A prospective study of Leptospirosis as a differential diagnosis of Dengue like illness

Abstract:

Background: Leptospirosis is both a zoonotic and environmental disease. The bacteria are hosted in animal kidneys for months and even years, and the bacteria are released in the environment by the urine of these animals. The transmission to humans occurs by contact with infected animals or contaminated water. There are different entry points for this contamination, it could be a skin abrasion, it could be through the mucous membranes, it can also occur through inhalation of droplets of urines for instance during farming activities and sometimes, it occurs by drinking water. Clinical presentation of leptospirosis mimics dengue as pyrexia with thrombocytopenia is common in both.

Methods: We have included all patients between age group of 0-18 years with complaints of fever. Lab investigation showed thrombocytopenia but negative dengue serology and raised SGOT/SGPT and no other obvious cause of illness. Hence leptospira serology was done.

Results: Total of 15 patients were cases of dengue like illness, out of which Leptospira serology samples came positive in 60% (9). Total number of cases of dengue like illness are 15 out of which 66.6% patients belonged to >10 years (11-18) & 33.33 % patients were <10 years and gender ratio was 66.6% (10) male & 33.33% (5) females. The patients who were diagnosed as dengue like illness were given antibiotic- 46.6% (7) were given Doxycycline & 53.3% (8) cases were given Azithromycin. Clinical improvement with increase in their platelet count was seen within 48 hrs. of starting the antibiotic in all of them.

Conclusion: Leptospirosis should be considered as an important differential diagnosis while treating patient of dengue like illness. Consider treating such patient with doxycycline/azithromycin as this result in clinical improvement & may prevent any complications.

Keywords: Leptospirosis, zoonotic and environmental disease, dengue

1. Introduction:

Leptospirosis is one of the most important zoonotic bacterial infections worldwide.[1.2] it is most commonly affects resource-poor populations, resulting in significant morbidity and many deaths. The infection is estimated to account one million cases and around 58,900 deaths annually, with a fatality ratio of 6.85%.[3] Adolph Weil in 1886 first described leptospirosis as a enlarged spleen, febrile illness with icterus, renal failure and conjunctivitis associated with outdoor occupations where people came into contact with water.[4] Thus, the severe form was named as'Weil's disease'. The causative organism was first described by Stimson in 1907, who demonstrated the presence of spirochaetes in the kidneys of a patient dying of the disease; because of the question-mark shape of the organism the organism was named *Spirochaeta interrogans*.[1]

Leptospirosis is highly prevalent in the tropics areas, with 73% of cases occurring in South-East Asian countries, East Sub-Saharan Africa, the Caribbean and Oceania. It is common among the impoverished urban, semi-urban populations and rural farming populations; particularly affecting young male adults.[4] Human leptospirosis has diverse clinical illness and clinical manifestations in humans can range from a mild, self-limiting acute febrile illness to a severe, life-threatening condition with multiple organ dysfunction.[1.2] The clinical features of leptospirosis are similar in many other febrile illnesses, especially diseases seen in the tropics, such as dengue and other haemorrhagic fevers, rickettsial infection, malaria, and bacterial sepsis. While the majority present with uncomplicated fever, approximately 10% develop severe disease.[5] Pulmonary haemorrhage has recently been shown to be an important cause of mortality.[6] Incubation period shows wide variation, from 2-20 days, usually 7-12 days.[7]

The diagnostic tests are divided into those which provide tests for indirect evidence of infection (demonstration of antibodies to leptospirosis) and direct evidence of infection (demonstration of leptospires or its DNA, or culture).[8]

Preventive measures of leptospirosis are through avoidance of potential exposure to infection, and administration of pharmacological prophylaxis to individuals at high risk. Doxycycline 200 mg weekly, commencing one week prior to exposure, and continued through the period of exposure is recommended. No human vaccine is currently available till date.[9]

2. Aims & objectives:

1. To study leptospirosis as a differential diagnosis in patients with dengue like illness at our hospital during dengue outbreak

3. Methods:

We included all patients 0-18 years of age group presented with fever and lab investigation showed thrombocytopenia with negative dengue serology; raised SGOT/SGPT. Some of these patients were suspected to have leptospirosis for which leptospira serology was sent.

Comment [A1]: Please re write the sentence.

Comment [A2]: Since the number of objective is one, hence the numerical number may be avoided. Objective may be clear mentioning the time frame and the name of the institute.

Comment [A3]: Which test was employed?

3.1 Data collection: Total No. of patients under study - 15 cases were registered in Pediatric department of SSB Hospital in the month of August 2021 to October 2021. Data has been evaluated on the basis of Symptoms, Biochemistry and antibody testing of Leptospirosis. (Table no 1, 2 and 3)

Comment [A4]: Was this a record based study or a prospective study with enrolment of participants?

Was Institutional Ethics Committee/Board clearance obtained for the study?

Table no 1: Represents Symptoms of dengue like illness in Total No. of patients (15 cases).

Fever	Y	y	y	y	y	y	y	y	y	y	y	y	y	y	y
vomiting	y	y	n	y	y	y	y	y	y	y	y	n	y	n	y
Pain Abdomen	y	y	n	y	y	n	y	y	y	y	y	n	n	n	y

y=Yes; n= No; N=Negative

Table no 2: Represents Biochemistry of Total No. of patients (15 cases).

HB	13.8	13.4	13.9	17.4	12.1	14.2	14	10.6	11.9	17.4	16.4	11.3	11.9	13.9	11.6
PCV	45	41.1	41.9		37.1	43.4	43.1	33.2	37.9	52.4	49.6	36.5	36.6	41.1	37.1
TLC	8.1	4	3.2	6.8	7.6	2.5	8.3	5.1	3.5	10.4	5	3	4	5	5.5
Platelet	50	111	42	11	258	27	40	70	65	36	42	101	82	126	158
SGOT	902	903	796	236	50	433	618	213	61	252	597	48	95	284	97
SGPT	544	367	315	103	33	191	198	126	22	152	280	26	50	56	33
S. Bilrubin	0.5	0.5	0.3	0.5	0.2	0.4	0.3	0.3	0.5	0.6	0.3	0.3	0.4	0.2	0.7

Table no 3: Represents Antibody testing of Total No. of patients (15 cases).

Leptospira serology	11.28	17.61	15.55	N	N	N	N	11.28	9.42	9.75	13.66	9.7	10.62	-	-
Dengue NS1	N	-	-	N	N	N	N	N	N	N	N	N	N	N	N
Dengue IGG	N	-	N	N	N	N	N	N	N	N	N	N	N	N	N
Dengue IGM	N	-	N	N	N	N	N	N	N	N	N	N	N	N	N

Y=Yes ; N=Negative

Results:

A total of 15 cases of dengue like illness, Leptospira serology came positive for 60%(9) of them. (Figure no 1). Total number of cases of dengue like illness are 15 out of which 66.6%patients belonged to >10 years (11-18) & 33.33 % patients were <10 years. (Figure no 2) Total number of cases of dengue like illness are 15 out of which there were 66.6% (10) male & 33.33% (5) females (Figure no 3) The patients who were diagnosed as dengue like illness were given antibiotic 46.6% (7) were given Doxycycline & 53.3% (8) cases were given Azithromycin. There was clinical improvement with increase in their platelet count within 48 hrs. of Starting the antibiotic.(Figure no 4)

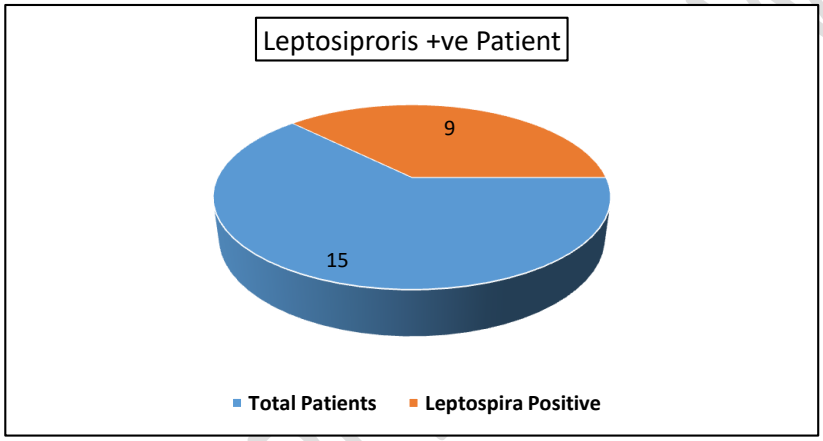

Figure no 1: 80% patients were suspected to be cases of Leptospira, hence Leptospira serology was sent out of it 60% (9) came out to be positive.

Comment [A5]: Spelling of Leptospirosis

Comment [A6]: Sentence construction may be improvised

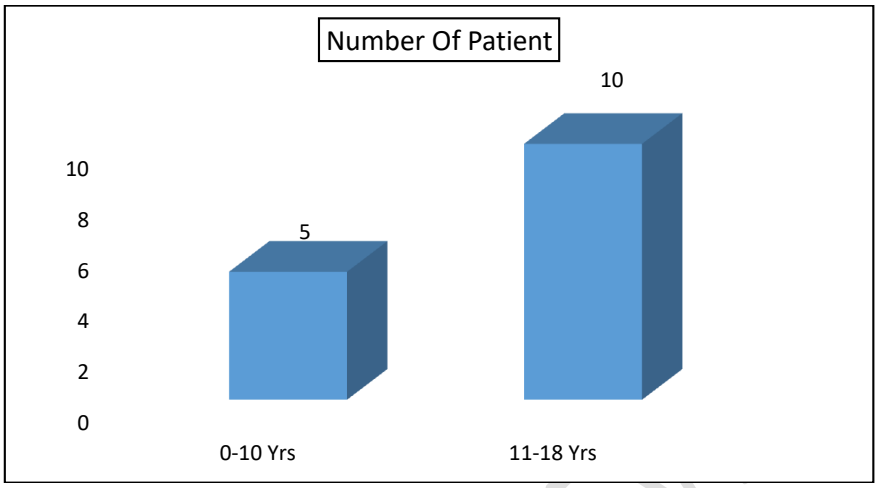

Figure no 2: Total number of cases of dengue like illness are 15 out of which 66.6%patients belonged to >10 years (11-18) & 33.33 % patients were <10 years.

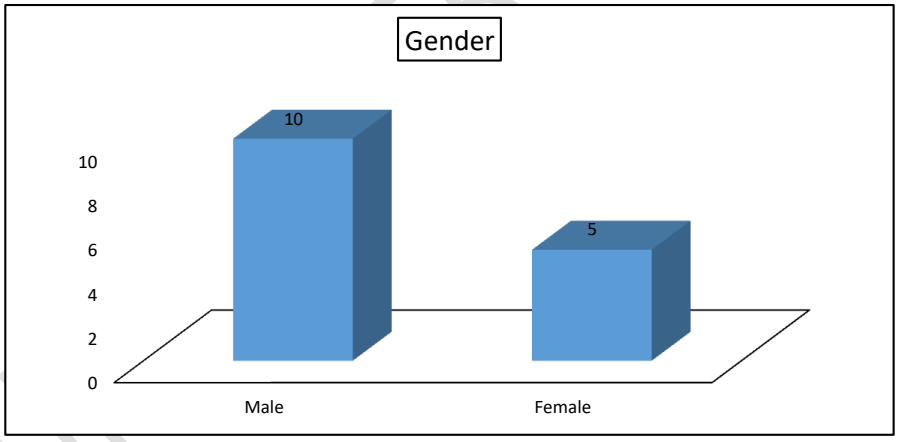

Figure no 3: Total number of cases of dengue like illness 15 Out of which there were 66.6% (10) male & 33.33% (5) females.

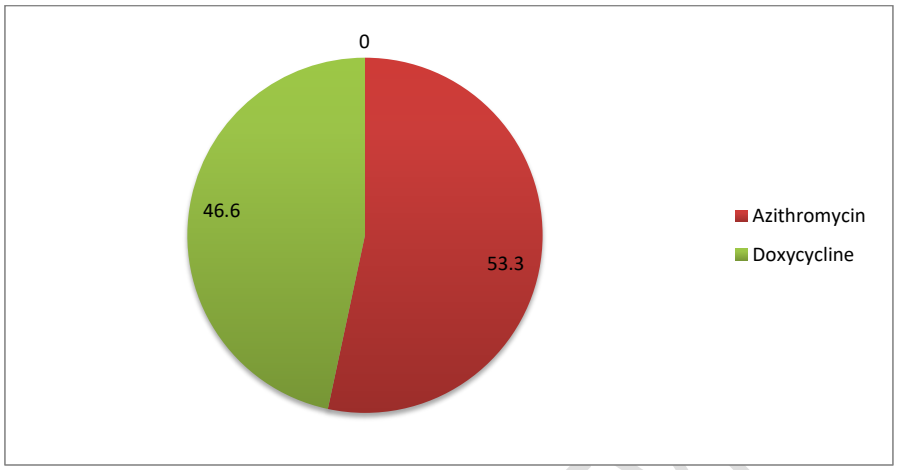

Figure no 4: The patients were diagnosed as dengue like illness were given antibiotic 46.6% (7) were given Doxycycline & 53.3% (8) cases were given Azithromycin. There was clinical improvement with increase in their platelet count within 48 hrs. of Starting the antibiotic.

Comment [A7]: Dose of Doxycycline and Azithromycin to be mentioned.

Discussion: Acute febrile illness (AFI) encompasses a broad spectrum of infectious causes; and remains poorly characterized in tropical regions of the developing world.[10] Commonly, health care providers in developing countries are in the need to apply syndromebased treatment protocols, due to the lack of diagnostic tests[11] Dengue virus (DENV) and leptospirosis are the most common causes of AFI.[12] There are studies have also reported the detection of leptospirosis among patients with dengue-like symptoms in other settings. Dircio-Montes, et al. 2012 established the prevalence of leptospirosis in patients with an initial diagnosis of dengue, they concluded that at least a sixth part of all cases were leptospirosis infection and should have been treated with antibiotics.[13] In a study, found a positive correlation between prevalence of dengue, leptospirosis and co-infection and rainfall. It is important to take into account other factors that affect the transmission of these infections, like relative temperature and humidity, before concluding that rainfall is the reason for the increased infections transmission.[14-16]

During dengue epidemic there are patients who test negative for dengue but present with fever & thrombocytopenia. Such patients are treated as dengue like illness but it was seen in our study that leptospirosis constituted major amount of the patient treated as dengue like illness. These patients are often missed and treated for viral fever only.

However, Leptospirosis should be kept in mind while treating such patients & diagnosis should be confirmed by sending leptospira serology. Treating these patients with doxycycline or azithromycin can shorten their course of illness, help in clinical improvement of the patient and prevent complications.

Limitations:

1. The Sample size is too small to check for statistically significant data
2. The cost of Leptospira serology is a limiting factor.

Conclusion: Leptospirosis should be considered as an important differential diagnosis while treating patient of dengue like illness especially those with deranged liver and kidney function. Consider treating such patient with doxycycline/azithromycin as this result in clinical improvement & may prevent any complications.

Recommdation: In all cases of dengue like illness, we can test for Leptospirosis so that treatment can be modified to give the optimal benefit to the patient in future.

Follow up/ Review: Ongoing prospective study.

Comment [A8]: Is this paper a part of a larger study? More participants to be included or the 15 patients will be followed up?

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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