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Understanding Leptospirosis: Global Trends, Environmental Drivers, and Public Health Strategies

Shafraaz Khan, Mabel Vaniqi, Anjini Naicker, Emily-Ann Underwood, Shanon Shyna Prasad

Leptospirosis is an important re-emergent global zoonosis, affecting mainly tropical and subtropical climate zones. Leptospira spp. are primarily transmitted through the urine of infected animals, most notably rodents, and can result in a broad spectrum of clinical manifestations including mild flu-like symptoms to severe conditions like Weil's disease which is characterized by jaundice, renal failure or hemorrhage. Although leptospirosis is a treatable disease, underreporting of the low and middle-income countries usually occurs for many reasons including diagnostic difficulties and variations in clinical presentation. Cumulatively, leptospirosis causes about 1.03 million cases and 58,900 deaths globally each year with the highest morbidity in South & Southeast Asia followed by Oceania (i.e., Australasia) as well as the Caribbean. The disease is also considered environmentally related and its transmission can be enhanced by flooding due to the presence of large amounts of water which helps promote the survival of bacteria in soil and water. Climate change increases the danger in large part by causing more frequent extreme weather events. As a result, it is imperative that outbreaks are contained with preventive measures - such as vaccination campaigns or environmental management and education of the public. These vaccines, while effective, are limited by their short-lived protection and serovar specificity. The mainstay of treatment remains antibiotics such as doxycycline and penicillin with prophylactic antibiotics in high infection exposure settings. There are still many research questions that require answers regarding the environmental dynamics of Leptospira, as well as socio-economic factors affecting disease transmission. Effective leptospirosis control requires an integration of human, animal and environmental health approaches. We need better surveillance, diagnostics and public health in recognition of the fact that leptospirosis has to be anticipated by governments as a priority disease for which stress should not fall on susceptible populations. Continued work on leptospirosis prevention should address these gaps to form a more complete picture of the solutions that can be applied.

Introduction

Leptospirosis, a zoonotic disease caused by pathogenic spirochete bacteria of the genus Leptospira, is an underappreciated but relatively common cause of human morbidity and mortality worldwide. This re-emerging zoonosis primarily occurs in tropical and subtropical regions, but it has a wide distribution with outbreaks reported from different geographic areas worldwide, which shows its rapid epidemic potential. It is predominantly transmitted via the urine of infected animals, particularly rodents, and can result in a wide range of disease from asymptomatic or mild flu-like illness to severe forms like Weil's Disease characterized by jaundice, renal failure, hemorrhage, etc. Leptospirosis is a treatable disease but despite this, it is frequently underreported, especially in low and middle-income countries because of its diagnostic difficulties and variations among clinical presentations.

Leptospirosis is a major public health problem of global concern, with an estimated 1.03 million cases and 58,900 deaths occurring annually worldwide. Morbidity rates are highest in South and Southeast Asia, Oceania, and the Caribbean. Its environmental nature of disease means its transmission depends on certain climatic conditions—particularly flooding to create optimal living situations for the bacteria in soil and water. Climate change compounds these risks by intensifying the occurrence of adverse weather events and thereby increasing disease spread into environments in which it can be sustained. Thus, to prevent and control leptospirosis efficiently relies on precautions including vaccination plans, environment regulations, as well as awareness for the public.

The current vaccines are of poor efficacy due to partial protection and serovar specificity; while antibiotics such as doxycycline and penicillin are the first-line treatment for leptospirosis with prophylaxis advised in high-risk environments. Nevertheless, many questions remain to be answered on the biology of Leptospira in environmental compartments critical for temporal changes presented here as well as its interactions with variables determining disease transmission at a geographical level. An integrated strategy at the interface of human, animal, and environmental health is necessary to fill these gaps. Greater surveillance, diagnostics, and public health interventions are needed to be aware of the burden of disease represented by leptospirosis and determine whether it meets these criteria in vulnerable populations. The global nature of leptospirosis and the diverse socioeconomic impact it creates prompted us to review both factors determining its ecoepidemiogenesis and transmission. By integrating existing research and exposing important gaps in knowledge, this review aims to facilitate a comprehensive view of the leptospirosis landscape that informs improved public health strategies and interventions.

Epidemiology of Leptospirosis

As a zoonotic illness, leptospirosis can occur anywhere in the world, although it is more common in tropical and subtropical regions. It is one of the diseases that can be treated and reported. Leptospirosis is a disease brought on by a kind of bacteria known as Leptospira, which enters the environment through the urine of sick animals. The most common cause of sepsis in humans is rats. It is often believed that rivers provide a significant risk of disease transmission to people. It has a wide range of defenses that enable it to evade the human immune system and spread infection. The illness is incredibly widespread, with a high death rate ranging from asymptomatic to multi-organ infection. It is usually moderate but has the potential to be fatal; it is also most likely to be severe and can quickly lead to Weil's disease, a deadly alignment form. Weil's disease is the combination of jaundice, bleeding, and renal failure. It is the type of affection most closely linked to severe leptospirosis. It is getting worse all around the world and appears to be co-occurring with a number of unrelated illnesses, such as dengue and malaria (Devi et al., 2021).

A Gram-negative bacterium that is a member of the Leptospiraceae family, Leptospira genus, and Spirochaetaes phylum is the cause of the neglected and reemerging zoonoses leptospirosis. These microorganisms have a 0.1 \m diameter, 6–20 m length, and a pointed tip that is usually folded into a distinctive hook shape. They appear spiral-shaped. Because of its two periplasmic axial flagella, which are situated beneath the cell membrane, Leptospira is incredibly mobile and may execute flexion, translation, undulation, and rotations around its central axis. Despite being a microaerophile, Leptospira can thrive in fully aerobioses environments. It thrives best at 28 to 30 degrees Celsius, yet it can also grow at 37 degrees. The pH range of 7.2 to 7.4 is optimal (Cilia et al., 2021).

An annual morbidity of 14.8 cases per 100,000 people was predicted by modelling the worldwide burden of leptospirosis, with 1.03 million cases and 58,900 deaths annually attributable to the disease. It is common for prevalence to be endemic at different intensities, ranging from extremely low in temperate zones to hyperendemic in tropical locations with considerable seasonality. Latin America and the Caribbean reported 35.8% (114/318) of the world's outbreaks, followed by Southern Asia with 12.9% (41/318) and North America with 10.7% (34/318). Out of all the outbreaks that happened in Latin America while the Caribbean, 45.6% (52/114) were in the Caribbean, primarily in Cuba (42 outbreaks), and 45.6% (52/114) were in South America, primarily in Brazil (28 outbreaks). At the national level, the United States of America (10.4%; 33/318), India (11.9%; 38/318), and Cuba (13.2%; 42/318) reported the greatest numbers of leptospirosis outbreaks (Munoz-Zanzi et al. 2020).

A study of seven tropical islands whose health services regularly check for leptospirosis: Reunion, Guadeloupe, Tahiti, Fiji, New Caledonia, Mayotte, and Futuna. Futuna had an average incidence ± standard error of 68.9±72.8, by far the highest and most variable. Between 2006 and 2010, there were four consecutive peaks in the incidence that were greater than 250 cases per 100,000 people (Fig 2E). Reunion Island, on the other hand, had the least varied and lowest incidence (0.71±0.72). 2018 saw the highest occurrence (5.25) on this island. We saw the

lowest incidence in Guadeloupe (2.3±1.8) between 2014 and 2016, with significant incidence peaks occurring often around the rainy season in the other years. Despite having low average incidences (2.3±3 and 2.7±1.9, respectively), Fiji and Tahiti both saw outbreaks that were significantly higher than the baseline, with incidences of 20 in 2013 for Fiji and 12.6 in 2010 for Tahiti (Douchet et al. 2024).
New Caledonia experienced a seasonally high incidence of leptospirosis with 2.72±3.6 cases per 100,000 people, while Mayotte reported 3.8±5.4 cases per 100,000. These incidences were significantly leveled by interannual outbreaks, with New Caledonia and Mayotte experiencing six and four peaks respectively, each surpassing 17 cases per 100,000. The seasonal dynamics in Reunion Island, Tahiti, Fiji, New Caledonia, and Mayotte can be categorized into two phases. The first half of the year (January to June/July) saw high incidence rates, which then declined during the latter half (June/July to December). Similarly, in the northern hemisphere island of Guadeloupe, incidence peaked later in the year and lasted from March to November. Mayotte recorded the largest seasonal amplitude, with the highest incidence of 12.9 cases per 100,000 people in April, part of a brief three-month peak. In contrast, Reunion Island had the smallest seasonal amplitude with a maximum incidence of 1.5 cases. Tahiti's highest incidence occurred in February at 4.5 cases per 100,000, followed by a secondary peak of 3.3 cases three months later. Futuna did not display a distinct seasonal pattern, with incidence rates fluctuating throughout the year (Douchet et al. 2024).

There is evidence linking human exposure to leptospirosis with flooding events, leading to a common association between outbreaks of the disease and flooding. Flooding is a significant factor in the spread of leptospirosis. Current knowledge suggests that climate change will have a considerable impact on the burden of leptospirosis. For instance, it is the only bacterial zoonosis known to be increasingly prevalent in Europe due to climate change, with recent increases observed, particularly in the Netherlands (ECDC, 2022). The epidemiology of leptospirosis is largely influenced by flooding, often triggered by severe weather events like typhoons, cyclones, or monsoons. The impact of prolonged and intense rainfall on human exposure to leptospirosis-contaminated environments is substantial enough that mass chemoprophylaxis decisions have been based on rainfall patterns. Climatic data have proven useful in predicting leptospirosis occurrences across various regions (Davignon et al. 2023).
The most significant risk factor among all of them was the existence of a cut or wound on the skin sustained while doing the work. It was noted that hardly any of the instances had worn gloves or boots as a kind of protection while at work. One possible explanation for this could be that the majority of agriculture-related tasks in India are still performed by humans and have not yet been mechanized. There is a custom of performing agriculture by hand and barefoot with the assistance of animals like cows, which increases the danger of direct contact with contaminated mud. The second-highest risk factor for the disease was coming into contact with polluted soil around the house. People in the Indian context are known to occasionally labor in the vicinity of their homes wearing any kind of footwear. The likelihood that the soil may become contaminated with contaminated pee is increased when there are a lot of rodents around the house. While the risk of infection is considerably increased when barefoot walking occurs and skin abrasion occurs. A risky occupational element occurs when someone works outdoors and comes into direct contact with mud, soil, or water. It has been established that poor environmental cleanliness and hygiene contribute to the illness. In a similar vein, our investigation revealed that a risk factor was the existence of drainage within a 15-meter radius of the residence. During the ten months of the rainy season, Udupi experiences abundant rainfall. The overflow of sewage or drainage occurs during the rainy season, further polluting the environment (Kamath et al., 2014).
The results of the study demonstrate the role that poverty, climate, and location play in the global distribution of leptospirosis. Tropical nations represented 73% of the estimated cases worldwide and had the highest projected illness incidence. This trend can be linked to social and environmental factors that support the survival of the bacteria in soil and surface water, the presence of reservoir animals, and the possibility of human exposure to these infection sources (Costa et al., 2015). Leptospirosis is another disease that spreads more easily in tropical climates. It frequently seasonal and becomes more prevalent

during times of intense rains. The illness is widely acknowledged as a health issue affecting urban slum residents, pastoralists, and poor rural subsistence farmers (Cunha et al., 2022). We discovered that lifespan, which acts as a partial stand-in for poverty, is a reliable indicator of the prevalence of diseases in a given nation. Lastly, our model showed an inverse relationship between country percent urbanization and leptospirosis incidence, despite the fact that urban slum environments are a developing and increasingly significant setting for leptospirosis transmission. This relationship partly reflects the high prevalence of leptospirosis in rural areas and also reflects the widely acknowledged link between poverty and lower aggregate country-level percent urbanization (Costa et al., 2015).

The study identified regions within the underdeveloped world where leptospirosis prevalence may be significantly underestimated. In South and Southeast Asia, large populations, particularly in India and Indonesia, were found to have a substantial annual morbidity rate from leptospirosis. Specifically, India had an estimated incidence of 19.7 cases per 100,000 people (95% CI 6.8–36.8), while Indonesia reported 39.2 cases per 100,000 people (95% CI 12.8–78.0). Despite the endemic spread and documented significant outbreaks in these countries, regular surveillance for leptospirosis has not been conducted.

A significant limitation of the study was the lack of comprehensive data on disease prevalence in certain geographic areas, particularly in parts of Africa. In this region, only two studies provided data on illness and mortality rates. Although the burden estimates for Africa might be unreliable, increasing evidence suggests they are credible. Leptospirosis is recognized as an animal health issue in Africa, with Leptospira found in a variety of wild and domestic animals. A recent population-based study in northern Tanzania reported an annual incidence of 75–102 cases per 100,000 people.

To validate these estimates for Africa and other regions with limited data, additional locally representative studies are crucial. However, such efforts require significant time and resources, which may delay decision-making regarding the implementation of control measures and the enhancement of surveillance systems (Costa et al., 2015).

Comparative Analysis of Leptospirosis in Humans and Animals

Infection pathways for leptospirosis vary between species, influencing transmission dynamics. Both humans and animals can acquire the bacteria from contaminated water, soil, or through direct contact with infected animals. Understanding these pathways is crucial for developing effective prevention strategies. Humans can contract leptospirosis through direct exposure to infected animals. This can occur when open wounds or mucous membranes come into contact with the urine or body fluids of infected animals (Bradley & Lockaby, 2023). Such direct transmission is considered less common compared to indirect pathways. More frequently, leptospirosis is acquired through indirect contact with contaminated water, soil, or vegetation (Narkkul et al., 2021, Khalili et al., 2020).
This mode of transmission is particularly significant during rainy seasons or in areas with poor sanitation, where the bacteria can survive in the environment for extended periods. Animals, particularly domestic and livestock species, can become infected through direct contact with the urine or body fluids of other infected animals. This direct transmission plays a crucial role in maintaining the cycle of infection within animal populations. Similar to humans, animals can also experience indirect transmission through contaminated environments (Gizamba & Mugisha, 2023, Narkkul et al., 2021). This highlights the importance of environmental conditions in the epidemiology of leptospirosis.

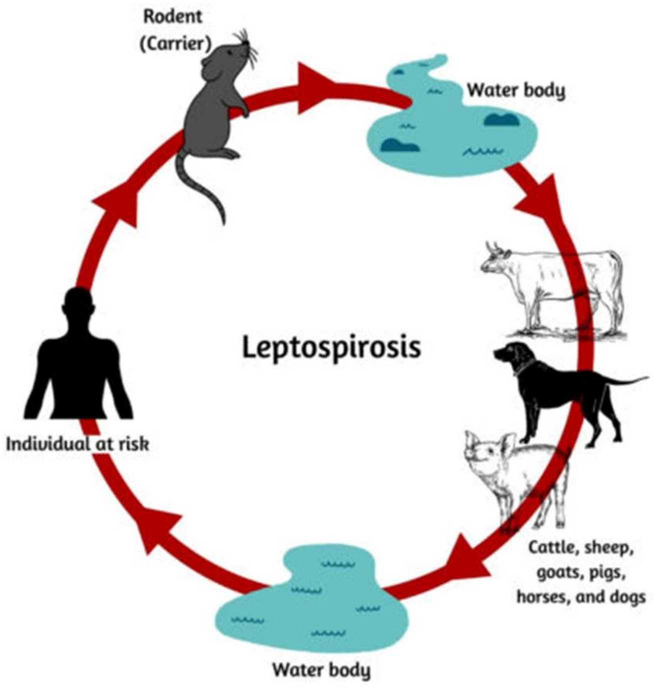

Fig 1.0 Transmission of Leptospirosis. Gayathri, R., Archana, V., & Ramya, M. (2022). Molecular diagnostic methods for the detection of leptospirosis. *Journal of Pure and Applied Microbiology*, *16*(2), 782–795. https://doi.org/10.22207/jpam.16.2.24

Identifying socio-environmental elements such as urbanization, flooding, and inadequate sanitation will be essential, as these factors have been shown to elevate the likelihood of leptospirosis outbreaks. Moreover, analyzing demographic vulnerabilities, including age, occupation, and comorbid health conditions, will provide insights into human susceptibility. Disadvantaged communities often lack access to effective public health measures, increasing their risk of infection (Bradley & Lockaby, 2023). Behavioral Factors such as swimming in contaminated water and outdoor work raise the risk of infection (Narkkul et al., 2021, Khalili et al., 2020) and consumption of water from multiple sources correlates with higher infection rates (Narkkul et al., 2021). For animals, factors like farming practices, rodent populations, and habitat encroachment play significant roles in increased transmission rates. Poor sanitation and overcrowding in domestic settings can lead to higher infection rates among livestock and pets (Khalili et al., 2020). Outbreaks in animals are often associated with environmental changes such as heavy rains (Gizamba & Mugisha, 2023). Hence, future research should holistically integrate these risk factors to formulate comprehensive public health strategies aimed at reducing the incidence of leptospirosis in both humans and animals, ultimately curbing the cycle of infection and enhancing community resilience against this zoonotic disease.

Zoonotic Aspects of the disease

It is essential to identify the reservoirs of leptospirosis, primarily including rodents, livestock, and wild animals, as they play a critical role in the transmission cycle. Further research should also underscore the importance of addressing environmental and human factors that influence these reservoirs' interactions with various habitats. Rodents are traditionally recognized as primary reservoirs for *Leptospira*, playing a pivotal role in many urban outbreaks (Narkkul et al., 2021). Their ability to thrive in human-inhabited areas enhances the likelihood of transmission to humans. Humans can become infected through contact with urine or tissues of infected animals, particularly rodents, which are significant reservoirs for the bacteria (Bradley & Lockaby, 2023). Domestic animals such as cattle, buffaloes, dogs, and cats are significant reservoirs of leptospirosis. Their close interaction with humans facilitates the potential spread of the disease, especially in agricultural or rural settings where human-animal contact is common (Khalili et al., 2020). In rural areas, wildlife species can also act as reservoirs for leptospirosis. Seasonal changes that affect animal behavior and environmental conditions can lead to increased interactions between wildlife and domestic animals, thus amplifying the risk of transmission (Gizamba & Mugisha, 2023).

Understanding the important factors of leptospirosis zoonosis is crucial for developing effective strategies for prevention and control. These factors include the ecology of the Leptospira bacteria, the role of various animal reservoirs—particularly rodents, livestock, and wildlife—in the transmission cycle, environmental conditions that favor the survival of the bacteria, and the socio-economic conditions that facilitate human exposure. Numerous mammals can serve as reservoirs for *Leptospira*, including livestock, companion animals, and wildlife, contributing to the widespread nature of the disease (Sykes et al., 2022). There are over 20 species of *Leptospira*, categorized into more than 300 serovars, with various levels of pathogenicity affecting different hosts (Soo et al., 2020, Azócar-Aedo, 2023).

Domestic animals such as dogs and livestock can harbor the bacteria, although dogs have not been identified as a major source of zoonotic infection (Sykes et al., 2022).

Comparative Epidemiology in Humans and Animals

Epidemiology in Humans: Leptospirosis symptoms can range from asymptomatic to severe illness, including organ failure and death. Long-term health impacts occur in about 30% of cases. The incidence of human leptospirosis varies significantly by region. In Tanzania, for example, studies report incidences of 75-102 cases per 100,000 persons annually (2007-2008) and 11-18 cases per 100,000 persons annually (2012-2014) (Motto et al., 2021). In some regions, human seroprevalence is low (e.g., 0.3% in Chile) but indicates a public health concern due to the potential for outbreaks (Azócar-Aedo 2023).

Epidemiology in Animals: Domestic animals (dogs, cattle, pigs) and wildlife serve as primary reservoirs for *Leptospira*, shedding the bacteria in their urine. In Chile, seroprevalence rates are notably high, with dogs showing a prevalence of%, while cattle exhibit a lower prevalence of 5.6% (Azócar-Aedo 2023). The prevalence in animal populations is influenced by environmental conditions, including high rainfall and poor sanitation, which facilitate the bacteria's survival and transmission. The disease transmission dynamics depend on interactions between various host species and their environments. Wild animals also contribute to the epidemiology of leptospirosis, although specific prevalence rates in wildlife are less frequently documented.

Both humans and animals primarily contract leptospirosis through environmental exposure, although humans are more likely to contract it via occupational hazards. Prevalence is generally higher in animal populations compared to humans, indicating that while humans are affected, the disease is more endemic among animal populations. The interconnectedness of human and animal health underscores the need for integrated surveillance and prevention strategies.

Roles of Veterinary Public Health

Certain professions, such as veterinary work, animal husbandry, and wildlife management, carry a higher risk of exposure due to frequent handling of potentially infected animals (Bradley & Lockaby, 2023). Its management requires an integrated approach that considers the health of humans, animals, and the environment, often referred to as the One Health approach (Pal et al., 2021). Veterinary public health plays a crucial role in the diagnosis of leptospirosis through several key functions: Surveillance and Monitoring animal populations for signs of leptospirosis to identify potential outbreaks. Diagnostic Testing- Utilizing advanced diagnostic methods such as serology tests and polymerase chain reaction (PCR) to identify the presence of Leptospira in both humans and animals (Pham & Tran, 2022, Pal et al., 2021). Epidemiological Investigation- Assessing environmental factors and the history of exposure in both animals and humans to enhance diagnostic accuracy (Pham & Tran, M 2022). Collaborative Efforts- Working alongside public health officials, veterinarians, and ecologists to streamline disease surveillance and response strategies (Viroj et al., 2021). Education and Training- Providing training for veterinary professionals on the latest diagnostic techniques and the importance of reporting cases to public health authorities (Hernández-Rodríguez & Trujillo-Rojas, 2022). Risk Assessment- Evaluating the risk of transmission from animals to humans, especially in high-risk environments (Pal et al., 2021). Data Collection- Compiling and analyzing data on animal infections to inform public health strategies (Viroj et al., 2021). Improving Testing Methods- Advocating for and implementing better diagnostic assays that can facilitate early identification of infections (Sykes et al., 2022).

The treatment of leptospirosis relies heavily on veterinary public health practices, which include: Antibiotic Therapy- Administering effective antibiotics based on the susceptibility of the Leptospira strains involved (Hernández-Rodríguez & Trujillo-Rojas, 2022). Supportive Care- Implementing supportive measures for affected animals and humans to improve outcomes (Pham & Tran, 2022). Multisectoral Collaboration- Ensuring cooperation among veterinarians, public health officials, and environmental scientists to develop integrated treatment strategies (Pal et al., 2021). Monitoring Resistance- Tracking antimicrobial resistance patterns to ensure the effectiveness of treatment protocols (Pham & Tran, 2022). Public Education- Raising awareness about leptospirosis prevention and treatment options among the public and healthcare professionals (Viroj et al., 2021). Research and Development- Supporting research initiatives aimed at discovering new treatment methods or improving existing ones. Vaccination Programs- Promoting vaccination in at-risk animal populations to reduce the incidence of the disease (Pal et al., 2021). Emergency Response- Developing rapid response plans for outbreaks that involve both animal and human health sectors (Hernández-Rodríguez & Trujillo-Rojas, 2022).

Impact of Climate Change on Leptospirosis Trends

Climate Factors Influencing Leptospirosis Incidence include: Heavy Rainfall and Flooding- Climate change is expected to increase the frequency and severity of heavy rainfall and flooding, which are significant determinants of leptospirosis outbreaks. These events bring contaminated water closer to human populations and increase contact with reservoir animals. Temperature Variability- Warm and humid conditions favor the survival of pathogenic leptospires. However, extreme heat can also lead to desiccation, making certain regions less suitable for the bacteria. Studies indicate that there is a complex relationship between temperature and disease incidence, with both high and low temperatures affecting the dynamics of leptospirosis outbreaks. Seasonal Patterns- Increased temperatures and rainfall can influence seasonal trends of leptospirosis, with certain climatic conditions leading to higher transmission rates during specific times of the year (Douchet et al., 2022, Douchet et al., 2024). Geographical Influence- Certain geographic areas, such as low-lying and flood-prone regions, are more susceptible to outbreaks. Urbanization and agricultural practices contribute to the risk, as these environments often have higher rodent populations, which are key reservoirs for leptospirosis (Douchet et al., 2022, Bradley & Lockaby, 2023). Zoonotic Transmission- Climate change intensifies the interaction between humans, wildlife, and environmental factors, increasing the likelihood of zoonotic disease transmission. This is especially concerning in socioeconomically disadvantaged communities, which may lack access to adequate healthcare (Bradley & Lockaby, 2023).

Effects of changing weather patterns on disease incidence

The key Weather Factors Affecting Leptospirosis Incidence include: Rainfall- Heavy rainfall and flooding are consistently associated with increased cases of leptospirosis. Extreme weather events can wash away contaminated soil and bring reservoir animals closer to human populations, facilitating transmission (Douchet et al., 2024). A cumulative rainfall anomaly of 20 mm has been shown to increase the risk of leptospirosis by 12% within a week (Cunha et al., 2022). Temperature- The relationship between temperature and leptospirosis incidence can vary. For instance, warmer temperatures may promote the growth of leptospires, while lower temperatures have been shown to be more favorable for the bacteria's survival in some regions (Douchet et al., 2024). In certain tropical islands, high temperatures alongside rainfall can lead to increased rodent populations, which are key reservoirs for the bacteria (Douchet et al., 2022). Humidity- High humidity levels can also contribute to the transmission dynamics by maintaining favorable conditions for leptospire survival. Seasonality- Seasonal patterns of leptospirosis incidence are often aligned with cyclic rainfall in tropical regions, indicating a strong seasonal effect driven by weather changes. Climate Lags- There are significant lags between weather events and the reported cases of leptospirosis. Typically, a lag of one to two weeks is observed following increased rainfall or temperature anomalies before an uptick in cases is noted (Cunha et al., 2022). Extreme Weather Events- Events such as floods can lead to outbreaks due to increased contamination of water sources and heightened human-animal contact (Douchet et al., 2022). Long-term Climate Patterns- Long-term climate phenomena, such as the El Niño Southern Oscillation (ENSO), can influence inter-annual variability of leptospirosis cases by impacting rainfall and temperature patterns, which subsequently affect rodent populations and environmental contamination. Geographic Variability- The impact of climate factors can vary significantly across different regions and islands, suggesting that localized studies are essential for understanding leptospirosis dynamics in specific areas (Douchet et al., 2024).

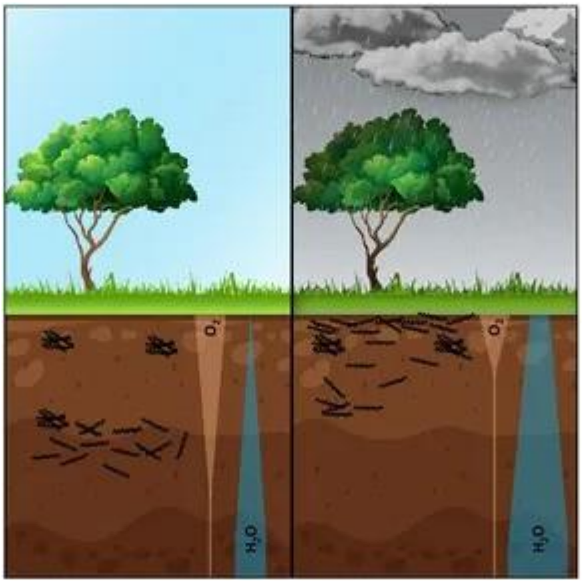

Fig 2.0 Effects of Rainfall on Leptospira. Davignon et al (2023). Leptospirosis: Toward a better understanding of the environmental lifestyle of Leptospira. *Frontiers in Water, 5*, 1195094. https://doi.org/10.3389/frwa.2023.1195094

This illustration describes a possible scenario where leptospires, bacteria that require both oxygen and water, must adjust their behavior depending on the soil's depth. After rainfall, water fills the soil, pushing the oxygen-rich layer closer to the surface. To survive, leptospires that need oxygen may move upward in the soil to access this oxygen, while still ensuring they have enough moisture. If the soil becomes too dry, these bacteria might form a biofilm, a protective layer that helps them retain water and survive. This biofilm also helps the bacteria exchange nutrients and survive in challenging conditions. This scenario could explain why human infections often increase after floods. When heavy rains disturb the soil, they can spread leptospires from their biofilms, potentially leading to more widespread contamination. However, this is just a theory, and more research is needed to confirm these ideas and better understand how leptospires adapt to their environment (Davignon et al 2023)

Influence of Natural Disasters on Outbreaks

Natural disasters, particularly floods, significantly influence the occurrence and spread of leptospirosis, a bacterial disease caused by the Leptospira bacteria. Below are detailed insights into how these disasters contribute to outbreaks. Mechanisms of Influence include the contamination of water sources. Natural disasters often lead to the flooding of areas, which can contaminate water supplies with Leptospira bacteria. This is particularly concerning in regions where sanitation infrastructure is inadequate. Other aspects include: Environmental Exposure- Floodwaters can expose populations to the bacteria, especially in urban areas where people may wade through contaminated water. The risk increases significantly after heavy rainfall or flooding events (Suk et al., 2020, Nazir et al., 2024). Ecosystem Changes- Flooding creates favorable conditions for the survival and proliferation of rodents, which are common reservoirs for leptospirosis. The presence of multiple animal reservoirs increases the likelihood of human exposure. Increased Incidence Post-Disaster- Historical data shows a marked increase in leptospirosis cases following natural disasters. For instance, outbreaks were reported in Brazil, Fiji, Italy, Malaysia, and the Philippines after significant flooding events (Walika et al., 2023). Temperature and Weather Patterns- Warmer temperatures and increased rainfall correlate with higher incidence rates of leptospirosis, which can be exacerbated by climate change and the frequency of flooding (Walika et al., 2023, Suk et al., 2020). Poor Sanitation and Infrastructure- Urban areas with high poverty levels, inadequate sanitation, and living conditions close to contaminated water bodies are at greater risk of leptospirosis outbreaks following natural disasters (Nazir et al., 2024). Occupational Hazards- Individuals working outdoors, especially in agriculture or in cleanup operations after disasters, face heightened exposure risks to leptospirosis (Suk et al., 2020, Munoz-Zanzi et al., 2020). Public Health Strain- Natural disasters can overwhelm healthcare systems, complicating the diagnosis and treatment of leptospirosis due to increased patient loads and limited resources (Nazir et al., 2024).

Leptospirosis Outbreaks following natural disasters also have an Impact on Vulnerable Populations. These include: Increased Risk in Slum Areas- Populations living in slums or areas with poor waste management are more susceptible to outbreaks due to their living conditions and proximity to contaminated water sources.

Economic Consequences- The rise in leptospirosis cases can lead to significant economic impacts, including loss of productivity and increased healthcare costs, particularly affecting agricultural communities. Health Complications- Leptospirosis can lead to severe health complications such as liver failure, kidney damage, and meningitis, disproportionately affecting those with limited access to healthcare (Nazir et al., 2024, Munoz-Zanzi et al., 2020). Awareness and Education Gaps- Lack of awareness about leptospirosis transmission and prevention among populations and health workers can hinder effective control measures following disasters. Healthcare Accessibility- Limited access to healthcare services in remote and disadvantaged areas further complicates the management of leptospirosis outbreaks after natural disasters (Nazir et al., 2024).

Correlation between Temperature, Rainfall and Leptospirosis cases

Environmental factors, especially meteorological conditions, play a significant role in the transmission and incidence of this disease. Positive Association with Rainfall- Studies have consistently shown that increased rainfall correlates with a rise in leptospirosis cases. Specifically, a 1 mm increase in rainfall with a lag of 1 week can lead to an increase of approximately 0.1% in incidence rates of leptospirosis (Gutiérrez , 2021). Increased rainfall and flooding create conditions favorable for the survival of *Leptospira* in the environment (Md-Lasim et al., 2021). Lag Effect- The most significant association occurs with short-term lags, typically 1 to 2 weeks after rainfall events, indicating that the risk of infection rises shortly after heavy rains or flooding (Cunha et al., 2022). Seasonal Patterns- Leptospirosis outbreaks often coincide with seasonal heavy rainfall, particularly in tropical regions, where the pathogen can survive in contaminated environments for extended periods (Wichapeng et al., 2021, Cunha et al., 2022). Geographical Variability- The relationship between rainfall and leptospirosis can vary by region, necessitating localized studies to understand specific dynamics and implement effective interventions (Phosri, 2022).

Correlation with Temperature: Leptospira thrives in tropical and subtropical climates, where warmer temperatures and increased rainfall facilitate its persistence in the environment. Regions, particularly in tropical areas, report higher incidences of leptospirosis due to the local prevalence of the pathogen. (Bradley & Lockaby, 2023). Negative Association with Temperature- There is evidence of a negative relationship between temperature and leptospirosis cases, particularly with a lag of around 4 weeks. Higher temperatures may reduce the incidence of leptospirosis, suggesting that cooler, wetter conditions are more conducive to the survival of the Leptospira bacteria. Soil Moisture Influence- The negative association with temperature highlights the importance of soil moisture for the bacteria's survival, as higher temperatures can decrease moisture levels and thus reduce bacterial activity. Variable Lag Periods- Different studies report varying lag times for temperature effects—some report a significant impact at 4 weeks, while others suggest longer lags may be relevant, indicating the complexity of these interactions (Gutiérrez, 2021). Combined Effects of Temperature and Rainfall: Integrated Analysis- Studies that analyze the effects of both rainfall and temperature together suggest that both factors interact significantly in influencing leptospirosis outbreaks. The integrated approach allows for a better understanding of how these meteorological variables contribute to disease incidence over time (Phosri, 2022). Public Health Implications- Understanding the correlation between these factors is crucial for public health strategies, especially in urban areas where flooding can lead to increased exposure to contaminated water sources (Cunha et al., 2022).

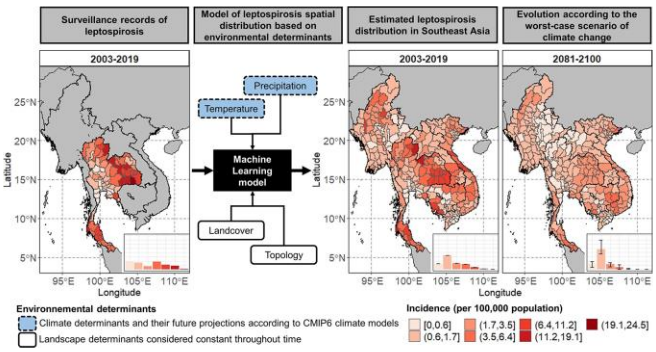

Fig 3.0 Weather Variables on Disease incidence. Douchet, L., Goarant, C., Mangeas, M., Menkes, C., Hinjoy, S., & Herbreteau, V. (2022). Unraveling the invisible leptospirosis in mainland Southeast Asia and its fate under climate change. *Science of the Total Environment*, *832*, 155018. https://doi.org/10.1016/j.scitotenv.2022.155018

Predictive modelling of future Leptospirosis Trends in the context of Climate Change

Predictive modelling for leptospirosis trends involves understanding how climate factors influence the incidence of this zoonotic disease. The models primarily focus on: Climate Variables- Key determinants include precipitation and temperature, particularly with time lags of 0 to 2 months prior to the onset of symptoms. Seasonality- The models can accurately forecast seasonal dynamics of leptospirosis, highlighting that wet months, characterized by high precipitation, correspond to increased disease incidence. Inter-annual Variability- The influence of climate events such as El Niño-Southern Oscillation (ENSO) is notable, as these can lead to significant fluctuations in disease incidence across different years due to changes in environmental conditions and rodent populations, which are primary reservoirs for the disease (Douchet et al., 2024).

Key Findings from the Modelling: Importance of Precipitation- The modelling shows that lagged precipitation (especially 2 months prior) is a strong predictor of leptospirosis incidence, with the wettest months leading to higher predicted cases. Temperature Effects- While both high and low temperatures can increase incidence, the relationship varies significantly across different islands, indicating a complex interaction that requires localized models. Local Specificity- The models must account for local environmental characteristics and human behaviors that affect disease transmission, as generic models may overlook these nuances (Douchet et al., 2024). Epidemic Prediction- A novel pattern-oriented integrated model was developed to predict outbreak dynamics, including early sensing and environmental determinants, allowing for better preparedness and response strategies (Convertino et al., 2021). Environmental Indicators- Factors such as land use, soil type, and water pH are essential for understanding leptospiral survival and distribution but were not included in all models, indicating a gap in predictive capacity (Douchet et al., 2024, Convertino et al., 2021).

Future Trends and Projections include: Increased Outbreak Frequency- As climate change progresses, the conditions necessary for leptospirosis outbreaks are expected to become more common, particularly in tropical regions where the disease is already prevalent (Bradley & Lockaby, 2023). Impact of Extreme Weather Events- The correlation between extreme weather events and leptospirosis incidence underscores the need for enhanced surveillance and disease management strategies as climate change continues to escalate these events (Douchet et al., 2022, Bradley & Lockaby, 2023). Socioeconomic Disparities- The impacts of climate change on leptospirosis will disproportionately affect lower socioeconomic groups, exacerbating existing health disparities and increasing vulnerability to outbreaks (Bradley & Lockaby, 2023). Potential for Regional Variability- While some regions may see increased incidence due to climate change, others might experience a decline in disease rates. This variability highlights the importance of localized studies to understand the specific impacts in different areas (Douchet et al., 2022). Need for Improved Environmental Understanding: Research into the environmental persistence of leptospires and the dynamics of transmission is critical for effective disease management and response strategies (Douchet et al., 2022, Bradley & Lockaby, 2023).

Challenges and Future Directions: Data Limitations- The reliance on satellite data for climate variables poses challenges, as localized climate conditions may not be accurately represented, leading to underestimation of incidence peaks. Need for Localized Models- Future research should focus on developing finer-scale models that incorporate local data and specific environmental conditions to improve predictive accuracy. Human Behavior- Understanding the social and recreational activities that contribute to transmission risk, especially during events like triathlons, is crucial for enhancing prediction capabilities (Douchet et al., 2024).

Adaptation and Mitigation Strategies to address the Impact of Climate Change on Leptospirosis

Adaptation Strategies: Enhanced Surveillance Systems- Implementing early warning systems (EWS) to monitor environmental conditions and predict leptospirosis outbreaks based on climate indicators such as rainfall and flooding patterns.

Public Health Education- Raising awareness about leptospirosis prevention among communities, especially those in high-risk areas, to encourage practices that reduce exposure to contaminated water. Improved Water Management- Developing better drainage systems and managing water resources to minimize flooding risks, thereby reducing potential exposure to Leptospira bacteria (Kim et al., 2020). Infrastructure Resilience- Strengthening infrastructure, such as roads and sanitation systems, to withstand extreme weather events and prevent disease transmission through contaminated environments (Convertino et al., 2021). Community Involvement- Engaging local communities in monitoring and reporting disease outbreaks, which can enhance community resilience and response to public health threats. Research and Development- Investing in research to understand the epidemiology of leptospirosis and its relationship with climate variables, which can inform policy and intervention strategies (Kim et al., 2020). Agricultural Practices- Encouraging sustainable agricultural practices that reduce flooding and improve soil management to limit the proliferation of Leptospira in farming areas (Convertino et al., 2021). Vector Control- Implementing measures to control rodent populations, which are primary hosts for Leptospira, especially in urban settings prone to flooding (Semenza et al., 2022).

Mitigation Strategies: Climate Change Mitigation Policies- Advocating for and implementing policies aimed at reducing greenhouse gas emissions to limit the severity of climate change impacts. Urban Planning- Designing urban areas to be more resilient to flooding through green spaces and permeable surfaces that absorb rainwater. Ecosystem Management- Protecting and restoring natural ecosystems, such as wetlands, which can act as buffers against flooding and reduce the transmission of waterborne diseases (Convertino et al., 2021). Intersectoral Collaboration- Collaborating across health, environmental, and agricultural sectors to create comprehensive strategies that address the multifaceted challenges posed by climate change. Policy Frameworks- Developing integrated policy frameworks that include health considerations in climate adaptation strategies, ensuring a holistic approach to public health and environmental management. Funding and Resources- Allocating adequate resources for climate adaptation projects that specifically target zoonotic disease prevention. Monitoring and Evaluation- Establishing mechanisms for ongoing evaluation of adaptation and mitigation efforts to improve their effectiveness and make necessary adjustments (Kim et al., 2020). Capacity Building- Training health professionals and community leaders on the impacts of climate change on health, focusing on prevention and response strategies for leptospirosis (Convertino et al., 2021).

Pathogenesis and Transmission

The disease leptospirosis is a resurgent infection brought on by gram-negative bacteria. It is a member of the genus Leptospira, family Leprospiraceae, and phylum Spirochetes. mostly infectious illnesses, such as leptospirosis, brought on by a broad range of pathogens, including bacteria, fungi, and viruses (Rajapakse, 2022). Globally, there are about 500,000 high-risk cases, with a 30% annual death rate. Leptospirosis poses a serious threat to public health due to its high morbidity and fatality rates (Devi et al., 2021). When comparing older men and women, the prevalence is higher among young and middle-aged men. This infection can spread to humans when a cut or mucous membrane is exposed to germs. Exposure can occasionally happen by direct or indirect contact. direct interaction with an animal through their exposure to indirect touch skin lesions, contact with moist skin, inhalation, in addition to surface proteins are the main ways that Leptospira enter the body (Malim, Shaadan, & Ideris, 2019).

Additionally, it destroys the endothelium of tiny vessels and causes ischemia in the muscles, liver, kidneys, and lungs. Thrombocytopenia may also happen in certain situations. Three types of leptospirosis have been identified, ranging from milder cases of anicteric icteric to more severe cases of Weil's illness. These lead to failure of multiple organs. The final diagnosis of leptospirosis is made using microbiological techniques or serology. The degree for queasiness at presentation determines how leptospirosis is treated. The severity of the clinical presentation might range from multi-organ failure to asymptomatic. MAT and primary serological tests are the potential leptospirosis diagnostics. Therefore, leptospirosis is ten times more common in tropical. Animals that are afflicted can spread the infection through their urine, which can contaminate water or soil via skin abrasions or mucous membrane penetration, pathogenic leptospirosis enters the body and spreads via the hematogenic pathway. Leptospirosis in humans can induce a wide range of symptoms, the majority of which are immunological expressions. The worst versions of the illness can be fatal and cause multiple organ damage, muscle aches, lung bleeding, hepatic dysfunction, and vascular damage (Malim, Shaadan, & Ideris, 2019).

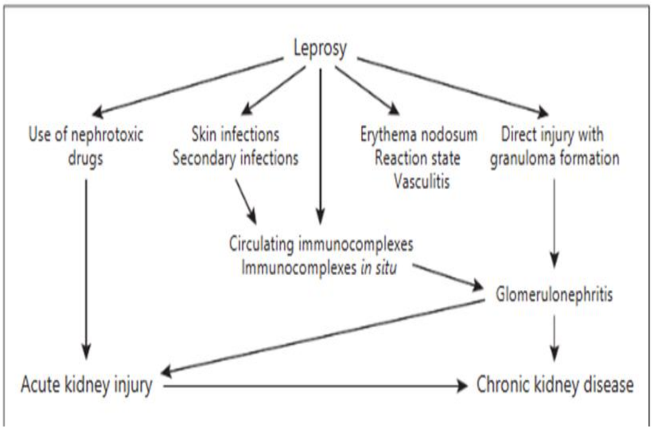

Fig 4.0 The Complications of Leprosy. Silva, G., Junior, Srisawat, N., Sirivongrangson, P., Fayad, T., Sanclemente, E., & Daher, E. (2021). Neglected tropical diseases and the kidneys. *Contributions to Nephrology*, 201–228. https://doi.org/10.1159/000517724

Humans can contract the organism through portals of entry such as conjunctivae, mucous membranes, or wounds or abraded skin. Contact with pee-contaminated soil or water (such as floodwater, ponds, rivers, streams, or sewage), intake of food or water contaminated by urine or urine-contaminated water, or direct contact with the urine or reproductive fluids of sick animals are examples of human exposures that can result in infection. Rarely, animal bites have also resulted in transmission. The question of whether Leptospira can pierce healthy skin is up for debate. Although extremely rare, human-to-human transmission has been linked to breastfeeding and sex (“UpToDate,” n.d.).
The course of infection and the emergence of disease are well-documented at the scale of the host animal or human. However, the paucity of contemporary genetic tools for pathogenic Leptospira spp. mutagenesis means that the processes of disease at the cellular and molecular level remain poorly known. A tiny number of critical virulence factors have been discovered thanks to the recent advancements in transposon mutagenesis and the creation of a very limited number of guided leptospiral mutants. Surprisingly, it has been demonstrated that several leptospiral proteins that are thought to have a virulence-related role are not necessary for virulence in animal models. This suggests that pathogenic Leptospira have a high level of functional redundancy. Leptospira have been found to have a vast number of potential adhesins that interact with various components of host tissue; however, hardly any of these have been genetically verified to play a crucial role in pathogenesis (Adler, 2014).
It is customary to characterize acute leptospirosis as a biphasic illness. Early on in the infection, leptospires spread to all tissues and cause a wide range of clinical symptoms, leading to bacteremia in the first few days following the incubation phase. With the exception of the kidneys, eyes, and brain, where leptospires can live for several months, the immune host response helps remove the parasite from nearly all host tissues. A carrier animal's infection is identical to that of a susceptible host in every way, with the exception that leptospires are able to successfully remain in the renal tubules and the animals only exhibit minimal symptoms of aberrant histology or weight loss. Thus, asymptomatic sick animals that actively maintain and shed bacteria can be considered true reservoirs. This is because chronic disease transmission in the environment depends on these animals (Davignon et al., 2023b).
Rats in particular are widely believed to be the primary sources of Leptospira infection and were found to be asymptomatic carriers of the illness as early as 1917. Injecting blood, urine, or kidney emulsion from asymptomatic rats intraperitoneally killed guinea pigs, demonstrating the vitality and pathogenicity of the leptospires present in their reservoir hosts. All mammalian species have the potential to act as chronic carriers and reservoirs if they come into contact with the co-adapted Leptospira strain. For example, L. interrogans serovar Lai is often asymptomatic in mice but extremely pathogenic in humans. L. borgpetersenii serovar Ballum is persistently carried in the kidneys of Mus musculus mice for up to 117 days. Post-infection, in the absence of illness symptoms. Comparable findings have been documented for L. borgpetersenii serovar Hardjo, L. interrogans serovar Canicola in dogs, L. interrogans serovar Pomona in pigs, and L. interrogans serovar Hardjo in cattle. The immune system of the host has a role in identifying whether the animal is a susceptible or reservoir. Leptospires, for example, are rapidly cleared from

the blood and organs, with the exception of kidney tubules, which may be partially explained by the increasing evidence that they are more readily detected by innate immune cells in chronic carriers (Davignon et al., 2023)

Morbidity and Mortality

Warnasekara, Srimantha, and Agampodi (2021) present a detailed analysis of the global burden of leptospirosis using Sri Lanka as a case study. Health planning demands a comprehensive understanding of disease burdens, yet accurate assessments of diseases like leptospirosis remain challenging, particularly in lower and middle-income countries (LMICs) due to data deficiencies and sampling biases. The paper highlights three main reasons for the underestimation of leptospirosis: underreporting, lack of diagnostic tools, and diverse clinical features.

Routine reporting in many LMICs, including Sri Lanka, is hampered by non-digitalized hospital information systems and the tedious nature of manual reporting, leading to significant underestimation. The authors note that notification systems are often incomplete, particularly in the private sector, which handles a significant portion of healthcare but lacks consistent reporting protocols. Additionally, complementary medicine practices and outpatient departments also contribute to underreporting (Warnasekara et al., 2021).

The lack of effective diagnostic tools further complicates accurate disease estimation. Current diagnostic methods, including culture, direct visualization, molecular detection, and antibody detection, all have limitations, making clinical, biochemical, and epidemiological parameters crucial for diagnosis. However, these methods are not always available outside major cities like Colombo, contributing to the underestimation of cases (Warnasekara et al., 2021).

Clinical features of leptospirosis vary widely, from mild flu-like symptoms to severe, multi-systemic involvement, which can be misdiagnosed due to similarities with other diseases like dengue and hantavirus. This diversity, coupled with concurrent disease outbreaks common in tropical regions, poses additional diagnostic challenges (Warnasekara et al., 2021).

Predictive models have been developed to aid in leptospirosis detection, yet their clinical utility is limited by complexity. Simplified models that integrate clinical, biochemical, and epidemiological data could enhance diagnostic accuracy. The authors suggest that improving notification systems, developing region-specific diagnostic tools, and continuously updating clinical profiles are crucial steps towards better disease burden estimation (Warnasekara et al., 2021).

Costa et al. (2015) conducted a systematic review to estimate the global burden of leptospirosis, a life-threatening zoonotic disease that affects vulnerable populations such as rural farmers and urban slum dwellers. Despite its severity and global distribution, leptospirosis remains a neglected disease due to the lack of comprehensive global estimates for morbidity and mortality. The authors reviewed published studies and databases to extract information on disease incidence and case fatality ratios, using linear regression and Monte Carlo modeling to obtain adjusted estimates of disease morbidity and mortality for different regions and demographics. The review identified 80 studies from 34 countries, revealing significant regional disparities in the quality of data, particularly in Africa where few quality studies were available. The regression model, incorporating variables such as population structure, life expectancy, proximity to the equator, and urbanization, accounted for 60% of the variation in disease incidence. The authors estimated that annually there are approximately 1.03 million cases and 58,900 deaths due to leptospirosis worldwide. The highest morbidity and mortality rates were observed in regions such as South and Southeast Asia, Oceania, the Caribbean, and East Sub-Saharan Africa, with adult males aged 20-49 years being the most affected demographic.

Leptospirosis, transmitted through contact with animal reservoirs or contaminated environments, has a broad geographical distribution. The disease is prevalent among subsistence farmers, cash croppers, pastoralists, and urban slum dwellers, and can spread rapidly following extreme weather events and disasters. The review highlighted the emergence of leptospirosis in new settings due to globalization and climate change, and the increased risk in urban slum environments due to rat-borne transmission.

The authors noted that the major burden of leptospirosis is due to its severe manifestations, such as pulmonary hemorrhage syndrome and acute kidney injury, with case fatality rates exceeding 10% and 70%, respectively, for these conditions. Misdiagnosis is common, as leptospirosis can present with non-specific symptoms similar to other febrile illnesses like malaria and dengue. The lack of reliable diagnostic tests has further contributed to the underreporting of cases and deaths.

The study's methodology involved screening 32 electronic databases and additional grey literature for relevant studies published between 1970 and 2008. The data extraction process followed PRISMA guidelines, and the quality of studies was assessed by independent raters. The final estimates were derived using a multivariable regression model that predicted disease incidence based on country-specific indicators and a Monte Carlo model to adjust for incomplete diagnostic testing.

Costa et al. (2015) concluded that leptospirosis is a leading zoonotic cause of morbidity and mortality, particularly in resource-poor regions. The study underscores the need for improved surveillance, diagnostics, and targeted interventions to address the disease burden. The findings provide a basis for policy-making and the implementation of One Health approaches to leptospirosis prevention and control.

Torgerson et al. (2015) offer a comprehensive assessment of the global burden of leptospirosis, measured in terms of Disability Adjusted Life Years (DALYs). This metric combines both the years of life lost (YLLs) due to premature mortality and the years lived with disability (YLDs) due to the disease. Despite leptospirosis being a significant zoonotic disease with severe health impacts, its global burden has been underestimated, particularly in resource-poor regions.

The authors utilized data from a parallel publication that estimated global morbidity and mortality of leptospirosis to calculate the DALYs. They estimated approximately 2.90 million DALYs are lost annually due to leptospirosis, with the majority (about 96%) resulting from premature mortality (Torgerson et al., 2015). The highest burden was observed in tropical regions of South and Southeast Asia, the Western Pacific, Central and South America, and parts of Africa. Males, particularly young adult males aged 20-49, bear the brunt of the disease burden, accounting for approximately 80% of the total DALYs.

The study highlights the severe forms of leptospirosis, such as pulmonary hemorrhage syndrome and acute renal failure, which contribute significantly to the YLLs. The case fatality rate for these severe forms can exceed 50%. The authors also discuss the difficulties in diagnosing leptospirosis due to its clinical similarities with other febrile illnesses, contributing to underreporting and misdiagnosis.

Torgerson et al. (2015) used a disease model to estimate the YLDs, incorporating various clinical manifestations and their respective disability weights. They found that non-fatal cases often lead to significant morbidity, including acute renal and pulmonary failure, and chronic sequelae such as extreme fatigue and myalgia, which can last for months to years. Despite these chronic effects, the YLDs represent a smaller fraction of the total DALYs compared to the YLLs.

The authors performed sensitivity analyses to test the robustness of their estimates, finding that the YLLs dominated the total DALY calculations, regardless of variations in disability weights. This underscores the critical need for accurate mortality data to improve disease burden estimates.

The study's findings emphasize the need for improved surveillance, diagnostics, and public health interventions to address leptospirosis, especially in the most affected regions. The authors call for more comprehensive data collection and reporting to better understand and mitigate the global impact of leptospirosis.

Guernier, Goarant, Benschop, and Lau (2018) conducted a systematic review to investigate the epidemiology, pathogen diversity, and animal reservoirs of leptospirosis in the Pacific Islands. The Pacific Islands, due to their environmental conditions, are highly favorable for the transmission of leptospirosis, a neglected zoonosis with the highest incidence in tropical regions, particularly Oceania. Despite recent reports of emergence and outbreaks in the region, the epidemiology and drivers of transmission remain poorly documented, especially in the more isolated and less developed islands.

The authors performed a literature search using four international databases for articles published between January 1947 and June 2017. They also included grey literature available on the internet. In total, they identified 148 studies describing the epidemiology of leptospirosis across 25 Pacific Islands. However, data availability varied significantly between islands, with no information from four Pacific Islands. Human leptospirosis was reported from 13 islands, with 63% of studies conducted in Hawaii, French Polynesia, and New Caledonia. Animal leptospirosis was investigated in 19 islands, involving 14 host species, primarily pigs (18% of studies), cattle (16%), and dogs (11%). Only 13 studies provided information on both human and animal leptospirosis from the same location (Guernier et al., 2018).

The review found that leptospirosis is widespread in the Pacific Islands, showing some epidemiological heterogeneity. Serology results indicated diverse serogroups both in humans and animals, with rodents, cattle, pigs, and dogs identified as likely important carriers. However, the relative importance of each animal species in human infection needs further clarification. The authors recommend that epidemiological surveys with appropriate sampling designs, pathogen typing, and data analysis are necessary to improve understanding of transmission patterns and to develop effective intervention strategies (Guernier et al., 2018).

The findings underscore the importance of integrated studies using an eco-epidemiological approach that includes human, veterinary, and environmental factors to fully understand leptospirosis transmission in the Pacific Islands. Improved diagnostic facilities and better health infrastructure are critical for accurate diagnosis and effective management of leptospirosis in these regions (Guernier et al., 2018).

Guerra (2013) provides an in-depth review of leptospirosis, a zoonotic disease caused by the spirochete Leptospira, highlighting its global distribution, public health impact, and the challenges associated with its diagnosis, treatment, and prevention. Leptospirosis is considered the most widespread zoonosis globally, with higher incidences in tropical and subtropical regions, where it ranges from 10 to 100 cases per 100,000 individuals. The disease is particularly prevalent in environments with poor sanitation, stagnant waters, and frequent human-animal interactions, such as agricultural and recreational activities. Epidemics are often triggered by flooding and natural disasters like hurricanes and earthquakes (Guerra, 2013).

The review emphasizes the re-emergence of leptospirosis as a significant public health concern due to increased human encroachment into wildlife habitats and the effects of global climate change. Climate change, by altering environmental conditions, can extend the survival of Leptospira in the environment and expand the habitats of reservoir species to higher elevations and latitudes. This has led to an increased incidence of the disease globally, necessitating improved surveillance and early detection methods to mitigate its impact. In the United States, leptospirosis was reinstated as a nationally notifiable condition in 2012 to better monitor and control its spread (Guerra, 2013).

Diagnosis of leptospirosis poses significant challenges due to its nonspecific clinical presentation, which can mimic other febrile illnesses such as dengue and influenza. The current gold standard for diagnosis is the microscopic agglutination test (MAT), which, despite its limitations, remains the primary method for confirming infection. However, the MAT is labor-intensive and costly, highlighting the need for more accessible and rapid diagnostic tests, such as polymerase chain reaction (PCR), particularly in resource-limited settings. Early diagnosis and treatment are crucial to reduce morbidity and mortality associated with severe forms of the disease, which can include hepatic, renal, or pulmonary dysfunction and hemorrhagic manifestations (Guerra, 2013).

Prevention strategies for leptospirosis include improved surveillance, mass prophylaxis during outbreaks, and vaccination. Although vaccines have been developed and used regionally, their feasibility for widespread use, especially in endemic areas, remains uncertain due to various barriers, including the identification of locally circulating serovars and the assessment of vaccine safety and efficacy. The World Health Organization's Leptospirosis Burden Epidemiology Reference Group (LERG) uses the disability-adjusted life year (DALY) metric to quantify the global burden of the disease, aiding in the formulation of effective prevention and control policies (Guerra, 2013).

Guerra concludes that significant challenges remain in accurately determining the global burden of leptospirosis due to inadequate surveillance systems and diagnostic capabilities. Long-term studies and coordinated efforts between public health and veterinary sectors are essential for developing and implementing effective strategies for the prevention and control of leptospirosis, in line with the One Health approach (Guerra, 2013).

Bradley and Lockaby (2023) provide an extensive review on the environmental aspects of leptospirosis, a significant zoonotic disease caused by the bacterium Leptospira. The disease is prevalent globally, with higher incidences in tropical and subtropical regions, disproportionately affecting socioeconomically disadvantaged communities. The authors underscore the importance of understanding the pathogen's environmental phase to enhance disease management and prevention strategies.

The review highlights the environmental persistence of Leptospira in soil and water, emphasizing the pathogen's ability to survive, persist, and potentially reproduce in these environments. Laboratory studies have shown that Leptospira can survive in waterlogged soil, which is critical for understanding its environmental transmission cycle. However, there is a lack of detailed field-based studies examining Leptospira prevalence, survival, and transmission in natural settings (Bradley & Lockaby, 2023).

The authors discuss the challenges in diagnosing and reporting leptospirosis due to its nonspecific symptoms, which often mimic other febrile illnesses like dengue and influenza. The current diagnostic standard, the microscopic agglutination test (MAT), is labor-intensive and costly, limiting its use in resource-poor settings. Improved diagnostic methods, such as quantitative real-time polymerase chain reaction (qPCR) tests targeting pathogenic Leptospira genes, are needed to facilitate active surveillance and better public health responses.

Bradley and Lockaby (2023) identify several key areas for future research, including the need for comprehensive field studies to assess the environmental conditions that support Leptospira survival and persistence. They highlight the importance of understanding the pathogen's interactions with environmental factors such as pH, temperature, and nutrient levels, which can vary widely across different habitats. The role of biofilms and microbial interactions in facilitating Leptospira survival in soil and water also requires further investigation.

The review also addresses the impact of climate change on leptospirosis transmission, noting that increased temperatures and extreme weather events can extend the habitat range of reservoir species and enhance the pathogen's environmental survival. These changes may lead to more frequent and severe outbreaks, particularly in regions with inadequate infrastructure and public health resources.

In addition to environmental factors, the authors emphasize the importance of socio-economic conditions in influencing leptospirosis risk. Poor sanitation, lack of access to clean water, and inadequate waste management contribute to higher exposure rates in disadvantaged communities. The review calls for targeted public health interventions and improved surveillance systems to address these disparities and reduce the disease burden.

Bradley and Lockaby (2023) conclude by stressing the need for a One Health approach, integrating human, animal, and environmental health perspectives to effectively manage and control leptospirosis. This approach requires collaboration across disciplines and sectors to develop comprehensive strategies for disease prevention and control.

Lau et al. (2016) conducted a comprehensive study on leptospirosis in Fiji, focusing on identifying risk factors and environmental drivers of transmission. Leptospirosis, a zoonotic disease prevalent in the Pacific Islands, saw significant outbreaks in Fiji following severe flooding in 2012, resulting in 576 reported cases and a 7% case-fatality rate. The study aimed to provide evidence to improve public health mitigation and intervention strategies using an eco-epidemiological approach.

The researchers conducted a cross-sectional seroprevalence study involving 2,152 participants from 81 communities across Fiji's three main islands. They collected data through questionnaires and geographic information systems (GIS) to assess various risk factors related to demographics, individual behavior, contact with animals, socioeconomics, living conditions, land use, and the natural environment. The study found that 19.4% of participants had antibodies indicative of previous or recent infection (Lau et al., 2016).

Key risk factors identified through multivariable logistic regression analysis included male gender, iTaukei ethnicity, living in villages, lack of treated water at home, working outdoors, living in rural areas, high poverty rates, proximity to major rivers, presence of pigs in the community, high cattle density, and high maximum rainfall in the wettest month. These factors highlight the complex and multifactorial nature of leptospirosis transmission, with significant contributions from environmental conditions and socio-economic status (Lau et al., 2016).

The study also underscored the impact of climate change, population growth, and urbanization on leptospirosis transmission in Fiji. Severe weather events and flooding are expected to intensify in the South Pacific due to climate change, exacerbating the risk of leptospirosis. Additionally, rapid population growth and urbanization often lead to the development of slums, where poor sanitation and close contact with animals increase disease transmission (Lau et al., 2016).

The researchers emphasized the need for improved public health interventions and environmental management to control leptospirosis effectively. They suggested targeting high-risk groups with health promotion activities and educational materials, particularly focusing on males, farmers, and the iTaukei population. Public health measures should also aim to improve water treatment facilities and reduce exposure to untreated water and floodwaters. Furthermore, the study highlighted the importance of integrated eco-epidemiological approaches to understanding and mitigating the risks of zoonotic diseases like leptospirosis (Lau et al., 2016).

Reid, Rodney, Kama, and Hill (2017) explore the development of multisectoral strategies for zoonotic diseases, focusing on leptospirosis in Fiji. Leptospirosis, caused by bacteria of the genus Leptospira, poses significant health risks, especially in tropical regions like Fiji. This study examines the complexity of managing zoonotic diseases, which requires collaboration across various sectors, including health, agriculture, labor, and local government. The need for such a collaborative approach is underscored by the different agendas and organizational cultures that must be aligned to address the disease effectively. The researchers employed a realist review methodology combined with systems thinking frameworks to determine optimal strategies and governance for leptospirosis prevention and control in Fiji. This process involved facilitated workshops with multiple stakeholders to identify needs, issues, and potential interventions. The research was informed by interviews with bureaucrats from different government ministries, synthesizing locally available data on the impact of leptospirosis (Reid et al., 2017).

The study found that leptospirosis often receives widespread attention only during outbreaks, usually triggered by media coverage of deaths or numerous hospitalizations. Despite this, all ministries expressed support for a multisectoral strategy, designating the Ministry of Health and Medical Services (MHMS) as the lead agency. The final consultation workshop set a goal to reduce the case fatality rate attributable to leptospirosis by 50% by 2020, focusing on four overarching strategies: improved clinical management, enhanced surveillance, improved communication to minimize risk and promote health-seeking behaviors, and strengthened coordination and governance structures (Reid et al., 2017).

Leptospirosis in Fiji is associated with strong seasonality, particularly during periods of heavy rainfall and flooding, which exacerbate the spread of the disease. Indigenous (iTaukei) Fijian males aged 15-45 are disproportionately affected due to higher exposure through occupational and recreational activities. The disease is transmitted indirectly through contact with water or mud contaminated by the urine of infected rodents or domestic animals (Reid et al., 2017).

The realist review process identified several key findings. There is a broad recognition of the mortality associated with acute outbreaks of leptospirosis, but a poorly defined understanding of its impact across different sectors. Multi-sectoral collaboration was found to be effective during acute outbreaks but required higher-level governance to sustain collaboration during endemic phases. Stakeholders generally viewed leptospirosis as a human health problem, driven primarily by human mortality and morbidity, rather than an issue with broader economic and social costs (Reid et al., 2017).

To achieve the set goal, the study proposed several specific actions under the four strategies. These included developing triaging systems based on syndromic case detection, improving diagnostic capacities, standardizing surveillance processes, and enhancing risk communication. A significant effort was recommended to build the capacity of community health workers to provide education and behavior change programs, particularly targeting high-risk groups. Strengthening governance structures was also emphasized, with a proposal for a collaborative framework involving key ministries and stakeholders (Reid et al., 2017).

The authors conclude that a multisectoral approach, involving the systematic review of evidence and the engagement of diverse stakeholders, is essential for effective leptospirosis control in Fiji. The process of deliberative consultation and the creation of a National Action Plan provide a foundation for ongoing collaboration and policy development. The global burden of leptospirosis is substantial and complex, with significant underestimation in many regions due to underreporting, lack of effective diagnostic tools, and diverse clinical presentations. In conclusion, a comprehensive approach integrating human, animal, and environmental health perspectives is essential for effective leptospirosis management and control. Improved surveillance, diagnostics, public health interventions, and multisectoral collaboration are critical to reducing the global burden of leptospirosis and mitigating its impact on vulnerable populations. These efforts must be supported by robust data collection, targeted research, and ongoing policy development to adapt to changing environmental and socio-economic conditions.

Clinical Manifestations and Diagnosis

The spectrum of clinical symptoms for leptospirosis varies between patients. Some symptoms may be very prominent and appear after 2 to 30 days after the initial exposure, while some patients may be asymptomatic. Leptospirosis can cause different features ranging from subclinical symptoms to the extent of pulmonary hemorrhage and Weil's syndrome. Fever is the most prominent feature seen in patients during their admission. Other symptoms may include chills, headache, and myalgia. Throbbing muscle aches on the calves and lower back, ocular findings in the subconjunctival region, and icterus, vomiting, feeling nauseated, diarrhea, abdominal pain, and dehydration may also be some of the symptoms that could be observed while being infected by leptospirosis. This infection has the potential to even cause multiple organ failure with the brain, lungs, liver, and kidney being the aim of infection. It can also progress into neuro-leptospirosis, acute respiratory distress syndrome, and hemorrhagic pneumonitis. In certain circumstances, the patient may have both renal failure and jaundice; this is called Weil's disease and is the most distinguishable form of leptospirosis. Acute respiratory distress syndrome may occur when the pulmonary edema and acute hemorrhagic alveolar syndrome culminates. Jaundice may be present according to the virulence of Leptospira. Heart abnormalities can also be seen in the infection. Various lab tests can also suggest an infection with leptospirosis, such as hematological results showing low platelet levels and mild leukocytosis, while the biochemistry results may indicate hyponatremia, hypokalemia, and increased serum creatinine levels. In certain circumstances, there may be an increase in creatine kinase and serum amylase levels as well. The severity of leptospirosis can be shown by meningoencephalitis. Guillain-Barre Syndrome, hemiplegia, and transverse myelitis are some other neurologic complications (Mohandas & Dhawan, 2021).

Laboratory Diagnostic Methods

There are various tests that could help with the detection of leptospirosis. However, for choosing which platform of testing to use, the date of collection of the sample is extremely essential as it may indicate that the virus is at the antigen or antibody phase. Serological tests and culture methods are some of the ways in which leptospiral could be detected. Levels of antibodies may rise after 3-10 days after the onset of symptoms, thus knowing the date of onset is extremely essential. During the initial 10 days of the infection, cerebrospinal fluid and blood cultures are extremely useful. Warthin-Starry stain is widely used in the histochemical departments as a staining for Leptospira. Urine cultures may be a very good method for the detection of Leptospira till even 30 days. This is because of the presence of the organism in the renal tubules. The Microscopic Agglutination Test (MAT) is regarded as the gold standard test for leptospirosis. Other tests include Enzyme-Linked Immunosorbent Assay (ELISA) IgM, Rapid Diagnostic Test, and Polymerase Chain Reaction (PCR) tests. The differential diagnosis for leptospirosis may be difficult as the symptoms are similar to dengue, influenza, malaria, toxoplasmosis, hepatitis, and dengue hemorrhagic fever; thus, MAT is the preferred method of testing to prevent misdiagnosis (Yadav & Kumar, 2021).

Leptospiral pulmonary hemorrhage has emerged in recent years in various places around the world. Clinicians are often concerned about how to correctly establish the diagnosis of leptospirosis.

The gold standard, which is MAT testing, detects the serovar-specific antibodies. IgM levels for detection of leptospirosis may not truly indicate if it is a true infection as these antibodies can be present for many months. The various methods of detection of leptospirosis mentioned above may only be able to produce reliable results if the essential components for testing are provided; this means that details such as the date of onset need to be provided so that the laboratory knows which stage of infection the patient is in and test the sample according to the stage of infection. MAT testing is regarded as the gold standard because of its high sensitivity, which has the ability to test group-specific antibodies (Patel, 2014). There are several diagnostic methods, but it may also not be viable to do some of the tests routinely because of their low sensitivity, expense, or other technical limitations. The diagnosis is often challenging because the cases are either mild or asymptomatic. Factors such as cross-reactivity may also contribute to false positive results (Levett, 2013; Evangelista & Coburn, 2022).

196

Table:1 Summary of laboratory diagnosis of leptospirosis

Test	Advantages	Disadvantages	Correlation of Clinical Disease with Investigations at different stages of disease						
			Sample	1st week	2nd week	3rd week	4th week	Month-years	Years
A. Microscopy: -Dark Field (DFM) -Immunofloresence -Light -Immunoperoxidase staining	Convenient for visualizing leptospires in blood, urine, rarely in CSF	DFM-Lacks sensitivity and specificity, approximately 10⁴ leptospires/ml are necessary for one cell per field to be visible under DFM	Blood	+	-	-	-	-	-
			CSF	+/-	+/-	-	-	-	-
			Dialysate Fluid	+/-	+/-	-	-	-	-
-Silver staining -Warthin-Starry stain -Immunohistochemistry -Quantitative buffy coat	Demonstration of leptospires in tissues		Urine:Convalescent shedder	-	+	+	+	+/-	+/-
			Reservoir host	-	+	+	+	+	+
B. Culture:	Gives confirmed diagnosis	Cumbersome							
C. Serology: a) Antibody Detection Paired sera required to confirm diagnosis. Fourfold or greater rise in titer between paired sera confirms diagnosis	Positive from 2nd week of illness onwards		Normal Response	-	+/- (high titres)	+ (high titres)	+ (high titres)	+/- (declining titres)	+/- (declining titres)
-Serogroup Specific Tests -Microscopic Agglutination Test (MAT)	Gold Standard, High sensitivity, Detection of group-specific antibodies possible	Complex due to requirement of maintaining strains for the preparation of live antigens	Early Treatment	-	+/- (low titres)	+ (low titres)	+ (low titres)	+/- (declining titres)	+/- (declining titres)
			Delayed Response	-	-	-	+/-	+	+/- (declining titres)
-Genus Specific Tests -IgM ELISA -IgG ELISA -Indirect Fluorescent -Antibody Tests (IFAT) -IgM Dipstick -Macroscopic Slide Agglutination -Lateral Flow Assay -Indirect hemagglutination assay -Microcapsule agglutination -Counterimmunoelectrophoresis -Complement Fixation	Most widely used laboratory method for leptospira diagnosis, Time taken to perform assay varies from 30 seconds to 4 hours		Anamnestic Response	-/+	+/-	-	-	-	-
b) Antigen Detection -Radioimmunoassay (RIA) could -Enzyme linked immunosorbent assay (ELISA) -Chemiluminescent immunoassay -Staphylococcal coagglutination	Greater specificity than dark field microscopy, Can detect upto 10⁴ to 10⁵ leptospires/ml		Blood	+	-	-	-	-	-
			CSF	+/-	+/-	-	-	-	-
			Dialysate Fluid	+/-	+/-	-	-	-	-
			Urine:Convalescent shedder	-	+	+	+	+/-	-
			Reservoir host	-	+	+	+	+	+
D. Molecular diagnosis: -Dot blotting -In situ hybridization -PCR	Successful method to detect *Leptospira* DNA in serum and even better in urine in the first week of infection, also used to detect *Leptospira* DNA in tissues for post-mortem diagnosis, which is useful when conventional methods fail.	Sensitivity lower than PCR,not extensively used for diagnosis. Inability of most PCR assays to identify the infecting serovar							

Ahmad et al: Laboratory diagnosis of leptospirosis

J Postgrad Med September 2005 Vol 51 Issue 3

Fig 5.0 Laboratory Disgnosis of Leptospirosis Arumugam, Y., Rahman, M. A., Chadee, D. D., & Mathew, S. (2005). Laboratory diagnosis of leptospirosis. *The Journal of Microbiology, Immunology and Infection*, *38*(3), 184-192.

There are several diagnostic methods, but it may also not be viable doing some of the tests routinely because of its low sensitivity, expense or other technical limitations. The diagnosis is often challenging because the cases are either mild or asymptomatic. Factors such as cross reactivity may also contribute to false positive results

Table 3 Advantages and disadvantages of common diagnostic tests for leptospirosis

	Microscopic demonstration	Culture	Serology MAT	Serology ELISA IgM	Serology rapid tests IgM	Molecular testing
Specimen collection	Blood, urine, CSF	Blood, urine, CSF, tissues	Blood	Blood	Blood	Blood, urine, CSF, tissues
Window of positivity	1st wk: blood, CSF 2nd wk: urine	1st 10 d	From Day 10–12	From Day 6–8	From Day 6–8	From Day 5–10 in blood
Processing time	Available in 1 h	2 wk to 4 mo	Several wks if not locally available	Available in 1 d	Available in 15–30 min	Available in 1 d
Early diagnosis	No	No	No	No	No	Yes
Definitive diagnosis if positive	No	Yes	Yes (seroconversion)	Yes (seroconversion)	Yes (seroconversion)	Yes
Identification	No	Yes (if MAT or molecular testing available)	Yes	No	No	Yes (by additional molecular tests)
Remark	Low sensitivity and specificity Not recommended for diagnosis	Low sensitivity, slow, difficult	Gold standard but very difficult	Needs confirmation by MAT	Needs confirmation by MAT	The only sensitive test at the acute phase
Equipment required	Dark field microscope	Specific culture media	Reference laboratory only	Standard laboratory	Laboratory equipment not required	Special equipment, dedicated laboratory space, highly skilled personnel

Fig 6.0 Advantages and Disadvantages of common laboratory tests. Arumugam, Y., Rahman, M. A., Chadee, D. D., & Mathew, S. (2005). Laboratory diagnosis of leptospirosis. *The Journal of Microbiology, Immunology and Infection*, *38*(3), 184-192. https://doi.org/10.1016/j.jmii.2013.03.001,.

Prevention and Control Measures

Vaccines and Prophylaxis

Leptospirosis can be prevented by administering vaccinations to both humans and animals. Because of cross-reactivity, certain vaccines can provide protection against serovars other than the ones used in their manufacturing (Matsuo, Isogai, & Araki, 2000). They can, however, be dependent on the serotype and unable to elicit an immunological response against other serovars (Sonrier et al., 2000). Furthermore, developing vaccines is hampered by the genetic and phenotypic variability of infectious leptospires. Typically, inactivated vaccinations are administered to cattle and domestic animals. It is also used on vulnerable human populations in various nations. But they aren't employed everywhere because of human side effects, a lack of cross-protection, and a short immunity period (Grassmann, Souza, & McBride, 2017).

There are several types of leptospirosis vaccines available, with bacterins being the most common.

These vaccines are created from whole, inactivated cells. Despite their widespread use, bacterins have several drawbacks, including high production costs, potential for both systemic and localized reactions, and a relatively short duration of immunity. Additionally, they only provide protection against antigenically similar serovars. Consequently, polyvalent vaccines are often administered to domestic animals such as cattle. The duration of immunological protection from these vaccines varies based on the adjuvants used, ranging from six months to three years. Human vaccine formulations have shown efficacy rates between 60% and 100% (Koizumi & Watanabe, 2005).

Recombinant DNA vaccines offer several advantages, including stability, low production costs, and the ability to induce long-term humoral and cell-mediated immune responses against multiple serovars. These vaccines are highly immunogenic and have been developed to target conserved genes in pathogenic leptospires. In animal models, genes such as LipL32, OmpL1, and LipL41 have been inserted into various vectors to develop effective vaccines (Bashiru & Bahaman, 2018).

Chemoprevention prophylaxis is another option for treating leptospirosis; it is primarily utilized in situations where there is a high risk of infection and forced exposure. Weekly oral administration of 200 mg of doxycycline has been shown to considerably lower morbidity and mortality while also reducing clinical infection. However, it does not prevent infection (Sehgal et al., 2000).

Hygiene, PPE, and Environmental Control

Using protective clothing to cover wounds and lower the chance of disease appearance is one way to prevent leptospirosis (WHO, 2008). Other methods include wearing personal protective equipment, such as overalls, gloves, boots, and goggles, when around livestock to avoid exposing skin or mucous membranes. Hands should be cleaned after coming into touch with animals and their byproducts, and rodent populations should be kept under control to avoid leptospirosis. Additionally, areas used for animal breeding must be cleaned. In addition, individuals ought to undergo routine laboratory and clinical testing, particularly in cases where an infection is suspected. Pets and cattle must also be vaccinated. It's crucial to stay away from swimming in animal-accessible areas, treating human water sources with chlorine, and boiling water before drinking it. Similarly, preventing water clusters from forming in work zones is crucial to lowering the risk of leptospirosis outbreaks (Official Mexican Standard NOM-029-SSA2-1999, 1999). Staying away from the carrier host and contaminated environment lowers the risk of infection. Increasing public knowledge of leptospirosis is crucial, particularly for those in high-risk categories, since this will enable early detection and appropriate treatment (WHO, 2009). This can be accomplished by implementing interventions or education campaigns that encourage high-risk groups to adopt preventative health practices (Rahman et al., 2018).

Designing control measures requires knowledge of the eco-epidemiology of bacteria in the environment and in animal hosts, as well as the identification of Leptospira reservoirs. Since the virulence of different Leptospira serovars might vary, it is impossible to determine the exact level of health risk associated with leptospirosis. However, it is also possible for the infection to be undetected and asymptomatic, which would lead to an underestimate of the seroprevalence. Therefore, in order to adopt or modify vaccination methods, it is vital to ascertain the precise number of individuals who are seropositive and to research which serovars are present in the affected area (Richard & Oppliger, 2015; Sanchez-Montes et al., 2015). Once thought to be a common illness in tropical regions, some researchers predict that changes in temperature, an extended wet season, and flooding events brought on by climate change could expand the disease's distribution area and increase the incidence of leptospirosis and spirospira in the coming years (Lau et al., 2010) so there are a lot of information gaps that need to be filled.

Vaccination Strategies

The creation of vaccines is aided by fundamental studies in molecular biology and microbiology of *Leptospira*. One example of fundamental research that has advanced and will continue to advance our knowledge of pathogenesis and virulence factor identification is *Leptospira* mutagenesis. In order to identify viable vaccine candidates and analyze protein sequence variations among various *Leptospira* spp., genomic and pangenomic investigations are crucial to the development of a universal leptospirosis vaccine. Reverse vaccinology (RV) has to be used more extensively in leptospirosis cases as it hasn't been adequately investigated yet. An in vitro validation is necessary after possible vaccine candidates are found, especially to verify the location of antigens on the leptospiral cell surface. A potential vaccine candidate's immunogenicity can now be evaluated.

The immune response against leptospiral antigens has been strengthened by the use of a number of adjuvants and delivery methods. The most often used are Freund's adjuvant and aluminum hydroxide (alhydrogel), however other substances, such as flagellin (Monaris et al., 2015), CpGs (Bacelo et al., 2014), and liposomes have been investigated. Since Freund's adjuvant has a high reactogenicity, it cannot be used on people. It is helpful for the initial screening of vaccine antigens and has been effectively incorporated into leptospirosis vaccine formulations (Silva et al., 2007).

The most often used adjuvant in human vaccines, alhydrogel, has only shown evidence of limited protection in vaccinations to date. As of late, additional adjuvants—MF59 (squalene), AS01 [monophosphoryl lipid A (MPL), QS21], AS03 (α-tocopherol, squalene, and polysorbate 80), AS04 (MPL combined with alhydrogel), and virosomes (liposome/VLPs)—have entered the market and been given approval for use in the formulation of human vaccines (Stassijns et al., 2016). The potential adjuvants for leptospirosis vaccinations have not yet been tested.

Rational immune response regulation is challenging to achieve with leptospirosis vaccines since little is known about the protective immune response that should be elicited by the vaccination. Humoral immunity is thought to be responsible for protection; anti-LPS antibodies are protective in animal models and can be passively transmitted between animals (Pizza et al., 2000). Leptospires are most likely removed from the bloodstream by phagocytosis, which is followed by opsonization. However, in some hosts, such as cattle, cellular immunity induction is as significant (Pizza et al., 2000). Until recently, there were no published findings of a link between antibody titer elicited by leptospiral recombinant vaccines and challenge resistance. However, an oral immunization technique based on LigA indicated that survival was dependent on achieving a minimum antibody titer in a 2-week period following inoculation (Lourdault et al., 2014). If this can be replicated, it will be a very significant discovery. The lack of immunological correlates is a serious restriction in target identification utilizing RV because they are needed for the in vitro screening of prospective vaccine candidates, such as the bactericidal assay for *Neisseria meningitidis* (Pizza et al., 2000) and the opsonophagocytosis assay for *Staphylococcus aureus* (Etz et al., 2002).

Efforts to develop a universal leptospiral vaccine have so far fallen short of expectations, and alternatives to whole-cell inactivated leptospiral vaccines have not lived up to the original hype. The few (about thirty) leptospiral proteins that have been studied utilizing different vaccine strategies—such as subunit, DNA, prime-boost, encapsulated, and live avirulent strains—have been emphasized in a number of reviews. Less than a small percentage of these have been successful. But the availability of various genome sequences, along with developments in bioinformatics (like RV) and the study of virulence components exposed to the surface, can help find better candidates for vaccines (Pizza et al., 2000; Etz et al., 2002).

The next task is to create in vitro tests for high-throughput screening of these vaccine candidates based on correlates of immunity. Although there are a number of leptospirosis animal models, standardizing them is essential for the rigorous analysis of protection data. A universal vaccine must prioritize cross-protection, which calls for the discovery of vaccine candidates that are conserved across infectious *Leptospira* species (Lourdault et al., 2014). Our limited knowledge of the (protective) immune response has made it more difficult to choose adjuvants wisely for use in vaccine formulations. Ultimately, even if the research is making progress, a universal leptospirosis vaccine is still a long-term objective.

Environment and Vector Control

Due to a dearth of fieldwork and research on the properties and dynamics of soils, there are currently several gaps in the literature concerning leptospirosis and soils. The strains of *Leptospira* that are found in the environment are largely unknown to us. Since soils contain strains of *Leptospira* from all across the genus, future research should aim to evaluate the entire diversity of *Leptospira* that live, persist, and reproduce in soils (Thibeaux et al., 2018).

First, the absence of surveillance restricts our current knowledge of the effect of ambient waters on the leptospirosis transmission cycle. This is partly due to the high costs and difficulties associated with detection technologies. *Leptospira* measurement in the environment is limited by the fact that methods are frequently tailored to sample under specific conditions rather than others, which causes variability between situations that makes data difficult to interpret. For instance, clogging of the sample filters due to physiochemical characteristics of the water, such as elevated concentrations of suspended solids, dissolved organic carbon, and other dissolved nutrients, can complicate the sampling of environmental water sources using methods that incorporate filtration (Riediger et al., 2016).

The increased understanding of where risk associated with environmental conditions is most severe along with opportunities for reducing the risk of leptospirosis outbreaks are likely to arise from studying trends along the urban–rural gradient, as many of the increased risks associated with increased rates of leptospirosis are related to decisions about land management and infrastructure. For instance, as cattle herds get closer to cities, prevalence rises along the urban–rural gradient (Yatbantoong & Chaiyarat, 2019). The mechanism underlying this tendency is unknown at this moment, hence more research is required to understand the transmission cycles among domestic animals. There also appears to be a prevalence trend of leptospirosis among small mammal populations that occurs along the urban-rural gradient, with different prevalence of infection in urban, suburban, and rural ecosystems (Yusof et al., 2019). The mechanics underlying this are also unknown. This demonstrates the dearth of knowledge on the cycles of *Leptospira* transmission in wildlife. Efforts to control the disease will be ineffective unless we have a good understanding of the pathways of transmission, components to environmental persistence, and the most likely hazards of spillover from environmental sources. As a result, it is critical to investigate the disease's dynamics along the urban-rural gradient, as well as *Leptospira*'s environmental persistence, survival, and reproduction. To increase communities' ability to reduce disproportionate exposure to leptospirosis through targeted public health outreach, we need to learn more about *Leptospira*'s environmental persistence and survival (Freudenberg, Pastor, & Israel, 2011).

Treatment and Management

Leptospirosis typically manifests with mild clinical symptoms that may resolve spontaneously (Haake & Levett, 2015; Chacko et al., 2021). Treatment varies based on the severity of the infection. For moderate leptospirosis, oral doxycycline is commonly prescribed, with a recommended dosage of 100 mg twice daily for a week. Other oral antibiotics include amoxicillin (500 mg/day for 7 to 10 days), ampicillin (500-750 mg/day for 7 to 10 days), and azithromycin (500 mg/day for 3 days) (Wang, Jin, & Węgrzyn, 2007; Monahan, Miller, & Nally, 2009; Lucheis & Ferreira, 2011). This approach can reduce the duration of the illness.

In addition to treating active infections, doxycycline can be administered prophylactically to individuals traveling to regions where leptospirosis is endemic, as well as to those in high-risk occupations like water sports athletes and veterinarians. For prophylaxis, a weekly dose of 200 mg of oral doxycycline is recommended, and this should continue as long as there is a risk of exposure. While doxycycline can reduce the severity of leptospirosis, it does not prevent the infection.

For severe leptospirosis, characterized by renal and hepatic failure, intravenous penicillin G sodium at a dose of 1.5 million units every 6 hours for one week is recommended (Fraga et al., 2024; Watt et al., 1988). Other antibiotics that can be used to treat severe leptospirosis include amoxicillin, ampicillin, azithromycin, doxycycline, and tetracycline. However, doxycycline is not recommended for children and pregnant women (Fraga et al., 2024). Besides antibiotics, treatment options may include steroids, natural medicines derived from medicinal plants, synthetic chemicals, and probiotics.

Due to the high mortality rate associated with severe pulmonary symptoms of leptospirosis, close monitoring of patients is essential. Antimicrobial therapy should be combined with mechanical respiratory ventilation to manage pulmonary hemorrhage. In addition to the aforementioned antibiotics, cefotaxime and ceftriaxone are also effective treatment options for leptospirosis (Griffith, Hospenthal, & Murray, 2006; Panaphut et al., 2003).

Even though antibiotic treatment for leptospirosis is highly effective, some patients may experience Jarisch-Herxheimer responses (JHRs). JHR is a brief immunological occurrence that frequently occurs in patients receiving therapy for syphilis, leptospirosis, and other spirochete diseases. Clinically, it presents as transient constitutional symptoms such as fever, chills, headaches, and myalgias. The onset of JHR was noted 24 hours following antibiotic ingestion. This characteristic can be recognized as a worldwide issue in the context of leptospirosis treatment with antibiotics (Friedland & Warrell, 1991). Some antibiotics are not appropriate for treating leptospirosis, despite the fact that a broad variety of antibiotics can be used to treat the disease. Consequently, *Leptospira* species are not susceptible to vancomycin, rifampicin, metronidazole, or chloramphenicol (Faine et al., 1999; Morgan, 2004).

Control and prevention are significant actions that can be thought of as viable solutions to stop leptospirosis from spreading. Effective strategies for preventing the spread of leptospirosis and the transfer of *Leptospira* bacterial agents include promoting hygiene and reducing environmental contamination through rodent control in both rural and urban regions. Concurrently, vaccination against leptospirosis is a significant preventive measure for domestic and livestock animals as well as people in high-risk employment (Hotez & Ferris, 2006).

A variety of approaches, including antibiotic therapy and newly developed treatments like probiotics and unique chemicals, are effective in treating leptospirosis. A treatment plan based on the severity of the infection still mostly uses antibiotics, such as doxycycline. While probiotics have the potential to influence gut microbiota and boost immune responses, more investigation is required to determine exactly what impact they play in the treatment of leptospirosis. Further intriguing directions for potential therapeutic interventions are provided by the investigation of bacteriophages and new chemicals. Mitigating the impact of this widespread zoonotic disease on global health requires sustained work to improve our understanding of leptospirosis pathophysiology and treatment approaches.

Challenges in Treatment

At least 20 of the 69 species of the genus Leptospira are known to be pathogenic, and its more than 260 serovars are divided into 24 serogroups by the serological classification system, which is based on the lipopolysaccharide (LPS) composition of the bacterial outer membrane (Vincent et al., 2019). There are commercial leptospirosis vaccinations available, particularly for veterinary usage, and they include inactivated leptospires (Ellis, 2015). These formulations do, however, have well-known drawbacks, such as protection against serovar restriction and the generation of transient immunity (André-Fontaine et al., 2003; Suepaul et al., 2010; Sonada et al., 2018; de Oliveira et al., 2021).

Leptospira spp. have limitations due to the lengthy incubation period, difficulty in accurately quantifying growth, and use of serum in bacterial culture media, despite being susceptible to a wide range of antimicrobial agents, including fluoroquinolones, macrolides, β-lactams, and tetracyclines. Despite these issues, leptospirosis preventive and treatment have been made easier by the use of microdilution techniques (Haake & Levett, 2015). Leptospira species demonstrate inherent resistance to diverse antimicrobial drugs; however, the precise mechanisms behind this resistance are yet unknown (Adler et al., 1986). Still, resistance to actidione, neomycin, polymyxin, nalidixic acid, vancomycin, rifampicin, and sulfonamides has made it easier to create selective media for isolating leptospires (Kumar et al., 2016). One may wonder why there hasn't been a noticeable rise in antibiotic resistance in Leptospira given this observation. Leptospiral infections are often monomicrobial, which limits the potential for horizontal resistance gene acquisition. Furthermore, there is no experimental evidence of foreign DNA uptake by Leptospira spp., despite genomic analyses supporting this hypothesis. Finally, human leptospirosis is a dead-end illness; human-to-human transmission is extremely infrequent (Faine et al., 1999; Morgan, 2004).

Discussion and Analysis

The Leptospirosis review is an in-depth analysis of this important zoonosis: its epidemiology, environmental drivers, the public health attempts to alleviate disease, and strengthen control efforts characterized by a call for integrated approaches as society moves forward. The group also discusses the ambitions, inconsistencies, and directions for future studies of leptospirosis.

Epidemiology of Leptospirosis

The epidemiologic profile of leptospirosis indicates its ubiquitous distribution in tropical/subtropical regions, with higher prevalence rates among low- and middle-income countries (LMICs). The paper also underscores the annual worldwide load of about 1.03 million cases with some 58,900 deaths, greatest happening in South and Southeast Asia (Oceania) and Caribbean regions. These data reinforce the public health importance of leptospirosis, particularly in regions with poor sanitation and limited healthcare infrastructure that face continued environmental exposure to Leptospira spp.

Nonetheless, the review also lays bare serious shortcomings in epidemiological data too — poor studies overall and dearth of some regions like Africa. The absence of well-organized surveillance and reporting systems in a lot of low- and middle-income countries (LMICs) leads to gross underestimation cancer burden. In addition, the wide spectrum in clinical presentations of leptospirosis (from mild flu-like syndromes to severe forms such as Weil's disease) makes diagnosis and reporting more complex, thereby increasing the chance for misdiagnoses or underreporting.

Environmental and Climatic Drivers

This review shows clearly that the main impact of flooding as associated with climate change on Leptospira transmission stems from increased bacterial survival in waterlogged soil and surface waters. The more often and the harder this happens, then especially in these places at risk it might lead to yet more cases of leptospirosis. The analysis correctly suggests that more attention should be given to those environmental drivers in predicting and preventing fatal outbreaks. Nonetheless, the authors argue that we still require more localized research to understand region-specific dynamics. Further study is needed on the contribution of biofilms and microbial interactions to Leptospira survival in nature.

Public Health Implications

This review highlights the importance of a One Health perspective that actively combines clinical, veterinary, and environmental management in order to address leptospirosis. Given that Q fever is a zoonotic disease, involving multiple epidemiological reservoirs such as rodents, livestock, and wildlife, it would be necessary to take this holistic approach.

Vaccination, public education, and environmental management are emphasized as integral to leptospirosis control strategies. Yet, the serovar-specific and short-lived immunity elicited by current vaccines drives the ongoing search for more efficacious and broadly protective vaccine(s). Recombinant DNA-based vaccines of very high immunogenic response have the promise to broaden and advance the way across many challenging infectious diseases.

The most relatively important class of antibiotics that are used in treatment for leptospirosis include doxycycline and penicillin. It is also emphasized in the review that prophylactic antibiotics are necessary for high-risk settings, but should be weighed against worries about antibiotic resistance and feasibility of such measures.

Diagnostic Challenges

Accurate and prompt diagnosis of leptospirosis is essential for effective treatment and control. The review summarizes different diagnostic techniques: Microscopic Agglutination Test (MAT), Enzyme-Linked Immunosorbent Assays (ELISAs), and Polymerase Chain Reaction. Yet, every approach is hampered by levels of sensitivity and specificity that may be low under conditions similar to those found in many resource-poor environments.

Increased diagnostic capacity, especially in LMICs, is important for improving surveillance of and reporting on human leptospirosis. Better research should focus on the creation of faster, cheaper, and more attuned diagnostics. Second, simplified predictive models incorporating clinical, biochemical, and epidemiological data could provide better diagnostic accuracy that would enable early outbreak detection.

Socio-Economic and Behavioral Factors

The socio-economic ground is an essential player in the dispersion of leptospirosis. All are due to poverty, poor sanitation, and close human-animal interaction in rural areas or urban slums. The review also draws attention to the necessity of implementing targeted public health measures in high-risk populations, including subsistence farmers, herders, and urban slum dwellers.

In addition, occupational exposure and recreational activities in contaminated environments are behavioral factors that also increase the risk of leptospirosis. This is an important aspect of a holistic strategy given the fact that educational campaigns informing them about precautionary practices are core to leptospirosis prevention.

Future Directions and Recommendations

In conclusion, the review provides a solid basis to understand the multifaceted nature of leptospirosis, and identifies several areas for future research as well as for policy development:

Improved Surveillance Systems and Data Reporting: There is an urgent need to strengthen surveillance systems in LMICs while at the same time improving mechanisms used in reporting. Completeness of the data could be improved with digitalization through integration (hospital information systems) and private sector reporting.

Environmental Dynamics: Field studies will be necessary to elucidate the environmental persistence and transmission dynamics of Leptospira. Studying biofilms, microbial interspecies interactions, and environmental factors like pH and temperature will give us a greater understanding of the ecology associated with this pathogen.

Effective Vaccines: There are effective vaccines in use, but further research is needed to develop a better vaccine providing wide and long-lasting protection due to recombinant DNA vaccines which have raised considerable attention during recent years as well as other measures developed for more broad-acting approaches, including constant monitoring of newer serovars emerging at various locations around the world.

Diagnostic Instruments: There is a need for promoting the development of cost-effective, rapid, and more sensitive diagnostic tools to enable early detection and treatment, especially in resource-constrained regions.

Public Health Education: Wide-ranging public education programs are needed to alert high-risk populations about strategies for leptospirosis prevention.

Integrated One Health Approach: The success of leptospirosis control strategies can be improved if a comprehensive and integrated One Health approach involving human, animal, and environmental health sectors is implemented.

The review covers a multifaceted analysis of leptospirosis, highlighting the complexity of its interaction with environmental, socio-economic, and climatic factors. Strategies to reduce this global burden should be focused on an effective, integrated approach towards the reduction of their determinants and vulnerabilities, which includes targeting gaps in surveillance (human, animal), diagnostics (health services), and public health infrastructure. Further investigation, focused interventions, and multisectoral cooperation will be needed to create successful programs for disease control and prevention of this re-emerging zoonosis.

Conclusion

Leptospirosis is a continuing international health problem that affects tropical and subtropical regions. Leishmaniasis is a complex public health problem and its transmission involves intricate interaction among environmental, climatic, and socio-economic factors. Leptospirosis remains under-recognized, especially in low-middle-income countries (excluding China) despite major progress that has been made towards the diagnosis and treatment of leptospires. Leptospirosis is a highly preventable disease; it calls for an integrated approach to human, animal, and environmental health. Growing evidence shows that an integrated approach, involving enhanced surveillance systems and diagnostics for the identification of both human and animal cases followed by specific public health interventions are necessary to reduce the disease burden. This takes into account that climate change escalates the conditions for leptospirosis transmission and should be complemented by proactive measures in relation to strategies on climate adaptation and mitigation. Although vaccines exist, they are serovar specific and generate short-lived immunity. Hence, more profound investigation of the environmental dynamics of Leptospira and the development of better vaccines are mandatory. Heavily targeted areas should have public education and awareness campaigns in place to assist with prevention efforts. A food- and water laboratory-testing center on the lines envisioned by the authors is an important advance in leptospirosis diagnostics and prevention. The facility will strengthen outbreak detection and response, in turn meaning improved public health results. In conclusion, the prevention of leptospirosis needs to be multi-pronged strategies and cut across all sectors. All of these abject failures in surveillance, diagnostics, and public health infrastructure can be addressed directly with respect to bovine tuberculosis by externally imposed requirements for introduction without concurrent disease risks, and furthermore should indeed also be informed at a political level from the premise that much resurgent zoonosis will not only find its further basis in environmental changes responsive to ecological landscapes but ultimately such change is nurtured through clinically affecting socioeconomic practices. The research must go on and efforts should be joined worldwide to come up with a complete strategy for preventing Leptospirosis.

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Shafraaz Khan. Technical Higher-Grade officer for Fiji Center of Disease Control Food and Water Lab 2024
Contact- shafmedt@gmail.com
shafraaz.khan@health.gov.fj

Mabel Vaniqi. Laboratory Technician for Fiji Center of Disease Control 2024
Contact- mabelvaniqi29@gmail.com

Anjini Naicker. Laboratory Scientist for Fiji Center of Disease Control 2024
Contact- anjininaicker55@gmail.com

Emily-Ann Underwood. Laboratory Scientist for Fiji Center of Disease Control 2024
Contact- em.lesione@gmail.com

Shanon Shyna Prasad. Laboratory Scientist for Fiji Center of Disease Control 2024
Contact- shanonlabt@gmail.com