered 100%, 89% in study by D. B. Zala, Vikram Khan and V. K. Das et al.[10]

The association between level of elevated SGOT, SGPT, total bilirubin, direct bilirubin and ALP at admission between survived patients and death patients among study subjects were found to be significant. This showed that those patients who died had raised levels of transaminase and bilirubin than those who survived. This is comparable with study done by Gaurang Parmar, Dilip Kava and Shreyash Mehta et al.

The association between levels of SGOT, SGPT, total bilirubin, direct bilirubin and ALP on admission, 3 weeks and 6 weeks were found to be statistically significant. This showed that patients who survived had raised levels of bilirubin and transaminases on admission and gradually returned to normal levels by 3 weeks and 6 weeks. This is comparable to study done by H. Sahira, R. Jyothi and J.T. Ramani Bai et al.

CONCLUSION

Liver involvement in leptospirosis was mainly in the form of raised level of transaminases and bilirubin. High SGOT, SGPT and bilirubin levels were more in patients who expired than survived patients. There was significant reduction in SGOT, SGPT and bilirubin level among survivors at 3 weeks and 6 weeks when compared to admission. Patients with high SGOT, SGPT and total bilirubin levels had prolonged hospital stay. Long-term follow up are required to assess the future complications among patients with leptospirosis.

Limitations of the Study- Study was conducted in a tertiary care center where referral bias cannot be avoided. Period of study was from August to June. Cases during July could not be taken as study was done in a limited period of time. Being a monsoon month, significant number of cases can be expected in July, which is not included in this study.

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