

Leptospirosis- the neglected disease



Clinical picture and epidemiology at the Andman Islands India

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1 Abstract

Leptospirosis is a worldwide public health problem and yet often being overlooked. Few studies are carried out on it and relatively little is known about it.

Regional Medical Research Centre in Port Blair, India, is the reference centre in Asia on leptospirosis and during two month I went there to study the disease.

In the Andaman Islands I examined 15 patients with leptospirosis, 11 of them were men and 3 were women. Most of the patients were hospitalized and had different syndromes due to leptospirosis. All patients had fever. Common symptoms were body ache, headache and chills. A few patients developed pulmonary, renal and liver complications.

Leptospirosis is potentially lethal but a treatable disease. It can mimic a lot of other diseases like influenza, dengue fever, hepatitis and meningitis.

Diagnostic methods are complicated in leptospirosis. The quick methods are based on antibodies and you always have to consider the time it takes to develop antibodies and the variety in ability to develop antibodies among individuals. Other tests available need qualified personnel and the golden standard test, MAT, based on antibodies agglutination is based on individual observations and hard to standardize. This test is only confirmatory with paired blood samples, which are difficult to obtain in clinical practice.

The Andaman Islands is an endemic area with atypical presentation of leptospirosis. The doctors have to treat patients with antibiotics on wide indications, in clinically suspected cases to prevent the fatal complications of the disease.

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2 Introduction

Leptospirosis is an acute bacterial infection caused by spirochetes belonging to the genus *Leptospira*[1] that can lead to multiple organ involvement and fatal complications. It has a wide geographical distribution and occurs in tropical, subtropical and temperate climatic zones [2]. Most countries in the South East Asia region are endemic to leptospirosis[3].

A number of leptospirosis outbreaks have occurred during the past few years in various countries particularly in South America [4, 5] and India[6, 7, 8]. Some of these were as a result of natural calamities such as cyclone and flood.

Leptospirosis is considered as the most widespread zoonosis in the world [9] Leptospirosis affects human beings and many other species of vertebrates. It can present in a wide spectrum of clinical manifestations [10]. The syndrome of icteric leptospirosis with renal involvement is referred to as Weil's disease. Another recognized clinical form is that presenting with severe pulmonary haemorrhage [4, 7, 8]. Other complications include acute respiratory failure [9], myocarditis[10], meningitis and renal failure[11]. Uveitis has recently been recognized as a late complication of leptospirosis [12, 13]

Pulmonary haemorrhage is perhaps the most fatal complication in leptospirosis. At the Andamans, a significant higher case fatality ratio has been observed amongst patients who develop pulmonary haemorrhage as compared to patients with other clinical presentations [8].

Renal failure can be a fatal complication but in most cases it can be reversed with conservative measures such as maintaining fluid and electrolyte balance and symptomatic therapy [8]. Other complications such as meningitis rarely become fatal. Myocarditis may sometimes cause intractable hypotension and cardiac arrhythmias and might become fatal.

Leptospirosis, being a zoonotic disease with a large variety of animal species acting as carriers, is difficult to eliminate and perhaps even control in tropical developing countries. The bacteria are adapted to the environment of the tropical region with plenty of rainfall and it is often difficult to avoid exposure of the people to animals or contaminated environment. Because of this, early detection and prompt treatment and creating awareness about the disease among the people and the public health professionals are the steps that could be taken to reduce the magnitude of the problem [15].

2.1 Morphology

The leptospire are spirochaetes that belong to the family Leptospiraceae, in the order Spirochaetales. Other spirochaetes are *Treponema* and *Borrelia*. [14]

Spirochaetes are helically coiled, thin bacteria, classed in the order Spirochaetales. Since leptospire are too thin to be seen under microscope they are best visualized under darkfield microscopy. Seen by darkfield illumination in fluid media, leptospire are thin, helical, motile organisms, ranging from 10 to more than 20µm long, often hooked at one or both ends. They spin constantly on their long axis, so that the hooked ends appear as loops. The rotatory movement occurs in both directions alternately and they also move in flexion and extension.

Leptospire are gram-negative but with a surface architecture resembling gram-positive and gram-negative bacteria [14].

Leptospira are grown at 28-30 degrees and pH 7-8. They are slow growers and it can take 7-10 days to yield $1-2 \times 10^8$ cells per ml. The pathogenic leptospira can survive for days to months in wet soil and fresh water with pH7-8 but only for a few hours in salt water [15].

2.2 Classification of leptospira

Presently two different classification systems- one based on phenotypic characters and other on the genetic homology are being used. In the phenotypic classification there are two species namely, the *L. interrogans* (pathogenic) and the *L. biflexa* (non-pathogenic). Both the species have several serovars and serovar is the basic taxon, which is defined in the basis of surface antigenic makeup. Closely related serovars are arranged in serogroups.

Based on genetic homology in DNA hybridization experiments, 15 genomic species have been described in the genus Leptospira [4].

2.3 Leptospirosis in the world

The Caribbean and Latin America, the Indian subcontinent, Southeast Asia, Oceania and to a lesser extent Eastern Europe, are the most significant foci for the disease, including areas that are popular travel destinations [24].

But leptospirosis is found wherever experts in leptospirosis, astute and aware medical and veterinary practitioners and epidemiologists and adequate specialist laboratory facilities for accurate diagnosis is available [14].

2.4 Historical Aspects

In 1882, Adolf Weil reported his description of a clinical syndrome characterized by splenomegaly, jaundice and nephritis (Weil 1886, as quoted in Levett 2001) commonly referred to as Weil's disease which became synonymous with leptospirosis.

Leptospire were first identified as a cause of Weil's disease in Japan, where it was common among coal miners (Faine 1994)

2.4.1 Epidemics on the Andamans, Andaman Haemorrhagic fever

A severe seasonal epidemic of febrile jaundice [25], [26], was observed amongst the free-living convicts of the penal settlement [26]. The hepato-renal involvement was thought to be a complication of malaria that was common among the convicts but no malaria parasites were observed (Wolley). The similarity of the disease to Weil's description of haemorrhagic jaundice was recognized by later researchers. Detection of leptospire in urine and liver samples of the patients gave further support to the diagnosis [25].

A detailed description of the epidemiology and clinical course of leptospirosis was given by Taylor and Goyle (1931). After Taylor and Goyle's work in the 1930s nothing further is known regarding the occurrence of leptospirosis in the half century that followed [6].

During the late 1980s, seasonal outbreaks of mysterious febrile illness were reported. This time the disease manifested itself in the form of severe haemoptysis in the most cases. The name Andaman haemorrhagic fever (AHF) was used to describe this disease because the aetiology remained unknown for 15 years. The mystery was unravelled in 1995 during an outbreak in Diglipur in North Andaman. This was the first report of severe pulmonary haemorrhage as a complication of leptospirosis in India. (Sehgal et al 1995)

2.5 Laboratory diagnosis

Laboratory diagnosis is broadly classified into direct evidences (isolation of organism or demonstration of leptospire by dark field microscopy or amplification of specific fragment of leptospiral DNA) and indirect evidence (detection of antibodies to leptospire) [27].

2.5.1 Dark ground microscopy

The principle of Dark Ground Microscopy (DGM) is that the object is illuminated only by light rays that are scattered by the object. DGM appears to be a simple and rapid procedure and in old textbooks mentioned as a useful tool in diagnosis of leptospirosis but this is not true in clinical practice. The organism is only present in blood during a short period during the acute stage of the disease and the concentration is too low to allow detection by direct microscopy. The leptospiral shedding in urine is intermittent. Moreover serum proteins and cell fragments may mimic leptospire. DGM also requires technical expertise and reading the results is always subjective [15].

2.5.2 Staining techniques

Various silver impregnation techniques are used for the staining of leptospire in body fluids and tissues. However these techniques have the same limitations as DGM and therefore not recommended for direct diagnosis of leptospirosis [15].

2.5.3 Isolation of leptospire

Isolation of leptospire from clinical specimens is the strongest evidence for confirmatory diagnosis. Isolation and identification is the method of choice to identify circulating serovars in a particular

geographical region. In addition locally isolated and identified strains will be more useful to be used as antigens in MAT as local strains were found to be more sensitive and strongly reactive than reference strains. Moreover the local strains will be used for the development of vaccine. However the technique has several drawbacks. Leptospire are slow growing organisms and require several days or weeks to yield cultures and weeks to month for identification. Prior administration of antibiotics greatly reduces the chances of successful isolation [15].

2.5.4 Microscopic Slide Agglutination Test (MSAT)

The basic principle of the test is similar to other slide agglutination tests used in other infectious diseases such as enteric fever or brucellosis.

There can be different ways to prepare the antigens. One may either use a single serovar or multiple serovars to prepare the antigens.

The test is easy to perform and read. The antigen is broadly reactive and stable for six month at 4 to 8 C. It is more sensitive than Microscopic Agglutination Test (MAT) in the early stage of the disease but a high percentage of false positive reactions are observed, probably due to lack of standardization and quality control of the antigen preparation. The number of false negative reactions are comparatively low [15].

2.5.5 Microcapsule Agglutination Test (MCAT)

The test is based on the principle of passive agglutination and employs carrier micro-capsule particles on the surface of which ultrasonicated leptospiral antigens are observed. The test is simple to perform, easy to read and does not require any special expertise or equipment. But the test is not confirmatory and it is costlier.

2.5.6 Lepto Lateral Flow

This test is based on the binding of specific IgM antibodies to the broadly reactive heat extracted antigen prepared from non-pathogenic Patoc 1 stain. IgM antibodies bound to the broadly reactive antigen are detected with an anti human IgM gold conjugate contained within the test device.

The test is very quick and both serum sample as well as blood can be used to perform the test.

Disadvantage is that the test is expensive [15].

2.5.7 LEPTO Dipstick

By using a broadly reactive leptospiral antigen Leptospira-specific IgM antibodies are detected in human sera.

The LEPTO-dipstick is easy to perform and read, requires only a single dilution and does not require any special equipment. The dipstick has a long shelf-life even at room temperature. The test has good sensitivity, specificity and predictive values comparable to those of IgM ELISA. This makes LEPTO-dipstick the test of choice for routine use at the peripheral level, particularly in developing countries. The limitation of the test includes its inability to give information about the infecting serovar because of its genus-specific nature and requires at least 3 hours of incubation [16].

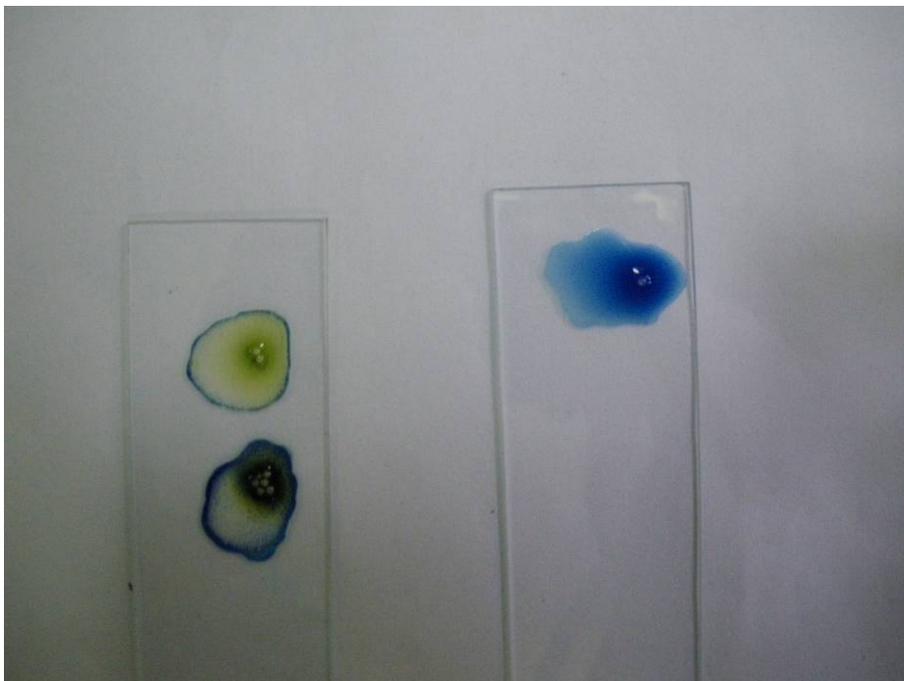
2.5.8 Lepto Dri Dot

This is a card agglutination test based on the binding of leptospira specific antibodies in patients' serum to the broadly reactive antigen coated on latex particles leading to a fine agglutination.

The Dri Dot test is simple to perform and results can be obtained within 1 minute. The test can be stored at room temperature with no special equipment required and it is easy to perform. Its sensitivity is higher than that of IgM ELISA but its specificity is lower [17].

2.5.9 Latex Agglutination test

This test was developed on Regional Medical Research Centre in Port Blair. Latex beads are coated with outer- and inner membrane of leptospira from a local isolate and coloured so that they can be visualized after agglutination. The same amount of latex beads and serum sample are mixed and agglutination is observed within 30 seconds.



Picture 1. To the left a positive latex agglutination test. To the right no agglutination was present.

2.5.10 Microscopic Agglutination Test (MAT)

The test remains the corner stone of sero-diagnosis of leptospirosis and a helpful tool in understanding the epidemiology of the disease.

MAT is ideally performed on paired serum samples (acute and convalescent). The criterion for a definite diagnosis of current leptospiral infection is a four fold rise in titre or seroconversion. However, in actual practice, obtaining paired samples from patients is very difficult. Very often the diagnosis is made on a single sample received during the initial stage of the disease. This has led to a debate on the cut-off titre to be used as a diagnostic titre indicating current leptospiral infection. The cut off titre for single MAT depends on the baseline titre in the community in a particular geographical region. Since the agglutinins stay for a prolonged period of time after infection a proportion of healthy individuals will have detectable levels of antibodies. At the same time, in true patients it takes some time for the antibodies to reach detectable levels. These two sets of people account for the false positive and the false negative results of the test [18].

Since Andaman island is a highly endemic area for leptospirosis with more than 50 per cent seroprevalence [19], a higher proportion of individuals have high titres compared to other parts of India. Because of this the specificity is lower at lower cut-off titres [18].

The usual method for carrying out MAT is to mix equal volumes of series of serum dilutions and leptospira culture in the wells of microtitre plates. The serum antigen mixture is allowed to react for a certain period at certain temperature. The degree of agglutination and endpoint titre are determined by examining a drop of the mixture by dark field microscopy.

A battery of antigens, covering the range of serovars that are expected or likely to be circulating in a particular geographical area, where the patient becomes infected, should be used.

Criteria for serological diagnosis of leptospirosis by using MAT are seroconversion or four fold rise in antibody titre in paired sera. A minimum titre of 1:400 or more in a single serum sample is needed.

However, the significant titre in the case of single serum samples may vary from one geographical area to the other [15].

2.5.11 Criteria for a definite and presumptive diagnosis of leptospirosis

The criteria for a definite diagnosis usually used in well established laboratories are:

- Isolation of leptospire from clinical specimen.
- Four-fold or greater rise in MAT titre between acute and convalescent-phase serum specimens run parallel.
- Sero-conversion from a titre <1 in 20 to 1 in 80 in between acute and convalescent phase samples run in parallel.

Isolation of leptospire is laborious and takes several weeks or months. Sero-conversion or rise in titre is the central dogma of serological diagnosis but requires second convalescent-phase sample which is difficult to obtain. Therefore, the criteria for definite diagnosis have greater application in establishing the

endemicity of the disease in a particular geographical region rather than in routine diagnosis. Once the endemicity is defined in a particular region, criteria for a presumptive diagnosis can be used for diagnosis and case management [15].

Criteria for presumptive diagnosis:

- A MAT titre of 100/200/400 or above in single sample based on endemicity.
- A positive result in IgM Based immunoassay, slide agglutination test or latex agglutination test.
- Demonstration of leptospirosis directly or by staining methods [15].



Picture 2. Leptospira are adapted to the environment of the tropical Andman islands and it is often difficult to avoid exposure.

2.6 Epidemiological characteristics

On the Andaman Islands the incidence of the disease usually shows two peak seasons, one during July and the other during October-November. This coincide with the paddy sowing and harvesting time and the people get exposed to wet and waterlogged rice fields, as well as they have contact with animals like cattle, buffaloes, goats and dogs. Young adults are common among patients with high exposure to waterlogged agricultural fields that might be contaminated with animal urine and, thus, harbour leptospires.



Picture 3. Waterlogged agricultural fields.

At 26 of December 2004 the tsunami and earthquake severely affected the islands, particularly the southern group. It killed 5.000-10.000 and left many low-landed areas permanently under water. During the post-tsunami there was an apparent decrease in incidence of leptospirosis, perhaps a result of reduced agricultural activities and ingression of salt water into agricultural fields[22].



Picture 4. Low landed area permanently under water after the tsunami and earthquake 2004.

2.6.1 Transmission

Leptospirosis is a direct zoonosis. Rodents are considered as reservoirs host for leptospiral infection but domestic animals play an important role in the transmission [22].

The leptospire live in the renal tubules of the carrier animal [15].

2.7 Clinical features

The incubation period can vary between 2-30 days but usually range from 5-14 days [14]. Most patients present with mild fever and recover without any complications [8].

There is a wide spectrum of clinical presentations of Leptospirosis. The illness may be mild and self-limiting or severe and possible fatal. Outcome may depend on the infecting serovar, number of infecting leptospire, the condition of the infected person and available medical care. About 5-15%, of those infected with the serovars known to cause severe disease, have been reported to develop severe icteric disease but that figure depend on how many mild cases that are diagnosed. The mortality rate in severe types of leptospirosis is 5-40% [14].

2.7.1 Classic symptoms

- Anicteric febrile illness

The typical leptospirosis is biphasic. The first septicemic phase lasts for 4-7 days and is characterized by acute systemic infection and leptospira in the blood and in cerebrospinal fluid. This is followed by a period of one to three afebrile and asymptomatic days and then the second immune phase starts with fever and leptospira in the urine and lasts for 4-30 days or longer. This bifasic course may not be seen in all patients.

Common symptoms are sudden onset of fever (typically 39°C) sometimes with rigors and chills, headache, muscle pain and tenderness, malaise with or without vomiting. Chest pain, dry cough and haemoptysis may occur. Some patients can develop mental symptoms of restlessness, confusion and delirium.

The most characteristic findings on examination are conjunctival suffusion and severe myalgia. Conjunctival suffusion is bilateral and usually associated with subconjunctival haemorrhage. Myalgia is most commonly located in the lower limbs and is so severe that even touching the muscle causes intense pain [15].

- Icteric leptospirosis (Weil's Disease)

In some patients the septicemic phase progress to severe icteric illness with renal failure. Jaundice is the most important clinical feature of the severity of illness and is due to hepatorenal necrosis, intrahepatic cholestasis and increased bilirubin load from absorption of tissue haemorrhage. The liver is often enlarged and tender.

Renal involvement is the most serious complication and is the most common cause of death in icteric leptospirosis. Oliguria can occur as early as the fourth day of illness but more often in the second week. Meningeal symptoms are frequent but overshadowed by hepatic and renal features.

Severe bleeding, cardiac and pulmonary complications are frequent. Toward the end of the second week the patient is deeply jaundiced, ureaemic and haemorrhagic and become comatose. Death may occur in this stage due to renal failure and the mortality rate may be as high as 15-40%.

In those who are not severely ill, recovery takes place in the second week [15].

- Haemorrhagic pneumonitis

Pulmonary haemorrhages usually occur in the second week of severe forms of icteric leptospirosis, but occasionally it can occur within 24-48 hours of onset of the illness. The onset is sudden with fever, headache, generalized body ache, cough that is dry in the beginning but becomes streaked with blood after a few days. The patient becomes breathless and toxic. Massive haemoptysis may cause asphyxiation and death. Mortality in these cases is very high, around 50-70% if they arrive late to the hospital [15].

- Overlapping symptoms

The clinical course has two separate syndromes, hepato-renal and pulmonary. Some degree of overlap can be seen. In the Andamans, the incidence of pulmonary complications of leptospirosis appears to be quite high. These complications tend to occur early and with a dramatic nature. The exact pathogenesis behind this acute respiratory failure is not well understood but available information indicates that the cause can be disseminated intravascular coagulation (DIC) and adult respiratory distress syndrome (ARDS) [8].

2.8 Pathogenic mechanisms

Leptospirosis is a primary bacteraemic infection. Localisation of leptospire at the site of entry does not occur in natural conditions. Leptospire are not pyogenic bacteria; they do not cause inflammatory reactions except through secondary tissue damage.

The central lesion, characteristic of all forms of leptospirosis, is damage to the walls of small blood vessels, leading to leakage and extravasation of cells, including haemorrhages. Other lesions follow as secondary effects [14].

Paradoxically, the most obvious adhesion of leptospire to cell surfaces, in the renal tubules, does not appear to damage the cells, nor lead to inflammation around the affected tubules in the absence of repair or scarring from the acute infection, in most animals.

The primary lesion in all forms of leptospirosis in all animals, including humans, is damage to the membranes of the endothelial cells of the small blood vessels, caused by leptospiral toxin. The immediate effect is to loosen the junction between cells, allowing fluid and leptospire to migrate into extravascular spaces, followed by erythrocytes wherever the damage is severe and prolonged. The secondary effects of ischemic changes, anoxia and increased pressure in the tissues reinforce damage resulting in cellular functional disintegration and death. [14]

2.9 Differential diagnosis

Leptospirosis with its varied manifestations may mimic a large number of disease processes.

Anicteric:

Viral fever, malaria, enteric fever, influenza or pyelonephritis.

Icteric:

Viral hepatitis, septicaemia with jaundice, malaria.

Haemorrhagic pneumonitis:

Bacterial pneumonitis, pulmonary tuberculosis and military tuberculosis

2.10 Treatment

Antibiotic treatment is effective within 7 to 10 days after infection and should be given immediately on diagnosis or suspicion.

The drug of choice is benzyl penicillin by injection in the doses of five million units per day for five days. Patients who are hypersensitive to penicillin can be given erythromycin 250 mg four times daily for five days. Doxycycline 100 mg twice daily for ten days is also recommended. Tetracyclines are also effective but contraindicated in patients with renal insufficiency, in children and pregnant women [15].

Injection of Hydrocortisone 100mg every 8 hourly is also given in severe cases.

Doxycycline has been used as a chemo prophylactic agent for short time exposure, but it cannot be recommended for routine continuous use or for a long-term occupational exposure [29].

2.11 Study area: The Andaman and Nicobar islands

Five hundred and seventy two islands, small and big, are scattered in the south-eastern region of the Bay of Bengal. They stretch for about eight hundred kilometres and out of the total area of 8,249 square kilometers, ninety-two per cent is covered with forests of various types. More than half the area has been declared as tribal reserves, national parks and wildlife sanctuaries.

The native inhabitants of the Andaman Islands are the Negrito tribes, classified into the Great Andamanese, the Jarwas, the Onges and the Sentinentelse. The Sentineles still remains isolated from the rest of the world. Two Mongoloid tribes, the Nicobarese and the Shompen, live in the Nicobar Islands.

The islands remained isolated from the rest of the world until the British decided to explore them during the last quarter of the eighteenth century.

Following the first war of independence of India, the convicted freedom fighters were transported to the penal settlement of Port Blair. They belonged to different parts of British India, Pakistan and Myanmar and followed different religions like Sikhism, Hinduism, Christianity and Buddhism. These people then stayed in the Islands and inter-caste and inter-religious marriages caused the complete blending of religions and culture. People speaking Hindi, Bengali, Telegu, Tamil, Urdu, Malayali, Nicobari and Punjabi today live together in the islands. Today the total population of the Union Territory of Andman and Nicobar islands is

356.265. Five hundred of them are negrito aboriginal, twenty-two thousand Nicobarese and three hundred Shompen [23].

2.12 Disease reporting system on the Andaman and Nicobar Islands

In Andaman and Nicobar Island Director of health services is collecting and compiling data from the all islands.

In Port Blair there are one hospital, GB Pant and 5 urban health centres. The urban report and all the wards in GB Pant report to medical records library at GB Pant, they report to the Health information system and they report to the Director of health services.

Then there are 28 health centre throughout the Islands and each centre have 5 sub-centre with one nurse in charge. The sub-centre reports to the health centre and the health centre to the Health information system and to the Director of health services. There are 83 diseases that they have to report monthly.

This is a very complicated process and after 4 weeks work I had to realise that information on the incidence of leptospirosis was not available. .

3 Study objectives:

To study the following aspects of leptospirosis at the Andaman islands,

1. Epidemiology
2. Clinical manifestations
3. To compare the incidence pre and post tsunami
4. Diagnostic methods.

3.1 Study setting for situation Analysis

Urban:

Visit to GB Pant Hospital, Port Blair, interaction with Medical Specialists.

Primary Health Centre (PHC), Garacharma

Rural:

Visit to PHC, Manglutan

Visit to Community Health Center (CHC), Rangat, Middle Andaman

3.2 Methodology:

- Aquisition of data from GB Pant hospital for computing Case fatality ratio.

- Surveillance data from Health Information System (HIS), Directorate of health services, Andaman and Nicobar Islands- number of reported cases and deaths from all over Andaman and Nicobar Islands.
- Patients reporting at GB Pant, CHC Rangat and Garacharma PHC during the study period (between 28 of October to 23 of December) for description of the clinical spectrum of the disease.
- The patients were examined with the help of local professionals and interviewed through a questionnaire. Only confirmed cases of leptospirosis was included in the study. Criteria considered four-fold rise or seroconversion in MAT or a positive Latex agglutination test was required.
- Administering a pre-tested questionnaire for identify risk factors of leptospirosis.



Picture 5. Dr. Sameer Sharma waiting for patients at Rangat CHC.

4 Results

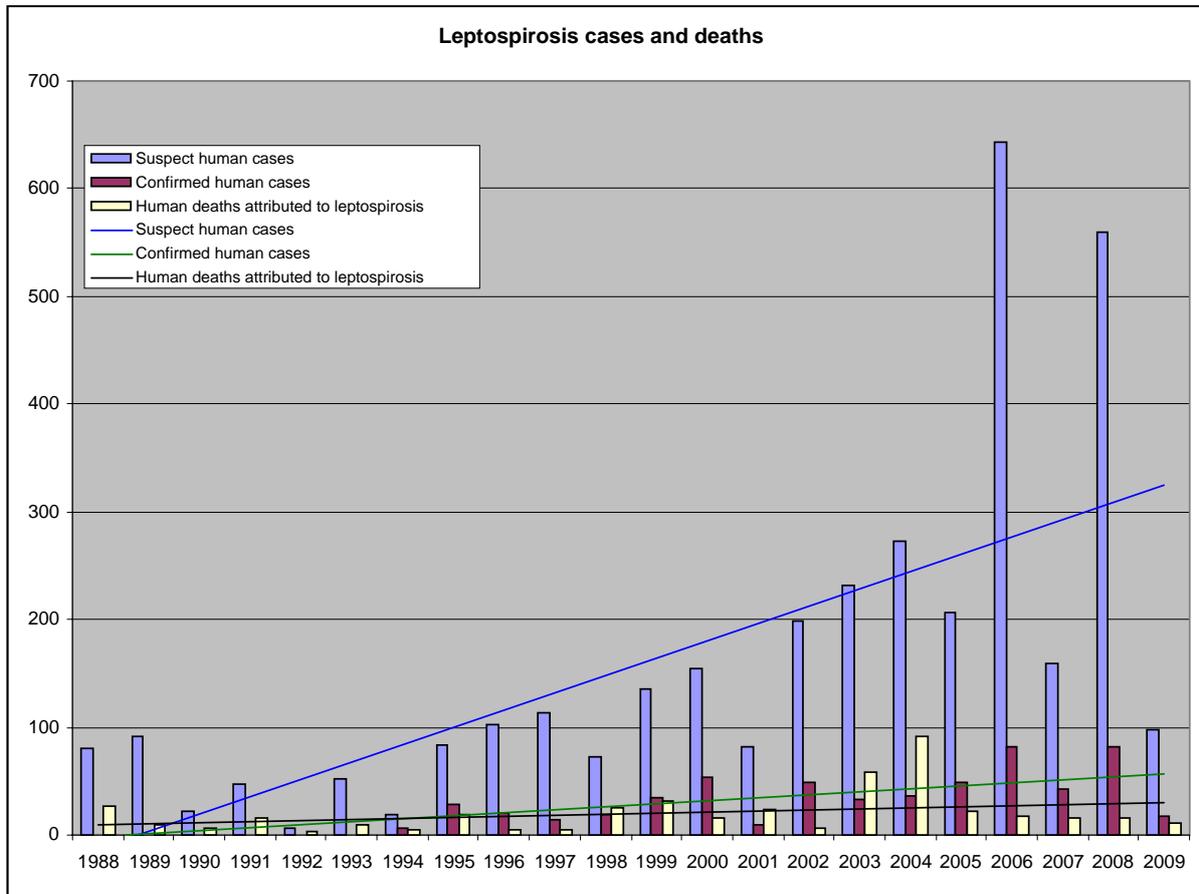


Figure 1. Suspected cases, confirmed cases and deaths due to leptospirosis at the Andaman Islands.

Information was collected from the Regional medical research centre in Port Blair. Samples were collected from all over Andaman islands. Some years studies were conducted by researchers at the centre and more samples were taken. Suspected cases have therefore a big variation in number over the years. The overall trend is a rise in suspected cases and also in the number of confirmed cases and deaths due to leptospirosis.

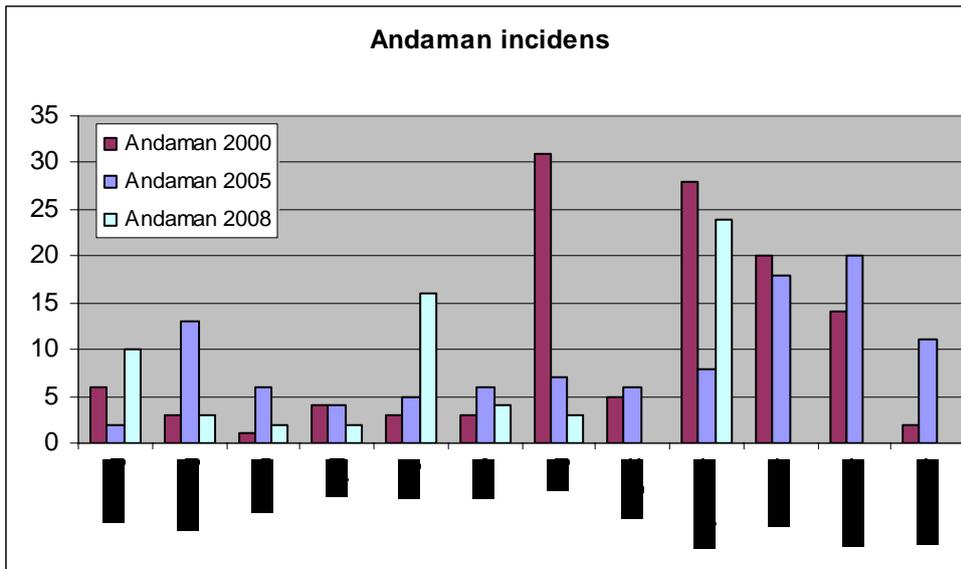


Figure 2. Number of cases with leptospirosis at the Andaman Islands.

Information was taken from the Director of health services at GB Pant in Port Blair. The only available information was from year 2000, 2005 and 2008.

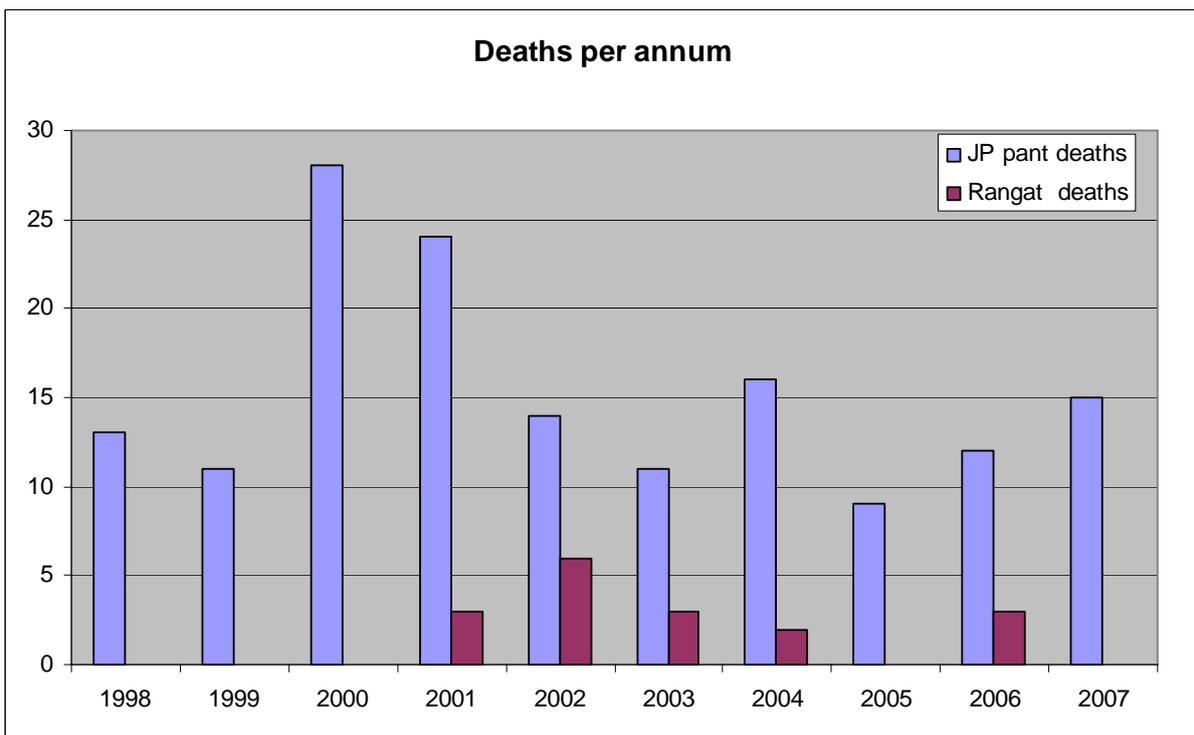


Figure 3. Number of fatal cases of leptospirosis at GB Pant Hospital, Port Blair and Rangat Clinical Health Centre.

Information on deaths due to Leptospirosis is kept in a different department at GB Pant. The information was much more complete.

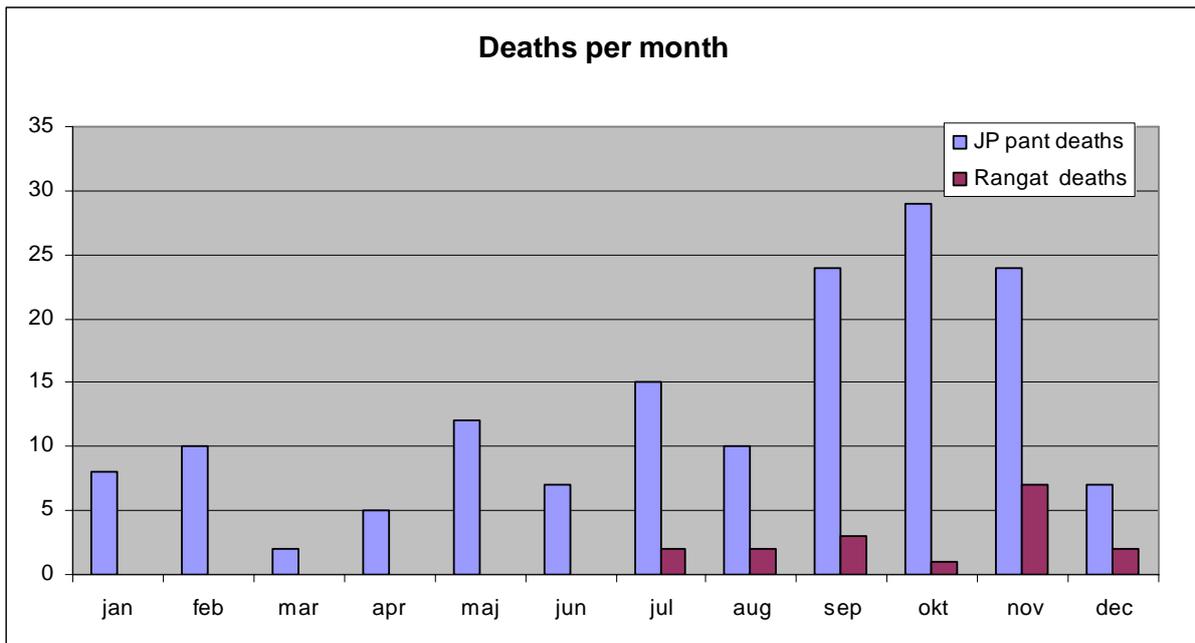


Figure 4. The monthly distribution of deaths at GB Pant and Rangat CHC from 1998 to 2007.

As shown in Fig 4, a small peak is seen in July and a larger peak in September, October and November.

4.1 Laboratory Results

During my stay in Andaman Island I examined with the help of local medical professionals, questioned and took blood samples from 31 patients. 16 of them were from a small hospital in Rangat, one from a primary health centre in Port Blair and 14 from GB Pant hospital. We performed Latex agglutination test on all the samples and 14 came out positive. Age of the patients ranged from 14 to 50 year. The 14 patients included 11 (79%) men and 3 (21%) women. The mean age was 29 years. Women were younger (mean age: 23) than men (mean age 31). 71 per cent of the patients were in the age group 15-34 year.

All the samples, except for three were taken during the first week of illness, two during the second week and one during the third.

We also performed MAT on all the collected samples but due to different difficulties only one sample from each patient was taken. To get an ideal result from MAT you need to take one sample during the acute phase and a second sample during the convalescence phase.

The cut-off titre for MAT on a single sample on the Andaman Islands is 400 or more. Out of my samples 5 had a significant titre in MAT.

4.2 Syndrome-wise analyse

4.2.1 Mild form

Nine patients presented with a mild form of leptospirosis. In most cases the first symptom was high grade fever. Two patients first symptom was headache and one was severe joint-pain. Since it is very important to detect leptospirosis in an early stage it is important, as a clinician, to know that the clinical picture can vary a lot. It is also impossible to know in advance which patient that will develop complications without early treatment.

Case 1: 25-year old man

He was working as a policeman in Port Blair and was admitted at GB Pant 19/11/2009.

He had a sudden onset of high fever, 39 degrees, and chills the day before admission and developed arthritis in one knee, body ache and a dripping nose.

During examination the man was very warm, sweating and freezing. Malaria smear was negative. He had no crepitation, icterus, hepat-splenomegaly and no conjunctival involvement. The patient was started on crystalline penicillin every sixth hourly.

Blood sample for Leptospirosis 19/11/09 was positive (Latex agglutination test).

The day after the patient was feeling better and fever had come down. After two days in the hospital the patient was discharged.

After a week the patient was reviewed, he was still tired but went back to work the day after.

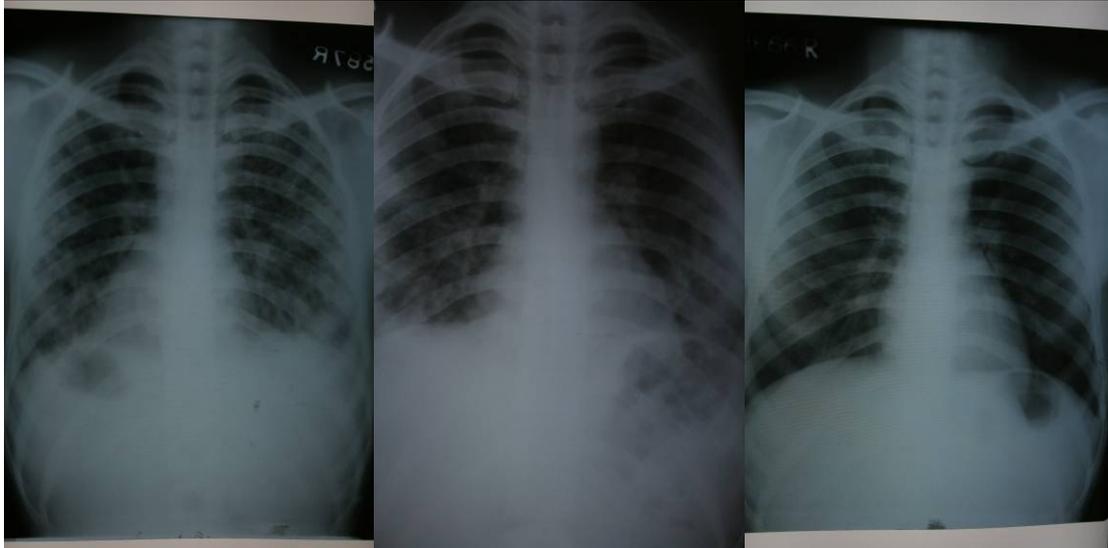
4.2.2 Hepato-renal syndrome

I met two patients with classical presentation of hepato-renal failure. They were both very sick with high grade fever, general body ache, diarrhoea, pain in abdomen, icterus and scanty urine. One of them had severe calf tenderness on palpation which is a classical symptom. The second patient had developed ascites, hepatomegaly and subconjunctival haemorrhages.

4.2.3 Pulmonary syndrome

Three of the patients had pulmonary involvement with cough, breathlessness, haemoptysis and crepitations on auscultation.

All 3 had patients was investigated with X-rays where the bleeding was visualized.



These 3 X-rays were taken from one of the patients every third day during the treatment as the symptoms from the lungs improved.

The overall impression was that these patients were severely ill and that they had a very dramatic and unpredictable course.

Case 2: 45 year old woman

Just before my arrival in Port Blair this patient with dramatic pulmonary involvement was admitted at GB Pant.

The woman came to the hospital on the 25 of October 2009 5.40 in the morning.

She had a history of fever and chills for more than 7 days. The last days she had been vomiting and coughing. One vomit was with blood.

On examination blood pressure was 110/80, pulse 120 and a few crepitations over left lung

The following blood test was taken:

S-glucose: 109	(Ref. 80-120mg %)
S-Urea: 40	(10-50mg %)
S-Creatinine: 1.1	(0.8-1.4mg %)
S-Bilirubin: 0.9	(0-1.0mg %)
Hemoglobin: 7.4	
Enteric fever blood Widal: neg.	
Malaria smear: neg.	

She was started on treatment for leptospirosis with intravenous fluid, benzyl penicillin every sixth hourly, ranitine every 8 hourly, paracetamol and other symptom releasing drugs.

The next day she was still having fever but the vomiting had stopped. BP 120/80, pulse 115

Crepitations are now auscultated over both lungs

She was started on hydrocortisone and injection of ceftriaxone 1 g*2 (antibiotics for gastro-intestinal infection)

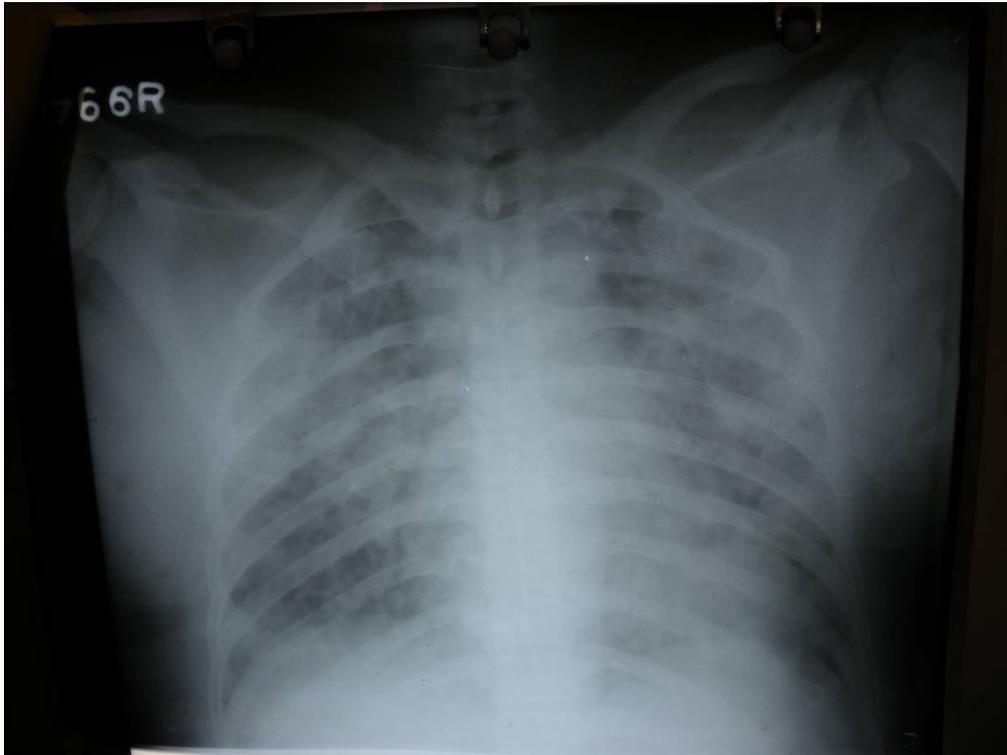
After a few hours the patient was gasping for air and vomiting coffee coloured vomit. She was tachypnoeic and pulse and blood pressure was not recordable.

She was given hydrocortisone and oxygen.

Fifteen minutes later she was stable with pulse 120 and blood pressure 190/70.

Soon after the gasping started again and the patient expired.

Cause of death: Cardiorespiratory arrest due to leptospirosis



The X-ray was taken post mortem and shows bilateral infiltrate. The days she came to the hospital she had only crepitations on one lung. It is likely that the bleeding in the lung was spread to both the lungs within 24 hours.

4.2.4 Mixed Hepato-renal and Pulmonary

The patient I met with hepatorenal failure and pulmonary haemorrhage was not confirmed with blood test, but the clinical picture strongly indicates that diagnosis and therefore I chose to present that case.

Case number 3: 17 year old woman

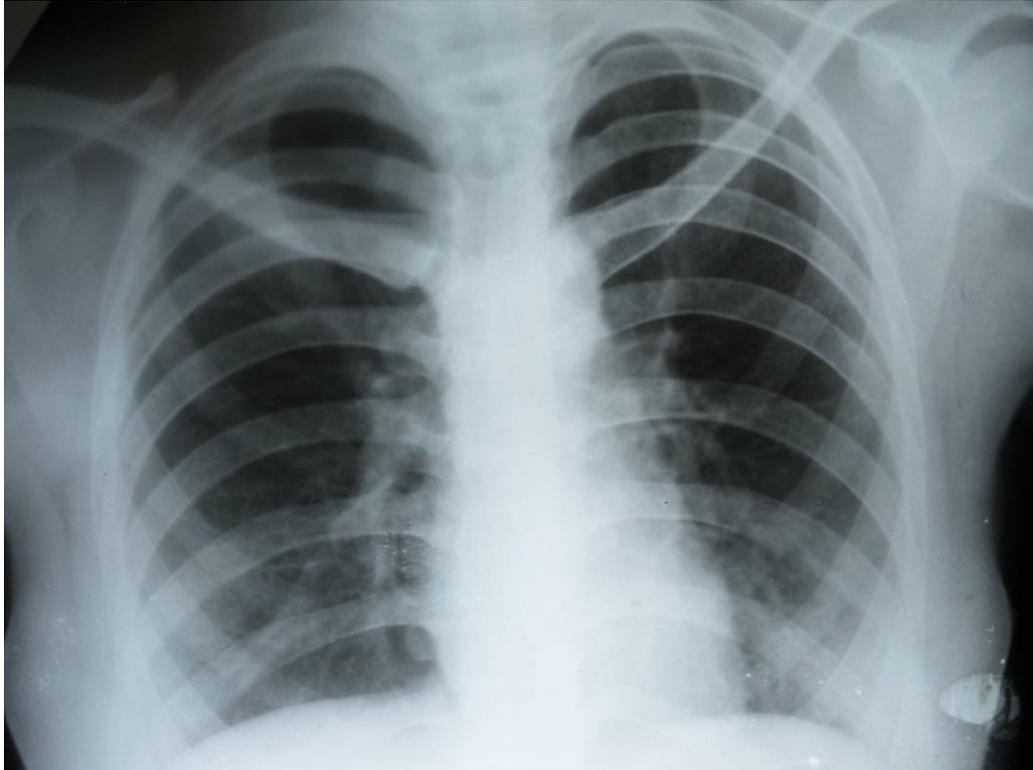
A 17 years old woman from a small village outside Rangat on middle Andaman was admitted to CHC in Rangat on 10/11/09.

Suspected diagnosis: Leptospirosis with acute renal failure and hepatorenal involvement.

She had a history of fever, vomiting, breathing difficulties, whole body pain and burning pain in epicondrium for the last 2 days.

On examination she looked ill and had difficulties in breathing. She had ronchi on auscultation, conjunctival suffusion and was clearly icteric. Her urine output was reduced and she was mildly dehydrated. Blood pressure 100/70, pulse 98,

Abdomen was palpated with no hepato-or splenomegaly, CNS normal.



X-ray: Some findings but not typical for leptospirosis.

The following blood test was taken:

S-glucose: 9.1 mgs% (Ref. 80-120mgs %)

Urea: 106 mgs % (10-50mgs %)

Creatinine: 3.1mgs % (0.8-1.4mgs %)

Bilirubin: 3.0 mgs % (0-1.0mgs %)

Latex agglutination test for leptospirosis: neg

The patient was started on injection of paracetamol, injection of beryfyllin (broncho-dilator) twice daily, benzyl penicillin every 6 hour, hydrokortison every 8 hours, lasix 2mg every 8 hourly, intravenous Ringer and dextros, Ranitec (alfa blocker), Vitamin K injection every 8 hourly, oxygen and backrest. The patient was in need of dialysis and was sent to GB Pant hospital in Port Blair. She was transported in an ambulance together with 3 other patients during the night. The journey took 5 hours on very bumpy roads.

The day after she reached GB Pant at 9.30 am.

On examination, added to the findings from the days before, was dyspnea, body pain, coated tongue and she was bleedings from lips and gums. Blood pressure 90/70, takycardia.

Blood test shows:

S-glukos 56 (Ref. 80-120mgs %)

Urea 36.0 (10-50mgs %)

S-bilirubin 0.7 (0-1.0mgs %)

Lepto rapid test: neg

In the afternoon blood pressure was 100/60 and pulse 120. Crepitations over both lungs and mild subconjunctival bleeding on left eyes.

Additional treatment with metronidalzole was started.

Two hours later bleeding from the mouth starts, pulse was rapid.

Ten minutes later the patient died.

Case number 4: 28 year old man

A 28 year old man working as a policeman came to GB Pant 2/12/09 with low grade fever, headache, body ache (especially calf tenderness) and cough since 3 days. He was frequently passing watery stool, had been vomiting 20-25 times and was not passing urine, only 2-3 yellowish drops, since 3 days.

On examination the patient is conscious and oriented, dyspnotic, dehydrated and icteric.

Puls was feeble (in shock), blood pressure 94/80 and tachycardia. Lungs are clear bilaterally with deep, rapid breathing and abdomen was palpated with mild tenderness over right hypocondrium. Calf muscles where very tender.

After he was given dopamine blood pressure was 110/70.

Blood samples taken:	S- Urea: 167	(10-50mgs %)
	S-Creatinine 4.6	(0.8-1.4mgs %)
	S- Potassium: 5.4	(3.3-4.9 meq/L)
	S- Bilirubin: 12.7mgs %	(0-1.0mgs %)
	S- glucose: 122	(80-120mgs %)
	S-sodium: 134	(132-144meq/L)
	Cholesterole: 135	(130-200mgs%)
	ASAT: 190	(0-40 IU/L)
	ALAT: 198	(0-40 IU/L)
	Lepto rapidtest: negative	
	Dengue rapid test: negative	
	HbsAg rapid test: negative	

Suspected diagnosis: Leptospirosis with hepato-renal syndrome

He was treated with KAD, oxygen and intravenous fluid and treated with Pantocid, Flagyl, Emitec, Crystallin penicillin.

The day after he was conscious and orientated but breathlessness with no cough, no haemoptysis and clear lungs. Puls rate was 114 and temperature 37,3 degrees Celcius.

He underwent haemodialysis the first time that day. After dialysis the patient felt better. For the coming days the level of creatinine was fluctuating and he was given dialysis the 4/12, 7/12, 9/12 (when creatinine was more then 4).

On the seventh of December rectal bleeding started.

Two days later the patient felt fine but observing all his vital parameters you got another picture. His respiratory rate was high and he was breathless with high puls rate, temperature was high, he was still strongly icteric and still bleeding from rectum.

On the tenth of December he was moved to Chennai for futher treatment. His condition was very serious.

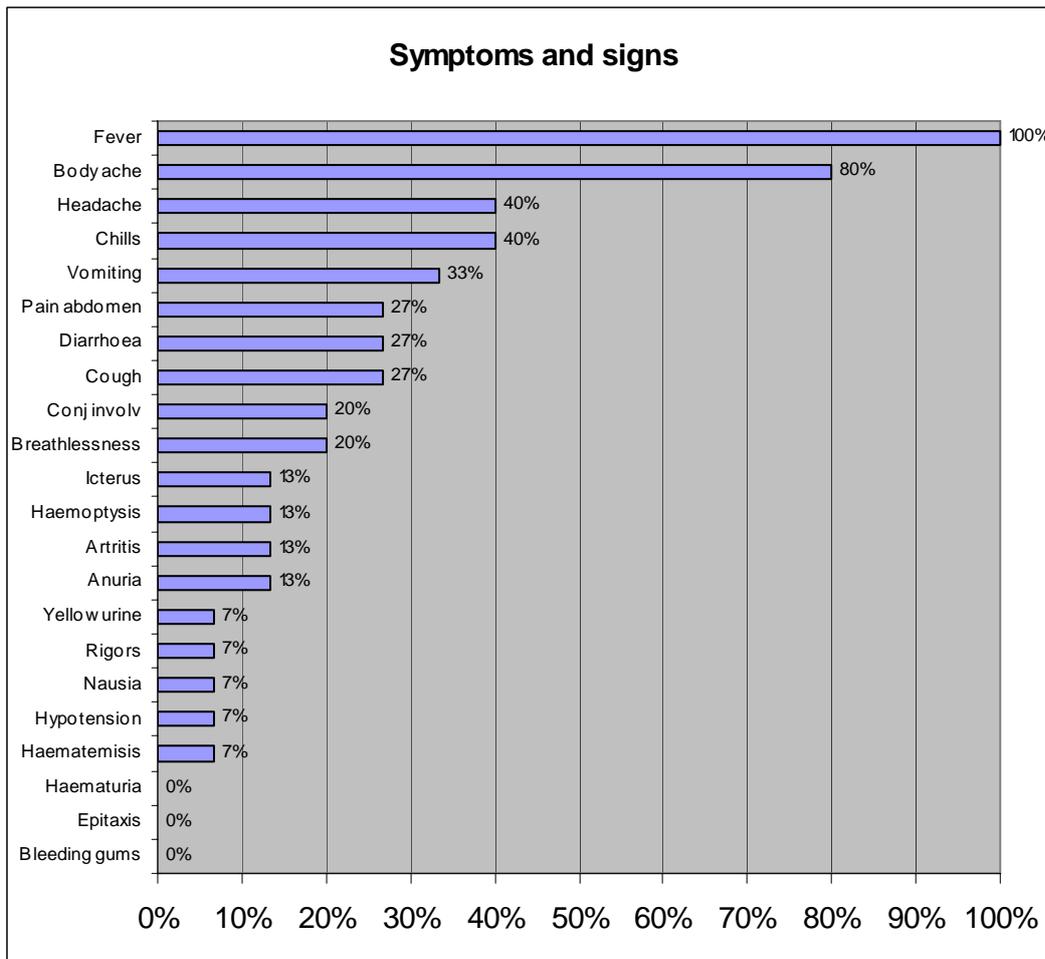


Figure number 5

Out of my patients with leptospirosis all had fever and most of them had body ache. Headache, chills and vomiting was also a common symptom.

5 Discussion

Leptospirosis is a common disease on the Andaman Islands and in the tropical world. The overall impression during my stay was that most people and medical staff on the Islands are aware of the disease and its various complications.

All the patients I met were treated with benzyl penicillin or doxycycline, the recommended treatment. Severe cases were treated with cortisone.

The mild cases improved soon after given correct treatment. Icteric cases were all hospitalized during a long time and with slow improvement. Pulmonary cases were the most unpredictable clinical presentation.

A few of the doctors I interviewed said they had seen less cases of leptospirosis the last couple of years. They all agreed this was due to the awareness among doctors to treat patients on a wide indication with antibiotics.

Higher prevalence in men is universal and is usually attributed to their outdoor activities [28]. This was also the case among my patients with 79% men and 21% women.

Risk-groups and risk factors

Andaman Islands are known to be endemic for leptospirosis with the majority of the population exposed to the disease. There are seasonal post-monsoon outbreaks with considerable mortality. The island have a suitably environment with heavy rainfall and waterlogging of the land to maintain the infection and transmission to humans. The majority of the affected population belong to the agricultural community or work with slaughterhouses or animal farms or live in the forest. Sero-prevalence of leptospirosis among high-risk population of the Andaman Islands is 52.7% according to a study in 2006 [20] but most of the time it is sub clinical.

A study of risk-factors from 2007 (A.P Sugunan et al) showed that most of the risk-factors were fairly common among people living in the highly endemic area around Rangat, with a prevalence in range of 25-80 per cent. A few of the factors such as use of stream water and well water were rare. The factors that had a significant different prevalence among cases and controls were house with thatched roof and use of stream water for drinking among the factors related to house and environment, cattle and pig among the animals in house and barefoot walking, wounds, harvesting, cleaning sewage, clearing garbage and working standing in water among behavioural and occupational factors studied. [21].

I was told many times that around 10 years ago leptospirosis was only seen among farmers and people working in wet conditions. Now the disease is seen both in rural and urban areas and among all categories of professions. This correlates well with the patients I saw. Most of them came from rural, wet areas in lowland but a few were from rural, dry areas or highland. Most of them had animal in the house but a few did not. They were house wives, students, governant servants, policemen, carpenters and agricultural workers.

These observations of a shift in categories of patients are not described in any articles or studies I have read and are only observations the doctors I have met.

The number of human cases worldwide is not known precisely. According to WHO incidences ranges from 0.1 to 1 per 100.000 per year in temperate climate to 10-100 in 100.000 in the humid tropics. During outbreaks and in high risk-groups this number may be higher.

Picture number one shows suspected, confirmed cases and deaths and the information were taken from Regional Medical Research Centre in Port Blair. Data was collected from all over Andaman Islands from 1998 to 2009(except December). There is a big variation in number of suspected cases. Blood samples can

be taken by staff from the centre but most samples are taken if researchers from the centre are sent to conduct a study. Some year staff went to Manglutan PHC on every day basis to take samples on suspected cases. The overall trend shows a rise in number of suspected cases but I am not sure this reflects that there actually are more cases today. Leptospirosis was not well known among medical staff and in the community until 20th century and it is possible that the diagnosis is suspected more often now.

The trend for confirmed cases is also positive. I have no information on the clinical symptoms of these patients and in an endemic community it is hard to tell anything from these numbers.

There is no obvious rise in number of cases of leptospirosis during the tsunami or during the reconstruction work after the tsunami. The flooded areas after the tsunami were filled with salty water and it is thought among researchers at the centre that leptospiras did not survive in the salty water.

Picture number two shows incidence from 2000, 2005 and 2008 and was taken from Directorate of health services at GB Pant. The reporting system on the Andman Island is very complicated, 28 health stations are supposed to report 83 different diseases each month. Many of the centre lack adequate material to confirm diagnosis and are situated far away from the RMRC. It is also possible that they have sent the report to GB Pant but the staff did not keep it properly because the former students from Sweden included statistics in their report that I was not able to trace even though we tried for several weeks.

Information on deaths due to leptospirosis was kept at a different department and much more complete. I took information from GB Pant and Rangat CHC which was the hospitals I spent most time at. They show a peak in July and in September, October and November and correlated well with the harvest season. These are the months when many people come in contact with contaminated water in the paddy fields harvesting rice.

The Andaman Islands are in need of better diagnostic methods and surveillance system. Today nobody knows how great the disease burden is.

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