Review Article

Leptospirosis: A Review on Zoonosis in Indian Scenario

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Abstract

Leptospirosis is a zoonotic contagious bacterial disease of animals affecting both humans and animals (Slack, 2010). Leptospirosis goes by many names like 7-day fever, harvest fever, field fever, canefield fever, mild fever, rat catcher's yellows, Fort Bragg fever, pretibial fever, rice field worker disease (Mosby's Medical Dictionary, 2015) etc. It has historically been known as black jaundice and in Japan it is called Nanukayami fever. It is caused by corkscrew-shaped spirochaete bacteria of the genus Leptospira (Slack, 2010). It causes various symptoms ranging from none to mild sickness such as headaches, muscle pains, and fevers and even severe with bleeding from the lungs or even meningitis (Bride et al., 2005). In case of Weil's disease, the person becomes icteric having kidney failure and bleeding (Bride et al., 2005). Sometimes it causes a lot of bleeding into the lungs then it is known as severe pulmonary hemorrhage syndrome (Klopfleisch et al., 2011).

Key words: Animals, Leptospirosis, Spirochaete, Zoonosis

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Introduction

The disease was first described by physician Adolf Weil in 1886 in Germany when he reported an "acute infectious disease with enlargement of spleen, jaundice, and nephritis" (Stimson, 1907). Inada and Ito first identified *Leptospira* as the causative organism in 1908 (Inada and Ito, 1908; Inada *et al*., 1916). It is estimated that seven to ten million people are infected by leptospirosis annually. Almost one million cases

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of severe leptospirosis are observed every year claiming around 58,900 lives. Annual rates of infection vary from 0.02 per 100,000 in temperate climates to 10 to 100 per 100,000 in tropical climates. The disease is most common in tropical areas of the world but may occur anywhere. Outbreaks may occur in slums of the developing world. Weil's disease and severe pulmonary haemorrhage syndrome result in death rates greater than 10% and 50%, respectively, even with treatment. As symptoms aren't clear it's may go unnoticed and thus cause serious problems. Leptospirosis is one of the most important diseases of public health importance.

Etiology

Leptospirosis is caused by the spirochaete bacteria belonging to genus *Leptospira* of family Leptospiraceae under the class Spirochaetes. The genus *Leptospira* is divided into two species based mainly on their pathogenicity; *L. interrogans* consisting of pathogenic strains and *L. biflexa* consisting of non-pathogenic saprophyte strains. These species again consist of many serovars of *Leptospira*. The varied numbers of serovars are due to difference in agglutination reaction because of the surface lipopolysaccharide (LPS) of the bacteria. There are approximately more than 225 serovars for *L. interrogans* and more than 60 serovars for *L. biflexa* (Mohammed *et al*., 2011).

Leptospires are motile and aerobic, can't survive dry environment, heat, acids and basics disinfectants but can sustain alkali pH up to pH 7.8 (Johnson and Faine, 1984). The bacteria can only be visualized using a dark field or phase contrast microscope. Though they are gram negative in nature, gram's staining isn't done for visualization of the bacteria. Silver impregnation staining, immunoperoxidase staining or immunofluorescence should be done to observe these bacteria (Terpstra, 2003). Being aerobic in nature, the bacteria can be cultured media enriched with vitamins like B1 and B12, long-chain fatty acids, and ammonium salts at 28-30°C. The fatty acids are the sole source of carbon and are utilized by β-oxidation (Evangelista and Coburn, 2010). The widely used media for culture of *Leptospira* is Ellinghausen–McCullough/ Johnson–Harris (EMJH) medium, which contains oleic acid, bovine serum albumin and polysorbate (Tween). Addition of 5-fluorouracil and antibiotics such as nulidixic acid or rifampicin makes the medium inhibitory for common laboratory contaminants (Evangelista and Coburn, 2010). The growth is often slow and thus the culture should be discarded only after 13 weeks. Very low amount of agar can be used to create a semi solid medium in which the bacteria grows and creates a highly turbid zone below the surface of the media. This is due to the optimum oxygen tension in that area and this is called as Dinger's ring or Dinger's disk (Mohammed *et al*., 2011).

The pathogenic strains can't be differentiated from non-pathogenic ones on basis of their morphology. So to differentiate pathogenic and saprophytic strains some tests like pathogenicity to test animals, conversion to spherical forms in 1M NaCl, growth in presence of 8-azaguanine (225mg/l) and growth at 13°C are

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conducted. Saprophytes are able to grow at 13°C and in presence of 8-azaguanine and also are converted to spherical forms in presence of 1M NaCl which the pathogenic bacteria fails to do though *L. interrogans Icterohaemorrhagiae* can grow at 10°C. An ELISA test, in which the antigens of only pathogenic leptospires can react with the monoclonal F9-4 antibodies, can also be used (Terpstra, 2003).

Transmission

Leptospirosis is mostly transmitted by the urine of an infected animal and is contagious as long as the urine is still moist as the bacteria can't survive dryness for a longer period (Bharti *et al*., 2003). Although *Leptospira* have been detected in reptiles and birds, only mammals are reported to transmit the bacteria to humans and other animals. No report exist which shows the pathogen moving from reptiles or birds to humans. The disease infects a wide range of natural rodent and non-rodent as reservoir hosts which include foxes, rabbits etc. Rats, mice, and moles are important primary hosts but animals like dogs, cows, sheep etc are also responsible for disease transmission (James and Berger, 2006).

Pet dogs mainly contract leptospirosis, mostly from licking the urine of infected mice in the house or outside and thus act as source of infection to others (McKay, 2001). The type of habitats most likely to carry infective bacteria are moist and damp areas like riverbanks, muddy livestock rearing areas where there is a regular passage of wild or farm mammals (Kohn *et al*., 2010). The disease is, seasonal in temperate climates and year-round in tropical climates and directly with the amount of rainfall. Leptospirosis is also reported to be transmitted via the semen of the infected animals (Wasiński and Dutkiewicz, 2013). Humans can only become infected through contact with food, water, or soil that is contaminated with urine from these infected animals. This may happen by swallowing contaminated food or water or through skin contact. No human to human transmission is reported (Wasiński and Dutkiewicz, 2013).

It is an occupational hazard for many people who work outdoors or with animals, such as: farmers, mine workers, sewer workers, slaughterhouse workers, veterinarians and animal caretakers, fish workers, dairy farmers etc. where there is presence of water lodging conditions (James and Berger, 2006). The disease has also been associated with swimming, wading and rafting in contaminated lakes and rivers. As such, it is a recreational hazard for campers or those who participate in outdoor sports. Persons who actively participate in such activities in tropical or temperate climates are in a very high risk zone. In addition, incidence of leptospirosis infection among urban children appears to be increasing (Langston and Heuter, 2003).

Epidemiology

Leptospirosis is an infectious disease caused by *Leptospira interrogans* complex, which has over 20 serogroups and more than 200 serovars. Rodents, domestic & wild animals form the reservoir of infection where domestic animals such as cattle, dogs, and pigs may act as carriers for several months (temporary

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carrier) while rodents usually remain carrier throughout their life (permanent carrier). Rodents are therefore considered as the major reservoir of infection. Leptospires are excreted in the urine of the animals and they affect man when he comes into contact with urine of infected animals, directly or indirectly (Shivakumar, 2008).

Leptospirosis can occur in both urban and rural areas. In urban areas of developing countries, a contaminated environment due to various factors such as overcrowding, inadequate drainage and sanitation facilities for man and animals, presence of stray animals, domestic rats, bandicoots, unhygienic slaughter houses and people walking bare foot contribute to the spread of the illness (Shivakumar, 2008). Persons of all ages and races are susceptible. In India, urban leptospirosis has been reported from Chennai and Mumbai while rural leptospirosis has been reported from Gujarat, Kerala and Andamans. Non-reporting of leptospirosis from other states of India does not mean that it is absent in those parts (Shivakumar, 2008).

Indian Scenario

Leptospirosis is reported to be of endemic importance from many States of India.

Andaman and Nicobar Islands

Andaman and Nicobar Islands are endemic for leptospirosis since early part of the 20th century. Outbreaks of Andaman Hemorrhagic fever (AHF) were reported since 1988. This was proved to be leptospirosis in 1994. 524 cases of AHF (leptospirosis) were reported from 1988-97 (Sehgal, 1998; Singh *et al*., 1999; Shivakumar, 2008).

Gujarat

The disease is endemic in south Gujarat since 1994. The endemic districts are Valsad, Navsari and Surat (Patel *et al*., 2006; Shivakumar, 2008).

Maharashtra

Leptospirosis has been reported regularly since 1998. 2355 cases and 167 deaths were reported in 2005, mainly due to large outbreak during the post monsoon floods. The number of districts in Maharashtra reporting leptospirosis has expanded from two in 1998 to ten districts in 2005 (Karande *et al*., 2002, 2003; Shivakumar, 2008).

Kerala

Leptospirosis is endemic in many areas of Kerala. Kolenchery is in the midlands of Kerala. In this area leptospirosis was rarely diagnosed before 1987. Since then an annual increase in incidence was observed (Kuriakose *et al*., 1997; Shivakumar, 2008).

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Tamilnadu

Leptospirosis has been reported from Chennai since 1980's. The leptospirosis laboratory at Institute of Microbiology, Madras Medical College was established in 1994 (Ratnam *et al*., 1983*a*, *b*; Chinari Pradeep *et al*., 1999; Shivakumar, 2008).

Puducherry

In a study of 33 icteric patients from Puducherry, 22 had altered sensorium and 20 had multi-organ failure and thrombocytopenia and 13 patients died (39.3%) (Dutta and Christopher, 2005; Shivakumar, 2008).

Karnataka

Leptospirosis outbreaks have been reported from 15 districts of Karnataka. The highest incidence of cases have occurred in Bangalore city, Uttara kannada, Shimoga, Bidar, Gulbarga, Udupi and dakshina kannada districts. During the year 2004, 152 cases and 11 deaths were reported and during 2005, 224 cases and 19 deaths were reported.

Odisha

After the cyclone during the October-November 1999, 142 patients with febrile illness and hemorrhagic manifestations were evaluated. 28 (19.2%) had evidence of leptospirosis which was confirmed by MAT. 6 were positive by culture / PCR (Joint Publication by Office of WHO, Representative to India, New Delhi and Regional Medical Research Centre (ICMR), WHO Collaborating Centre for Diagnosis, Research, Reference and Training in Leptospirosis, 2006; Shivakumar, 2008).

Other States

Data from Andhra Pradesh, Uttar Pradesh, West Bengal and Delhi were analysed. Evaluation of acute febrile patients in Uttar Pradesh revealed that 7% had leptospirosis (25/ 346). 17 of the 25 patients had jaundice. In a study of 55 cases of leptospirosis in Hyderabad, 52 % had renal failure and jaundice occurred in 42%. Out of 42 persons with jaundice who were evaluated in Calcutta, 10 (23.8 %) were found positive for leptospirosis. 75 patients from Delhi with symptoms of leptospirosis were evaluated, 32 were found positive for leptospirosis and 5 died. 180 febrile patients from urban slums of Delhi were evaluated and 27 (15 %) were positive for leptospirosis (Shivakumar, 2008).

Pathogenesis

The bacteria enter the body through small abrasions, mucosa, conjunctiva and genital tracts. It involves some chemotactic interactions and then transmembrane passage. The bacteria settle down in the convoluted tubules of the kidney and thus keep on shedding the pathogen in urine. The period of shedding varies from

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a few weeks to many months. After the bacteria reach a higher concentration in blood and tissue, there is tissue damage due to endotoxins secreted by the pathogen. Hemolysin is also secreted by the bacteria and leads to damage of blood cells. Endothelium gets damaged which leads to ischemia and other complications. The exact molecular basis of virulence is yet unknown however the humoral response has been observed to be active in first week of infection leading to phagocytosis by macrophages and neutrophils (Mohammed *et al*., 2011).

Signs and Symptoms

In humans, the disease is characterized by variety of symptoms, including high fever, vomiting, jaundice (yellow skin and eyes), red eyes, headache, chills, muscle aches, , abdominal pain, diarrhoea, rash etc. Many of these symptoms can be mistaken for other diseases. In addition, some infected persons may have no symptoms at all. Illness usually begins abruptly with fever and other symptoms. The symptoms appear after an incubation period of 7–12 days (NHS, 2012).

Leptospirosis may occur in two phases-

- The first phase (acute or septic phase) ends after 3–7 days of illness with the appearance of antibodies against *Leptospira* and the disappearance of all the bacteria from the bloodstream. The patient is asymptomatic for 3–4 days until the second phase begins with another episode of fever.
- The hallmark of the second phase is meningitis (inflammation of the membranes covering the brain) the illness lasts from a few days to 3 weeks or longer. Without treatment, recovery may take several months

Majority of the cases of the leptospirosis are mild form. However, there has been reports of severe disease, which develops during the second stage or occurs as a single progressive illness. The classic form of severe leptospirosis is known as Weil's disease, which is characterized by liver damage (causing jaundice), kidney failure, and bleeding. The disease affects brain also causing meningitis, encephalitis of brain tissue with same signs and symptoms; and lung affected as the most serious and life-threatening of all leptospirosis complications. The infection is often incorrectly diagnosed due to the nonspecific symptoms. The patients of leptospirosis are likely to be misdiagnosed as malaria, dengue hemorrhagic fever, and viral hepatitis etc. (Mosby's Medical Dictionary, 2013).

Diagnosis

On infection the bacteria can be found in blood and cerebrospinal fluid (CSF) for the first 7 to 10 days (invoking serologically identifiable reactions) and then moving to the kidneys. After 7 to 10 days the microorganism can be found in fresh urine. Hence, early diagnostic efforts include isolation from blood or other clinical materials through culture of pathogenic leptospires. Diagnosis of leptospirosis is confirmed with tests such as enzyme-linked immunosorbent assay (ELISA) and polymerase chain reaction (PCR).

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The Microscopic Agglutination Test (MAT) is still considered the gold standard test in diagnosing leptospirosis according to CDC. Live *Leptospira* are to be cultured regularly and agglutination reaction is carried out to check the species and serovar of the pathogen. It is a very laborious and expensive method and needs live bacterial antigen to test. That's why this test is only conducted in specially designed labs (Picardeau *et al*., 2014).

Differential diagnosis is difficult as the signs and symptoms match a lot of diseases. Focus should be made towards the medical history like low-lying areas, seasonality, contact with stagnant contaminated water or rodents in vicinity support the leptospirosis hypothesis and serve as indications for specific tests. *Leptospira* can be cultured in Ellinghausen-McCullough-Johnson-Harris medium (EMJH), which is incubated at 28° to 30°C. Due to its slow growth in laboratory media, culture techniques are useless for diagnostic purposes but are commonly used in research.

Treatment

Antibiotics like amoxicillin, doxycycline, ceftriaxone etc. are used. Fluid therapy can be advised as per the requirement. Persons with symptoms suggestive of leptospirosis should contact a health care provider as soon as possible.

Prevention

Leptospirosis has been an underreported disease and there are a few reliable global incidence data as the disease is not detected in common laboratory tests. As the symptoms are very much similar to many other diseases and the bacteria being destroyed by common antibiotics, the disease is very hard to detect in a population. The risk of leptospirosis can be greatly avoiding water contaminated with animal urine or contact with potentially infected animals. Occupational workers should wear protective clothing or footwear. Any skin cuts should be covered with waterproof dressing while swimming in freshwater to protect against a range of infections. In pet dogs, vaccination against the bacteria protects the animal and the house hold. Human immunization also helps to provide a certain degree of protection against infection but only available in countries like China and Cuba (McBride *et al*., 2005). Immunization of local reservoirs of the pathogen like dogs and livestock should be implemented in the areas prone to leptospirosis like low-lying areas, damp and muddy environment, locality with high rice cultivation etc. Destruction of mice and rodents is a necessary step towards prevention of leptospirosis and many other rodent borne infections.

References

1. Bharti, A.R., Nally, J.E., Ricaldi, J.N., Matthias, M.A., Diaz, M.M., Lovett, M.A., Levett, P.N., Gilman, R.H., Willig, M.R., Gotuzzo, E. and Vinetz, J.M. (2003). Leptospirosis: a zoonotic disease of global importance. *The Lancet. Infectious Diseases*, 3(12): 757–771.

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 DOI 10.5455/ijlr.20171020111742

2. Chinari Pradeep, K.S., Sumathi, G., Vimala Ranga Rao, G., Shivakumar, S. (1999). Leptospirosis laboratory. Chennai Medical College – A three year experience in sero- diagnosis (1995- 1997). *Indian J. Med. Microbiol*., 17(10): 50-51.
3. Costa, F., Hagan, J.E., Calcagno, J., Kane, M., Torgerson, P., Martinez-Silveira, M.S., Stein, C., Abela-Ridder, B. and Ko, A.I. (2015). Global Morbidity and Mortality of Leptospirosis: A Systematic Review. *PLoS Neglected Tropical Diseases*, 9(9): e0003898.
4. Dutta, T.K. and Christopher, M. (2005). Leptospirosis – An Overview. *J. Assoc. Phys. India*, 52: 545-551.
5. Evangelista, K.V. and Coburn, J. (2010). *Leptospira* as an emerging pathogen: a review of its biology, pathogenesis and host immune responses. *Future Microbiology*, 5(9): 1413–1425
6. Inada, R. and Ito, Y. (1908). A report of the discovery of the causal organism (a new species of *spirocheta*) of Weil's disease. *Tokyo Ijishinshi*, 1915: 351–360
7. Inanda, R., Ido, Y., Hoke, R., Kaneko, R. and Ito, H. (1916). The Etiology, Mode of Infection and Specific Therapy of Weil's disease. *J. Exper. Med*., 23(3): 377–402.
8. James, William D. and Berger, Timothy G. (2006). Andrews' Diseases of the Skin: clinical Dermatology. *Saunders Elsevier*
9. Johnson, R.C. and Faine, S. (1984). *Leptospira*, In: Krieg, N.R. and Holt, J.G. (eds.) *Bergey's manual of systematic bacteriology*. Williams & Wilkins, Baltimore, 1: 62-67
10. Karande, S., Kulkarni, H., Kulkarni, M. *et al*. (2002). Leptospirosis in children in Mumbai slums. *Indian Journal of Pediatrics*, 69: 855-858.
11. Karande, S., Bhatt, M., Kelkar, A. *et al*. (2003). An observational study to detect leptospirosis in Mumbai, India. *Archives of disease in childhood*, 88(12): 1070-1075.
12. Klopfleisch, R., Kohn, B., Plog, S., Weingart, C., Nöckler, K., Mayer-Scholl, A. and Gruber, A.D. (2011). An Emerging Pulmonary Haemorrhagic Syndrome in Dogs: Similar to the Human Leptospiral Pulmonary Haemorrhagic Syndrome? *Vet. Med. Int*., 33: 928541.
13. Kohn, B., Steinicke, K., Arndt, G., Gruber, A.D., Guerra, B., Jansen, A., Kaser-Hotz, B., Klopfleisch, R., Lotz, F., Luge, E. and Nockler, K. (2010). Pulmonary abnormalities in dogs with leptospirosis. *J. Vet. Intern. Med*., 24(6): 1277–1282.
14. Kuriakose, M., Eapen, C.K. and Paul, R. (1997). Leptospirosis in Kolenchery, Kerala,India. Epidemiology, Prevalent local serogroups and serovars and a new serovar. *European Journal of Epidemiology*, 13(6): 691-697.
15. Langston, C.E. and Heuter, K.J. (July 2003). Leptospirosis. A re-emerging zoonotic disease. *Veterinary Clinics of North America, Small Animal Practice*, 33(4): 791–807.
16. Leptospirosis. *NHS*. 11 July 2012.
17. McBride, A.J., Athanazio, D.A., Reis, M.G. and Ko, A.I. (2005). "Leptospirosis". *Current Opinion in Infectious Diseases*, 18(5): 376–86.
18. McKay, James E. (2001). Comprehensive health care for dogs. *Creative Pub. International*. pp. 97
19. Mohammed, H., Nozha, C., Hakim, K., Abdelaziz, F. and Rekia, B. (2011). Leptospira: Morphology, Classification and Pathogenesis. *J. Bacteriol. Parasitol.*, 2: 120
20. Mosby's Medical Dictionary (9th Ed.). *Elsevier Health Sciences*. 2013. pp. 697
21. Patel, B.K., Gandhi, S.J. and Desai, D.C. (2006). Clinico-epidemiological aspects of leptospirosis in south Gujarat. *Indian J. Med. Microbiol*., 24(4): 322-326.
22. Picardeau, M., Bertherat, E., Jancloes, M., Skouloudis, A.N., Durski, K. and Hartskeerl, R.A. (2014). Rapid tests for diagnosis of leptospirosis: current tools and emerging technologies. *Diagn. Microbiol. Inf. Dis.*, 78(1): 1–8.
23. Ratnam, S., Sundararaj, T., Thiagarajan, S.P. *et al*., (1983*a*). Serological evidence of leptospirosis in jaundice and pyrexia of unknown origin. *Ind. J. Med. Res*., 77:427-430.
24. Ratnam, S., Suramaniam, S. and Madanagopalan, T. (1983*b*). Isolation of leptospirosis and demonstration of antibodies in human leptospirosis in Madras, India. *Trans. R. Soc. Trop. Med. Hyg*., 77: 455-458.

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DOI 10.5455/ijlr.20171020111742

25. Report of the Brainstorming meeting on Leptospirosis Prevention and control. Mumbai, 16- 17 February 2006. Joint Publication by Office of WHO, Representative to India, New Delhi and Regional Medical Research Centre (ICMR), WHO Collaborating Centre for Diagnosis, Research, Reference and Training in Leptospirosis.
26. Sehgal, S.C. (1998). Emergence of leptospirosis as a public health problem. *Proceedings of the third round table conference. Series leptospirosis, Ranbaxy science foundation*, 3: 7-12.
27. Shivakumar, S. (2008). Leptospirosis- Current scenario in India. In: *Medicine Update*, Vol. 18, Chap. 106. pp. 799-809, DOI: 10.13140/2.1.4905.6968
28. Singh, S.S., Vijayachari, P., Sinha, A. *et al*. (1999). Clinical-epidemiological study of hospitalized cases of severe leptospirosis. *Indian J. Med. Res*., 109: 94-99.
29. Slack, A. (2010). "Leptospirosis.". *Australian family physician*, 39(7): 495–498.
30. Stimson, A.M. (1907). Note on an organism found in yellow-fever tissue. *Public Health Reports*, 22(18): 541.
31. Terpstra, W.J. (2003). *Human Leptospirosis: Guidance for Diagnosis, Surveillance and Control*. World Health Organization. International Leptospirosis Society
32. Wasiński, B. and Dutkiewicz, J. (2013). Leptospirosis—current risk factors connected with human activity and the environment. *Ann. Agric. Environ. Med*., 20(2): 239–244.

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