# One Health Approach for Understanding and Managing Animal Leptospirosis in India

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## Abstract

Leptospirosis is a zoonotic disease of significant public health concern globally and in India, where a diverse range of animal hosts contribute to its perpetuation and spread. This paper reviews the epidemiology of leptospirosis in various animal species in India and underscores the importance of the One Health approach in overcoming complacency towards its management. The interconnectedness of human, animal, and environmental health is central to understanding the disease's dynamics. This approach exposes the shortcomings of isolated efforts and the necessity for comprehensive strategies that foster intersectoral collaboration, supported by appropriate policies, educational initiatives, and technological advancements. This review highlights the critical roles of various stakeholders, from government and policymakers to health professionals and the general public in implementing and promoting One Health initiatives. Despite the challenges, the review illustrates the significant potential of the One Health approach in mitigating the impact of leptospirosis in India, with insights valuable for other zoonotic diseases. This review concludes by outlining future directions and recommendations, focusing on advancements in leptospirosis prevention and control and identifying areas necessitating further research. By addressing complacency and promoting proactive, integrated actions, we can effectively manage leptospirosis, thereby protecting both animal health and public health in India.

**Keywords:** Leptospirosis, One Health, India, Epidemiology, Livestock, Wildlife, Disease control

## Introduction

### Leptospirosis: An Invasive Zoonotic Threat

Leptospirosis, a zoonotic disease caused by the pathogenic bacteria of the Leptospira genus, thrives with alarming pervasiveness across the globe.[1, 2] Leptospirosis afflicts an extensive array of mammalian species, encompassing humans, livestock, and a diverse array of wildlife. [3] With an unusual ability to occupy diverse mammalian hosts, the organism has a complex life cycle. The life cycle involves a maintenance host harboring a chronic renal infection, contrasting the incidental host susceptible to acute disease episodes with potential severe outcomes including Weil's disease or pulmonary hemorrhagic syndrome.[4] Leptospirosis has a protean clinical presentation, ranging from mild, flu-like conditions to potentially fatal complications including jaundice, renal failure, and hemorrhage.[5] The broad spectrum of manifestations and symptomatic overlaps with other febrile illnesses pose significant diagnostic challenges, often culminating in underreporting and misdiagnoses.[4] Transmission of this disease to humans and other animals is primarily via direct or indirect contact with urine from infected animals, entering the body through skin cuts or mucous membranes of the mouth, nose, and eyes. Flooded regions and water bodies contaminated with the urine of infected animals serve as hotspots for leptospirosis transmission.[6] Global incidence estimation is a complex task, rendered challenging due to variations in surveillance and reporting across countries. Nevertheless, the yearly worldwide tally of severe leptospirosis in humans is estimated to surpass a million cases, with a death toll approximated at 58,900 cases.[1] Resource-limited, tropical countries bear the highest burden, due to their conducive conditions for survival and propagation of Leptospira.

The One Health paradigm recognizes the intricate relationship between human health, animal health, and the environment health, with the objective of optimizing health outcomes.[7, 8] This concept is critically relevant to leptospirosis, a zoonotic disease hosted in animal reservoirs.[9] This review addresses the application of One health concept for understanding the epidemiology and control of leptospirosis in India, emphasizing the importance of a One Health approach for effective disease management. The One Health strategy has proven effective in managing leptospirosis through veterinary health measures, such as screening and vaccinating domestic animals in high-risk areas, and environmental health initiatives that improve sanitation and water quality.[10] These measures reduce human infection risk and environmental burden of Leptospira. The approach fosters multi-sectoral data sharing, enabling early detection of leptospirosis outbreaks and swift intervention to limit disease spread.[11] Nonetheless, there is a prevailing complacency in implementing the One Health approach to leptospirosis.[3, 12] This complacency can delay diagnosis and treatment, inhibit effective prevention strategies, and obfuscate disease patterns (Table I).[13,14]
The root causes of this complacency include

coordination gaps due to institutional and professional barriers, lack of awareness of the One Health approach, and resource constraints in both human and veterinary health sectors. Limited availability of diagnostic tools and surveillance systems compounds the problem, reducing capacity to detect and monitor leptospirosis in human and animal populations.[15] Overcoming this complacency is imperative to enhance leptospirosis management and reduce its impact on human and animal health. The review further explores the ethical dimensions of the One Health approach (Fig.1), underscoring principles like harm minimization, duty of care, solidarity, healthcare equity, and research ethics. By fostering interdisciplinary collaboration and a holistic understanding of leptospirosis, the One Health approach can significantly contribute to strategies to reduce the disease's impact on human, animal, and environmental health in India.

**Table 1: Types of Complacency in Leptospirosis Research and Management in India**

| Type of Complacency | Description |
|---|---|
| Geographic Complacency | Focus on Gujarat, Maharashtra, and Kerala, neglecting other endemic regions. |
| High-Risk Group Complacency | Underrepresentation of certain high-risk groups, ignoring their specific risks |
| Intervention Research Complacency | Absence of studies on diverse interventions like dialysis, human vaccines, and personal |
| Community-Level | Limited focus on systemic |
| System and Policy-Level Complacency | Lack of research on governance and health system readiness. |
| Seasonal Risk Complacency | Inconsistent consideration of seasonal risks like monsoons and flooding |
| Disease Course Complacency | Few studies explored alternative therapeutic measures for leptospirosis. |
| Animal Transmission Complacency | Limited focus on animal vaccines or birth control programmes to control disease spread. |
| Health System Response Complacency | Inadequate studies evaluating health system readiness. |
| Innovative Approach Complacency | Limited use of multicomponent interventions in studies |
| Non-Endemic Areas Complacency | Minimal focus on non-endemic regions in leptospirosis management studies. |
| Lesser-Known Intervention Complacency | Absence of studies on novel interventions like dialysis or vaccines. |
| Health System Infrastructure Complacency | Limited research into healthcare infrastructure. |

## 2. Leptospirosis

### 2.1. An Overview

Leptospirosis is caused by spirochete bacteria from the Leptospira genus, falls within the phylum Spirochaetes and comprises over 64 species based on molecular classification, differentiated through a variety of genetic techniques such as DNA-DNA hybridization and 16S rRNA phylogeny.[16] However, for practical epidemiological and diagnostic purposes, the serological classification, which identifies over 300 serovars based on surface-exposed lipopolysaccharides (LPS), is frequently used.[17] The Leptospira genome is unique among bacteria for its two circular chromosomes and the presence of lateral gene transfers and multiple pathogenicity islands, indicating its genomic plasticity and evolutionary adaptation to diverse environments.[18]

Morphologically, Leptospira bacteria are slender, helically coiled, and possess internal flagella or endoflagella that are located in the periplasmic space. The coordinated rotation of these endoflagella provides Leptospira with their distinctive translational motility, which is not only important for their survival in aqueous environments but is also aid in host tissue invasion during infection (Fig. 2).[19] The Leptospira bacteria thrive in warm and humid conditions and can survive for months in damp soil and stagnant water bodies, especially those rich in organic matter and with slightly alkaline pH. This remarkable environmental resilience helps to maintain the transmission cycle in nature, particularly in areas with frequent flooding or swamps.[6, 20]

### 2.2 Transmission Dynamics

Leptospira, a bacterium with a broad host range, primarily persists in the environment due to the widespread distribution, high population density, and chronic infection nature of rodents.[9] Humans, incidental hosts, usually contract the disease through direct or indirect exposure to the bacteria found in the urine of infected animals, water, or soil.[21] Upon entering a host, Leptospira spreads, affecting various organs, notably the liver and kidneys.

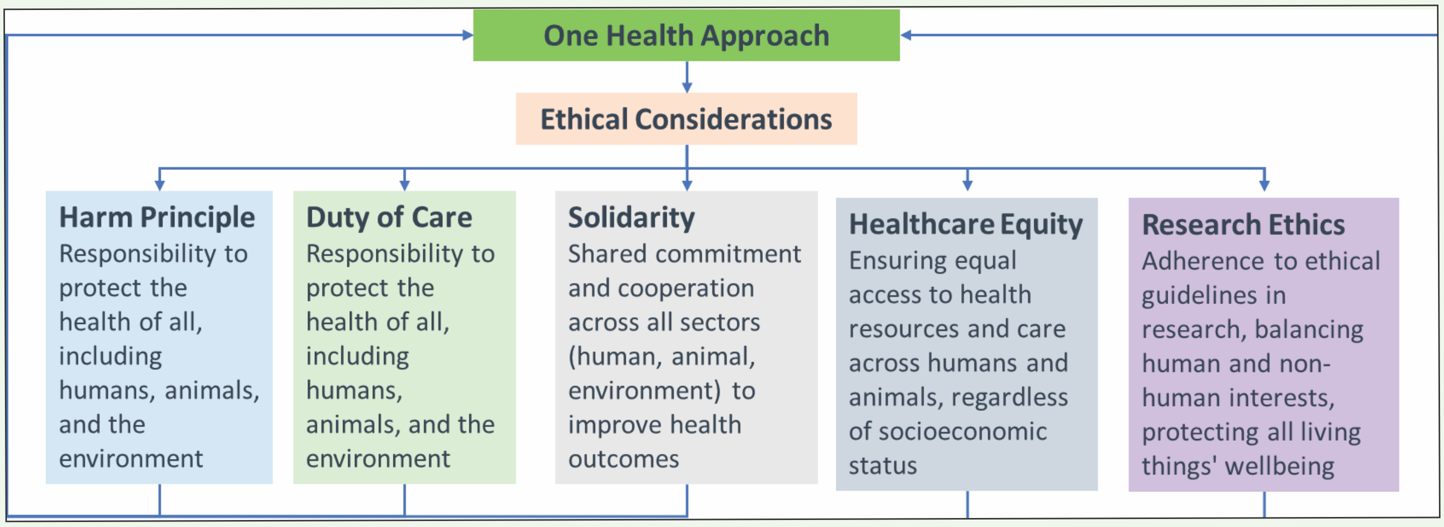


**Figure 1: The Ethical Principles Guiding the One Health Approach**

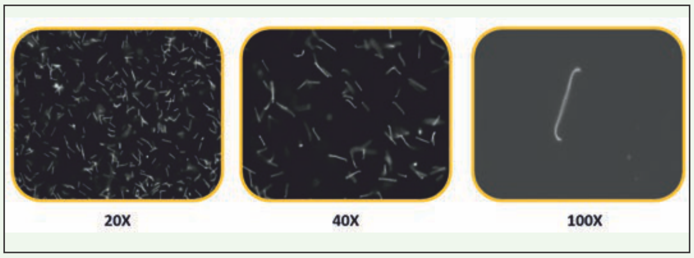


**Figure 2: The Ethical Principles Guiding the One Health Approach**

This targeting induces jaundice and renal impairment - classic severe leptospirosis symptoms. Moreover, the bacteria can colonize renal tubules, promoting urinary shedding and further spread of the disease.[6, 22] The complex transmission dynamics incorporate multiple hosts and environmental factors. Rats, primary Leptospira reservoirs, harbor the bacteria in their renal tubules and excrete it in their urine, often asymptotically.[9] This shedding, especially prevalent in urban areas with dense rodent and human populations, is instrumental in spread of leptospirosis Here, humans frequently contract the infection through exposure to rodent urine-contaminated water or soil, especially in sanitation-poor areas.[4]

Livestock, such as cattle, pigs, and horses, heavily influence epidemiology of leptospirosis in rural and agricultural settings. These animals, infected similarly to humans, often suffer from reproductive disorders and milk drop syndrome, causing economic losses.[9] They can become chronic Leptospira shedders, contaminating the environment and contributing to reinfection cycles in livestock and potential transmission to other animals and humans.[9] Wildlife also plays a key role in leptospirosis transmission dynamics. Wild rodents, marsupials, and carnivores can harbor and shed Leptospira, potentially contaminating natural water sources, soil, and vegetation.[23] This contamination poses risks to humans engaged in recreational activities and domestic animals in these areas. Humans contract the infection through occupational or recreational exposure to Leptospira-contaminated environments (Fig. 3)[4]. Farming, mining, abattoir work, veterinary practice, and certain water-related recreational activities notably heighten Leptospira exposure risk. The intricate interplay of these hosts and environments sustains the lifecycle of Leptospira, underscoring the need for a multi-sectoral and transdisciplinary approach, epitomized by the One Health Concept, in leptospirosis control and prevention (Fig. 4).[2]

### 2.3. Human leptospirosis, its Impact on Human Health, Livestock Productivity and Economy

Estimates suggest that leptospirosis affects more than one million people annually, leading to 58,900 deaths worldwide.[1] Livelihoods, particularly in resource-limited settings, are also severely affected by leptospirosis. The disease frequently affects vulnerable populations such as farmers, slaughterhouse workers, and others exposed to infected animals or contaminated water or soil.[4] Among the Asian countries, it has been estimated that China has the second largest burden estimate (301,688 DALYs, 95% UI: 119,388–525,491 or 22.05 DALYs per 100,000 population, 95 UI: 8.82–38.81) after India (684,369 DALYs, 95% UI: 290,213–1,217,287 or 56.35 DALY per 100,000 population, 95% UI: 23.90–100.23).[25] A country-level evidence gap map in India highlighted limited data and research gaps on the epidemiology of leptospirosis, indicating the need for more comprehensive studies to understand the disease burden and risk factors better.[26]

Despite these valuable studies, a country-level evidence gap map highlighted limited data and research gaps on the epidemiology of leptospirosis in India, signaling the need for more comprehensive studies to better understand the disease burden and risk factors.[26] A few of seroprevalence studies in India have provided valuable insights into the prevalence and distribution of leptospirosis in different regions. For instance, a study

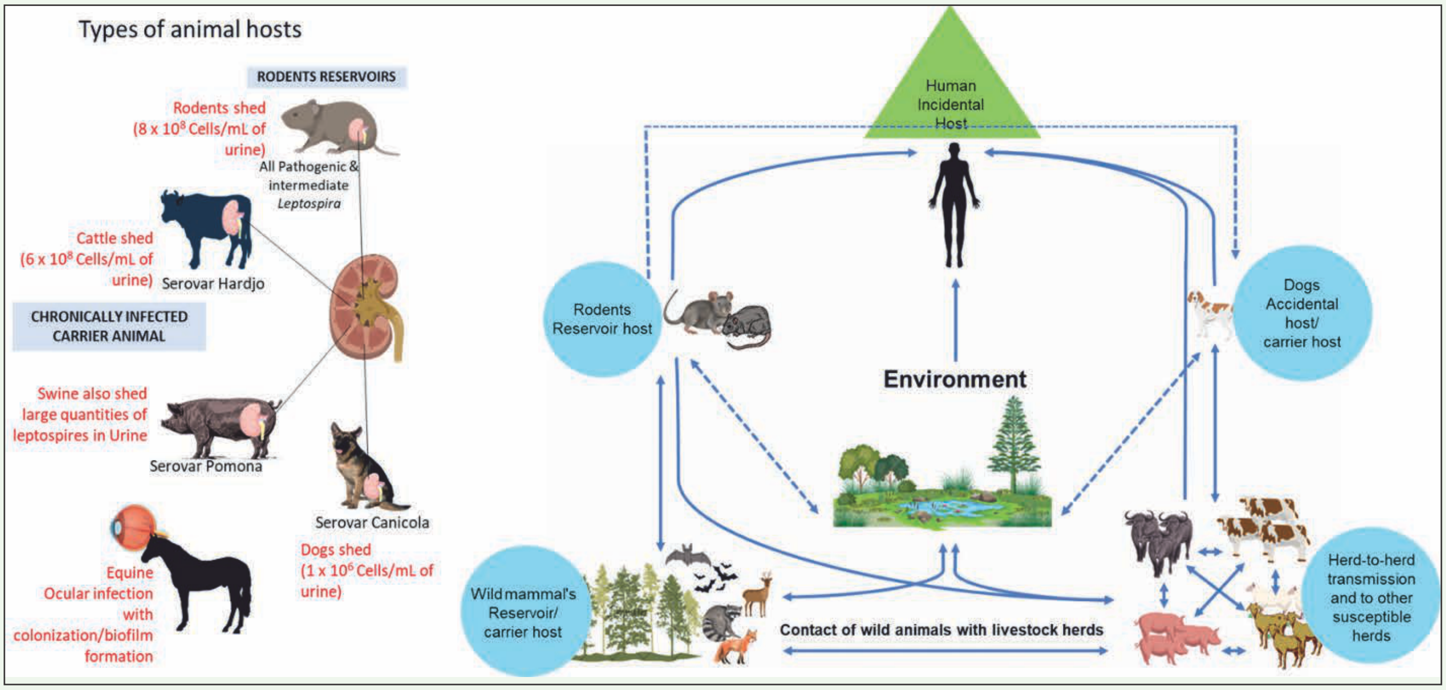


**Figure 3: Leptospirosis Transmission Cycle: A diagram showingthe zoonotic transmission cycle of leptospirosis, including the roles of different animal reservoirs, the environment, and human.**

conducted in the South Andaman Island found an overall seroprevalence of 10.9%, with higher rates in rural subjects compared to urban subjects. The most common infecting serogroup was Icterohaemorrhagiae, followed by Grippotyphosa, and the study suggested a shift in infecting serogroups possibly linked to changing trends in the animal population.[27] Another population-based case-control study in the Kodagu district of southern India identified environmental and occupational factors associated with leptospirosis risk, including flooding or water collection near houses, proximity to open sewers, direct contact with mud or water during work, animal farming, and the presence of rodents in houses.[28]

In Lucknow, Uttar Pradesh, a study focused on pediatric patients with acute febrile illness and found a seropositivity rate of 10% through IgM ELISA. Contact with infected animals and contaminated environments were highly associated with seropositivity, and common clinical symptoms included fever, chills, myalgia, headache, abdominal pain, and cough.[29] An outbreak investigation in Keerakadu village, Tamil Nadu, traced leptospirosis to contaminated water from an unprotected well. The outbreak was controlled through patient isolation and treatment, prophylactic antibiotics for the community, and recommendations for regular water chlorination and well protection.[30]

Studies have also explored the clinical profile, management strategies, and outcomes of patients with leptospirosis in different regions of India. In North India, an increase in leptospirosis incidence was observed over the years, with severe complications such as renal failure, respiratory failure, neuroleptospirosis, and disseminated intravascular coagulation (DIC). Early diagnosis and treatment were emphasized to reduce mortality. [31] In South India, a study investigated the co-infection of dengue and leptospirosis, revealing significant associations between clinical features like rashes and bleeding gums and co-infection. Laboratory parameters like thrombocytopenia were also linked to co-infection.[32] During the Coronavirus disease-2019 outbreak, one study described the clinical profile and outcome of leptospirosis patients and stressed the need to consider leptospirosis as a differential diagnosis for acute febrile illnesses, especially in tropical regions with specific risk factors.[33]

Southern India recorded a notable positivity rate of 25.6%, followed by 8.3%, 3.5%, 3.1%, and 3.3% in the north, west, east, and central regions, respectively. Rapid urbanization, climate change, poor sanitation, and improper waste management have contributed to an increase in leptospirosis outbreaks in recent years. [34]

The economic repercussions are due to various factors, such as reduced milk yield, weight loss, infertility, abortion, and even death in severe cases, which directly reduce the productivity of livestock.[9, 35] In cattle, leptospirosis is often associated with reproductive disorders, including abortion, stillbirths, and infertility.

Besides, the illness may also lead to decreased milk production and anorexia, which directly influence the dairy industry's profitability. Furthermore, the need for veterinary care and treatments for infected animals adds to the cost burden.[36]

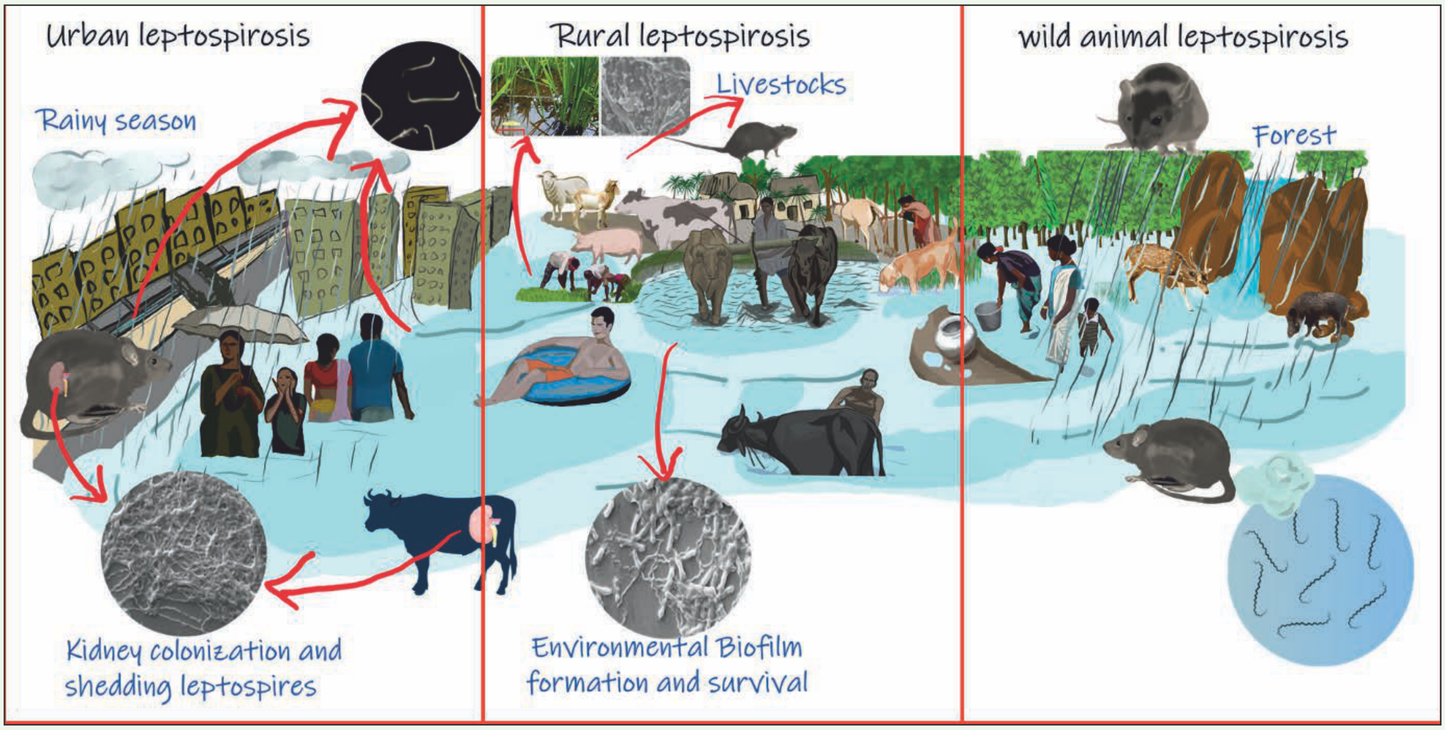


**Figure 4: Illustration showing overall risk group, hosts and environmental risk factors for Urban, rural and wild leptospirosis.**

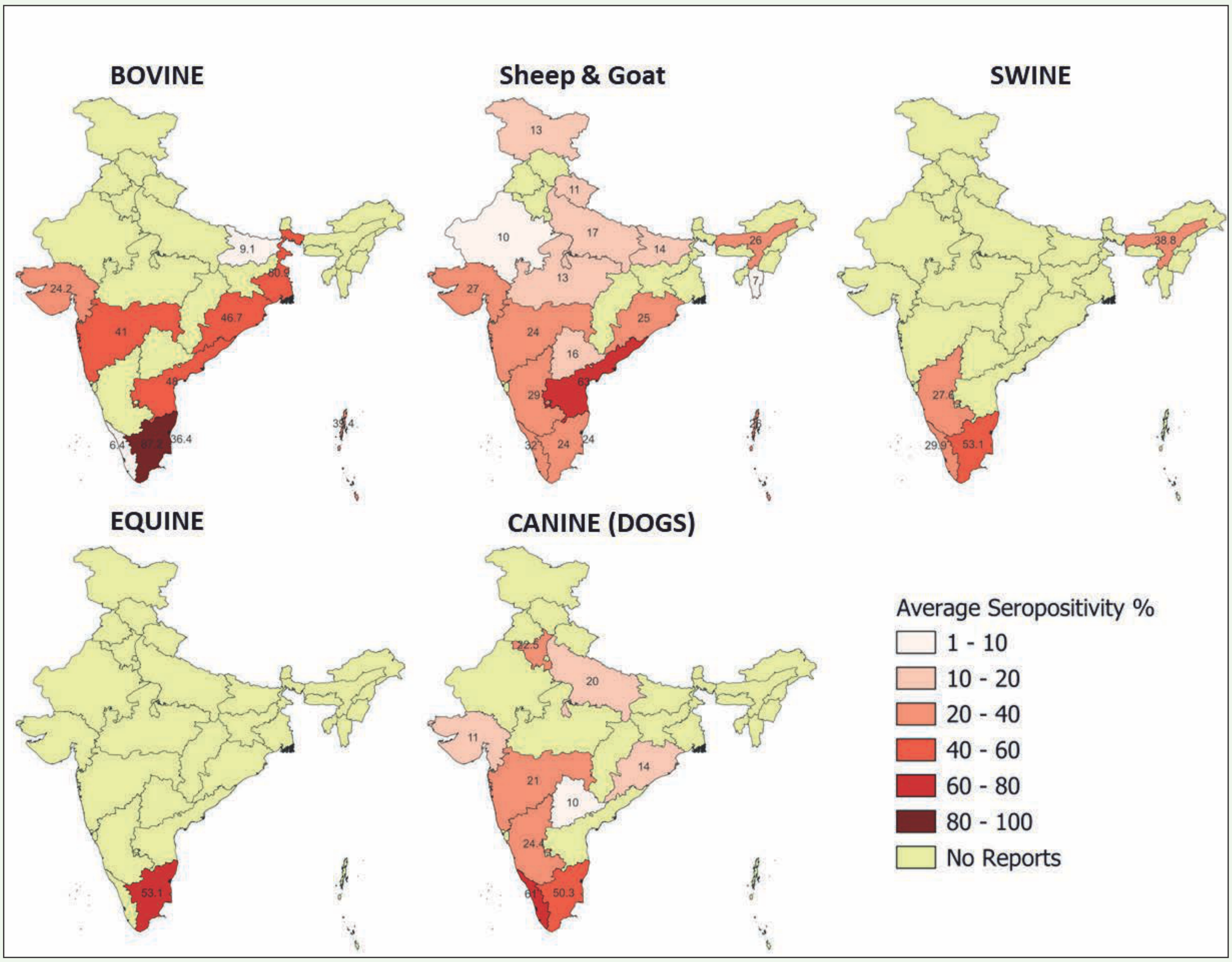


**Figure 5: Prevalence of Animal leptospirosis depicted in India map (published data for year 2000 to 2021)**

**Table 2: Preventive Measures: This table outlines the main preventive measures for leptospirosis, the rationale behind them, and their expected impact on disease control.**

| Strategy | Stakeholders | Expected Outcome |
|---|---|---|
| **Joint Surveillance programmes** | Public health officials, veterinarians, environmental health specialists | Early detection and prevention of outbreaks |
| **Coordinated Vaccination programmes** | Veterinarians, livestock owners, public health officials | Reduced disease prevalence in animal reservoirs, reduced transmission to humans. |
| **Environmental Risk Management** | Environmental health professionals, urban planners, community leaders | Reduced environmental exposure to Leptospira, reduced transmission |
| **Public Health Education** | Stakeholders: Public health officials, community health workers, educators | Increased awareness and adoption of preventive measures, reduced exposure to the disease. |
| **Livelihood Support programmes** | Government agencies, NGOs, community leaders | Reduced dependence on high-risk activities, and decreased exposure to the disease. |

**Table 3: Preventive Measures: This table outlines the main preventive measures for leptospirosis, the rationale behind them, and their expected impact on disease control.**

| Stakeholders | Roles |
|---|---|
| Government Health Agencies | Development and implementation of policies, surveillance programmes, funding research and control initiatives, public health education |
| Non-Governmental Organizations (NGOs) | Disease awareness campaigns, support in executing control measures, conducting research, providing resources and aid |
| Veterinary Professionals | Disease diagnosis and control in animals, public education on zoonotic diseases, reporting cases to health agenciesinterventions like dialysis, human vaccines, and personal protective equipment. |
| Medical Professionals | Diagnosis and treatment of human cases, health education, reporting casesand WASH interventions. |
| Academia and Research Institutions | Conducting research on disease pathogenesis, diagnostic methods, treatments, and prevention strategies; training future professionals |
| Communities/General Public | Adherence to prevention measures, reporting suspected cases, participation in awareness programmes |
| Agricultural Sector | Implementing animal health practices to prevent disease, reporting suspected cases in livestock therapeutic measures for leptospirosis. |
| Pharmaceutical Companies | Development of effective treatments and vaccines, research and developmentvaccines or birth control programmes to control disease spread. |
| Technology Companies | Development of health technologies for disease surveillance, diagnostics, data sharing |

Similarly, in pigs and small ruminants such as sheep and goats, leptospirosis has been linked to reproductive problems and failure to thrive in newborns, leading to significant productivity losses. Anorexia, weight loss, and other clinical symptoms can also affect the growth rate and market weight of pigs, sheep and goats. [9, 37] The impact of leptospirosis on the equine industry is also considerable. Horses infected with Leptospira can develop recurrent uveitis, potentially leading to blindness, and suffer from kidney disease and abortion, affecting their health and performance.[38]

Moreover, the disease has implications for wildlife and the associated tourism industry. Rodents and other wildlife species often serve as asymptomatic carriers, contributing to the spread of disease.[39] Overall, the economic burden of leptospirosis on livestock productivity is vast and extends to various sectors, including dairy, meat, wool, and hide production, as well as the associated industries such as tourism.

**2.3. Animal Leptospirosis in India**

Animal leptospirosis in India exhibits marked regional variability due to different climatic conditions, farming practices, and the diversity of potential animal reservoirs.[26] Prevalence rates and implicated serovars differ from region to region, with studies reporting evidence of the disease in animals such as dogs, swine, horses, rodents, and even captive wild animals (Fig. 5). Understanding this geographical and host variability is crucial for developing targeted control strategies to mitigate the impact of leptospirosis in India.[26]

In the case of bovine leptospirosis, India faces a matter of particular concern, given the considerable variation in prevalence rates and serovar distributions across its diverse regions. [26] Studies conducted in various states have reported a complex epidemiological landscape. For example, in Andhra Pradesh, [40,41] it was found leptospirosis prevalence rates of 56.23% and 19.65%, respectively, with multiple serovars identified, including Hebdomadis, Pomona, Sejroe, Ballum, Australis, Grippotyphosa, Autumnalis, Javanica, and Canicola. Similarly, in Gujarat, prevalence ranged from 5.77% to 38.55%, with several serovars detected, such as Sejroe, Hebdomadis, Ballum, Australis, Pomona, Canicola, Icterohaemorrhagiae, Autumnalis, and Tarassovi.[42, 43] Such variations underscore the necessity for region-specific surveillance and targeted control measures.[26]

Leptospirosis in sheep and goats also presents a unique epidemiological landscape in India. The prevalence rates vary across regions, with states reporting rates from 7% to 63%. [44, 45] In the northern region,[45] prevalence rates of 13% in Jammu and Kashmir, 10% in Rajasthan, and a slightly higher rate of 11% in Uttarakhand were reported. The western state of Gujarat demonstrated a notably high prevalence ranging from 12% to 52%, with a wide array of serovars identified.[45-48] In the southern states of Karnataka and Kerala, prevalence rates of 29% and 28% to 36% were reported, respectively, with Pomona, Australis, and Grippotyphosa being the most common serovars.[45, 49] Such variations emphasize the need for tailored surveillance and control measures to address this public health concern.[26]

Canine leptospirosis, a significant zoonotic disease in India, presents diverse epidemiological profiles across different regions. Studies have reported prevalence rates ranging from 10.98% to 77.7 %.[50, 51] The regional prevalence and serovar distribution underscore the need for sustained surveillance and region-specific control measures.[26]For instance, in northern India, Uttarakhand reported a prevalence of 20%, with prominent serovars including Autumnalis, Icterohaemorrhagiae, Grippotyphosa, and Canicola.[50, 51] In contrast, Kerala reported an alarming prevalence of 71.12% with a wide array of serovars identified.[52]

Swine leptospirosis poses an emerging public health challenge in India, with varying seroprevalence rates across different regions. For example, a study in Assam reported a seroprevalence of 38.8%, predominantly identifying Ballum as the leading serogroup in swine. [53] In contrast, Kerala reported a seroprevalence of 35.92%, with a variety of serogroups identified. [54]

Leptospirosis poses a significant health risk to the equine population in India. A study in Chennai reported a distressing seroprevalence rate of 76.05% in horses, with predominant causative serovars being Leptospira Pomona and Leptospira Grippotyphosa.[55] The high prevalence in urban centres like Chennai requires stricter surveillance measures, particularly due to the significant public health risk posed by asymptomatic carriers.[56]

Leptospirosis extends beyond rodents to various animal species in India. Captive sloth bears have shown seropositivity, with Pyrogenes being the most common serovar.[57] Wild animals like Sambhar, Cheetal, Tiger, and Elephant also showed seropositivity, indicative of the disease's broad host range.[58] Additionally, captive elephant handlers have demonstrated antibodies against multiple Leptospira serovars, highlighting the disease's risk for individuals in proximity with potential animal reservoirs.[59] Zoological parks and animal rescue centres often house leptospirosis, with significant seropositivity reported among various animal species and staff.[60, 61] Continued research and collaboration across disciplines are essential to address this public health challenge effectively.

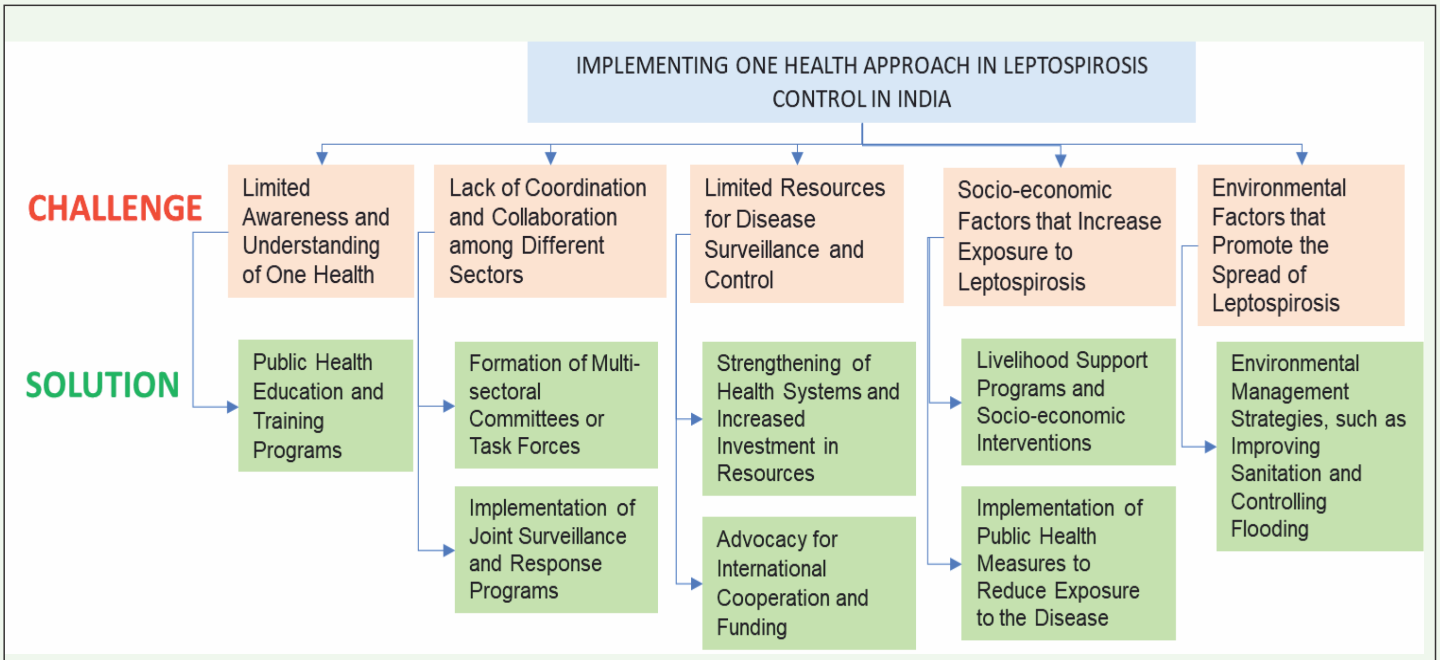


**Figure 6: Challenges and Barriers to implementing the One Health approach in leptospirosis control in India and their potential solutions**

## 3. Recommendations for future research, policy, and practice

Addressing the spread and impact of leptospirosis in India necessitates a multifaceted, interdisciplinary approach. This strategy encompasses numerous spheres, from research to diagnostics, policy integration, surveillance systems, public awareness, and increased funding.

**a. Enhanced Interdisciplinary Research:** This is a pivotal aspect of managing the complexities of leptospirosis. A collaborative effort between various stakeholders such as public health and veterinary professionals, policymakers, researchers, and the private sector can lead to better disease management.[62] The interdisciplinary approach combines human and veterinary medicine, epidemiology, environmental science, and social science. Research should focus on the epidemiology and ecology of leptospirosis, the role of various animal reservoirs, environmental factors contributing to Leptospira survival and transmission, and socioeconomic and cultural factors influencing disease exposure and health-seeking behaviours (Table I & II).[63]

**b. Improved Diagnostics and Technological Innovations:** The limitations of current diagnostic methods necessitate investment in research and development of rapid, accurate, and affordable diagnostic tests.[35, 46, 64] Novel technologies such as point-of-care diagnostics, advanced vaccines, and digital health platforms can greatly enhance disease detection, prevention, and management. In addition, AI can aid in predictive modelling and risk mapping, enhancing surveillance capabilities.[65]

**c. Effective Vaccines:** For both humans and animals, the creation of cross-protective vaccines that can provide immunity against a broad range of Leptospira serovars is vital.[66]

**d. Integrated Surveillance Systems and Standardization:** Surveillance systems need to amalgamate data from human, animal, and environmental health to track disease trends and detect outbreaks early. This integration necessitates digital technologies for real-time data reporting, visualization, and analysis. Standardization of diagnostic and reporting protocols, along with centralized data management platforms, will enhance the surveillance system.[67]

**e. Policy Integration:** Policies should address leptospirosis across different sectors, including strategies for rodent control, waste management, water and sanitation, land-use planning, and livestock management. Inclusion of leptospirosis in the national list of notifiable diseases at least in the endemic areas can enhance disease reporting and response.[68]

**f. Community Engagement, Education, and Public Awareness:** Efforts need to be made to increase community knowledge about leptospirosis, especially among high-risk groups. Education programmes and public advocacy campaigns can inform about personal protective measures, safe water and sanitation practices, and responsible pet and livestock management.

**g. Capacity Building and Funding:** Investing in training programmes for health professionals, veterinarians, laboratory staff, and field workers is crucial. A well-trained workforce is key to effectively diagnosing, preventing, and controlling leptospirosis. Additionally, advocating for more resources to support research, control programmes, and capacity-building initiatives related to animal leptospirosis is essential.

**h. Climate Change Adaptation:** With climate change potentially influencing the transmission dynamics of leptospirosis, research into its impacts and the development of climate-adaptive control strategies are required.[69]

With these strategies in place, India can make substantial strides toward a more integrated, effective, and sustainable approach to controlling animal leptospirosis, ultimately benefiting the health of humans, animals, and the environment (Fig. 6).[62]

## 4. Conclusion

It is evident that leptospirosis remains a significant public health challenge in India, especially in regions where there is close interaction between humans, animals, and the environment. This zoonotic disease not only poses a significant threat to human and animal health but also reflects the broader systemic and environmental issues at play, such as sanitation, waste management, and land use.

A One Health approach – emphasizing the interconnectivity between human, animal, and environmental health – offers a promising strategy for managing leptospirosis. This strategy recognizes the need for collaboration among various stakeholders, including veterinary and public health professionals, policymakers, researchers, and the private sector. Yet, the effective implementation of One Health approach in India faces challenges due to complacency, resource constraints, and lack of public awareness.

The review emphasized the need for interdisciplinary research, improved diagnostics, effective vaccines, integrated surveillance systems, policy integration, community engagement, capacity building, climate change adaptation, and the importance of technological innovations such as Artificial Intelligence in managing leptospirosis. Investments in these areas can facilitate the early detection and rapid response necessary to control the spread of leptospirosis and limit its impacts on public health. It's also imperative to advocate for increase funding and resources to support research, control programmes, and capacity-building initiatives related to leptospirosis. These efforts must be complemented with community engagement and public awareness campaigns about the risks and preventive measures associated with leptospirosis.

## Author Contributions

KVK conducted the literature search, performed data analysis and wrote the rough draft of the manuscript. PPB, SM, and AP extracted and interpreted the data as well as edited the draft. CHB handled language, copy editing and rewriting the manuscript. VB provided guidance and support for the research, designed and conceptualized the idea, interpreted the data and edited the manuscript. BRG offered support. All authors reviewed and approved the final edited manuscript.


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## Conflicts of Interest

No conflicts to declare

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