

## Istituto Zooprofilattico Sperimentale della Lombardia e dell'Emilia – Romagna "Bruno Ubertini" Centro di Referenza Nazionale per la Leptospirosi

# BOLLETTINO BIBLIOGRAFICO Edizione n. 2025/07 Luglio 2025

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In-house IgM dot-blot assay for serodiagnosis of human leptospirosis: development, standardisation, and performance evaluation

(2025) Microorganisms, 13 (6), art. no. 1307

DOI: 10.3390/microorganisms13061307

ABSTRACT: Laboratory confirmation of human leptospirosis relies on serological tests, with the microscopic agglutination test (MAT) as the reference. However, due to its complexity, there is a need for a simpler and more accessible diagnostic method. This study aimed to standardise and develop an IgM dot-blot test with a whole-cell antigen from saprophytic Leptospira biflexa serovar Patoc for diagnosing human leptospirosis. After checkerboard titration standardisation, IgM dot-blot was performed with paired serum samples from 124 MAT-confirmed leptospirosis cases and 143 serum samples from healthy and diseased individuals as the control group. Repeatability and reproducibility were also evaluated. An IgM dot-blot kit was then developed and compared to the PanbioTM Leptospira IgM ELISA using 144 serum samples from patients with suspected leptospirosis. The IgM dot-blot showed a sensitivity of 58.1% and 96.0% when performed on acute and convalescent samples, respectively. Specificity was 94.4%. The repeatability and reproducibility of the IgM dot-blot showed 100% consistency. Comparison of IgM dot-blot and IgM ELISA showed almost perfect agreement, with a Kappa index of 0.81. The developed IgM dot-blot offers a robust alternative to existing methods, requiring minimal specialised equipment and fewer reagents than IgM ELISA. The good performance of this IgM dot-blot immunoassay makes it a promising tool for diagnosing human leptospirosis, potentially increasing diagnostic capacity, especially in places with limited resources.

LANGUAGE OF ORIGINAL DOCUMENT: English

Hejduk L., Müller N., Rathner A., Štěrba J., Hung S.-C., Chyan C.-L., Rego R.O.M., Strnad M.

Navigating infection by pathogenic spirochetes: the host-bacteria interface at the atomic level

(2025) Protein Science, 34 (7), art. no. e70185

DOI: 10.1002/pro.70185

ABSTRACT: Pathogenic spirochetes bind and interact with various host structures and molecules throughout the course of infection. By utilizing their outer surface molecules, spirochetes can effectively modulate their dissemination, interact with immune system regulators, and select specific destination niches within the host. The three-dimensional structures of multiple spirochetal surface proteins have been elucidated, providing insight into their modus operandi. This review focuses on the structural characteristics of these sticky molecules and their functional implications, highlighting how these features contribute to the pathogenicity of spirochetes and their ability to persist in the host and vector environments. Recognizing the structural motifs and ligands to which these important virulence determinants bind could open new avenues for developing strategies to block colonization by spirochetal pathogens.

LANGUAGE OF ORIGINAL DOCUMENT: English

Andrade A.C.D.S., Bonato F.G.C., Santos I.C.D., Iukava L.K., Charnovski S.G.D., da Silva B.P.B., Suci Junior E.M., Pretto-Giordano L.G., Piau Junior R., Ribeiro R.N., Gazim Z.C., Silva G.C.C., Barbosa L.N., Gonçalves D.D.

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Presence of Leptospira spp. in nonhuman primates and wild felids from a Brazilian zoo

(2025) Vector-Borne and Zoonotic Diseases

DOI: 10.1089/vbz.2025.0020

ABSTRACT: Introduction: Leptospirosis is a zoonotic disease caused by the bacterium Leptospira spp., which is divided into saprophytic and pathogenic. Transmission in zoos can occur due to infected urine in poorly sanitized environments, rodents, and animal accumulation. Aim: This study investigated the presence of antibodies and DNA of Leptospira spp. in nonhuman primates and wild felids from a zoo in western Paraná, Brazil. Materials and Methods: Samples were collected through chemical restraint and venipuncture. Antibody testing was performed by microscopic agglutination test and polymerase chain reaction (PCR). Results: Of the 24 samples analyzed (17 capuchin monkeys and 7 felines), 12.5% presented antibodies for the Butembo serovar, all in primates. No feline showed reaction or DNA amplification. Conclusion: The results highlight the importance of studies on leptospirosis in wild animals in captivity, considering factors such as biome and management of the zoo, which houses rescued species that cannot be reintroduced into the wild.

LANGUAGE OF ORIGINAL DOCUMENT: English

Moroni B., Meletiadis A., Di Nicola M.R., Garcia-Vozmediano A., Pitti M., Dipietromaria G., Zoppi S., Bergagna S., Pinnelli V., Guasco C., Acutis P., Pastorino P., Prearo M., Esposito G.

### Prevalence of Salmonella, Cryptosporidium and Leptospira in Invasive Pond Slider (Trachemys scripta) in North-Western Italy

(2025) Veterinary Medicine and Science, 11 (4), art. no. e70439

DOI: 10.1002/vms3.70439

ABSTRACT: Natural lakes and ponds typically feature green areas where people engage in recreational and sporting activities. In Italy, these areas are often inhabited by non-native freshwater turtles, even at high densities. However, freshwater turtles have been identified as natural carriers for various pathogens that can be transmitted to humans, making their sanitary monitoring crucial to prevent accidental transmission through direct or indirect contact. In this study, we investigated the presence of three potentially zoonotic pathogens, namely Salmonella, Leptospira and Cryptosporidium, in a group of 83 freshwater turtles (Trachemys scripta) captured in Piedmont, Northwest Italy. Overall infection prevalence was 9.6%. Salmonella spp. was detected in ten specimens of T. s. elegans and Cryptosporidium ducismarci in one specimen of T. s. scripta. Salmonella enterica subsp. diarizonae was confirmed in ten freshwater turtles. No Leptospira DNA was detected. Our findings highlight that turtles, as asymptomatic carriers of zoonotic pathogens, contribute to environmental contamination and public health risks, underscoring the need for sanitary monitoring of invasive alien species under a 'One Health' approach.

LANGUAGE OF ORIGINAL DOCUMENT: English

Abil O.Z., Kundu S., Midon L.M., Gomes-Solecki M.

#### TLR4 competence and mouse models of sublethal leptospirosis

(2025) PLOS Neglected Tropical Diseases, 19 (5), art. no. e0013163

DOI: 10.1371/journal.pntd.0013163

ABSTRACT: Mice are slowly being accepted as alternative models for investigation of leptospiral infection. The strain often used to analyze sublethal disease (C3H/HeJ) expresses a hyporesponsive tlr4 gene in its cells and thus the model is deemed immunocompromised. To help resolve this scientific concern we compared infection of mice expressing competent tlr4 (C3H/HeN, C57BL6) versus tlr4 hyporesponsive mice (C3H/ HeJ) with Leptospira interrogans serovar Copenhageni strain Fiocruz L1-130 over a period of two weeks. We found that the two mouse strains with a functional tlr4 gene (C3H/HeN and C57BL/6) developed clinical and

molecular signs of leptospirosis less pronounced but not significantly different than tlr4 hyporesponsive C3H/HeJ, as quantified by weight loss, survival curves, presence of Leptospira 16S rRNA in blood and urine and burden of viable spirochetes in kidney as compared to the respective uninfected controls. Analysis of serologic immune factors in the three strains revealed increased IgM and IgG3, and a general absence of inflammatory markers at two weeks post infection. Our data suggests that TLR4 function is not sufficient to cause susceptibility to leptospirosis. We conclude that C3H/HeN and C57BL/6 are appropriate mouse models of sublethal leptospirosis.

LANGUAGE OF ORIGINAL DOCUMENT: English

Martin B.M., Sartorius B., Mayfield H.J., Cadavid Restrepo A.M., Kiani B., Then Paulino C.J., Etienne M.C., Skewes-Ramm R., de St Aubin M., Dumas D., Garnier S., Duke W., Peña F., Abdalla G., de la Cruz L., Henríquez B., Baldwin M., Kucharski A., Nilles E.J., Lau C.L.

Geospatial analysis of leptospirosis clusters and risk factors in two provinces of the Dominican Republic (2025) PLoS neglected tropical diseases, 19 (6), pp. e0013103

DOI: 10.1371/journal.pntd.0013103

ABSTRACT: BACKGROUND: Drivers of leptospirosis transmission can vary across regions, leading to spatial clustering of infections. This study aims to identify clusters of leptospirosis seroprevalence in the Dominican Republic (DR) and factors associated with high-risk areas. METHODOLOGY/PRINCIPAL FINDINGS: We analysed data from two provinces, Espaillat and San Pedro de Macoris (SPM), obtained on a national survey conducted in 2021 (n = 2,078). Samples were tested by microscopic agglutination testing (MAT) to detect leptospirosis antibodies. We used flexible spatial scan statistics to locate significant clusters for seropositive individuals (all serogroups combined) in each province and calculated risk ratios (RR) at the household and community level. Environmental and sociodemographic risk factors associated with clusters were assessed by logistic regression. One cluster was identified in each province. Participants living inside a cluster were more likely to live further from health facilities (OR 1.86, p < 0.001 and OR 4.41, p = 0.044 by motorized travel time in Espaillat and SPM, respectively). Cluster participants were also less likely to live in areas of higher population density (OR 0.76, p < 0.01 and OR 0.29, p < 0.001 in Espaillat and SPM, respectively) and in communities with higher gross domestic product (GDP) (OR 0.70, p < 0.001 and OR 0.42, p < 0.001 in Espaillat SPM. and respectively). Additional risk factors varied between Espaillat and SPM. CONCLUSION/SIGNIFICANCE: Our findings confirm the clustered spatial pattern of leptospirosis and highlight that transmission drivers vary by province. While both provinces show higher transmission in impoverished areas, modifiable factors differ, requiring tailored public health interventions.

LANGUAGE OF ORIGINAL DOCUMENT: English

Sawangpol C., Aimyong N., Phosri A.

Epidemiological changes in the incidence of human leptospirosis in Thailand: findings from the National Disease Surveillance System from 2013 to 2022

(2025) Infectious Diseases Now, 55 (6), art. no. 105108

DOI: 10.1016/j.idnow.2025.105108

ABSTRACT: Objectives: To describe the epidemiological changes in leptospirosis incidence from 2013 to 2022, and to further quantify factors associated with leptospirosis mortality in Thailand. Methods: We analyzed the epidemiological trends of leptospirosis incidence using data from the National Disease Surveillance System

from January 2013 to December 2022 and estimated potential factors associated with leptospirosis mortality using a multiple logistic regression model. Results: A total of 25,006 cases were reported during the study period, with an average incidence rate of 3.8 cases per 100,000 population. The incidence rate gradually decreased from 2013 to 2021, followed by a sharp increase in 2022. The case fatality rate increased steadily from 2013 to 2015 and then began to decline after 2015. A higher incidence rate was observed in men than in women, in individuals aged ≥15 years than in children <15 years, in residents of rural areas than urban areas, in people living in the southwestern region than in those living in other regions, and in individuals engaged in agriculture. We also observed that age groups, regions of residence, healthcare facilities and services, and duration from symptom onset to treatment initiation were significantly associated with a mortality risk from leptospirosis. Conclusion: A decreasing trend in leptospirosis incidence was observed from 2013 to 2021, followed by a recent increase in 2022, indicating that it is crucial to enhance the current surveillance system for implementing targeted interventions and to develop appropriate guidelines for reducing leptospirosis incidence and mortality by controlling the associated prognostic factors.

LANGUAGE OF ORIGINAL DOCUMENT: English

Hassan M., Rosli S.N.Z., Mohamed Tahir N.A., Mohamed N.A., Mohd Sukri K., Azmi L., Mohammad N.

### Enhancing leptospirosis screening using a deep convolutional neural network with microscopic agglutination test images

(2025) Biology Methods and Protocols, 10 (1), art. no. bpaf047

DOI: 10.1093/biomethods/bpaf047

ABSTRACT: Leptospirosis poses substantial challenges to global public health. In Malaysia, leptospirosis is endemic, with annual cases peaking during the monsoon season. The microscopic agglutination test (MAT) is the gold-standard serological method for confirmation of leptospirosis. However, it is labor-intensive and timeconsuming, as it relies on the subjective interpretation of medical lab technicians. This study describes the development of a semiautomated workflow for Leptospira screening by integrating a TensorFlow and customdesigned Keras-based Deep Convolutional Neural Network (DCNN) with conventional MAT. We used a dataset of 442 positive and 442 negative MAT images, which consisted of a mixture of Leptospira serovars from Malaysia to train the model. The model was subjected to hyperparameter tuning, which modulated the number of convolutional layers, filters, kernel sizes, units in dense layers, activation functions, and learning rate. Verification of our tested model compared to the verified patient MAT results achieved the following metrics: a Precision score of 0.8125, a Recall of 0.9286, and an F1-Score of 0.8667. Combining our model with the current Malaysia Leptospira workflow can significantly speed up, reduce inaccuracies, and improve the management of leptospirosis. Furthermore, the application of this model is practical and adaptable, making it suitable for other labs that observe MAT as their Leptospira diagnosis. To our knowledge, this approach is Malaysia's first hybrid diagnostic approach for Leptospira diagnosis. Scaling up the dataset would enhance the model's accuracy, making it adaptable in other regions where leptospirosis is endemic.

LANGUAGE OF ORIGINAL DOCUMENT: English

Chen X., Xie X., Liu X., Liu J., Zhang W., Cao Y.

Role and mechanism of butyric acid in hamster leptospirosis

(2024) Chinese Journal of Veterinary Science, 44 (8), pp. 1743 - 1748

DOI: 10.16303/j.cnki.1005-4545.2024.08.22

ABSTRACT: Leptospirosis is a global natural zoonotic infectious disease. Research shows that shortchain fatty acids, metabolites of gut microbiota, are involved in host immune regulation and affect disease progression. This experiment was conducted to investigate the role of short-chain fatty acids in leptospirosis. The results showed that supplementation of short-chain fatty acid butyric acid could significantly improve the survival rate of leptospirosis in hamsters. In vitro experiments showed that butyric acid treatment inhibited the expression of Cat and Gsr genes in macrophages after infection with Leptospira, but enhanced the expression of NOX1 and NOX4 genes. At the same time, butyric acid treatment enhanced macrophage ROS levels after leptospirosis infection, and high levels of ROS enhanced the bactericidal function of macrophages. In vivo experiments also confirmed that butyric acid protects hamsters against acute leptospirosis by regulating ROS production. Collectively, the short-chain fatty acid butyric acid, a metabolite of gut microbiota, enhances the bactericidal function of macrophages by regulating ROS expression, thereby protecting the host against leptospirosis.

LANGUAGE OF ORIGINAL DOCUMENT: Chinese

Vivero-Tellez D., Contreras-Ortíz J.A., Flores-Martínez E., Gracia-Ramos A.E.

Weil's disease with multi-organ dysfunction: a diagnostic challenge

(2025) Clinical Medicine and Research, 23 (1), pp. 26 - 31

DOI: 10.3121/cmr.2025.1963

ABSTRACT: Leptospirosis is a zoonotic disease caused by spirochetes from the species Leptospira. Weil's disease, the more severe manifestation of leptospirosis, is characterized by a combination of jaundice, renal injury, and hemorrhages. Diagnosing severe leptospirosis in patients with acute life-threatening multi-organ dysfunction at presentation can be challenging because of the non-specific clinical manifestations. This report describes a case of severe leptospirosis with jaundice, acute renal dysfunction, severe thrombocytopenia, pulmonary hemorrhage, and unusual manifestations, including rhabdomyolysis, acalculous cholecystitis, and pancreatitis, which required a comprehensive diagnostic evaluation of possible causes to confirm the diagnosis. The case highlights the importance of clinicians considering leptospirosis in the differential diagnosis of a patient with cryptogenic sepsis who develops multiple organ dysfunction.

LANGUAGE OF ORIGINAL DOCUMENT: English

Gong L., Lyu T., Tian H., He H., Ding Y., Liu J., Xie X., Zhang W., Cao Y.

Protective effect of Angelica sinensis polysaccharide on leptospiral infection in golden hamster

(2025) Chinese Journal of Veterinary Science, 45 (5), pp. 1060 - 1066

DOI: 10.16303/j.cnki.1005-4545.2025.05.23

ABSTRACT: To explore the protective effect of Angelica sinensis Polysaccharide (ASP) on leptospiro-sis induced by pathogenic Leptospira infection, the golden hamster model of leptospirosis was selected for the experiment. The Leptospira and Leptospira + ASP groups were intraperitoneally injected with Leptospira interrogans serovar Lai strain 56601 (IX 106 per hamster). After infection, the Leptospira + ASP group was injected intraperitoneally with ASP (50 mg/kg) for three consecutive days, while the Leptospira group was injected intraperitoneally with normal saline for three days. The experiment employed methods such as daily observation of the clinical symptoms of golden hamsters, statistics of the survival status of each group of golden hamsters, pathological damage of liver, kidney, and lung, bacterial load in organs, and the expression of inflammatory cytokines (IL-Iß and TNF-a). The results indicated that ASP could effectively alleviate the

clinical symptoms of the infected hamsters, enhance the survival rate, ameliorate the pathological damage of the body, reduce the bacterial load in various organs, and mitigate tissue inflammation. This study demonstrated for the first time that ASP has a protective effect on leptospirosis, providing medication guidance for the clinical treatment of leptospirosis.

LANGUAGE OF ORIGINAL DOCUMENT: Chinese

Taborda M., Takahashi J.P.F., Nascimento J.B.F., Mari J.F., Oliveira V.F., Magri A.S.G.K., Nastri A.C.S.S., Magri M.M.C.

Gastrointestinal mucormycosis associated with leptospirosis: should we be concerned during major floods? (2025) Revista do Instituto de Medicina Tropical de Sao Paulo, 67, pp. e35

DOI: 10.1590/S1678-9946202567035

ABSTRACT: Gastrointestinal mucormycosis (GIM) and leptospirosis are two severe diseases associated with high morbidity and mortality rates. The coexistence of these two conditions has not yet been reported in the literature. This study presents a case involving this rare association. A 49-year-old man from Sao Paulo, Brazil, was hospitalized with acute abdominal pain, low blood pressure, and jaundice. He had a history of contact with floodwater and ingestion of contaminated water, was hospitalized with acute abdominal pain, low blood pressure, and jaundice. Upon ICU admission, he developed jaundice, acute renal failure requiring hemodialysis, and alveolar hemorrhage necessitating intubation. Leptospirosis was confirmed by serological tests and treated with ceftriaxone for 14 days. Two weeks later, he developed severe enterorrhagia, requiring a massive transfusion and a total colectomy with terminal ileostomy. Histopathology revealed necrotizing granulomatous inflammation with hyphae indicative of mucormycosis. He was treated with amphotericin B for 7 weeks, followed by posaconazole. Abdominal CT scans over the next five months showed complete clinical and radiological improvement. The association between mucormycosis and leptospirosis has not been previously documented, highlighting the diagnostic challenges and the critical importance of early detection. Successful management in this case required timely surgical intervention combined with prolonged antifungal therapy.

LANGUAGE OF ORIGINAL DOCUMENT: English

Ortiz-Prado E., Izquierdo-Condoy J.S., Salazar-Santoliva C., Vasconez-Gonzalez J.

Leptospirosis deaths in children in the Amazon: syndemic inequities

(2025) The Lancet, 405 (10497), pp. 2275

DOI: 10.1016/S0140-6736(25)01204-8

LANGUAGE OF ORIGINAL DOCUMENT: English

Shulga O.D., Romaniuk A.S., Kotsiuba O.G.

Guillain-Barre syndrome as a complication of leptospirosis associated with Hebdomadis serovariant

(2025) Psychiatry, Neurology and Medical Psychology, 12 (2), pp. 270 - 278

DOI: 10.26565/2312-5675-2025-28-11

ABSTRACT: Background. Leptospirosis is an acute, naturally focal zoonotic infection caused by various serogroups of Leptospira, with a wide range of transmission mechanisms. The relevance of this infectious disease in modern medicine remains high not only in Ukraine but worldwide, with an estimated 350,000 to 500,000 severe cases reported annually. The clinical course can range from mild to severe, involving multiple

organs and systems, potentially leading to disability or even death. Complications affecting the nervous system are of particular clinical significance, occurring in only 10-15% of cases, yet they can result in serious outcomes. Cases involving the development of Guillain-Barré syndrome are extremely rare, highlighting the scientific and clinical importance of analyzing such cases. The presented case is notable for the development of secondary Guillain-Barré syndrome with profound peripheral tetraparesis, bilateral facial nerve palsy, central-type pelvic organ dysfunction, severe pain and amyotrophic syndromes, as well as impaired gait and loss of self-care ability. Purpose - to describe a rare clinical case of Guillain-Barré syndrome associated with leptospirosis caused by the Leptospira Hebdomadis serovar. Materials and methods. This paper presents the findings from clinical observation and diagnostic studies of Guillain-Barré syndrome associated with leptospirosis in a patient treated at the infectious disease and neurology departments of the Volyn Regional Clinical Hospital. Results. The patient was diagnosed with a severe form of leptospirosis, complicated by the development of secondary Guillain-Barré syndrome. The diagnosis of leptospirosis was confirmed via microagglutination and lysis testing, which yielded a positive result at a serum dilution of 1:400 with the Hebdomadis serovar. Despite a comprehensive therapeutic approach, the patient's condition rapidly deteriorated, marked by progressive neurological deficits, including ascending symmetrical weakness with areflexia and autonomic dysfunction. These symptoms indicated a rapidly advancing involvement of the nervous system characteristic of Guillain-Barré syndrome. The clinical features of leptospirosis and its impact on the nervous system were assessed based on the patient's complaints, neurological examination, and diagnostic test results. Conclusions. This report describes the first documented case in the literature of Guillain-Barré syndrome associated with the Leptospira Hebdomadis serovar. The uniqueness of the case lies in the development of severe neurological impairment due to delayed medical intervention. This case underscores the importance of early diagnosis and heightened physician awareness regarding potential neurological complications of infectious diseases.

LANGUAGE OF ORIGINAL DOCUMENT: English

Saranya S., Chellapandi P.

### Evolutionary insights into the geographic spread of pathogenic and opportunistic Leptospira strains (2025) Microbial Pathogenesis, 206, art. no. 107825

DOI: 10.1016/j.micpath.2025.107825

ABSTRACT: Leptospirosis, a global health concern caused by Leptospira sp. is largely unknown due to its elusive phylogeographic distribution and flow. Therefore, this study aimed to understand the geographical distribution and evolutionary changes of pathogenic, non-pathogenic, and opportunistic strains of Leptospira. This study used genome-scale data, 16S rDNA gene sequences, and virulence proteins to construct precise phylogenetic trees using robust bootstrapping techniques. Phylogenomic studies indicated that pathogenic Leptospira strains constituted a distinct cluster from opportunistic and non-pathogenic variants. The pathogenic strains coalesced, creating a central group in the phylogenetic tree based on the 16S rDNA gene. Pathogenic strains had a close evolutionary relationship with non-pathogenic and opportunistic strains, since they shared the outer membrane protein L. The opportunistic strains formed a clearly defined clade, suggesting that there were no evolutionary transitions between them. Nevertheless, we found potential transitions between the pathogenic and non-pathogenic strains. Additionally, this study unveiled the participation of prominent countries in the dissemination of Leptospira strains to various geographical areas, such as Thailand, the USA,

Peru, Italy, Turkey, Malaysia, New Caledonia, Brazil, and Iran. This work provides novel perspectives on the evolutionary shift, geographical dissemination, and emergence of highly pathogenic Leptospira strains.

LANGUAGE OF ORIGINAL DOCUMENT: English

Merker Breyer G., Noronha Arechavaleta N., Corrêa da Silva B., Rocha Jacques da Silva M.E., Costa Torres M., Cadó Nemitz L., da Rosa Marques R., Borges Meurer F., Linden G.A., Soares Weyh T., Maboni Sigueira F.

### Canine leptospirosis in flood-affected areas of Southern Brazil: molecular assessment and public health implications

(2025) Infectious Disease Reports, 17 (3), art. no. 63

DOI: 10.3390/idr17030063

ABSTRACT: Background: Southern Brazil faced massive rains and floods in May 2024, which led to social, infrastructural, and One Health issues affecting over 478 municipalities and 2.3 million people. Exposure to floodwater increased the risk of bacterial infections, including leptospirosis. Despite the zoonotic nature of leptospiral infections, only human leptospirosis is subject to mandatory reporting, while canine cases are less closely monitored. Considering the extent of this climatic event, many emergency shelters were created for rescued dogs, highlighting the need to monitor infectious diseases to mitigate the spread of hazardous pathogens. Methods: We performed a molecular assessment of canine leptospirosis in Porto Alegre and its metropolitan region. A total of 246 dogs rescued from the flooded areas underwent molecular diagnosis targeting lipL32. In addition, positive samples were identified by sequencing of the partial secY gene. Results: A total of 9 (4%) dogs were positive for Leptospira spp. Molecular and phylogenetic analyses of secY from the positive samples determined that the circulating strains belonged to L. interrogans (n = 8)— Icterohaemorrhagiae and Pomona as the suggested serogroups—and L. kirschneri (n = 1). Conclusions: Our findings point out the challenges in diagnosing and controlling leptospirosis during severe climatic events and reinforce the need for preventive sanitary measures to mitigate the dissemination of Leptospira spp., including the adoption of a mandatory notification system for canine leptospirosis.

LANGUAGE OF ORIGINAL DOCUMENT: English

Lewicka A.J., Lyczakowski J.J., Pardyak L., Dubniewicz K., Latowski D., Arent Z.

### Beyond serology: saccharide profiling enables identification of antigenically similar Leptospira and prompts re-evaluation of bacterial lipopolysaccharide evolution

(2025) Frontiers in Molecular Biosciences, 12, art. no. 1581587

DOI: 10.3389/fmolb.2025.1581587

ABSTRACT: Leptospirosis is a zoonotic infectious disease of growing importance in both human and veterinary medicine. Gram-negative spirochetes of Leptospira are traditionally classified into serovars based on their antigenic identity, which must be ascertained to design effective treatment procedures for humans and appropriate vaccination strategies in pets and livestock. Unfortunately, identifying Leptospira serovars is challenging and currently requires access to a wide panel of reference strains, animal-derived antisera, or monoclonal antibodies. Here, we describe a new method for the identification of Leptospira serovars that is based on monosaccharide composition analysis of the polysaccharide part of bacterial lipopolysaccharide (LPS) structures. Our approach requires no animal sacrifice and can be implemented in any laboratory equipped for chromatographic analysis. An LPS sugar fingerprint that is specific to each bacterial isolate that we studied can be generated. Importantly, sugar profiling of LPS enables distinguishing Leptospira serovars

that are antigenically very similar. Using our new approach, we discover that the LPS structures of two cattle pathogens belonging to two different species: Leptospira interrogans and Leptospira borgpetersenii, and to one serovar: Hardjo, can be distinguished despite sharing major similarities. Through extensive phylogenetic analysis, we reveal which specific glycosyltransferases of the LPS biosynthesis rfb locus likely drove the emergence of these similarities and identify a single glycosyltransferase that might have contributed to the formation of saccharide differences in the LPS structure. Our findings have implications for future work on the evolution of bacterial polysaccharide synthesis and highlight the importance of preventing horizontal gene transfer between pathogenic bacteria.

LANGUAGE OF ORIGINAL DOCUMENT: English

Yalung J.R.V., Realina R.C.A., Rodriguez V.M., Santiago V.A.T., Tangkengco E.S., Valerozo M.M., Villaflor C.M., Yapit A.D.C., Lirio M.R.F.

Molecular and structural characterization of proline-rich peptides in Apis mellifera to Leptospira interrogans: exploring potential therapeutic applications of Apidaecin to LipL32

(2025) Microbial Biosystems, 10 (2), pp. 152 - 159

DOI: 10.21608/mb.2025.376684.1295

ABSTRACT: Leptospirosis is a disease caused by the gram-negative bacterium Leptospira interrogans, with limited treatments contributing to its growing global burden. This study investigates Apidaecin, a proline-rich antimicrobial peptide (PRAMP) from Apis mellifera (honeybee), targeting LipL32, a key virulence factor of Leptospira interrogans. Using an in-silico approach, ProtParam analyzed Apidaecin's molecular characteristics. Notably, theoretical isoelectric point, instability index, aliphatic index, and hydropathicity were 10.95, 81.52, 46.63, and-1.717, respectively. Furthermore, AlphaFold Protein Structure Database generated the three-dimensional structures of the proteins, and molecular docking via LZerD Protein Web Server identified Model 1 as the most favorable binding interaction, attaining a Ranksum score of 42, and consistent ranks of 14 in GOAP, DFIRE, and ITScore. Model 2 follows with a score of 64 and Model 3 scores 77. Models 4 and 5 perform poorly, with Ranksum score of 150 and 157, mainly due to high GOAP ranks of 137 and 92, respectively. Results also suggest that Apidaecin's high proline content (28.1%) enhances its bacteriostatic activity via ribosomal restraining capacity to inhibit elongation of protein. This structural property allows Apidaecin to target gram-negative bacteria without damaging the host membrane, making it a promising therapeutic candidate. Moreover, the nature of the findings stems primarily from computational predictions, providing valuable preliminary insights. Thus, these in silico findings require further experimental validation, particularly in vitro assays, in vivo studies, and clinical evaluations, to assess its pharmacokinetics, efficacy, and safety for human use.

LANGUAGE OF ORIGINAL DOCUMENT: English

Kumari A.M.U.P., Vidanapathirana J., Amarasekara J., Karunanayake L.

Provider cost estimation of leptospirosis at district general hospital Monaragala, Sri Lanka

(2025) BMC Infectious Diseases, 25 (1), art. no. 816

DOI: 10.1186/s12879-025-11211-y

ABSTRACT: Introduction: The rising number of leptospirosis patients and escalating healthcare costs strain the sustainability of free healthcare systems in developing countries like Sri Lanka, posing significant challenges to resource allocation and financial stability in these regions. The objective of this study is to assess

the healthcare provider's cost of managing leptospirosis at the District General Hospital, Monaragala, Sri Lanka. Methods: A hospital-based cost estimation study was conducted in DGH Monaragala using the scenario building technique, to assess the provider cost of laboratory confirmed leptospirosis patients using three standard management profiles as uncomplicated ward treated, complicated ward treated and ICU treated. Results: The provider cost per uncomplicated leptospirosis patient treated in the ward was Rs. 5,449.39 per day (Rs. 5,993 with 10% inflation), totaling Rs. 21,797.54 for an average 4-day stay (Rs. 23,976 with inflation). For complicated cases, the cost per day was Rs. 5,695.35 (Rs. 6,264 with 10% inflation), with a total of Rs. 39,867.43 for an average 7-day stay (Rs. 43,853 with inflation). ICU costs varied by complication: renal (Rs. 26,538.79/day), cardiac (Rs. 28,212.39/day), pulmonary (Rs. 29,657.10/day), neurological (Rs. 26,444.85/day), and multi-organ failure (Rs. 28,363.17/day). The total provider cost for laboratory-confirmed leptospirosis cases at DGH Monaragala was Rs. 7,916,564.52, with 34.7% allocated to managing 11 complicated ICU cases. Conclusions and recommendations: The provider cost of leptospirosis in DGH Monaragala was high. Given the inherent challenges in limiting exposure, it is imperative that control efforts prioritize early detection and treatment.

LANGUAGE OF ORIGINAL DOCUMENT: English

Badri M., Sheikhdavoodi N., Nikkhahi F., Eslahi A.V., Karanis P.

### A case of severe leptospirosis complicated with massive rhabdomyolysis and acute kidney injury: a case report

(2025) Journal of Medical Case Reports, 19 (1), art. no. 316

DOI: 10.1186/s13256-025-05378-w

ABSTRACT: Background: Leptospirosis is a reemerging waterborne zoonotic infection with a significant global health importance. The manifestations are ranged from mild febrile illness to severe conditions, including Weil's disease and rhabdomyolysis-induced acute kidney injury. Case presentation: Here we report a case of a 27-year-old Iranian male patient with a history of mountain climbing who developed severe leptospirosis. The patient presented massive rhabdomyolysis, acute kidney injury, and respiratory distress, initially suspected to be related to his physical activity. The leptospirosis infection was confirmed using an enzyme-linked immunosorbent assay. Despite hydration and broad-spectrum antibiotic therapy, the patient's condition demanded intensive care and hemodialysis. Finally, the patient recovered completely, underscoring the critical need for timely diagnosis and intervention in leptospirosis cases. To date, there have been no reports of leptospirosis-associated rhabdomyolysis in Iran. Additionally, cases of rhabdomyolysis caused by leptospirosis are rare worldwide. Conclusion: This is report reveals the reemergence of leptospirosis, particularly in environments conducive to the survival of Leptospira bacteria, and the significance of awareness and preventive measures, especially for susceptible populations.

LANGUAGE OF ORIGINAL DOCUMENT: English

Putz E.J., Andreasen C.B., Boggiatto P., Palmer M.V., Fernandes L.G.V., Tibbs-Cortes B.W., Stasko J.A., Hamond C., Olsen S.C., Nally J.E.

#### Peromyscus spp. deer mice as rodent model of acute leptospirosis

(2025) Emerging infectious diseases, 31 (7), pp. 1365 - 1376

DOI: 10.3201/eid3107.241579

ABSTRACT: Leptospirosis is a global zoonotic disease affecting humans, wildlife, companion, and domestic animals. Incidental hosts can contract the disease directly or indirectly from asymptomatic reservoir hosts, most commonly small rodents. The Golden Syrian hamster is recognized as the dominant rodent model for acute leptospirosis because the animals are susceptible to many serovars and are used to maintain laboratory strains and test bacterin vaccine efficacy. However, hamsters are primarily used in survival-based studies, and investigations into host immune response and disease pathogenesis are limited. We found that Peromyscus leucopus white-footed deer mice are susceptible to acute leptospirosis, and thus might be an alternative rodent model. Furthermore, similar to hamsters, deer mice produce circulating foamy macrophages in response to Leptospira challenge. Deer mice exhibit differences in response to different serovars, clinical disease severity, kidney and liver lesions, and an overall sex effect, with male mice demonstrating more severe clinical signs and higher bacterial burden.

LANGUAGE OF ORIGINAL DOCUMENT: English

Saengsuwan L., Woradet S., Chaimay B.

Renal function associated with mortality among patients with leptospirosis in upper Southern Thailand: a hospital-based case-control study

(2025) Journal of Health Research, 39 (3), pp. 227 - 233

DOI: 10.56808/2586-940X.1136

ABSTRACT: Background: Leptospirosis is a major public health issue in tropical regions. This study investigated the association between renal function and mortality among leptospirosis patients in upper southern Thailand. Methods: A hospital-based case-control study was conducted on leptospirosis patients from 2012 to 2018. Cases were patients who died, while controls were survivors (1:3 ratio). A total of 42 cases and 126 controls were included. Data were sourced from the Office of Disease Prevention and Control 11, Nakhon Sri Thammarat, and medical records. Key renal function indicators included blood urea nitrogen (BUN), creatinine (Cr), and estimated glomerular filtration rate (eGFR). In-hospital mortality was the primary outcome. Statistical analysis involved descriptive methods and multiple logistic regression. Results: Patients with elevated BUN (AOR ¼ 3.60, 95 % CI: 1.34e9.61), high Cr (AOR ¼ 6.08, 95 % CI: 1.95e18.99), and eGFR in stages 3e5 (AOR ¼ 4.43, 95 % CI: 1.68e11.70) had a higher mortality risk after adjusting for confounders. Conclusion: Impaired renal function, particularly elevated BUN, Cr, and advanced renal failure, increases mortality risk in leptospirosis patients. Early renal function assessment is crucial for reducing mortality.

LANGUAGE OF ORIGINAL DOCUMENT: English

Veena R.K., Jayashankar M., Vinod Kumar K., Padma M.R., Balamurugan V.

Geospatial distribution of Leptospira-specific antibodies in febrile illness cases from Dakshina Kannada, India (2022–2023)

(2025) Tropical Medicine and International Health, 30 (7), pp. 737 - 748

DOI: 10.1111/tmi.14132

ABSTRACT: Background: Leptospirosis, a significant zoonotic disease, remains a major public health challenge in Dakshina Kannada, Karnataka, India, particularly during the monsoon. Objectives: To conduct spatial and temporal analysis of leptospirosis and investigate serogroup-specific distribution of Leptospira antibodies among febrile illness cases in Dakshina Kannada district, Karnataka state, India during 2022–2023. Methods: A total of 3489 serum samples from human febrile illness cases were screened for Leptospira-

specific IgM antibodies using commercial ELISA. A subset of 1631 samples underwent the Microscopic Agglutination Test (MAT) with a panel of 20 serovars representing 17 serogroups. Additionally, PCR targeting the lipL32 gene was performed on a subset of samples to identify active infections. Spatial mapping of seroprevalence and serogroup distribution was carried out using QGIS software. Results: The overall seroprevalence was (657/3489) 19%. IgM ELISA detected antibodies in (593/3489) 17% of cases, while MAT confirmed a seroprevalence of (154/1631) 9%. Among 80 samples tested by LipL32 PCR, 13 (16%) were positive. Djasiman, Hurstbridge, Javanica, and Icterohaemorrhagiae were the most frequently detected serogroups. The highest positivity rates were observed in Moodabidri (29%) and Sulya (27%) Taluks. Fever was the most common symptom, and the 30–39 age group had the highest prevalence (23%, p < 0.05). Seasonal peaks corresponded with monsoon months. Conclusion: This study highlights the need for integrated diagnostics, including ELISA, MAT, and early molecular detection through PCR, to improve leptospirosis management during peak seasons. The findings support targeted interventions, such as water sanitation and rodent control, to reduce the burden in this region. Expanded surveillance of livestock, wildlife, and the environment is crucial for understanding reservoirs and contamination sources.

LANGUAGE OF ORIGINAL DOCUMENT: English

Gompo T.R., Pandit S., Subedi D., Sapkota R.C., Pandey A., Nepal R., Tiwari A., Jyoti S.

### Seroprevalence and risk factors associated with Leptospira Hardjo among commercial dairy cattle farms of Rupandehi district, Nepal

(2025) BMC Veterinary Research, 21 (1), art. no. 442

DOI: 10.1186/s12917-025-04882-x

ABSTRACT: Background: Nepal relies on an agrarian-based economy, with the livestock sector contributing significantly to the national GDP. However, diseases like leptospirosis negatively impact cattle production and pose significant zoonotic risks. This study represents the first attempt to evaluate the risk factors of leptospirosis in cattle in Nepal. A cross-sectional study was conducted from March 2019 to April 2020 in 14 administrative units of the Rupandehi district. A total of 367 blood samples were collected from 206 cattle farms using a proportionate sampling procedure. An indirect ELISA was used to detect specific antibodies in serum samples against Leptospira interrogans serovar Hardjo. Farm management practices and knowledge of zoonotic diseases were assessed through interviews with animal owners from the 206 cattle farms. Regression analyses were conducted to analyze the herd and farm level risk factors. Results: The overall farm-level seroprevalence of leptospirosis was 4.85% (95% CI: 2.35-8.75), while the animal-level seroprevalence was 3.81% (95% CI: 2.10-6.30). Using multivariable logistic regression analysis, we found that farms with purchased cattle (farms that regularly introduce cattle from other farms) had a borderline significant increase in odds of leptospirosis (OR: 7.25, 95% CI: 0.88-59.46, p = 0.065) compared to farms that only keep homebred cattle. Additionally, larger farms (> 10 animals) were significantly associated with increased odds of leptospirosis (OR: 13.34, 95% CI: 1.64–108.42, p = 0.015) compared to smaller farms (≤ 10 animals). At the animal level, no statistically significant difference was observed in the multivariable mixed-effects logistic regression model, which included farm as a random effect. Conclusion: The detection of farms with positive serum samples highlights the persistent threat of leptospirosis to cattle production and its occupational hazards within Nepal's dairy sector. Farm-level risk factors, such farms with purchased cattle and larger farm sizes, emphasize the need for targeted control measures. Given the zoonotic nature of the disease and its ecological complexity involving multiple hosts, a One Health approach is essential. Collaborative efforts among stakeholders are needed to develop evidence-based policies, strengthen health system preparedness, and implement practical interventions that reduce transmission risks and the overall disease burden in both human and animal populations across the country.

LANGUAGE OF ORIGINAL DOCUMENT: English

U.K., Mustafa, Ummul Khair, E., Sauli, E., K.S., Kreppel, Katharina Sophia, J., Boenecke, Juliane, J., Brinkel, Johanna

Evaluation of the acceptability of ESIDA app, a smartphone-based clinical decision support application to improve infectious disease outbreak detection in Tanzania: clinician perspectives

(2025), 25 (1), art. no. 2197

DOI: 10.1186/s12889-025-23286-y

ABSTRACT: Background: Epidemic-prone infectious diseases (EPIDs) such as dengue fever, coronavirus disease 2019 (COVID-19), leptospirosis, Marburg virus disease, measles and cholera, to name a few, place a significant burden on the Tanzanian population and health system. Clinicians working in primary health facilities (PHFs), such as dispensaries, health centres, and basic hospitals, play a vital role in detecting cases and outbreaks. However, they often face challenges, including insufficient knowledge of these diseases and a lack of supporting resources, including surveillance guidelines, standard case definitions, and, most importantly, access to confirmatory diagnostic tests. Although Tanzania reports outbreaks of infectious diseases almost every year, a significant number of cases go undetected and contribute to delayed response and recurrent outbreaks. Smartphone-based clinical diagnostic decision support systems (CDSS) have been proven to help bridge case detection gaps. The Epidemiological Surveillance for Infectious Diseases in Sub-Saharan Africa (ESIDA) project proposed developing the ESIDA app, a smartphone-based CDSS, to aid clinicians in the detection of EPIDs. Before developing the app, the ESIDA project evaluated its acceptability among clinicians, the primary target users. The aim was to gather insights to inform the app development, ensuring its design and features are relevant and applicable in Tanzania context. Methods: In-depth interviews were conducted with 21 clinicians, including medical doctors and clinical officers from public and private facilities in the Dar es Salaam region, which has reported frequent outbreaks of dengue and cholera. Data were collected and analyzed using the Unified Theory of Acceptance and Use of Technology (UTAUT) model. Result: Clinicians were positive about the proposed ESIDA app and intended to use it once it was available. The facilitators and barriers to acceptability focused on performance expectancy, effort expectancy, facilitating conditions and social influence. Expected benefits, ease of use, and government involvement emerged as facilitators of acceptability, while high internet costs, workload, time constraints, infrastructure gaps, and patient resistance were identified as potential barriers. Conclusion: The development of the ESIDA app should prioritize maximizing system performance and benefits. They must also be user-friendly and in line with social norms. The necessary infrastructure must be in place for effective implementation.

LANGUAGE OF ORIGINAL DOCUMENT: English

S., Melo, Sebastián, A., Guallasamín-Miño, Andrea, P., Mosquera, Pamela, M., Carvajal, Mateo, M., Falconí, Mercy, J.D., Mosquera, Juan Daniel, D., Páez-Rosas, Diego, E.A., Diaz, Eduardo Alfonso, T.R., Pearson, Talima R., V.A., Barragán, Verónica Alexandra

Leptospira interrogans in the Galapagos sea lions (Zalophus wollebaeki)

(2025), 10 (1), art. no. 14

DOI: 10.1186/s40850-025-00235-1

ABSTRACT: Background: Leptospira are endemic and cause disease among California sea lions (Zalophus californianus), but the epidemiology of Leptospira in Galapagos sea lions (Z. wollebaeki) is almost completely unknown. Understanding the presence and circulation of this zoonotic pathogen is essential not only for the conservation of Galapagos sea lions, but also for assessing potential health risks to humans and other animals within the Galapagos archipelago. This study fills knowledge gaps by investigating Leptospira in this endemic host species to provide valuable insights into the dynamics of the pathogen in an isolated island ecosystem that is completely different from others in which Leptospira have been documented. Results: In 2016, serological analyses detected 24 positive samples in the "El Malecón" rookery (n = 43) and 18 positive samples in the "Punta Pitt" rookery (n = 33), confirming exposure to pathogenic Leptospira species. In 2017, we identified 15 (n = 29) and 13 (n = 30) positive samples, respectively. Molecular analyses further detected leptospiral DNA in 70.8% (n = 24) of sand with urine samples and 45.8% (n = 24) of kidney samples. Amplicon sequencing of the secY gene fragment yielded 10 consensus sequences, confirming the circulation of Leptospira interrogans among Galapagos sea lions. Conclusions: Our findings confirm that Galapagos sea lions are exposed to pathogenic Leptospira species and, for the first time, identify L. interrogans as the circulating species over two consecutive years. By expanding sampling across multiple rookeries, we provide a clearer picture of pathogen exposure in this endemic population. These results improve our understanding of Leptospira dynamics in marine mammals on remote islands, where management efforts aim to reduce disease risks from human activity, livestock, and synanthropic species.

LANGUAGE OF ORIGINAL DOCUMENT: English

S., Aguillon, Samantha, M., Turpin, Magali, G., Le Minter, Gildas, C., Lebarbenchon, Camille, A.O.G., Hoarau, Axel O.G., C., Toty, Céline, A., Duchet, Avril, L., Joffrin, Leá, R.V., Ramanantsalama, Riana V., P., Tortosa, Pablo Role of individual and population heterogeneity in shaping dynamics of multi-pathogen shedding in an island endemic bat

(2025), 21 (7 July), art. no. e1013334

DOI: 10.1371/journal.ppat.1013334

ABSTRACT: Understanding processes driving pathogen transmission in bats is critical to prevent spillovers and emergence events. Although substantial research has addressed this topic, few studies have directly examined shedding dynamics (as opposed to serological studies) and co-infection patterns using fine-scale spatio-temporal datasets. Here, based on the monitoring of 5,714 Reunion free-tailed bats (Mormopterus francoismoutoui) in 17 roosts over 24 months, we studied the co-shedding dynamics of paramyxoviruses (PMV) and Leptospira bacteria (LEPTO) in urine, and herpesviruses (HSV) in saliva. We evidenced all year long shedding with high prevalence of all three infectious agents (37% - 87%), as well as an exceptionally high level of co-shedding (59%), with both positive and negative interactions between infectious agents. Shedding patterns displayed temporal synchrony among roosts, with a peak during summer months, but were not influenced by roost size. Repeated shedding in recaptured bats supports within-host persistence, though underlying mechanisms remain to be identified. Our results also showed rapid HSV infection of juveniles (< 6 months), and suggest longer protection of juveniles by maternal antibodies for PMV and LEPTO. Reproductively-active individuals (both during the pregnancy and mating) were associated with increased PMV and LEPTO shedding, which could result from tradeoffs between reproduction and infection in both sexes, and/or an age-related bias with the progressive infection of older juveniles during reproductive periods. This

study highlights the significance of persistent shedding of multiple pathogens, including bacteria, and their intricate interactions within bat populations. Understanding how human-driven ecological changes may disrupt within-host processes and influence pathogen shedding in bats will help assessing the risk of pathogen spillover from bats to other species, including humans.

LANGUAGE OF ORIGINAL DOCUMENT: English

A.T., Ravindranathan, Anitha Thattamparambil, A., Mukundan, Aiswarya, S.N.T., Puthanpurayil, Sithara Nasar Thottathil, B., Kavuthodi, Bijesh, S., Karunakaran, Sunitha, R., John, Reena

Molecular and genomic characterization of Leptospira isolates in humans and its relation to disease severity (2025), 56, art. no. 100910

DOI: 10.1016/j.ijmmb.2025.100910

ABSTRACT: Objective: The study was conducted with the aim to find out the genomo species and serovars of Leptospira by gene sequencing among blood samples tested positive for Leptospira PCR and to identify the species associated with highest mortality. Methods: All samples with Ct value less than 35 were included in the study. After lipL32 PCR amplification and agarose gel electrophoresis, the amplified products were subjected to gene sequencing. Demographic details and mortality data were obtained from records. Results: 66 out of the 70 samples showed maximum similarity to L.interrogans in sequencing. Other species identified include L.kirschneri and L. noguchi (5 samples). Among those tested positive, 14 patients died. L.interrogans was frequently isolated (13/14)from those who died. The different serovars identified include serovar canicola/hardjo/copenhageni, manilae/bataviaea/lai/icterohaemorrhagiae. Of these, serovars identified in death include Serovar canicola/hardjo/copenhageni/ranaram/manila. Conclusion: Following sequencing, we identified the predominant species as L. interrogans (91 %) with case fatality rate of 19 %. They are found in animal population of our area, pointing the zoonotic potential of Leptospira. This highlights the need for sensitization of those with animal exposure regarding preventive strategies.

LANGUAGE OF ORIGINAL DOCUMENT: English

T., Ganasen, T., S.N.I., Mohd-Azami, Siti Nurul Izzah, J.J., Khoo, Jing Jing, T.L., Peng, T. L., J., Johari, Jefree, N., Sahimin, Norhidayu, Z., Ya'Cob, Zubaidah, S.A., AbuBakar, Sazaly A., S.K., Loong, S. K.

#### Rodent-borne zoonotic diseases in Southeast Asia: a narrative review

(2025), 42 (2), pp. 100 - 122

DOI: 10.47665/tb.42.2.003

ABSTRACT: Rodent-borne zoonotic diseases, including hantavirus pulmonary syndrome, leptospirosis, and rickettsiosis, significantly impact public health. However, there is a limited understanding of these diseases in Southeast Asia, a region emerging as a hotspot for zoonotic diseases. To address this, the authors reviewed the recent developments in prevalent rodent-borne diseases in Southeast Asia from 2000 to 2024. A comprehensive literature search was conducted in databases such as PubMed, Scopus, Web of Science, Google, and Google Scholar, using keywords like "rodent-borne diseases," "prevalence," "epidemiology," "humans," and "Southeast Asia.". Leptospirosis is widespread in several Southeast Asian countries. Malaysia and Thailand have established effective national surveillance systems, tracking annual cases and fatalities. For viral diseases, such as haemorrhagic fever with renal syndrome, most countries lack a structured reporting system. Vector-borne rodent diseases deal with similar underreporting, with diseases like bartonellosis and borreliosis noted only anecdotally, even in relatively-resourced countries like Thailand and Malaysia. This

underreporting is concerning, as the causative pathogens are often detected in rodent reservoirs and their arthropod vectors around these regions during biosurveillance studies. Invasive rodents have long infiltrated into human environments and thrive as successful commensal species, facilitating the transmission of zoonotic pathogens to humans. Therefore, robust surveillance systems, often essential in disease control are urgently needed across the Southeast Asian region. Further scientific research and biosurveillance studies are crucial in understanding the impact of these diseases on human health, rodent populations, and the environment. LANGUAGE OF ORIGINAL DOCUMENT: English

K., Hotta, Koma, T., Maruyama, Takahiro, T., Ito, Takamasa, T., Yonemoto, Takahiro, S., Kasai, Shunsuke, H., Imura, Haruki

Distinguishing Jarisch-Herxheimer reaction from septic shock in leptospirosis patients: a case study (2025), 26, art. no. e947704

DOI: 10.12659/AJCR.947704

ABSTRACT: Objective: Challenging differential diagnosis Background: The Jarisch-Herxheimer reaction is a transient response that occurs within 24 hours of antibiotic treatment for spirochete infections, such as syphilis, leptospirosis, Lyme disease, and relapsing fever, and can present with nausea, fever, chills, rigors, vomiting, hypotension, and skin lesions. This report describes the case of a 51-year-old woman who was working clearing land, with confirmed leptospirosis, who developed transient fever and hypotension following treatment with ceftriaxone (Jarisch-Herxheimer reaction). Case Report: A 51-year-old Japanese woman was admitted with fever and chills for 3 days. Two months prior, she had engaged in land clearance and drinking river water. She reported difficulty moving and joint pain but showed no signs of arthritis or spinal tenderness. Conjunctival injection was observed, and insect bites were absent. Laboratory findings indicated elevated white blood cell count and C-reactive protein level, liver dysfunction, and acute kidney injury. Suspecting leptospirosis and rickettsial infections, ceftriaxone (2 g every 24 hours) was initiated, but 3 hours thereafter, the patient developed chills, fever, and hypotension. Vasopressor administration proved insufficient, necessitating intubation and transfer to the Intensive Care Unit (ICU). Echocardiography findings ruled out cardiogenic shock. Despite a suspicion of septic shock, antibiotics were not escalated owing to a strong clinical suspicion of JHR. The patient's condition improved within 15 hours of antibiotic therapy. Vasopressors were discontinued on hospitalization day 3, and she was extubated. After completing ceftriaxone therapy (7 days), she was discharged on day 9. Conclusions: This report shows the importance of taking a detailed clinical history for patients at risk of exposure to spirochete infections, and highlights the association between antibiotic treatment and the occurrence of transient symptoms that can mimic episodes of parasitemia or sepsis.

LANGUAGE OF ORIGINAL DOCUMENT: English

M.S., Mohd Yusof, M. S., N., Ahmed, N., S.N.I., Bakhir, S. N.I., R.V., Shiva Shanghari, R. V., M., Hashairi Fauzi, M. The prevalence of leptospirosis infections among humans in Malaysia: a systematic review and meta-analysis (2025), 42 (2), pp. 201 - 212

DOI: 10.47665/tb.42.2.013

ABSTRACT: Leptospirosis is an infectious and zoonotic disease caused by pathogenic spirochetes of Leptospira. It affects global health issues, especially endemic in tropical and subtropical regions. This meta-analysis assessed the prevalence of leptospirosis in Malaysia and explored factors contributing to variability studies. A systematic review was conducted, which identified 301 records from six key databases. After

eliminating duplicates and applying the inclusion criteria, 24 studies were selected for qualitative and quantitative analysis. Pooled prevalence and heterogeneity were calculated using a random-effects model. The pooled prevalence of leptospirosis was 26.7% (95% CI: 20.5–34.0%) with high heterogeneity ( $I^2 = 97.43\%$ , p < 0.001). Thus, the reported prevalence decreased from 29.7% (2001–2010) to 18.1% (2011–2020). Additionally, cross-sectional studies reported a 27.4% prevalence, while prospective studies showed a higher rate (53.0%). Diagnostic methods affected the results, with MAT reporting 29.8% and combined PCR-MAT showing the highest prevalence at 31.9%. Leptospirosis remains common in Malaysia, demonstrating the need for better public health interventions, especially in flood-prone areas. Diagnostic techniques and surveillance must be improved and essential for better detecting and managing the disease.

LANGUAGE OF ORIGINAL DOCUMENT: English

C.J., Hernandez, Christopher Justin, G., Gunzel, Greici, C.G., Ritter, Clarice Gabardo, R.C.F., Bugs, Roberto Carlos Freitas, T., Rocha, Thiago, T.L., Fuller, Trevon L., P.M., Brasil, P. Maia, I.R., Dos Santos Varella, Ivana Rosângela, M., da Graça Pimenta Machado, Maria, C.G., Ramos, Carina Guedes

Leptospirosis? An epidemiologic investigation following the historic 2024 floods in Rio Grande do Sul, Brazil (2025) One Health, 21, art. no. 101146

DOI: 10.1016/j.onehlt.2025.101146

ABSTRACT: In May 2024, the Brazilian state of Rio Grande do Sul experienced an historic flood that affected millions of people. Hundreds of thousands of people were displaced by the record-breaking flood waters, exposing them to water-borne pathogens, including leptospirosis. With concern for an outbreak, local efforts focused on identifying and treating any potential cases of leptospirosis. Using data from a local database for people presenting with signs and symptoms compatible with leptospirosis, we conducted a retrospectiveprospective cohort study to estimate the incidence of confirmed cases. Of 539 patients reported to the database, a total of 485 patients were tested for leptospirosis and 303 were tested for Dengue (with 283 testing for both pathogens). We found 17 (3.5 %) confirmed cases of leptospirosis and 102 (33.7 %) confirmed cases of dengue fever. Most tested negative for both, with several confirmed cases of Hantavirus, Influenza A, and HIV. Although there were no significant differences between diagnoses and exposure risk factors, we did find several clinical differences, including headache, respiratory symptoms, diarrhea, acute kidney injury, jaundice, bleeding diathesis, and pulmonary hemorrhage. Leptospirosis was also found to be significantly associated with adverse clinical outcomes when compared to both dengue and the Unrelated/Unknown illness group and more likely to be of the male sex. These data reinforce the need for broader systematic surveillance for pathogens that may circulate in the event of major environmental disasters. Further, stronger diagnostics are urgently needed to distinguish between the causes of largely febrile outbreak in the face of a changing climate. LANGUAGE OF ORIGINAL DOCUMENT: English

A., Ahmad, Aqeel, U., Atta, Usama, A., Akgül, Ali, S., Sattar, Sadia, M.O., Ahmad, Muhammad Ozair

A study on mathematical modeling and control of leptospirosis transmission dynamics during a hurricane with asymptomatic measures

(2025) Modeling Earth Systems and Environment

DOI: 10.1007/s40808-025-02508-7

ABSTRACT:In order to examine the dynamics of disease transmission across human, animal, and environmental compartments, this study creates a unique fractal-fractional leptospirosis model utilizing the

Mittag-Leffler kernel. Important memory effects and hereditary characteristics of illness transmission are included in the model. Lyapunov functions is used to examine global stability and fixed-point theory to prove the existence and uniqueness of solutions. Finding equilibrium points, calculating the basic reproduction number R0, and doing a thorough parameter sensitivity analysis are examples of analytical outcomes. The importance of memory effects in transmission dynamics is shown by numerical simulations that show that reduced fractional order  $\xi$  and transmission rates  $\beta$  considerably impede illness progression. Flip bifurcation analysis is performed and it has been verified that model behaviour is bounded and flip bifurcation does not exist. According to our findings, R0 may be successfully decreased by strategically reducing contact rates  $\psi, \rho$  and environmental contamination  $k\theta$ , as well as by improving recovery rates  $k\theta, k\theta$  and sanitation measures  $k\theta$ . The visual confirmation of endemic equilibrium stability and compartmental interactions is provided by the 3D phase space analysis. This fractal-fractional architecture gives a strong mathematical basis for creating focused leptospirosis control techniques, as well as improved forecasting power.

E.A., Wikurendra, Edza Aria, J.U., Rangga, Josfirin Uding, A.Y.P., Asih, Akas Yekti Pulih, T.S., Sinulingga, Teguh Suranta

### Polymerase chain reaction-driven detection of Leptospira spp. in urban rat populations of Surabaya, Indonesia

(2025), 8, art. no. 100074

DOI: 10.1016/j.ijidoh.2025.100074

ABSTRACT: Objectives: Leptospirosis is a zoonotic disease caused by Leptospira spp., with rodents as the main reservoir. This study aims to detect Leptospira spp. in the urban rat population in Surabaya using the polymerase chain reaction (PCR) method and analyze its phylogenetic relationship. Methods: This laboratory-based surveillance study used a molecular approach to detect Leptospira spp. in the urban rat population from Genteng Village, Surabaya using PCR for detection and subsequent phylogenetic analysis of the positive isolates based on the partial lipL32 gene sequence. A total of 30 rat traps were set up, and 26 rats were successfully captured. Results: The PCR results showed that 22 of 25 Rattus norvegicus (88 %) were positive for Leptospira spp., whereas the single Rattus tanezumi and three other Rattus norvegicus were negative. With a prevalence rate of 84.6 %, these findings indicate a high risk of leptospirosis transmission in Surabaya. Phylogenetic analysis revealed that Leptospira DNA from Rattus norvegicus are closely related to Leptospira interrogans, a species known to be pathogenic to humans. Conclusions: These results strengthen the evidence that Rattus norvegicus plays a major role as a vector in the spread of leptospirosis in urban environments. Therefore, mitigation efforts, such as rodent population control, improved environmental hygiene, and community education, are needed to reduce the risk of leptospirosis infection.

LANGUAGE OF ORIGINAL DOCUMENT: English

A.I., Siddique, Aktarul Islam, B., Borkakoty, Biswajyoti, N.K., Bali, Nargis K., N., Sarmah, Neelanjana, M., Dutta, Mousumi, A., Jakharia, Aniruddha, null, I., Pal-Bhowmick, Ipsita, N., Kalimuthusamy, Natarajaseenivasan

Outbreak of leptospirosis caused by Leptospira wolffii with HAV coinfections in lower Assam, Northeast India in 2024: Clinical impact and public health implications

(2025) Indian Journal of Medical Microbiology, 57, art. no. 100923

DOI: 10.1016/j.ijmmb.2025.100923

ABSTRACT: Background: In February-March 2024, an outbreak of unknown fever and jaundice with multiple fatalities was reported in Goalpara District, Assam, India. This study aimed to identify the etiological agents responsible for the outbreak to guide public health interventions. Methods: Clinical samples from 30 individuals were collected and analyzed using serological and molecular techniques. Serological testing for Hepatitis A Virus (HAV), Hepatitis E Virus (HEV), and Leptospira was performed using IgM ELISA kits. Leptospira DNA was extracted and amplified using PCR targeting the 16S rRNA gene, followed by next-generation sequencing (NGS) for further analysis. Results: The results revealed HAV IgM antibodies in 23.33 % of cases (7/30), while 40 % (12/30) tested positive for Leptospira-specific IgM by ELISA. Additionally, PCR targeting the 16S rRNA gene confirmed Leptospira DNA in 53.33 % of the urine samples (8/15). Notably, 16.67 % (5/30) of cases exhibited coinfection with both HAV and Leptospira spp., challenging the clinical outcome. Sequencing and phylogenetic analysis of PCR-positive samples identified Leptospira wolffii (L. wolffii) as the causative agent, marking the first report of L. wolffii in human clinical samples from Northeastern India. Recently, L. wolffii, a member of the P2 subclade of Leptospira, has garnered attention due to its pathogenic potential. Conclusion: The findings along with reported fatalities, emphasize the pathogenic potential of L. wolffii and its likely introduction into the region, via cross-border transmission from neighboring Bangladesh, where the strain is prevalent. This study highlights the need for enhanced surveillance and research to monitor emerging Leptospira strains, particularly L. wolffii, in both human and animal populations, to better understand its epidemiology, pathogenicity, and public health implications.

LANGUAGE OF ORIGINAL DOCUMENT: English

D.B., Chagas, Domitila Brzoskowski, F.D., Santos, F. D.S., N.R., de Oliveira, Natasha Rodrigues, E.G., Noble, Eugenia Gutiérrez, M.A.C., Maia, Mara Andrade Colares, A.C.P., Seixas Neto, Amilton Clair Pinto, null, L., Yim, Lucía, M.J., Moreno, María Jesús, J.A., Chabalgoity, Jose A.

### Attenuated Salmonella Typhimurium expressing chimeric antigen from Leptospira as a recombinant vaccine candidate against leptospirosis

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ABSTRACT: Leptospirosis is a significant zoonotic disease caused by pathogenic spirochetes of the genus Leptospira. Attenuated Salmonella strains represent a promising vector for the development of safe and effective vaccines capable of eliciting a specific immune response. A chimeric Leptospira antigen (rQ1), previously described and based on the gene sequences of lipL32, lemA, and ligAni, was cloned into the pTECH2 vector for antigen expression in Salmonella Typhimurium LVR01. Hamsters were vaccinated orally (OR) and intramuscularly (IM) with 2 x 10^7 CFU of S. Typhimurium LVR01 carrying pTECH2/rQ1, pTECH2 alone, or PBS as a control. Vaccinations were administered twice, with a 14-day interval. Following OR and IM administration, serum samples were collected, and IgG antibodies against rQ1 were measured using indirect ELISA. The results showed that after the second immunization, IgG antibody levels in hamsters immunized IM with pTECH2/rQ1 were significantly higher (P < 0.0001) than in the control groups (PBS and pTECH2). Isotype analyses revealed significant levels of IgG2 (P < 0.05) in the group vaccinated IM with pTECH2/rQ1. However, the attenuated S. Typhimurium vaccine did not confer protective efficacy against homologous challenge in the hamsters immunized with pTECH2/rQ1. Further studies are necessary to explore this novel recombinant attenuated S. Typhimurium LVR01 vaccine and to further characterize the immune mechanisms involved.

LANGUAGE OF ORIGINAL DOCUMENT: English

T., Noel, Teola, R.B., Suepaul, Rod B., A.A., Adesiyun, Abiodun Adewale

Vaccination-challenge trials in beagle dogs using whole-cell Leptospira interrogans serovar Copenhageni vaccine: prevention of clinical leptospirosis, serological, leptospiremia, leptospiruria, cytokines, hematological, and pathological changes

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DOI: 10.3390/pathogens14070611

ABSTRACT: A killed, whole-cell vaccine was produced to induce immunity in dogs against leptospirosis. The vaccine, containing serovar Copenhageni, was produced and administered to 12 beagle dogs at both 8 and 12 weeks of age. Ten unvaccinated dogs of the same age group served as the control group. A live, virulent inoculum of Leptospira (1.52 × 109–4.40 × 109 leptospires per dog) was used to challenge the dogs at 2 weeks (Study 1) and 14 months (Study 2) post-booster vaccination. At regular intervals, pre- and post-challenge (PC), the microscopic agglutination test (MAT) was performed to measure antibody titers. Leptospiremia and leptospiruria were determined via culture, and the cytokine, biochemical, and pathological profiles of vaccinates and controls were also assessed. A high antibody response was measurable after booster administration. In Study 1 (onset of immunity), acute leptospirosis was observed in five (100%) out of five unvaccinated dogs. In contrast, no acute clinical leptospirosis developed in vaccinated dogs, except in one (20%) dog with mild clinical signs. In Study 2 (duration of immunity), mild clinical signs were observed in two (40%) of the control dogs, while all vaccinated dogs remained clinically normal. The incidence of leptospiruria and leptospiremia PC was lower in the vaccinated dogs compared to the unvaccinated group. Severe thrombocytopenia occurred in 100% (5/5) of the unvaccinated dogs in Study 1 that exhibited acute severe leptospirosis, whereas 80% (4/5) of the unvaccinated dogs in Study 2 showed mild to moderate thrombocytopenia 3 days after challenge. Four out of five unvaccinated dogs (80%) in Study 1 exhibited icteric tissues and hemorrhages in the lungs and mucosal surfaces of the stomach and intestines. A high IL-10 to TNF-α ratio, observed in the control group of both studies, and severe thrombocytopenia observed in the control group of Study 1, indicative of acute leptospiral disease, were detected. The vaccine prevented acute clinical leptospirosis and reduced the renal carrier state in beagle dogs, and further investigation is required using a larger sample size.

H., Stratton, Hayley, P., Rosengren, Patrick, T.L., Kinneally, Toni L., L., Prideaux, Laura, S., Smith, Simon, J.P., Hanson, Josh P.

### Presentation and clinical course of leptospirosis in a referral hospital in Far North Queensland, Tropical Australia

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ABSTRACT: The case-fatality rate of severe leptospirosis can exceed 50%. This retrospective cohort study examined 111 individuals with laboratory-confirmed leptospirosis admitted to Cairns Hospital, a referral hospital in tropical Australia, between January 2015 and June 2024. We examined the patients' demographic, clinical, laboratory and imaging findings at presentation and then correlated them with the patients' subsequent clinical course. Severe disease was defined as the presence of pulmonary haemorrhage or a requirement for intensive care unit (ICU) admission. The patients' median (interquartile range) age was 38 (24–55) years; 85/111 (77%) were transferred from another health facility. Only 13/111 (12%) had any comorbidities. There were 63/111 (57%) with severe disease, including 56/111 (50%) requiring ICU admission. Overall, 56/111

(50%) required vasopressor support, 18/111 (16%) needed renal replacement therapy, 14/111 (13%) required mechanical ventilation and 2/111 (2%) needed extracorporeal membrane oxygenation. Older age—but not comorbidity—was associated with the presence of severe disease. Hypotension, respiratory involvement, renal involvement and myocardial injury—but not liver involvement—frequently heralded a requirement for ICU care. Every patient in the cohort survived to hospital discharge. Leptospirosis can cause multi-organ failure in otherwise well young people in tropical Australia; however, patient outcomes are usually excellent in the country's well-resourced health system.

M.L., Mohd Napi, Muhammad Luqman, S.M., Mohamed Sultan, Suhana Mohamed, M.M., Abdullah, Mundzir M., H., Jamaluddin, Haryati, A.F., Ahmad Noorden, Ahmad Fakhrurrazi, M.L.P., Tan, Michael Loong Peng, M.K., Ahmad, M. K.

### Toward a molecular detection: statistical optimization on the preparation of 1-dimensional zno arrays as resistive based biosensors for Leptospira detection

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DOI: 10.1149/1945-7111/aded3a

ABSTRACT: In this study, one-dimensional zinc oxide (1-D ZnO) arrays with a nanostructure density of 84.9% and a diameter size of 150.04 nm were hydrothermally produced and optimized via the Box-Behnken design. The influence of precursor concentration (C), reaction time (t), and hydro-thermal temperature (T) on the growth of 1-D ZnO was investigated using response surface methodology (RSM). The optimized parameters for the synthesis of 1-D ZnO comprised 0.055 M of precursor solution, a reaction time of 5 h, and a hydrothermal temperature of 120 °C, yielding a nanostructure density of 84.9%, as confirmed by energy-dispersive X-ray analysis. Field-effect scanning electron microscopy showed that the average diameter of the optimized sample was 150.04 nm, which was close to the predicted value of 144.70 nm calculated from the statistical model. For DNA sensing, a minimum incubation time of 30 min at 50 °C and a drying time of 40 min were required for the optimal hybridization process. The fabricated resistive biosensors showed a good response toward DNA molecules with a sensitivity calculated of 1.98  $M\Omega$   $\mu$ M-1·cm-2, and a wide linear range from 10 fM to 1  $\mu$ M of target DNA with a detection limit of 10 fM.

LANGUAGE OF ORIGINAL DOCUMENT: English

R., Sarabandi, Roxana, A., Sarani, Ali, M., Rasekh, Mehdi, S., Sadr, Soheil, G.R., Abdollahpour, Gholamreza R., S., Nazemian, Shakiba, M., Khajehmohammadi, Mahdis, H., Borji, Hassan

Serovar typing and risk factors of Leptospira infection in dromedary camels (Camelus dromedarius) of Sistan and Baluchestan, Iran: an exploratory study, with a worldwide update of Leptospira infections in camels (2025), IJID One Health 7, art. no. 100065

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ABSTRACT: Objectives: Leptospirosis is a significant zoonotic disease of camels that poses an economic burden on livestock industries worldwide. Hence, the present study investigated the serovars and risk factors of Leptospira infection in camels in the Sistan and Baluchestan province, Iran, and compared it with the incidence and prevalence of Leptospira infection in camels worldwide. Methods: A total of 150 serum samples were collected from the camel population of Sistan and Baluchestan provinces, southeast of Iran, from the fall and winter of 2022 to the spring of 2023. The samples were then sent to the Leptospira Research Laboratory at the University of Tehran for the microscopic agglutination test. Results were compared against Leptospira

infection seroprevalence and epidemiology from other worldwide studies on Leptospira infection in camels to ascertain the significance of these zoonoses in Iran. Results: According to the results, 2 % of serum samples (3/150) were positive for Leptospira infections, and 4 % (6/150) were suspicious, with <1:100 titers. Moreover, of the three positive samples, two demonstrated reactivity to serovar Pomona, whereas the other positive sample demonstrated reactivity with serovar Icterohaemorrhagiae in the microscopic agglutination test. No significant difference in the prevalence of infection based on sex or age of camels was observed. The worldwide epidemiologic study of Leptospira infection in camels shows that the disease varies significantly in different regions regarding infection rates and pathogens. Conclusions: The results of this study indicate that Leptospira infection continues to be a significant threat to livestock health management in Iran. To control Leptospira infection in camels, there is a need for systematic monitoring and more comprehensive research to identify environmental and management factors that affect its spread.

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H., Su, Hui, K., Xu, Keye, W., Wang, Wuke, Y., Liu, Yuhui, G., Ping, Guohua, D., Bo, Dingyi

### Unveiling Leptospira prevalence and exposure in sanitation workers, a cross-sectional study in Ningbo City, China

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ABSTRACT: Background: The environmental presence of pathogenic Leptospira species poses a substantial threat to human health. Sanitation workers, due to their frequent exposure to contaminated soil or water, are at an increased risk of infection. This study aimed to better understand the risk factor of leptospirosis, pathogen exposure, and carriage among sanitation workers in Ningbo, so to help prevent and manage future outbreaks. Methods: A total of 306 samples were collected, comprising 102 whole blood samples, 102 serum samples, and 102 urine samples from sanitation workers which were categorized into 3 groups. Serum samples were analyzed using ELISA to detect IqM and IqG antibodies, qPCR targeting lipL32 and sec Y were employed on urine and whole blood samples. PCR were performed targeting sec Y followed by sequencing using Sanger method, alignment using DNASTAR MegAlign and MEGA X. Tested positive bio-samples subsequently cultured in EMJH broth supplemented with 5-fluorouracil to facilitate bacterial growth, and examined using a dark-field microscope. Results: The questionnaires results showed long working hours (most frequently reported risk factor 60.78%) and employment in garbage sorting (52.94%) were associated with elevated risk of infection (OR = 1.92 and OR = 1.68; p = 0.004 and p = 0.03, respectively), while use of boots (56.86%), masks (41.18%) and soaps (92.16%) can reduce the risk (OR = 0.33, OR = 0.55 and OR = 0.43; p<0.001, p = 0.03 and p = 0.007, respectively). 59.8% of participants tested positive for IgM. qPCR analysis targeting the sec Y gene revealed a positivity rate of 32.4% in blood samples and 7.8% in urine samples. Notably, the lipL32 gene was not detected in any samples. 42 secY gene amplicons obtained from whole blood samples and 8 from urine samples exhibited high sequence similarity to Leptospira interrogans (L. interrogans) when analyzed using DNASTAR MegAlign, clustering with L. interrogans (GenBank accession number OM456545.1). However, culture results showed negative through 2 months observation. Conclusion: This observation indicates the prevalence of a pathogenic L. interrogans subtype, which lacks the lipL32 gene, among asymptomatic sanitation workers. It is imperative for these workers to possess knowledge about infection risks and preventive measures to mitigate the likelihood of infection.

LANGUAGE OF ORIGINAL DOCUMENT: English