AKT PUBLICATION

Journal of Pharmaceutical Research and Integrated Medical Sciences (JPRIMS)
ISSN: 3049-1681 | Vol. 03, Issue-08, August-2026 | pp.-73-87

ORIGINALARTICLE https://jprims.in/

Leptospirosis/Weil's Disease: Pathogenesis, Epidemiology, Bio-Screening, Next-Generation Interventions Powered by AI, ML, Modeling, 3d Fingerprinting, Cover Etiology, Treatment Horizons, Fungal, Mosquito and Airborne Infection

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Abstract:

Leptospirosis or commonly referred to as Weil's disease is an emerging neglected zoonotic bacterial infection that poses great challenges globally due to its complicated epidemiology, varied presentations, and increased prevalence linked with climate change, urbanization, and environmental pollution. Despite advancements in the diagnostic procedures and treatment options with antibiotics, delayed diagnosis and inadequate surveillance systems still hinder disease control efforts. This review provides current information about the disease with regard to the causative agents, pathogenesis, epidemiology, bio-screening techniques, and therapies of leptospirosis together with new developments in artificial intelligence (AI), machine learning (ML), modeling, geospatial analysis, three-dimensional (3D) fingerprinting, digital pathology, and precision medicine. Some of the emerging technologies such as explainable AI, deep learning (DL), Geographic Information System (GIS), Bayesian, and Long Short-Term Memory (LSTM) model, biomarker-based diagnostics, and AI -based drug discovery have demonstrated significant potential in the context of disease surveillance, prediction of outbreaks, prognosis, and personalization of clinical interventions. This review further addresses aspects like vaccine development, digital health, and the difficulties of transitioning these technologies into practice. The integration of intelligent computing techniques and molecular diagnostics in conjunction with One Health surveillance may offer a promising approach to achieve early detection, precise treatment, and preparedness in leptospirosis.

Keywords: Leptospirosis; Weil's disease; Artificial Intelligence (AI); Machine Learning (ML); Bioscreening; Precision Medicine.

Received: May 19, 2026 **Revised: June 18, 2026** **Accepted: July 19, 2026** **Published: August 17, 2026**

DOI: https://doi.org/10.64063/3049-1681.vol3.issue8.000296

1. INTRODUCTION

The infection leptospirosis is also known as Weil's disease in the extreme form, and it is a neglected zoonotic disease of humans that results from bacteria of Leptospira genus[1]. Human infection occurs from direct contact with the urine of infected animals and contaminated environment. While most prevalent in tropical and sub-tropical countries, its burden across the globe is rising because of climate change, urbanization, floods, and environmental degradation. Failure to diagnose this condition at the early stage may cause several complications such as acute renal damage, hepatitis, pulmonary hemorrhages, myocarditis, and multiorgan failure.

Recent developments in molecular diagnostics, bioscreening techniques, AI, ML, geospatial modeling, and computational epidemiology have enhanced the diagnosis and surveillance of leptospirosis[2]. New advancements like explainable AI, digital pathology, 3D fingerprinting, and precision medicine provide new possibilities for early diagnosis, prediction of outbreaks, and personalized treatment methods. Nevertheless, the issues associated with heterogeneity of clinical presentation, limited access to diagnostics, and disjointed surveillance system pose significant obstacles for the management of the disease. This review presents a brief summary of current information about the etiology, pathogenesis, epidemiology, bioscreening, AI-based developments, treatment approaches, and future trends regarding leptospirosis[3].

1.1 Background and Context

Leptospirosis is an important zoonotic disease that occurs worldwide, resulting from pathogenic strains of Leptospira. The disease continues to be a public health problem especially in tropical and sub-tropical areas because of its increasing prevalence due to factors such as climate change, flooding, urbanization, poor hygiene, and occupational risks. Clinical presentation of the disease may vary from mild fever to severe Weil's disease[4]. Early diagnosis of the disease has been difficult since it presents similar symptoms as other diseases. Recent innovations in molecular technology, bioinformatics, AI, machine learning, geospatial analysis, remote sensing, and precision medicine have greatly contributed to disease surveillance, prediction, early detection, and personalized medicine leading to One Health approach to leptospirosis.

1.2 Objectives of the Review

The goals of this review include:

- To provide an overview of the etiology, pathogenesis, clinical presentation, and epidemiology of leptospirosis and Weil's disease.
- To discuss recent developments in bio screening techniques and molecular methods used for disease identification.
- To explore the involvement of AI, machine learning, computational models, geospatial approaches, and 3D fingerprints in disease diagnosis and surveillance.

- To present the latest treatment methods, new therapies, vaccine development, and AI-driven drug discovery for leptospirosis.
- To highlight the research gaps and future directions for precision medicine.

1.3 Importance of the Topic

The increasing significance of climate change, urbanization, environmental damage, and human-animal interface has added to the burden of leptospirosis cases around the world, emphasizing the need for better surveillance and early diagnosis[5]. The use of new technologies in the field of bioscreening, AI, machine learning, computational simulation, and precision medicine can be useful in this context. Hence, this review article combines scientific literature and technology in an effort to develop a more holistic view about leptospirosis.

2. PATHOGENESIS, ETIOLOGY AND EPIDEMIOLOGY

Leptospirosis is an intricate zoonosis whose development and evolution depend on the interplay of the disease agent, host, and environment. The detailed knowledge of the disease causation, epidemiology, mode of transmission, pathogenesis, and diagnostic methods is crucial for the prevention and treatment of this condition[6]. Recent discoveries in molecular biology, epidemiological monitoring, and bioscreening have provided a significant amount of information concerning disease transmission, host-pathogen relationship, and early detection. This section discusses the present state of research in relation to the etiology, epidemiological tendencies, pathogenesis, symptoms, and new diagnostic techniques of leptospirosis.

2.1 Etiology, Transmission, and Epidemiological Trends

Leptospirosis is an example of a zoonotic infectious disease that results from infection by leptospiral spirochetes of the genus Leptospira, which consists of at least 35 different species and more than 300 serovars[7]. The motile microorganism lives in moist conditions and affects human beings through contact with urine from infected animals directly or indirectly through water, soil, or vegetation. Infection by the microorganism occurs through cuts in the skin or mucous membranes and spreads through the bloodstream into several organs. The major reservoir host for the disease-causing microorganism is rodents, while other animals include cattle and domestic animals.

Geography of leptospirosis is greatly affected by climatic, environmental and socioeconomic factors. The disease is endemic in tropical and subtropical areas due to the presence of heavy rains, floods, bad sanitation, and poor disposal of waste products, which allow the bacteria to survive and spread[8]. Recent researches on leptospirosis indicate that climate change, urbanization, modification in the use of land and extreme climatic conditions have led to the spreading of leptospirosis geographically leading to an increased number of epidemics in both developed and underdeveloped nations. People working in agriculture, animal husbandry, sewage work, veterinary practice, army and in disaster relief work continue to be at high risk from this disease.

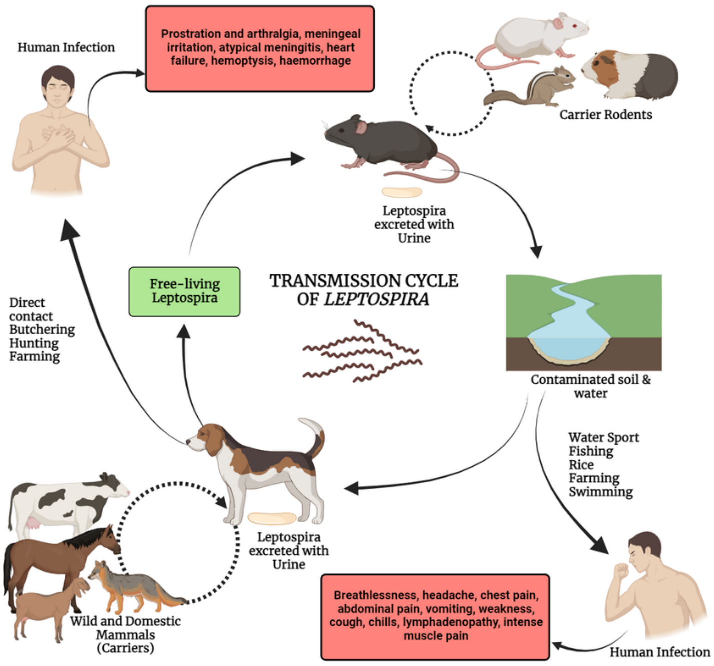

Figure 1. Schematic representation of the transmission cycle of Leptospira and major routes of human infection

Additional research now focuses on the role that environmental microbiota and ecology play in leptospiral maintenance[9]. The presence of fungi and biofilm in aquatic systems could potentially increase the survival of bacteria indirectly, but their exact role in the pathogen's transmission cycle is currently poorly defined. In addition, mosquitoes have not been known to be biological vectors for Leptospira, but mosquito-infested areas and leptospirosis cases occur in the same locations since both are common in wet environments with frequent rains and floods, standing water. Airborne transmission is also an uncommon mode of transmission, although there have been reports of inhalation of contaminated aerosols under specific occupational and laboratory settings.

2.2 Pathogenesis and Clinical Manifestations

Upon invasion through injured skin or mucosa, pathogenic Leptospira bacteria spread swiftly through the blood and induce leptospiremia, which is associated with the spread of bacteria in the body[10]. Bacterial pathogens have virulence factors such as outer membrane proteins, adhesins, lipopolysaccharides, and proteins that confer motility to enable adhesion to tissues and organs. Disease severity varies based on virulence of the bacteria, dose of infection, and immune response in the infected individual.

The immune response of the host is an essential determinant of the course of the disease. The activation of innate immune signaling pathways leads to the formation of pro-inflammatory cytokines, chemokines, and complement components, which are responsible for the elimination of bacteria but can also cause endothelial dysfunction and systemic inflammatory response[11]. Overactivation of the immune response can lead to a number of complications including tissue damage due to cytokines.

From a clinical standpoint, leptospirosis manifests itself in the form of fever, headaches, muscle pains, reddening of the eyes, vomiting, and stomach problems in the early stages. In its advanced form, leptospirosis leads to what is known as Weil's disease, which is defined as having jaundice, acute kidney problems, liver problems, pulmonary hemorrhaging, inflammation of the heart muscles, meningitis, thrombocytopenia, and multiorgan failure[12]. Among the reasons for the high mortality rate associated with leptospirosis include involvement of the lungs leading to respiratory distress syndrome.

2.3 Bioscreening and Diagnostic Advances

Diagnosis of leptospirosis at an early stage is difficult due to the similarity of symptoms with those of dengue, malaria, flu, COVID-19, and many other acute febrile diseases[13]. Standard tests for laboratory diagnosis of leptospirosis include the microscopic agglutination test (MAT) that serves as a gold standard of diagnosis through serology. Other common diagnostic tests include enzyme-linked immunosorbent assay (ELISA), bacterial culture, and polymerase chain reaction (PCR)s. MAT has the advantage of high specificity; however, it requires paired serum samples, live antigen suspensions, and special skills of laboratory workers for its use in practice[14]. PCR and quantitative PCR (qPCR) allow rapid and sensitive diagnosis during the early bacteremia phase of disease prior to antibodies production.

There have been significant improvements in the area of bioscreening techniques in recent times. Loop-mediated isothermal amplification (LAMP) enables the quick amplification of nucleic acids without complex laboratory equipment. It is especially well-suited for use in point-of-care testing because of this. CRISPR-based molecular diagnostic technologies have further contributed to improving the sensitivity and specificity of detection by providing programmable recognition of nucleic acids[15].

Omics technologies such as proteomics and metabolomics are becoming increasingly important to precision diagnostics. Omics approaches help in identifying new biomarkers linked to the progression of the disease, host immunity, and treatment response[16]. On the other hand, biosensors make use of nanotechnology and microfluidics along with electrochemical sensing for the fast and highly sensitive identification of pathogens. This integration of next generation biosensing devices with AI technologies is anticipated to aid in early diagnosis and improve the surveillance systems for leptospirosis.

3. AI-DRIVEN DIAGNOSIS, MODELING, AND NEXT-GENERATION INTERVENTIONS

With the fast growth of AI, ML, computational epidemiology, and digital health technology, the management of infectious diseases, such as leptospirosis, has been revolutionized. Traditional diagnostic and surveillance techniques have been known to experience limitations such as late diagnosis, different presentation of cases, and lack of capability in forecasting outbreaks[17]. The use of AI technology coupled with molecular diagnostics, medical imaging, environment surveillance, and epidemiology data has helped enhance the detection, risk assessment, prognosis assessment, and decision making by the public health community[18]. Also, the incorporation of explainable AI, spatial analysis, and precision medicine opens up possibilities of disease management using intelligent techniques.

3.1 AI, Machine Learning, and Disease Prediction

AI and ML have proved themselves useful in terms of diagnosing leptospirosis early and managing the disease clinically. The current methods of diagnosing this disease usually require laboratory testing, which may cause delays in treatment in the initial stages of the disease. ML algorithms can evaluate multiple types of data sets like clinical, laboratory, demographic, and environmental all together to recognize any patterns related to the disease that may not be visible through traditional statistics[19]. Supervised learning techniques such as Random Forest (RF), Support Vector Machine (SVM), Gradient Boosting, and XGBoost have shown great success in differentiating between leptospirosis and other febrile diseases.

The use of DL technologies has also broadened diagnostic abilities through the automation of analysis of highly complex medical information. Convolutional Neural Network (CNN) is proving to be an effective tool in classification of MAT images and digital microscopy slides[20]. The use of recurrent neural networks and hybrid DL systems is becoming more common in longitudinal data sets for the purposes of disease diagnosis and predicting the outcomes of a certain patient. Automated feature extraction from highly dimensional data set can help in identifying at-risk patients[21].

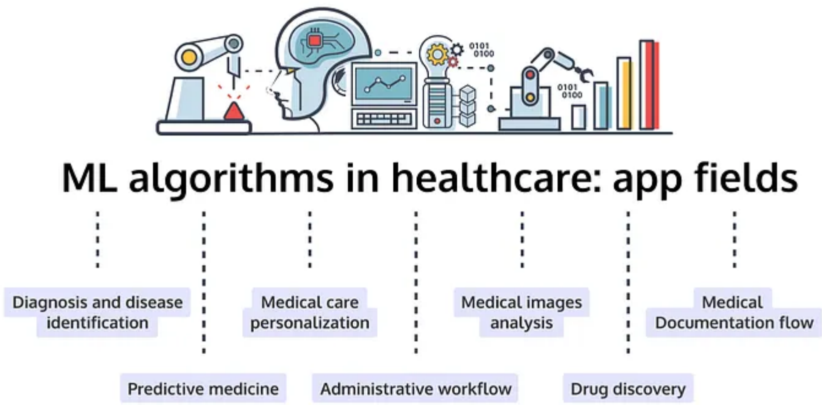

Figure 2. Applications of machine learning in healthcare relevant to leptospirosis diagnosis, prediction, and clinical decision support

However, even in the face of impressive accuracy of various AI models, their adoption in the field of medicine is dependent mostly on their ability to be transparent and interpretable. Explainable Artificial Intelligence (XAI), with methods such as SHAP and LIME, allows clinicians to get insight into how specific clinical variables affect diagnosis and prognosis[22].

Prognostic AI algorithms have also proven to be quite valuable in forecasting severity, mortality, intensive care unit admission, renal dysfunction, pulmonary hemorrhage, and multi-organ dysfunction. Using laboratory biomarkers, clinical parameters, imaging information, and demographics, such prognostic algorithms help healthcare professionals identify the risk early on and prioritize patients accordingly. Thus, AI prognostics is one more important step towards precision medicine.

3.2 Spatial Modeling and Intelligent Surveillance

Control of leptospirosis involves predicting patterns of disease transmission over time and space. The use of GIS, remote sensing techniques, and environmental models have greatly improved epidemiological surveillance through the incorporation of climate data, ecology, demography, and geography in developing disease risk maps[23]. This has helped in pinpointing areas with high transmission, susceptible populations, and conducive environmental conditions for pathogen survival.

With the recent developments in machine learning, there have been significant improvements in spatial epidemiology modeling. Bayesian modeling, support vector machines, artificial neural network, random forests, and LSTM networks are commonly used to identify non-linear associations between rain fall, temperature, humidity, vegetation indexes, land use patterns, and disease cases. DL models based on LSTM are especially effective at forecasting seasonal outbreaks owing to their ability to capture long-range temporal dependency in epidemiological time series[24]. Bayesian spatiotemporal models can provide probabilistic disease risk estimates, taking into account spatial heterogeneity and uncertainty.

The advent of GIS, remote sensing, and AI has led to the rapid evolution of intelligent warning systems that have the capability of predicting outbreak events in real time. Satellite imagery of environmental factors, meteorology, hydrology, and demographic data can continuously be monitored for high-risk regions prior to outbreaks[25]. Predictive surveillance technologies facilitate prompt public health actions, effective management of healthcare resources, and disease monitoring, especially as the incidence of leptospirosis changes due to climate change.

3.3 Precision Medicine and Future Technologies

New precision medicine paradigms are changing the paradigm of the diagnosis and treatment of leptospirosis through the convergence of molecular profiling, digital pathology, AI, and computational medicine. 3-D Fingerprinting systems utilize state-of-the-art imaging technology and molecular biomarkers and spatial tissue profiling techniques for the creation of comprehensive disease fingerprints, which increase pathogen discrimination and enable personalized therapeutics.

The use of digital pathology and AI-based microscopy further enhances diagnostics through automated microscopic image interpretation and minimizes observer variability. DL systems can automatically identify pathognomonic microscopic signs of the presence of the Leptospira organism, while at the same time, quantifying morphological alterations and inflammation[26]. The combination of digital pathology with proteomics and metabolomics biomarkers allows more comprehensive disease characterization and the establishment of precision diagnostic systems.

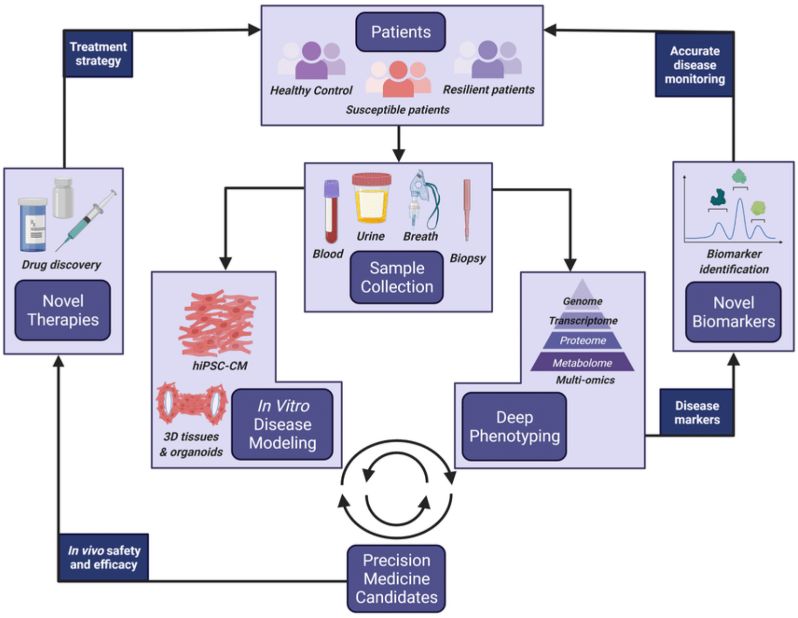

Figure 3. Integrated precision medicine workflow illustrating biomarker identification, multi-omics analysis, disease modeling, and personalized therapeutic strategies.

Artificial intelligence is also contributing to medical advancement in therapies through drug repurposing, personalized medicine, and digital health systems. ML can be used to discover existing drugs with possible anti-leptospiral properties based on molecular interaction, pharmaceutical database, and biological pathways, which means that there would be no need for conventional drug discovery processes, thus saving time and costs. Digital health systems also make it possible to have continuous monitoring of patients, telemedicine, use of wearables, and AI -based decision support systems, which allow for tailored therapies for each specific individual[27].

Table 1. Conventional Approaches and Emerging AI-Driven Innovations in Leptospirosis Management

Domain	Conventional Approaches	AI/Next-Generation Innovations	Clinical/Public Health Benefits
Etiology & Epidemiology	Clinical surveillance, outbreak reporting, environmental monitoring	GIS, remote sensing, climate modeling, spatiotemporal forecasting	Early identification of high-risk areas and improved outbreak preparedness
Disease Diagnosis	MAT, ELISA, PCR/qPCR, bacterial culture	ML diagnosis, CNN-based microscopy, AI-assisted image analysis	Faster diagnosis with improved sensitivity and reduced observer variability
Bioscreening	LAMP, CRISPR diagnostics, serological	AI-integrated biosensors, proteomics,	Early pathogen detection and precision

	assays	metabolomics, biomarker analytics	diagnostics
Disease Prediction	Clinical scoring systems and statistical models	Random Forest, SVM, XGBoost, Deep Learning, Explainable AI (SHAP/LIME)	Accurate disease classification, severity assessment, and mortality prediction
Spatial Surveillance	Field surveillance and epidemiological investigations	GIS mapping, Bayesian models, LSTM forecasting, remote sensing	Real-time surveillance and climate-driven outbreak prediction
Precision Healthcare	Conventional clinical management	3D fingerprinting, digital pathology, AI-assisted microscopy, personalized medicine	Individualized diagnosis and optimized therapeutic decision-making
Clinical Decision Support	Physician expertise and laboratory interpretation	AI-based decision support systems, digital health platforms, wearable biosensors	Improved clinical decision-making and continuous patient monitoring

4. TREATMENT HORIZONS AND TRANSLATIONAL PERSPECTIVES

Recent progress in the fields of antimicrobial therapy, intensive care, molecular diagnostics, and computer science has led to a marked improvement in the clinical management of leptospirosis. While traditional antibiotics still form the basis of the treatment of this condition, difficult cases of leptospirosis remain challenging to manage because of delayed diagnosis, multiorgan involvement, and quick progression of the disease[28]. The development of new trends such as biomarker-driven therapy, AI, personalized medicine, and digital health care is moving clinicians toward a new paradigm of care for patients with this disease.

4.1 Current Therapeutic Strategies

Early use of antibiotics is the first step in the management of leptospirosis, especially in the leptospiremic stage. In mild cases, patients can be treated with doxycycline, amoxicillin, or azithromycin, but in severe cases, patients are administered intravenous penicillin G or third generation cephalosporins like ceftriaxone or cefotaxime. Timely use of antibiotics prevents further spread of bacteria, reduces the course of the disease, and minimizes the chances of developing complications.

Patients suffering from severe leptospirosis usually need intensive care treatment due to multiple organ involvement. The ICU treatment is needed when patients come with sepsis, ARDS, hemorrhage in lungs, myocarditis, and neurological symptoms. The hemodynamic stability, mechanical ventilation, fluid replacement, and use of vasopressors are some of the main aspects of the critical care treatment.

Acute kidney failure is the most commonly observed complication associated with severe leptospirosis and might need renal replacement therapy. Hemodialysis or continuous renal replacement therapy can help manage electrolyte disturbance, metabolic acidosis, and fluid overload while increasing the chances of survival. Other supportive therapies include correction of electrolyte disturbances, nutritional therapy, blood transfusion in case of massive hemorrhage, and proper handling of liver, heart, and lung complications.

4.2 Emerging Therapeutic Innovations

The recent advances made possible in molecular medicine are paving the way for a biomarker-guided approach in the treatment of leptospirosis. Biomarkers such as proteomic, metabolomic, and inflammatory biomarkers are being evaluated based on their capability to determine disease severity, predict organ dysfunction, and assess therapeutic response. These biomarkers can be useful in early intervention and personalizing treatment while minimizing intensive care usage.

ML is revolutionizing drug discovery and optimizing therapy through analysis of pharmacological data sets, molecular interactions, and host-pathogen interaction network[29]. ML algorithms have proven promising in the discovery of drug repurposing candidates and determination of therapeutic efficacy, thus leading to a reduction in drug development time and expenses incurred in research.

Vaccines have also shown tremendous success along with personalized medicine in recent years. New recombinant vaccines and multi-epitope vaccines and reverse vaccine design strategies have been proposed as means to provide more comprehensive coverage against different strains of Leptospira. At the same time, the concept of personalized medicine combines genomic data, host markers, and clinical parameters for the development of individual treatments.

4.3 Clinical Translation and Future Implementation

Clinical success for novel technologies is achieved through the incorporation of digital health technology, AI, and precision medicine in daily healthcare operations[30]. Mobile apps, wearable devices, telemedicine services, and electronic health records allow the implementation of real-time patient monitoring, rapid medical communication, and healthcare access especially in rural and impoverished areas.

The use of precision medicine in managing infectious diseases entails the utilization of molecular diagnostics, bioscreening technology, and AI-based risk assessment tools and decision-making support tools to allow early diagnosis and personalized treatment. Explainable AI improves the trust of clinicians through accurate and interpretable predictive results that encourage evidence-based decision-making[31].

However, there are certain obstacles that continue to pose hindrances to their large-scale clinical application. The unavailability of high-quality datasets, absence of validation procedures, limited resources, data security problems, and regulatory problems prevent the widespread adoption of these innovative technologies in the field of healthcare. Overcoming these drawbacks with the help of multidisciplinary cooperation and healthcare policies will be crucial for successful deployment of these next generation technologies.

Table 2. Comparative Analysis of Recent AI and ML Studies in Leptospirosis

Author(s) & Year	Study	Methodology/Approach	Key Findings	Research Contribution
Sawesi et al. (2025)[32]	AI and DL for leptospirosis	Systematic review of ML/DL models	AI improved diagnosis and prediction but requires better clinical validation.	Summarized current AI applications and future directions.
Shirzad et al. (2023)[33]	Spatiotemporal disease modeling	MaxEnt spatial modeling	Climatic variables accurately identified high-risk areas.	Demonstrated AI-based spatial risk mapping.
Silva et al. (2024)[34]	ML for patient outcome prediction	Comparative ML algorithms	ML accurately predicted disease severity and outcomes.	Supported AI-based prognostic assessment.
Smith et al. (2019)[35]	Prediction of severe leptospirosis	Statistical risk-scoring model	Developed a simple score for predicting severe disease.	Provided a practical clinical risk assessment tool.
Suttirat et al. (2025)[36]	ML-based environmental risk analysis	ML using climatic and epidemiological data	Rainfall, temperature, and land use predicted outbreak risk.	Strengthened AI-driven surveillance and early warning systems.

5. DISCUSSION

With increased use of AI, molecular diagnostics, bioscreening techniques, spatial epidemiology, and precision medicine, the way in which leptospirosis is prevented, diagnosed, and treated is changing. The recent progress shows that the combination of computer methods with classical medicine and epidemiology helps detect diseases earlier, predict outbreaks, facilitate treatment decision making, and monitor population health[37]. Nevertheless, the effective transition into clinical practice needs rigorous validation, interdisciplinary cooperation, and standardization of implementation methods.

5.1 Interpretation and Analysis of Findings

The above evidence shows that leptospirosis is a multifactorial zoonosis whose successful treatment requires the convergence of biological, environmental, and technological knowledge[38]. In this regard, developments in molecular diagnostics, bio-screening technologies, AI, machine learning, geospatial analysis, and precision medicine have greatly enhanced the efficacy of diagnosis, forecasting of outbreaks, prognosis, and personalized management of patients. It becomes evident from the above that intelligent computing can serve to augment traditional medical practice[39].

5.2 Implications and Significance

This is a crucial step towards the effective implementation of diagnostics, predictive analysis, digital technologies for health care and biomarkers in the clinical setting[40]. Early detection and early interventions, as well as proper use of resources, are all possible through such approaches. In addition, a One Health approach which incorporates human, animal, and environmental surveillance, along with computational technologies, is an effective way of minimizing the disease burden of leptospirosis.

5.3 Research Gaps and Limitations

However, there are still some limitations that have prevented the wide application of new generation technology in the management of leptospirosis. There have been many AI models that are based on small and geographically constrained databases, thus having poor generalizability in other populations. Moreover, inconsistent surveillance systems, lack of external validation, poor integration of clinical and environmental information, and immaturity of 3D fingerprinting and biomarker-based precision medicine technologies pose substantial challenges.

5.4 Future Research Directions

Research must aim to develop AI tools that incorporate molecular diagnostics, bioscreening, environment surveillance, and epidemiology data into a single model to improve clinical decision making. More effort must be invested in multimodal data integration, precision medicine, wearable biosensors, digital health technologies, AI-based drug discovery, and vaccine development. The importance of increasing international collaboration by adopting the One Health approach and conducting multicenter validations cannot be overstated to advance clinical translation and global preparation for the next outbreak of leptospirosis.

6. CONCLUSION

Leptospirosis is an important disease in the group of neglected zoonosis with increasing global burden due to changes in the environment, urbanization, and climate variations. The review aims at discussing current advances in the etiology, pathogenesis, epidemiology, bioscreening methods, and treatment approaches to this infection with particular emphasis on the increasing importance of using AI, machine learning, geospatial methods, and precision medicine in disease surveillance, early diagnosis, prognosis, and personalized medicine. The use of these smart methods in combination with traditional medical approaches and One Health surveillance holds significant promise for disease control and patient management. Progress in the future will require standardization and validation, cooperation of multiple disciplines, and further development of diagnostics based on AI, digital health, vaccines, and precision infectious diseases.

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