

## Overview of Leptospirosis

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### Article Information     **Abstrak**

**Submitted:** 30 *Leptospirosis is one of the most important zoonoses worldwide and is a major public health problem in many countries. The disease is caused by spirochetes of the genus Leptospira and is transmitted through contact of abraded skin or mucous membranes with contaminated rodent urine, water, or soil. It is estimated that there are more than one million cases of severe leptospirosis per year worldwide. Leptospirosis can cause severe multiple organ failure with a mortality rate as high as 50%. Early recognition, diagnosis and treatment of leptospirosis can reduce morbidity and mortality. This overview will look out Leptospirosis thoroughly from the epidemiological burden, pathogenesis, clinical presentation and diagnosis, the current treatment and preventive leptospirosis.*

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## **Introduction**

Leptospirosis is one of the most important zoonoses in the world and a major public health problem in many countries, causing approximately 1 million cases and 60,000 deaths each year (Limothai et al., 2021), (Sykes, Reagan, Nally, Galloway, & Haake, 2022)

This illness arises from spirochetes belonging to the *Leptospira* genus and is spread through contact of skin abrasions or mucous membranes with rodent-contaminated urine, water, or soil. Leptospirosis presents a wide range of symptoms ranging from an asymptomatic febrile illness to a severe acute infection leading to organ failure and death (Bradley & Lockaby, 2023)

The spectrum of the disease is very broad and ranges from a clinically inapparent disease to a severe multisystem disease characterized by jaundice and acute renal failure, thrombocytopenia, and possibly fatal pulmonary hemorrhage. The wide variety of clinical manifestations of leptospirosis is part of the differential diagnosis of many febrile illness syndromes. In most cases, leptospirosis is confused with malaria and dengue, but the differential diagnosis certainly varies depending on the locally prevalent infectious disease (Bradley & Lockaby, 2023)

This disease occurs worldwide, but the incidence rate is highest in the world in tropical areas, although cases have been reported in temperate climates and developed countries. Certain occupational activities (e.g., agriculture, veterinary medicine, military training), recreational water immersion, poor living conditions, and seasonal rains in tropical areas are commonly associated with this disease (Li et al., 2022)

## **Epidemiology**

The transmission of leptospirosis is caused by the *Leptospira* bacteria, which is spread throughout the world and is transmitted directly or indirectly from animals to humans (zoonoses) (Rampengan, 2016)

Leptospirosis is very common in tropical areas, with 73% of cases occurring in this area, especially in Southeast Asia, eastern sub-Saharan Africa, the Caribbean, and Oceania. It is common among rural agricultural populations and poor urban and semi-urban populations, and particularly affects young adult males. Farmers, those in contact with livestock, those exposed to rodents in their workplaces, and people living in areas where sanitation is poor are most at risk. Recreational exposure has also been described in those who practice water sports. Urban plague usually occurs in environments with poor sanitary conditions and rats reproduce in large numbers. The overall incidence rate is stable globally; However, many major outbreaks have occurred over time in certain countries, in some cases related to flood-related natural disasters. Epidemics are often observed during floods, and changing environmental trends, with extreme weather patterns, can perpetuate these epidemics (Rajapakse, 2022). The World Health Organization (WHO) estimates the annual incidence of leptospirosis worldwide at 1.03 million cases and 58,900 deaths, with the greatest burden occurring in resource-poor tropical countries, including Latin American countries and Asia (Dreyfus et al., 2022)

The worldwide number of cases is estimated to be between 0.1 – 1 per 100,000 population per year in temperate climates to 10 or more per 100,000 population per year in the humid tropics. During an outbreak this figure may rise to 100 or more per 100,000. Although Leptospirosis can occur worldwide, there are a number of risk factors associated with the disease (Prabhu, Natarajaseenivasan, Uma, Thirumalaikolundusubramanian, & Joseph, 2014)

### **Pathogenesis**

The initial stage in the development of leptospirosis involves the breach of tissue barriers to enter the body. Leptospire enter the host via small abrasions, breaches of the surface integument, conjunctiva, mucous membrane, and genital track. This requires chemotaxis mechanisms for adhesion and transmembrane passages. The bacteria are then required to win the vascular compartment, However, they may settle in the convoluted tubules of the kidneys and be shed in the urine for a period of a few weeks to several months and occasionally even longer (Mohammed, Nozha, Hakim, Abdelaziz, & Rekia, 2011)

After the number of leptospire in the blood and tissues reaches a critical level, lesions due to the action of undefined leptospiral toxin or toxic cellular components and consequent symptoms appear. The succeeding phase in the pathogenesis involves the widespread dissemination through the bloodstream. Positive results for detecting leptospiremia through quantitative PCR are more probable within the initial 8 days of fever, primarily due to the introduction of blood into a leptospiral medium. In instances of heightened leptospiremia levels during infection, innate immune mechanisms are activated, subsequently prompting both tissue-specific and systemic responses. These responses contribute to severe consequences like a sepsis-like syndrome or organ failure, with the liver being a major target organ in leptospirosis (Haake & Levett, 2014)

### **Clinical Manifestation**

Human leptospirosis has diverse clinical manifestations. Clinical illness in humans can range from a mild, self-limiting acute febrile illness to a severe, life-threatening condition with multiple organ dysfunction (Fraga, Carvalho, Isaac, & Barbosa, 2024), (Haake & Levett, 2014), (Rajapakse, 2022), (De Vries et al., 2018)

The first symptoms (early phase) are fever, chills, severe headache, myalgia, nausea, vomiting, malaise and conjunctival hyperemia (Fraga et al., 2024). The headache is often severe and has been described as a bitemporal, frontal throbbing headache accompanied by retro-orbital pain and photophobia (Haake & Levett, 2014)

Muscular discomfort and tenderness are prevalent, notably affecting the calf muscles and lower back. An indicative sign for identifying leptospirosis is conjunctival suffusion, marked by the dilation of conjunctival vessels without purulent discharge, a feature commonly observed in leptospirosis but infrequently present in other infectious diseases. Additional ocular observations typically encompass subconjunctival hemorrhages and jaundice (Fraga et al., 2024)

Severe leptospirosis is characterized by dysfunction of multiple organs including the liver, kidneys, lungs, and brain. The amalgamation of jaundice and renal failure, referred to as Weil's disease, was initially documented in 1886 and continues to be one of the most readily identifiable clinical manifestations of leptospirosis (Haake & Levett, 2014)

Following adequate medical intervention, patients often encounter post-recovery symptoms, prominently including fatigue, headaches, weakness, paralysis, ocular manifestations, mood fluctuations, and depression. These indicators signify the lingering presence of leptospires in the patients, seemingly shielded by the host's immune response (Samrot et al., 2021)

### **Diagnosis**

Diagnostic tests for leptospirosis can be broadly utilized for both humans and animals, even though the objectives and methodologies may vary. Employing a comprehensive approach to leptospirosis diagnosis that incorporates various test methods enhances the accuracy of diagnostics (Sykes et al., 2022)

During the initial days of illness, a dependable laboratory diagnosis of leptospirosis involves the detection of *Leptospira* in biological fluids. Historically, this was accomplished through culture, utilizing the distinctive EMJH culture medium (Ellinghausen and McCullough, modified by Johnson and Harris), with subsequent examination of cultures through dark-field microscopy for up to 14 weeks (Goarant, 2016). However, the culture of leptospires does not contribute to an early diagnosis due to their slow growth (Yang et al., 2019)

Nucleic acid tests, such as the polymerase chain reaction (PCR) and antigen detection tests, can detect leptospiral DNA or antigens directly in blood, urine, or cerebrospinal fluid in the first days of the disease and are thus capable of yielding an early diagnosis. The introduction of real-time polymerase chain reaction (PCR) has expedited the processing time and enhanced both sensitivity and specificity (Goarant, 2016), (Yang et al., 2019)

Several days post-infection, the individual's immune system initiates a response, which may be observable in laboratory tests. The established serological method is the microscopic agglutination test (MAT), evaluating the patient's serum for its ability to agglutinate live *Leptospira* across various strains. MAT positivity typically occurs a week after the onset of the disease, notably later than immunoglobulin M (IgM). While MAT has been the predominant and widely employed method for diagnosing leptospirosis, it heavily depends on live cultures (Goarant, 2016)

The current reference standard for the diagnosis of leptospirosis is based on antibody detection by the microscopic agglutination test (MAT), with or without culture. Since anti-*Leptospira* antibodies appear only in the later stage of the disease, MAT and other serological tests, such as the immunoglobulin M (IgM) enzyme-linked immunosorbent assay (ELISA), are impractical in establishing an early diagnosis (Goarant, 2016)

## Management

Patients with suspected or confirmed leptospirosis with mild clinical features and no comorbidities may be managed as outpatients with regular follow up for identification of complications. Patients who have clinical features of organ involvement, or those who have comorbidities, must be admitted for in-hospital care (Rajapakse, 2022)

Early initiation of antibiotic treatment is likely to improve outcome. Adult outpatients with early disease should receive either doxycycline 100 mg orally twice per day For 7 days or azithromycin 500 mg orally once per day (Charan, Saxena, & Mulla, 2012), (Fraga et al., 2024), (Rajapakse, 2022)

Do the following investigations: complete blood count, C-reactive protein, creatinine, urea, electrolytes, liver transaminases. bilirubin, urine full report, Monitor urine output. Admit to hospital if there is jaundice, reduction in urine output, hematuria, cough, or difficulty breathing, or if clinically very ill (Rajapakse, 2022)

A shorter duration of the disease has been associated with the initiation of antimicrobial treatment following the onset of clinical signs. The WHO also suggests promptly initiating presumptive antibiotic treatment, emphasizing the empirical advantage of its commencement before the fifth day of the illness (Fraga et al., 2024)

Treatment for individuals with leptospirosis severe enough to require hospitalization typically involves intravenous administration of penicillin (1.5 million units IV every 6 h), ampicillin (0.5–1 g IV every 6 h), ceftriaxone (1 g IV every 24 h), or cefotaxime (1 g IV every 6 h). Ceftriaxone has demonstrated noninferiority to penicillin in treating severe leptospirosis and, with the added benefit of once-daily dosing, provides an alternative to intramuscular administration in situations where hospitalization is not feasible (Haake & Levett, 2014)

## Prevention

Strategies for prevention of leptospirosis are based on awareness of leptospirosis epidemiology and transmission mechanisms. Once the local epidemiology and transmission risks have been defined, it is possible to greatly mitigate risk by taking steps to reduce exposure and implement protective measures, immunization, and pre- or postexposure chemoprophylaxis (Haake & Levett, 2014)

- Prevention of leptospirosis is through avoidance of potential exposure to infection, and administration of pharmacological prophylaxis to individuals at high risk. It is advisable to use a weekly dose of 200 mg doxycycline starting one week before potential exposure and continuing throughout the exposure period. Doxycycline has been investigated for post-exposure prophylaxis in local populations following substantial rainfall in endemic regions. One of these studies revealed a decrease in the occurrence of symptomatic disease with post-exposure doxycycline prophylaxis. While alternatives like azithromycin or amoxicillin have not undergone similar studies, they may be contemplated in pregnant women, children, and individuals prone to photosensitivity (Haake & Levett, 2014), (Rajapakse, 2022)

- Typically, the administration of inactivated whole-cell vaccines to humans has been limited to those engaged in high-risk occupations or in reaction to floods and outbreaks (Haake & Levett, 2014). Human vaccination against leptospirosis is certainly a major goal of the research community. However, progress in this field has been extremely slow and the studies of vaccine safety are still in progress (Fraga et al., 2024)

### **Conclusion**

Leptospirosis is a zoonotic disease caused by a leptospira infection that is transmitted through contact with rodent urine, water, or soil contaminated by abrasions of the skin or mucous membranes. Leptospira infection enters the body through scratches on the skin, mucous membranes, conjunctiva, and oral route. Clinical manifestations may include fever, nausea, vomiting, weakness, muscle aches, headaches, and may cause severity such as functional organ failure.

Leptospirosis is one of the most important zoonoses in the world and is a major public health problem in many countries. This disease occurs throughout the world, but the incidence rate is highest in tropical areas. Poor living conditions and seasonal rainfall in tropical areas are commonly associated with this disease. The gold standard test for leptospirosis is the microscopic agglutination test. Early diagnosis and timely treatment will prevent a serious course of the disease. The therapy is administered medically with antibiotics and support. Early prevention by those with risk factors for infection is expected to protect against leptospirosis attacks.

## References

- Bradley, E. A., & Lockaby, G. (2023). Leptospirosis and the environment: A review and future directions. *Pathogens*, 12(9), 1167.
- Charan, J., Saxena, D., & Mulla, S. (2012). Prophylaxis and treatment for leptospirosis: where are the evidences? *National Journal of Physiology, Pharmacy and Pharmacology*, 2(2), 78.
- De Vries, S. G., Visser, B. J., Stoney, R. J., Wagenaar, J. F. P., Bottieau, E., Chen, L. H., Leder, K. (2018). Leptospirosis among returned travelers: a GeoSentinel site survey and multicenter analysis 1997–2016. *The American Journal of Tropical Medicine and Hygiene*, 99(1), 127.
- Dreyfus, A., Ruf, M.-T., Goris, M., Poppert, S., Mayer-Scholl, A., Loosli, N., ... Stenos, J. (2022). Comparison of the Serion IgM ELISA and Microscopic Agglutination Test for diagnosis of *Leptospira* spp. infections in sera from different geographical origins and estimation of *Leptospira* seroprevalence in the Wiwa indigenous population from Colombia. *PLOS Neglected Tropical Diseases*, 16(6), e0009876.
- Fraga, T. R., Carvalho, E., Isaac, L., & Barbosa, A. S. (2024). *Leptospira* and leptospirosis. In *Molecular medical microbiology* (pp. 1849–1871). Elsevier.
- Goarant, C. (2016). Leptospirosis: risk factors and management challenges in developing countries. *Research and Reports in Tropical Medicine*, 49–62.
- Haake, D. A., & Levett, P. N. (2014). Leptospirosis in humans. *Leptospira and Leptospirosis*, 65–97.
- Li, D., Liang, H., Yi, R., Xiao, Q., Zhu, Y., Chang, Q., Liu, T. (2022). Clinical characteristics and prognosis of patient with leptospirosis: A multicenter retrospective analysis in south of China. *Frontiers in Cellular and Infection Microbiology*, 12, 1014530.
- Limothai, U., Lumlertgul, N., Sirivongrangson, P., Kulvichit, W., Tachaboon, S., Dinhuzen, J., Praditpornsilpa, K. (2021). The role of leptospiremia and specific immune response in severe leptospirosis. *Scientific Reports*, 11(1), 14630.
- Mohammed, H., Nozha, C., Hakim, K., Abdelaziz, F., & Reikia, B. (2011). *Leptospira*: morphology, classification and pathogenesis. *J Bacteriol Parasitol*, 2(06).
- Prabhu, N., Natarajaseenivasan, K., Uma, A., Thirumalaikolundusubramanian, P., & Joseph, P. I. D. (2014). Leptospirosis now: epidemiology, progress, challenges and research gaps. *Elix Hum Physiol*, 67, 21173–21179.
- Rajapakse, S. (2022). Leptospirosis: clinical aspects. *Clinical Medicine*, 22(1), 14.
- Rampengan, N. H. (2016). (Peer Review) Leptospirosis.
- Samrot, A. V, Sean, T. C., Bhavya, K. S., Sahithya, C. S., Chan-Drasekaran, S., Palanisamy, R., Mok, P. L. (2021). Leptospiral infection, pathogenesis and its diagnosis—A review. *Pathogens*, 10(2), 145.
- Sykes, J. E., Reagan, K. L., Nally, J. E., Galloway, R. L., & Haake, D. A. (2022). Role of diagnostics in epidemiology, management, surveillance, and control of leptospirosis. *Pathogens*, 11(4), 395.
- Yang, B., de Vries, S. G., Ahmed, A., Visser, B. J., Nagel, I. M., Spijker, R., Leeftang, M. M. G. (2019). Nucleic acid and antigen detection tests for leptospirosis. *Cochrane Database of Systematic Reviews*, (8).



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