Review Article

Journal of Advanced Veterinary Research
(2024) Volume 14, Issue 6, 1065-1071

Deciphering leptospirosis: Insights into an emerging global threat

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ARTICLE INFO

Recieved: 31 March 2024

Accepted: 19 May 2024

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Keywords:

Infectious disease, *Leptospira*, Leptospirosis, Public health, Water.

ABSTRACT

Leptospirosis is caused by bacteria that are members of the *Leptospira* genus. This illness can occur in a variety of environments, although it is more prevalent in tropical regions where humidity and wetness greatly aid in its spread. Geographically broad, leptospirosis primarily affects tropical, temperate, and subtropical regions. Bacteria can enter the body through the vaginal system, mucosa, conjunctiva, and tiny abrasions. Hazardous germs are released into the urine when the bacteria settle in the complex kidney pathways. Leptospirosis symptoms are similar to those of other diseases, making diagnosis challenging. The majority of leptospirosis patients are resolved without problems. Laboratory techniques are used to research leptospirosis in humans and animals. Humans are classified as accidental hosts because they have had direct or indirect interaction with leptospirosis-infected animals. Leptospirosis infection can occur in at-risk groups who work in contaminated environments or animal shelters, such as abattoir and sewer workers, coal mines, plumbers, salver workers, agricultural workers, veterinarians, military personnel, abattoir employees, animals, meat handlers, and fishing industry workers. Antimicrobial therapy is one way to treat leptospirosis. Among the antibiotics are doxycycline, amoxicillin, ceftriaxone, ampicillin, penicillin, and erythromycin. Reducing the incidence of leptospirosis in domestic and wild animals can help manage the disease in people. Leptospirosis in wild animals is difficult to control, but in domesticated animals, vaccinations using inactivated whole cells or outer membrane preparations can effectively manage the disease.

Introduction

One of the most significant zoonotic infectious diseases in the world is leptospirosis. This disease mostly affects people with little resources, leading to high rates of morbidity and mortality (Costa *et al.*, 2015). An estimated 60,000 people die, and one million cases are reported each year from this illness, translating into a 6.85% case fatality ratio (Smith *et al.*, 2019). Numerous leptospirosis epidemics have shaken various regions of the world in recent years. The disease has since been recognized as a major outbreak that has lately spread to various countries as a result of the EcoChallenge Sabah 2000 competition in Malaysia (Sejvar *et al.*, 2003), as well as to India (Gupta *et al.*, 2023), China (Li *et al.*, 2022), Nicaragua (Schneider *et al.*, 2012), Southeast Asia (Cosson *et al.*, 2014), Brazil (Galan *et al.*, 2021), Africa (Gizamba and Mugisha, 2023), and the United States (Browne *et al.*, 2023). Leptospirosis is becoming more commonplace worldwide, particularly in underdeveloped nations.

Leptospirosis is caused by bacteria that are members of the *Leptospira* genus (Wilkinson *et al.*, 2021). There are two species in the *Leptospira* genus: *Leptospira biflexa* is non-pathogenic and *Leptospira interrogans* is a pathogenic species that causes leptospirosis (Yang *et al.*, 2023). Despite being one of the most common bacterial infections in the world, leptospirosis is categorized as a neglected tropical disease because cases are infrequently documented (Mwachui *et al.*, 2015). This illness can occur in a variety of environments, although it is more prevalent in tropical regions where humidity and wetness greatly aid in its spread (Md-Lasim *et al.*, 2021). Humans and several vertebrate animal species are susceptible to leptospirosis. Humans are thought to be incidental hosts of *Leptospira*, while animals are thought to be reservoir hosts of the parasite because human infection is brought on by exposure to tainted water (Sykes *et al.*, 2022).

Due to their frequent interaction with animals or water, some human vocations are linked to an increased risk of leptospirosis, including farmers, veterinarians, livestock breeders, and military personnel (Bradley and Lockaby, 2023). *Leptospira* infections linked to travel and leisure have been identified as potential causes of infection in affluent nations (Lau *et al.*, 2010). Activities that include the water, such swimming, canoeing, kayaking, and fishing, are responsible for many leptospirosis cases (Chiani *et al.*, 2023). Leptospirosis is linked to a wide range of clinical symptoms, such as meningitis, respiratory distress, pulmonary bleeding, and renal failure (Pongpan *et al.*, 2023). The availability of samples and the stage of the disease are used to diagnose leptospirosis. *Leptospira* can be found in laboratories using microscope examination, culture, serology, molecular techniques, and animal inoculation (Budihal and Perwez, 2014).

The germs known as *Leptospira* can live for weeks in the environment after colonizing the kidneys of diseased mammals and being expelled in their urine (Thibeaux *et al.*, 2020). Humans can contract the disease by coming into close contact with rodents, wildlife, livestock, pets, or by

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contaminating water and soil with the urine of infected animals. These bacteria most often enter the human body through mucous membranes (conjunctiva and oral mucosa), abrasions, and wounds; they most likely cannot pass through undamaged skin (De Brito *et al*., 2018). The interactions between people, animals, and the environment determine the risk factors for infection. Leptospirosis control efforts are focused on reducing the incidence of clinical illness through coordinated efforts to break the chain of transmission (Bradley and Lockaby, 2023).

Leptospirosis is classified as a "re-emerging disease" globally, meaning that although it seldom manifests, when it does, it can result in unusual outcomes (Lim, 2011). The driving factors for the transmission of this disease are caused by sociodemographic, climate, and environmental factors (Rahelinirina *et al*., 2019). Leptospirosis epidemics have recently been linked to several factors, including population increase, urbanization, climate change, flooding, and intensified agricultural practices to fulfill rising food demand (Baharom *et al*., 2023). The purpose of this review article was to explain the etiology, history, epidemiology, pathogenesis, clinical manifestations, diagnosis, transmission, risk factors, public health importance, economic impact, treatment and control of leptospirosis.

Etiology

Leptospira is the genus of Gram-negative spirochetal bacteria that cause leptospirosis (Samrot *et al*., 2021). This bacterium is elongated, helically coiled, aerobic, motile, and has a form resembling a "question mark" or hook that sets it apart morphologically from other spirochetes (Nakamura, 2022). Bacteria vary in size from 6 to 20 µm in length and approximately 0.1 µm in thickness. The optimal growth conditions for *Leptospira* are 28-30 °C and a pH of 7-8 (Tahara *et al*., 2018). The genus *Leptospira* was separated into two species: non-pathogenic saprophytic serovars found in *Leptospira biflexa* and pathogenic serovars found in *Leptospira interrogans* (Benacer *et al*., 2013). All serovars of *Leptospira interrogans* sensu lato and *Leptospira biflexa* sensu lato are included in this genetic classification, which has largely superseded the previous phenotypic classification (Sykes *et al*., 2022). Sensu lato is a Latin phrase that means "in a broad sense" and is frequently used taxonomically to denote a species complex.

This bacterium can live for days in fresh water and neutral or slightly alkaline damp soil (Md-Lasim *et al*., 2021). *Leptospira* cannot be seen under a light microscope due to their extremely low color. Phase contrast or dark field microscopy can be used to visualize these microorganisms (Vieira and Nascimento, 2020). The best staining method for these bacteria is silver impregnation (Rodríguez *et al*., 2013). When examined under an electron microscope, *Leptospira* have a cylindrical shape and are helically coiled around the force axis, with a diameter of 0.01–0.02 µm. They are made up of two axial filaments, which are the modified flagellum in spirochetal form, that are inserted sub-terminally at the tip of the body cells, with their free ends pointing in the direction of the cell center (Samrot *et al*., 2021).

There are now 22 species of *Leptospira* known to exist, at least 10 of which are harmful. Additionally, there are five species with unknown pathogenicity and seven species of saprophytes (Rajapakse, 2022). It's possible that in the future, more species will be described. There are several serovars of pathogenic *Leptospira* species, and each has a unique antigenic makeup. Currently, 26 serogroups comprising over 260 pathogenic serovars have been found (Harran *et al*., 2023). Based on the identification of antigenic features, this serological categorization is superior for epidemiological research and is more helpful in diagnosis.

Any mammal could become infected with *Leptospira*. Many serovars have primary (definitive) hosts or carriers, such as dogs for *L. interrogans* serovar Canicola (Piredda *et al*., 2022), cattle and sheep for *L. interrogans* serovar Hardjo (Salgado *et al*., 2015), pigs for *L. interrogans* serovar Pomona and *L. interrogans* serovar Brat islava (Bertasio *et al*., 2020; de Araújo *et al*., 2023), and mice for *L. interrogans* serovar Ictero haemorrhagiae and *L. interrogans* serovar Copenhageni (Vernel-Pauillac *et al*., 2021; Shetty *et al*., 2022). This has a greater impact on the bacterial spread in the environment than incidental hosts, such as people who are ill and less likely to transfer the infection. While animals infected with host-unadapted serovars are predicted to exhibit more severe clinical symptoms, definitive hosts are typically infected at a young age and typically exhibit minimal clinical disease (Rahman *et al*., 2020).

History

A common zoonotic illness called leptospirosis is brought on by infection with harmful *Leptospira* species (Sun *et al*., 2020). *Leptospira* can cause a wide range of illnesses in humans, from asymptomatic infections to severe multiorgan infection syndromes that have significant fatality rates. Adolf Weil initially described this illness, icteric leptospirosis with renal failure, in Heidelberg in 1886 (Afzal *et al*., 2020). Nonetheless, a comparable illness affecting sewage workers had been documented a few years prior (Rajapakse, 2022). Recent reviews have examined earlier accounts of illnesses that most likely correspond to leptospirosis. In ancient China, leptospirosis was undoubtedly recognized as a work-related risk when harvesting rice (Kim, 2019). This illness is known as akiyami or autumn fever in Japanese (Alexopoulou *et al*., 2024). In retrospect, it is evident that a distinct image of *Leptospira* jaundice first appeared in the early 1800s, several years before to Adolf Weil's description. There is a theory that suggests *Rattus norvegicus*'s westward range extension from Eurasia in the 18th century brought *L. interrogans* serovar icterohaemorrhagiae to Western Europe (Boey *et al*., 2019).

Leptospirosis's etiology was separately established in Germany and Japan in 1915. Inada and Ido in Japan found spirochetes and particular antibodies in the blood of Japanese miners afflicted with infectious jaundice, while two German medical groups examined German soldiers in the trenches of northeastern France who were afflicted with "French disease" (Levett, 2001). The two groups of German doctors, the first being Uhlenhuth and Fromme and the second being Hubener and Reiter, detected spirochetes in the blood of guinea pigs inoculated with the blood of infected soldiers (Levett, 2001). Unfortunately, these two groups of German doctors were so engrossed in the discussion about priorities that they failed to notice that Inada and Ido had published a study in both German and English eight months after their own. Following the release of Inada's research in Europe, leptospirosis was confirmed to have occurred on both sides of the Western Front.

In 1907, Stimson used silver staining to demonstrate that spirochete clusters were present in the renal tubules of a patient who had supposedly succumbed to yellow fever (Cerqueira and Picardeau, 2009). The resemblance to a question mark led Stimson to call it *Spirochaeta interrogans*, because spirochetes have hooked ends. Regretfully, this observation was disregarded for a long time. Work involving water was identified as a risk factor early on. While the possibility of *Leptospira* disease in dogs was known, it took some time to distinguish between canicola and *L. interrogans* serovar icterohaemorrhagiae infections in dogs. The role of rats as a source of infection in humans was identified in 1917 (de Oliveira *et al*., 2022). It took several years before leptospirosis in livestock was identified. Several monographs contain a wealth of information about the early stages of the discovery of leptospirosis.

Epidemiology

Geographically broad, leptospirosis primarily affects tropical, temperate, and subtropical regions. However, tropical regions like India (Gupta *et al*., 2023), China (Li *et al*., 2022), Nicaragua (Schneider *et al*., 2012), Southeast Asia (Cosson *et al*., 2014), Brazil (Galan *et al*., 2021), Africa (Gizamba and Mugisha, 2023), and the United States (Browne *et al*., 2023). *Leptospira* infections are prevalent in impoverished urban and semi-urban populations as well as rural farming groups, particularly affecting young men (Haake and Levett, 2015). Those who work with rats, farmers, livestock breeders, and residents of unsanitary locations are the most vulnerable populations to contracting this disease (Bradley and Lockaby, 2023). Urban epidemics frequently happen in areas with poor sanitation and a high breeding population of rats (Cerqueira and Picardeau, 2009).

Leptospirosis cases have significantly increased in emerging nations despite the disease's declining incidence rate in industrialized nations (Douchet *et al*., 2022). The incidence of leptospirosis is rising quickly in some nations, including Thailand, where it is being monitored (Suwanpakdee *et al*., 2015). There have been several documented outbreaks of leptospirosis. Although the incidence rate is largely steady worldwide, there are occasionally huge outbreaks in specific countries, some of which are connected to natural disasters like floods (Rehan *et al*., 2023). As a result, several post-flood outbreaks have happened in emerging nations with high population densities, such as Brazil, India, and the Philippines (Naing *et al*., 2019). This illness affects people's health worldwide and is thought to be detrimental to the global economy. Leptospirosis is estimated to infect one million people worldwide and cause the death of about 60,000 individuals annually (Smith *et al*., 2019).

Animals with *Leptospira* infection may be exposed to the bacteria either directly or indirectly through their urine or kidneys. Leptospirosis epidemiology revolves around kidney carriers, which are animals whose kidney tubules have been colonized by *Leptospira* (Chou *et al*., 2023). The bacteria are then expelled through urine and spread to other areas of the environment. However, tropical regions experience its expansion more frequently than nations with temperate climates. This is mostly because *Leptospira* can survive longer in warm, humid conditions. Thus, there are sizable regions where this disease is endemic in China, Oceania, Southeast Asia, the Caribbean, Africa, and America (de Vries *et al*., 2018). In this area, leptospirosis is irregular throughout the year, peaking in the summer months. Significant outbreaks have been documented after monsoons and extremely wet spells. Leptospirosis is endemic in Kerala, Tamil Nadu, and the Andaman Islands in India (Antima and Banerjee, 2023). However, with improved means of detecting this illness, reports of it have been made in nearly every region of India.

Pathogenesis

Bacteria can enter the body through the vaginal system, mucosa, conjunctiva, and tiny abrasions. Numerous chemotactic interactions and transmembrane pathways are needed for this. Hazardous germs are released into the urine when the bacteria settle in the complex kidney pathways (Barragan *et al*., 2017). There is a few-week to several-month period of shedding. Higher concentrations of bacteria in the blood and tissues cause tissue damage because the pathogen produces endotoxins. The bacteria also cause hemolysis, which causes blood cell damage (Gonçalves-de-Albuquerque *et al*., 2023). Ischemia and other problems result from damaged endothelial cells. A humoral response that results in neutrophil and macrophage phagocytosis has been found to be active during the first week of infection, even though the precise molecular basis of virulence is yet unknown (Bonhomme *et al*., 2020).

The primary injury is endothelial degradation in small blood vessels, which results in localized organ ischemia and causes meningitis, myositis, renal tubular necrosis, lung and hepatocellular damage, and placentitis (Sato and Coburn, 2017). The incubation period is determined by the infective dose, the organism's growth rate, toxicity, and immunity. Using a polyvalent analysis technique improves *Leptospira* pathogenicity characterization by lowering the uncertainties associated with individual testing, especially when phenotypic analysis is not entirely correlated with genotypic speciation (Samrot *et al*., 2021).

Given that nonpathogenic *Leptospira* do not enter cells with the same lethality as pathogenic *Leptospira*, it is possible that the invasive capacity of *Leptospira* is related to its pathogenicity (Ko *et al*., 2009). Damage to the endothelium of tiny arteries can cause ischemia damage to the renal parenchyma; in many animals, involvement can be chronic, resulting in the removal of vast numbers of *Leptospira* in urine (Sykes *et al*., 2023). It is a leading cause of contamination and infection in humans and other species. Bacteria can be present in cervical and vaginal secretions, sperm, breast milk, tears, and urine, and they are known to cause disease when in touch with humans (Cilia *et al*., 2020).

Clinical manifestations

The clinical symptoms of leptospirosis are highly varied. The average incubation period is 7-14 days, however it can range from 2 days to one month. Leptospirosis symptoms are similar to those of other diseases, making diagnosis challenging. The majority of leptospirosis patients are resolved without problems (Md-Lasim *et al*., 2021). However, misdiagnoses have resulted in leptospirosis becoming an infrequently reported disease. Leptospirosis in humans is divided into two phases: septicemia and immunity (De Brito *et al*., 2018). The acute or septicemic phase can last up to a week and is distinguished by the presence of *Leptospira* in the blood and cerebrospinal fluid. Symptoms such as fever, myalgia, chills, and headaches develop during this phase (Liu *et al*., 2024). The septicemia phase is followed by an immunological or delayed phase, which is characterised by antibody synthesis and the presence of *Leptospira* in the urine. At this stage, the disease spreads from the blood vessels to the body's important organs (Chancharoenthana *et al*., 2022). At this stage, the condition might be classified as anicteric or icteric. Anicteric leptospirosis is a milder variant that affects 90% of patients (Erdinc *et al*., 2006). Weil's disease, or icteric leptospirosis, is a severe form of the disease that affects 5-10% of patients and has a fatality rate of 5-40% (Ansari *et al*., 2023). It is distinguished by the involvement of several of the body's essential organs.

Leptospirosis develops swiftly and is characterised by a fever ranging from 100 to 105°F, along with persistent headaches. Pain is also felt in the lower body, specifically in the thighs and calves, but other regions of the body are also affected (Haake and Levett, 2015). Anorexia, nausea, vomiting, and constipation or diarrhoea are other symptoms of anicteric leptospirosis (Gasem *et al*., 2020). A person may have hallucinations and feel bewildered. Younger people may also exhibit symptoms of aseptic meningitis (Abdelrahim *et al*., 2021). Some people may develop gastroenteritis and stomach pain (Thalji *et al*., 2023). Encephalitis and uveitis have also been documented in some instances (Rajapakse, 2022). Conjunctival suffusion was also noted during the initial period in some instances, although there was no inflammatory discharge, ruling out genuine conjunctivitis (Arrieta-Bechara and Carrascal-Maldonado, 2022). Recently, anicteric leptospirosis has been linked to hemorrhagic pneumonia and acute respiratory syndrome (Chaikajornwat *et al*., 2020). Although the mortality rate for anicteric leptospirosis is nearly low, deaths have been reported in China (Becirovic *et al*., 2020).

Icteric leptospirosis (Weil's illness) affects a small percentage of persons. *Leptospira* serovar Icterohaemorrhagiae is responsible for the vast majority of icteric leptospirosis cases (Maroun *et al*., 2011). Jaundice is the most prevalent symptom, which can develop early in the disease or later in its progression. Hepatocellular necrosis develops, as does an increase in serum bilirubin levels (Małecki *et al*., 2018). Mild elevations in transaminases and alkaline phosphatase may occur. Death can also occur in the later stages, in the form of icteric leptospirosis caused by kidney failure (Ghasemian *et al*., 2016). The majority of people with renal failure have liver involvement. Cardiac involvement has also been reported in the form of myocarditis and pericarditis (Zechel *et al*., 2021). There have also been reports of pulmonary haemorrhage associated with leptospirosis (Gulati and Gulati, 2012). In most cases, leptospirosis infection leads to miscarriage in pregnant women (Selvarajah *et al*., 2021).

Fever and anorexia in cows are associated with a quick drop in milk production and atypical mastitis (Ibrahim *et al*., 2022). Pregnant cows are aborted if their placenta is retained. In addition, mild jaundice and severe anaemia occur, as do liver enlargement and renal edoema (Prajapati *et al.*, 2018). Hemoglobinuria, dyspnea, meningitis, fast dehydration, and mortality are all possible outcomes. Horses get conjunctivitis and recurrent ophthalmia (Wollanke *et al.*, 2022). Subclinical infections in pigs are prevalent, however they can result in abortions and the birth of weak piglets (Azócar-Aedo, 2023). Gastroenteritis, jaundice, and nephritis can all occur in dogs and cats (Klaasen and Adler, 2015; Mazzotta *et al.*, 2023).

Diagnosis

Laboratory techniques are used to research leptospirosis in humans and animals. The methods used involves isolating the causal agent and identifying *Leptospira* species antigens in tissues and body fluids using silver staining, immunochemistry, immunoperoxidase staining, immunofluorescence staining, and other Polymerase Chain Reaction (PCR) methods (Brown *et al.*, 2003). *Leptospira* in blood or urine has been detected directly using microscopic investigation (Budihal and Perwez, 2014). However, artefacts are frequently misidentified as *Leptospira*, and this approach has limited sensitivity and specificity.

Leptospira can be detected using a variety of polymerase chain reaction (PCR) techniques, but only a small number of these have been investigated in clinical trials. Additionally, multicenter studies examining a range of molecular diagnostic approaches have not been conducted (Ahmed *et al.*, 2012). The ability to confirm the diagnosis early in acute (leptospiremic) disease, prior to the development of immunoglobulin M (IgM) antibodies, when treatment is most likely to be effective, is the primary benefit of PCR (Mullan and Panwala, 2016). In severe situations where mortality occurs before seroconversion, PCR may have a high diagnostic value. DNA *Leptospira* was amplified from serum, urine, aqueous humour, and several autopsy tissues. Serum is the most appropriate specimen for early diagnosis (Al-Orry *et al.*, 2016). Urine from critically ill patients is frequently extremely concentrated and includes potent inhibitory action.

Blood, cerebrospinal fluid, and peritoneal dialysis fluid can all include *Leptospira* during the first ten days of an infection (Thalji *et al.*, 2023). Before starting antibiotic treatment, specimens should be taken when the patient has a temperature. At the bedside, inoculate one or two drops of blood straight into the culture media. *Leptospira* have been shown to survive many days in commercial blood culture media (Tantibhedhyangkul *et al.*, 2020). One week after being ill, urine can be cultured. As *Leptospira* cannot survive in an acidic environment, specimens should be collected aseptically into sterile containers free of preservatives and processed as quickly as possible for the best results. Cultures are carried out on commercially available albumin-polysorbate media such as Ellinghausen-McCullough-Johnson-Harris (EMJH) (Hornsby *et al.*, 2020). Primary culture is carried out in a semisolid medium with 5-fluorouracil as a selective agent. Because early growth might be rather slow, cultures are incubated at 30°C for several weeks. Molecular techniques like pulsed-field gel electrophoresis or conventional serological methods are used to identify isolated *Leptospira* to the serovar level (Mahtab *et al.*, 2019).

Leptospirosis is investigated indirectly through the identification of particular serum antibodies. These methods can be used to detect serum antibodies without distinguishing between serovars, such as various ELISA tests, indirect immunofluorescence, and spot agglutination tests, or to reliably identify the infecting serovar, such as the microscopic agglutination test (MAT) (Budihal and Perwez, 2014). The microscopic agglutination test (MAT) is considered the 'gold standard' serological test, despite the fact that it needs the laboratory maintenance of some *Leptospira* serovars (Goris and Hartskeerl, 2014). In addition, experts must read the outcomes of this test. The IgM ELISA test is quick and simple to perform, and it is widely used to diagnose acute leptospirosis (Dreyfus *et al.*, 2022). Except for isolation, none of the currently known diagnostic procedures are appropriate for investigating microbial pathogenicity (structure, products, and biochemical properties). Isolation is also required to appropriately classify agents into serogroups.

Transmission

Humans are classified as accidental hosts because they have had direct or indirect interaction with leptospirosis-infected animals (Evangelista and Coburn, 2010). Animals that become leptospirosis hosts can serve as carriers or reservoir hosts, the primary source of infection (Bradley and Lockaby, 2023). Although the presence of carrier animals is thought to be significant in leptospirosis transmission, it can arise via a variety of environmental factors. *Leptospira* are present everywhere in nature, but their main home is the renal system of host animals (Samrot *et al.*, 2021). Large rodents, animals, and marsupials can serve as carriers or reservoirs for leptospirosis (Medeiros *et al.*, 2020). *Leptospira* serovar Icterohaemorrhagiae has been linked to rodents (Boey *et al.*, 2019). Other serovars have been linked to other mammalian hosts. Cattle, for example, can become infected with Hardjobovis, Bratislava, Pomona, and Grippotyphosa, however more serovars have been recorded (Orjuela *et al.*, 2022). Pigs are frequently infected with serovars Pomona, Tarassovi, Bratislava, Grippotyphosa, Sejroe, and Icterohaemorrhagiae (Santos *et al.*, 2023), whilst Canicola and Icterohaemorrhagiae have been linked to infections in dogs (Santos *et al.*, 2021). Additionally, leptospirosis has been documented in a number of natural species, such as tiny insects, possums, deer, bats, and mongooses (Mgode *et al.*, 2021).

Leptospirosis can spread by direct or indirect contact. Direct transmission of *Leptospira* occurs through the tissue, bodily fluids, or urine of disease-carrying animals that are either acutely sick or asymptomatic (De Brito *et al.*, 2018). The most common method of entrance is through the skin. Bacteria can enter the blood or lymphatic system directly through the conjunctiva, or they can infiltrate the lungs via aerosol (Sun *et al.*, 2020). This disease in animals can spread transplacentally, hematogenously, through sexual contact, or by suckling from an infected mother (Samrot *et al.*, 2021). In animals, direct infection from mother to kid via the placenta has been observed, as has the presence of *Leptospira* in the genital tract. Meanwhile, the environment acts as an indirect transmission source (Thibeaux *et al.*, 2017).

Risk factor

Leptospirosis infection can occur in at-risk groups who work in contaminated environments or animal shelters, such as abattoir and sewer workers, coal mines, plumbers, agricultural workers, salver workers, veterinarians, military personnel, abattoir employees, meat handlers, and fishing industry workers (Md-Lasim *et al.*, 2021). Camping, fishing, hunting, and raising cattle all raise the risk of getting *Leptospira* (Guernier *et al.*, 2018). Aside from that, water sports such as canoeing, kayaking, swimming, and whitewater rafting provide a danger of transmitting leptospirosis (Walker, 2018). Men are diagnosed with leptospirosis at a higher rate than women, which has long been connected to men's overrepresentation in high-risk occupations (Mai *et al.*, 2022).

Leptospira can infect animals of all ages. However, leptospirosis is more common in young animals with higher morbidity (Tulu, 2020). Although leptospirosis affects practically all mammal species, including cattle, horses, sheep, dogs, goats, and pigs, the disease appears to be uncommon in cats (Azócar-Aedo, 2023). Specific management elements that increase the risk of infection include the inclusion of sick animals in herds, sharing pasture with infected animals, access to polluted water sources such as rivers, flood water, or drainage, and the purchase or loan of diseased male animals for natural insemination (Bradley and Lockaby, 2023).

Public health importance

Leptospirosis is a major threat to public health. *Leptospira* infections occur in natural rearing host populations via vertical and horizontal transmission, with rodents being the most important and widespread source of *Leptospira* infections (Boey *et al.*, 2019). Humans become infected with *Leptospira* largely through direct or indirect contact with infected animal urine (Haake and Levett, 2015). Other means of transmission include contact with infected animals and their bodily tissues, drinking contaminated groundwater, sexual intercourse, and trans-placental transmission (Wynwood *et al.*, 2014). The mortality rate for leptospirosis patients remains high due to diagnostic delays caused by a lack of infrastructure (Costa *et al.*, 2015).

The majority of leptospirosis patients are mild or asymptomatic. The overall case fatality rate is 1-5% (Smith *et al.*, 2019). Mortality rates vary by form and are higher among the elderly. The icteric type is rarely lethal. The icteric type, which affects 5-10% of all patients, has an overall mortality rate of 5-15%, with a fatality rate of 54% in severe cases involving the heart (Al Hariri *et al.*, 2022). The majority of people with kidney failure, liver disease, or anterior uveitis recover with normal kidney or liver function and vision (Ghasemian *et al.*, 2016). Individuals who have close contact with animals, agricultural workers, waste disposal personnel, and individuals who have come into touch with contaminated water should be made aware of the risk (Daud *et al.*, 2018). Infected animals should be treated, and there should be more awareness among at-risk communities (Goarant, 2016). As a recently emerging disease, its status requires serious consideration.

Economic impact

Depending on the animal species, the prevalence of animal illnesses recorded globally ranges from 2% to 46% (Allan *et al.*, 2015). There is no reliable method to determine the economic impact of animal infection due to the wide range of reported prevalence numbers and the influence of variables including climate, animal type, season, and research methodology (assaying serovars). When it leads to reproductive failure in animals that produce food, this disease becomes a significant economic issue (Selim *et al.*, 2024). Due to a decrease in milk and meat production, an infection of the reproductive system may trigger a "abortion storm" that results in significant financial losses (Sohm *et al.*, 2023). Since cattle and pigs are thought to be less resilient than small ruminants, these losses also seem to be more substantial in these animal species (Widiasih *et al.*, 2021).

Treatment

Leptospirosis in people should be treated as soon as possible to prevent serious consequences and possibly even death. Antimicrobial therapy is one way to treat leptospirosis. Among the antibiotics are doxycycline, ampicillin, amoxicillin, ceftriaxone, penicillin, and erythromycin (Hospenthal and Murray, 2003). Intravenous penicillin at a dose of 50,000–100,000 U/kg/day for seven to ten days is the recommended course of treatment for patients with severe leptospirosis infections (Charan *et al.*, 2013). Erythromycin, meantime, can be administered at 30–50 mg/kg/day in three to four doses over a period of seven to ten days to individuals who suffer from penicillin allergies (Moon *et al.*, 2006). Oral ampicillin (50-100 mg/kg/day) or amoxicillin (30-40 mg/kg/day) can be administered to the patient four times a day for seven to ten days in mild instances (Truccolo *et al.*, 2002). Doxycycline (2 mg/kg/dose) can be given twice daily for seven to ten days as a treatment for children over the age of eight (Sehgal *et al.*, 2000). Fever and most symptoms can be reduced with this medication. Dialysis treatment may be required for individuals with leptospirosis, and they should be closely monitored for any signs of renal failure (Chancharoenthana *et al.*, 2022).

The major objective of treating leptospirosis in animals is to contain the illness before the liver and kidneys sustain permanent damage. Antibiotic therapy is advised as soon as symptoms start to show up (Anugrah *et al.*, 2023). Because animals are usually treated only after the septicemia has stopped, treatment outcomes are frequently poor. Encouraging *Leptospira* carrier animals to dwell in groups safely is the second goal of treatment (Gomes-Solecki *et al.*, 2017). Other antibiotics like tetracycline, penicillin, ampicillin, doxycycline, streptomycin, and erythromycin are also used to treat leptospirosis (Chakraborty *et al.*, 2010).

The serovar may affect how well a treatment works. Blood transfusions, fluid treatment, and other forms of supportive care might also be required. Depending on the animal, this supportive care may be required; if the animal is seriously ill and in shock, fluid therapy may be needed (Monteiro *et al.*, 2021). On farms raising beef cattle, more abortions can be avoided by vaccinating all animals and treating them with antibiotics; in the case of dairy cattle, only diseased animals are typically treated because of the possible loss of milk sales (Mughini-Gras *et al.*, 2014).

Control

Reducing the incidence of leptospirosis in domestic and wild animals can help manage the disease in people. While there is limited control over leptospirosis in wild animals, vaccination with inactivated whole cells or outer membrane preparations can effectively manage the disease in domesticated animals (Wang *et al.*, 2007). There are leptospirosis vaccinations for dogs, cattle, and pigs (Orr *et al.*, 2022; Wilson-Welder *et al.*, 2021; Schommer *et al.*, 2021). Vaccines can prevent disease, but they cannot stop infection or organism shedding entirely. The vaccination only offers protection against the included serovar or closely related serovars, so immunity is essentially serovar specific (Bashiru and Bahaman, 2018). Antibiotic prophylaxis can also be used to stop illness in animals that have been exposed (Tabei *et al.*, 2022).

To mitigate the risk of leptospirosis transmission, measures such as improved hygiene, the use of slow-acting rodenticides to control rodent vectors, and avoiding contact with contaminated environments or infected wildlife, especially rodents, can all help lower the risk of infection (Khalil *et al.*, 2021). The key to preventing leptospirosis in people is the implementation of occupational hygiene practices for high-risk populations, which include the usage of waterproof shoes and gloves (Shafie *et al.*, 2021). Since drinking contaminated water has been related to multiple epidemics, it is advised that water be purified before consumption. Animals should not drink from or enter contaminated rivers (Wynwood *et al.*, 2014). Maintaining proper hygiene can lower the chance of infection in the cage and in the region where animals give birth (Goarant, 2016). It is advisable to choose replacement stock from animals free of leptospirosis. Before being reintegrated into the herd, animals that are not known to be *Leptospira*-free should undergo a 4-week quarantine and testing period (van den Brink *et al.*, 2023).

Conclusion

The bacteria *Leptospira* is the source of the zoonotic disease leptospirosis. Geographically broad, leptospirosis primarily affects tropical, temperate, and subtropical regions. Humans are classified as accidental hosts because they have had direct or indirect interaction with leptospirosis-infected animals. Antimicrobial therapy is one way to treat this illness. Reducing the incidence of leptospirosis in domestic and wild animals can help manage the disease in people.

Acknowledgments

This study was partly supported by the International Research Collaboration Top Over #500 funding from Lembaga Penelitian dan Pengabdian Masyarakat, Universitas Airlangga, Indonesia, in the fiscal year 2023.

Conflict of interest

The authors have declared no conflict of interest.

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