

Review

Not peer-reviewed version

Higher Occurrence of Leptospirosis in Humans and Animals Influenced by Hydro-Climatic Factors – a Review

Cintia Cavilha Juppa , <u>Álvaro Menin</u> , <u>Christina Pettan-Brewer</u> , Lenita Agostinetto , Ana Emilia Siegloch , <u>Bruna Fernanda da Silva</u>*

Posted Date: 24 March 2025

doi: 10.20944/preprints202503.1666.v1

Keywords: leptospirosis; Leptospira; climate changes; One Health



Preprints.org is a free multidisciplinary platform providing preprint service that is dedicated to making early versions of research outputs permanently available and citable. Preprints posted at Preprints.org appear in Web of Science, Crossref, Google Scholar, Scilit, Europe PMC.

Copyright: This open access article is published under a Creative Commons CC BY 4.0 license, which permit the free download, distribution, and reuse, provided that the author and preprint are cited in any reuse.

Disclaimer/Publisher's Note: The statements, opinions, and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions, or products referred to in the content.

Review

Higher Occurrence of Leptospirosis in Humans and Animals Influenced by Hydro-Climatic Factors—A Review

Cintia Cavilha Juppa ¹, Álvaro Menin ², Christina Pettan-Brewer ³, Lenita Agostinetto ¹, Ana Emilia Siegloch ¹ and Bruna Fernanda da Silva ^{1,*}

- Postgraduate Program in Environment and Health, Universidade do Planalto Catarinense, Lages 88509-900, Brazil
- ² Universidade Federal de Santa Catarina, Curitibanos 89520-000, Brazil
- Department of Comparative Medicine, School of Medicine, University of Washington, Seattle 98195, USA
- * Correspondence: brusilvabio@gmail.com

Abstract: Leptospirosis is a neglected zoonosis of global significance, associated with flooding and increased precipitation. This study aimed to identify hydro-climatic factors linked to leptospirosis in humans and animals through an integrative literature review. Searches were conducted in August 2024 in the SciELO, Scopus, and PubMed databases using the descriptors "Leptospirosis OR Leptospira" and "flooding" in Portuguese and English. Articles published in the last 10 years (2014-2024), describing the influence of climatic changes, such as heavy rains, floods, and temperature variations, on leptospirosis occurrence, were included. Review articles, conference abstracts, books, and irrelevant studies were excluded. Out of 240 studies, 55 were selected after screening. Findings show urban flooding, driven by high population density and poor drainage infrastructure, facilitates disease spread, while rural flooding increases bacterial dispersion via domestic and livestock animals, inadequate rodent control, and agricultural land contamination. The diversity of serovars highlights the disease's epidemiological complexity, with animals serving as reservoirs and links between environments and humans. Recommendations include strengthening basic sanitation to reduce exposure, rodent population control, implementing early warning systems to monitor climatic conditions, and adopting the One Health approach to integrate human, animal, plant and environmental health for effective leptospirosis control amid climatic changes.

Keywords: leptospirosis; *Leptospira*; climate changes; One Health

1. Introduction

Leptospira belongs to the order Spirochaetales, family Leptospiraceae, and genus Leptospira. These are spiral-shaped bacteria resembling corkscrews, distinguished from other spirochetes by the presence of terminal hooks in their structure [1,2]. However, all Leptospira species are morphologically similar, making it challenging to differentiate them based solely on physical characteristics [1].

Despite these morphological similarities, *Leptospira* species are divided into pathogenic, saprophytic, and intermediate groups. Pathogenic *Leptospira* have the potential to cause disease in animals and humans, residing in the renal tubules and genital tracts of certain animals (primarily rats) and exhibiting a more complex life cycle. Saprophytic *Leptospira* are free-living, reproducing in the environment, and are found in surface water, tap water, and moist soil [1]. Additionally, there is a third group, intermediate *Leptospira*, which is less documented. These species have low pathogenicity and may cause mild clinical signs in mammals [3].

The classification concept evolved after 1989 into two additional schemes: one based on serology, where the serovar is the basic taxonomic unit, and another based on DNA analysis using

molecular taxonomy to identify species [4,5]. Serological classification, based on the reactivity of surface antigens, led to the identification of serovars, most of which are pathogenic. These serovars are grouped into serogroups, which may exhibit cross-reactivity [4,5]. Serovars were determined using the Microscopic Agglutination Test (MAT) [5,6].

Alongside this classification, a genotypic classification of the *Leptospira* genus was established, leading to the description of additional species [7]. *Leptospira* species (genospecies) are classified based on DNA similarity, and within each species, serology is used to identify surface antigens and classify isolates into serogroups [8]. Currently, over 250 recognized serovars are distributed across 23 serogroups, many of which are associated with clinical diseases [8]. All pathogenic serovars for animals are also pathogenic for humans, with no host-adapted strains identified [7,9].

The primary transmission route of leptospirosis is through contact with water and soil contaminated by the urine of infected animals [10–14]. Infection occurs when the bacteria penetrate tissue barriers, facilitated by wounds, prolonged submersion of intact skin in contaminated water, or mucous membrane exposure [15].

In humans, leptospirosis can present a wide range of symptoms, including fever, headache, chills, muscle or body aches, nausea, vomiting, red eyes, abdominal pain, diarrhea, and skin rashes [16]. The diversity of symptoms often leads to confusion with other diseases, complicating diagnosis. Additionally, some individuals may remain asymptomatic, showing no signs of infection [16]. The incubation period ranges from 2 to 30 days and, in severe cases, the disease can progress to complications such as jaundice, kidney failure, hemorrhage (especially pulmonary), aseptic meningitis, cardiac arrhythmias, pulmonary failure, and hemodynamic collapse [17]. The case fatality rate of leptospirosis ranges from 5% to 15% in severe cases, exceeding 50% in patients with severe pulmonary hemorrhagic syndrome [17].

Animal leptospirosis presents clinical syndromes similar to those observed in humans, with hepatic, renal, and pulmonary involvement as the main manifestations. Common clinical signs include jaundice, hemorrhage, uveitis, uremic syndrome, and reproductive issues such as abortions [18–20]. Animals that survive the acute phase of the disease may become carriers, shedding *Leptospira* in their urine and contaminating the environment [20]. Many *Leptospira* serovars are associated with maintenance host animals, which acquire the infection easily and excrete the bacteria in urine for prolonged periods [8].

Due to its broad spectrum of clinical manifestations and challenges in early diagnosis, leptospirosis is frequently underreported, despite its significant impact on public health, particularly in tropical and subtropical regions [1]. Globally, the disease accounts for approximately 1,03 million cases and 58900 deaths annually, making leptospirosis one of the leading zoonotic causes of morbidity and mortality [21].

Brazil has the highest number of leptospirosis cases in Latin America, with approximately 4000 cases reported annually [11]. The relationship between flooding and leptospirosis incidence is well-documented [11]. During flood events, contaminated water spreads across urban and rural areas, increasing exposure for humans and animals and creating conditions conducive to bacterial proliferation [11]. Furthermore, the bacterium's persistence in moist environments and its ability to survive for extended periods in water or flooded soil make floods one of the primary risk factors for leptospirosis transmission [22,23].

The epidemiologic triad of agent, environment, and host is recognized as a key determinant in the occurrence and spread of leptospirosis and other infectious diseases [24]. Consequently, it encompasses all facets of One Health, a collaborative, multisectoral, and transdisciplinary strategy recognizing the inextricable link between human, animal, plant and environmental health [25]. This strategy aims to enhance understanding and strengthen initiatives to confront the challenges in preventing epidemics and epizootics, while also preserving the integrity of ecosystems, benefiting both humans and the biodiversity that supports them [26]. Considering the growing threat of climate change, particularly the increased frequency and intensity of flooding events, which exacerbate leptospirosis, this integrative literature review aims to identify the influence of climate change -

focusing on floods, precipitation, and temperature - on the occurrence of leptospirosis in humans and animals. Additionally, it seeks to report the diversity of serovars recorded during flood periods. These findings may contribute to the development of effective prevention and control strategies.

2. Materials and Methods

An integrative literature review was conducted through a systematic search for articles that contribute to answering the research question aimed at identifying the influence of climate change, focusing on flooding, precipitation, and temperature, on the occurrence of leptospirosis in humans and animals.

The search for scientific articles was carried out in the PubMed, SciELO, and Scopus databases, in Portuguese and English, in August 2024, using the Health Sciences Descriptors (DeCS/MeSH) "leptospirosis OR *Leptospira*" AND "flooding," identified in the title and/or abstract and/or keywords of the articles, with the same descriptors also being used in Portuguese.

Articles published in Portuguese and English within the last ten years (2014 to 2024), describing the influence of climate change, such as flooding, precipitation, and temperature, on the occurrence of human and animal leptospirosis, were considered. From the articles, the diversity of registered serovars was also identified. Review articles, conference abstracts, and books were excluded, as well as articles that did not meet the inclusion criteria described above. The identified articles were imported into the Rayyan platform, a tool specialized in systematic review screening [27].

After importing the articles, the Rayyan platform was used for detecting and excluding duplicate articles, which were manually reviewed to ensure their removal. Next, two independent reviewers proceeded to read the titles and abstracts of the included articles, classifying them according to the previously established inclusion and exclusion criteria.

In cases of disagreement between the two reviewers, a third researcher was consulted to read the article in question and decide on its inclusion or exclusion. The screening step was conducted blindly on Rayyan to avoid bias among reviewers during the selection process. The information from the articles included in the review was organized into tables highlighting the characteristics of each study.

3. Results

A total of 240 articles were identified in the databases, following the proposed inclusion criteria. After reading the titles and abstracts, 73 duplicate articles and 112 articles that did not meet the inclusion criteria were excluded. Thus, 55 potentially eligible articles were selected and read in full to ensure they met the established criteria. Figure 1 details the process of selecting the studies.

Regarding the type of study, 29 were cross-sectional studies (52.7%), seven ecological studies (12.7%), four epidemiological studies (7.3%), three case studies (5.5%), two case reports (3.6%), two meta-analysis (3.6%), two descriptive studies (3.6%), two experimental studies (3.6%), two mathematical models (3.6%), one cross-over study (1.9%), and one retrospective analytical study (1.9%), as represented in Figure 2.

Table 1 summarizes the databases of the articles with information about the authors, year of publication, country where the study was conducted, the journal in which the article was published, and the main related topic.

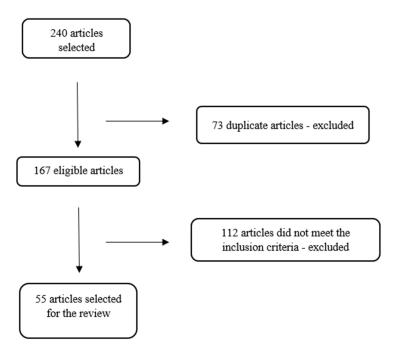


Figure 1. Diagram of the studies selected during the integrative review process.

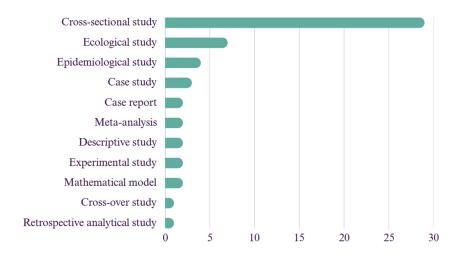


Figure 2. Illustration representing the types of studies included in the review.

Table 1. Data on authorship, database affiliation, country, publication journal, and main topic, presented in chronological order.

	Authors (year)	Databa se	Country of Study	Journal	Leptospirosis X Climate Change X Humans/Animals
1	Wójcik-Fatla et al. [28]	Scopus	Poland	Annals of Agricultural and Environmental Medicine	Occurrence of pathogenic Leptospira in water and soil samples.
2	Wynwood et al. [29]	Scopus	Australia	Tropical Biomedicine	Humans infected with serovar Arborea after flooding.

	A 1: (DI CN 1 (1	D: (1 1 :
3	Agampodi et	Scopus	Sri Lanka	PLoS Neglected	Disease outbreak in
	al. [30]			Tropical Diseases	humans in a dry region.
4	Pimenta et al.	Scielo	Brazil	Pesquisa Veterinária	Serovar prevalence in
	[31]			Brasileira	cattle.
5	Guimarães et al. [32]	Pubme d	Brazil	Ciência & Saúde Coletiva	Positive effect of
					precipitation on
					transmission.
					Environmental and
	Gracie et al.	Pubme d	Brazil	International Journal	socioeconomic factors
6				of Environmental	(densely urbanized areas,
0	[33]			Research and Public	flood-prone regions, and
				Health	altitude) in disease
					transmission.
_	Suwanpakdee	Pubme		Epidemiology and	Influence of flooding on
7	et al. [34]	d	Thailand	Infection	human disease.
					Report of two positive
	Matono et al.	Pubme		Journal of Travel	leptospirosis cases after
8	[35]	d	Japan	Medicine	traveling to a flooded
	[55]			1/10 dienie	area.
		Pubme		PLoS Neglected	Serovars involved and
9	Lau et al. [36]	d	Fiji	Tropical Diseases	environmental factors.
1	Sohail et al.			Journal of Equine	Seroprevalence and risk
0	[37]	Scopus	Pakistan	Veterinary Science	factors in equines.
-	[57]			Southeast Asian	Human seroprevalence
1	Gloriani et al.		Dhilinning	Journal of Tropical	of the disease after
1		Scopus	Philippine	Medicine and Public	floods.
1	[38]		S		nous.
1	A = 4 A = 1 -	Dl		Health	England and desired and the
1	Azócar-Aedo	Pubme	Chile	Zoonoses and Public	Factors associated with
2	& Monti [39]	d		Health	canine leptospirosis.
1	Ledien et al.	Pubme	Cambodia	PloS One	Development of a flood
3	[40]	d			indicator test.
1	Hayati et al.			Asian Journal of	Environmental factors
4	[41]	Scopus	Malaysia	Agriculture and	linked to leptospirosis
	. ,			Biology	risk in humans.
				Indian Journal of	Human seroprevalence
1	Syamsuar et	Scopus	India	Public Health	in flood-prone areas.
5	al. [42]	200740	1110110	Research and	
				Development	
1	liaz et al [42]	Scopus	Pakistan	Acta Tropica	Seroprevalence and risk
6	Ijaz et al. [43]	Scopus	Fakistan	Acia Hopica	factors in cattle.
1	Supe et al. [44]	t al. [44] Pubme	India	The National Medical Journal of India	Use of chemoprophylaxis
7					for leptospirosis in
					humans in flooded areas.
					,

1 8	Chadsuthi et al. [45]	Scopus	Thailand	BMC Infectious Diseases	Environmental factors in leptospirosis transmission in cattle and buffaloes.
1 9	Vitale et al. [46]	Pubme d	Italy	Journal of Infection and Public Health	Report of two symptomatic human leptospirosis cases.
2 0	Matsushita et al. [47]	Pubme d	Philippine s	PLoS Neglected Tropical Diseases	Association of rainfall and disease occurrence in humans.
2	Radi et al. [48]	Pubme d	Malaysia	The American Journal of Tropical Medicine and Hygiene	Environmental factors such as floods and water bodies in disease distribution in humans.
2 2	Mayfield et al. [49]	Pubme d	Fiji	The Lancet Planetary Health	Use of geographically weighted logistic regression for human epidemiology.
2 3	Sohail et al. [50]	Pubme d	Pakistan	Acta Tropica	Seroprevalence and risk factors in humans.
2 4	Togami et al. [51]	Pubme d	Fiji	The American Journal of Tropical Medicine and Hygiene	Occurrence of the disease in humans and factors such as floods.
2 5	Widiyanti et al. [52]	Scopus	Indonesia	Zoonoses and Public Health	Presence of bacteria in the environment, especially during floods.
2	Ding et al. [53]	Scopus	China	Environmental Research	Influence of floods on human cases.
2 7	Sumalapao et al. [54]	Scopus	Philippine s	Asian Pacific Journal of Tropical Medicine	Relationship between typhoons and increased disease occurrence in humans.
2 8	Naing et al. [55]	Pubme d	Australia	PloS One	Significant association between floods and increased risk of human leptospirosis.
2 9	López et al. [56]	Scopus	Argentina	Science of the Total Environment	Hydro-climatic factors in disease occurrence in humans.
3 0	Péres et al. [57]	Scopus	Brazil	Water	Influence of extreme hydrometeorological events and increased human hospitalization

					rates due to leptospirosis
					in Santa Catarina state.
	Goh et al. [58]	Pubme d	Malaysia	International Journal	Rat contact and shared
3				of Environmental	areas as risk factors for
1				Research and Public	shelter dogs and their
				Health	handlers.
3	Hamond et al.	Pubme	Uruguay	Transboundary and	Report of ovine
2	[59]	d	Oruguay	Emerging Diseases	leptospirosis.
3	Blagojevic et	Pubme	Serbia	Acta Veterinaria	Detection of leptospirosis
3	al. [60]	d	Servia	Hungarica	in wild mammals.
					Human epidemiology
3	Chery et al.	6	0	Pan American Journal	and correlation with
4	[61]	Scopus	Saint Lucia	of Public Health	precipitation and
					temperature.
					Detection of
3	Baki et al. [62]	Scopus	Malaysia	Malaysian Journal of	pathogenicity genes in
5		1		Microbiology	environmental samples.
					Identifying human
3		Pubme d	Brazil	Geospatial Health	disease clusters in
6	Silva et al. [63]				municipalities after
0					natural disasters.
					Higher risk of human
3	Gracie et al. [64]	Pubme d	Brazil	Cadernos de Saúde Pública	leptospirosis in
7					municipalities that
,					declared floods.
					Human disease cases
3	Syakbanah & Fuad [65]	Scopus	Java	Jurnal Kesehatan Lingkungan	after a cyclone and
8					-
					flooding. Mathematical model to
3	Chadsuthi et al. [66]		Thailand	Scientific Reports	
					evaluate cases in
9					humans, animals, and
					the environment.
4	Rahman et al. [67]		Malaysia	Journal of Veterinary Research	Disease prevalence in
0					cattle, goats, and sheep
					after flooding.
4	Keenum et al.	l. Pubme Pue	Puerto	Environmental Science	Presence of bacteria in
1	[68]	d	Rico	& Technology	water systems after
_	[]	THEO		a recitiology	flooding.
4	Mgode et al.	Pubme	Tanzania	Pathogens	Disease prevalence in
2	[69]	d		2 dato geno	cattle.
4	Taylor et al.	Pubme	Great	Preventive Veterinary	Disease prevalence in
3	[14]	d	Britain	Medicine	dogs.
4	Yanagihara et	Sconie	Ianan	Microbiology	Presence of <i>Leptospira</i> in
4	al. [70]	Scopus	Japan	Spectrum	the environment.

					Climatic and
4 5	Silva et al. [71]	Scielo	Brazil	Ciência e Saúde Coletiva	environmental factors in
					human leptospirosis
				Colcuva	occurrence.
					Occurrence of human
4	Taunton et al.	Pubme	Australia	Communicable	
6	[72]	d	Australia	Diseases Intelligence	leptospirosis after heavy rains and flooding.
4	Marteli et al. [73]	Pubme d	Brazil	Geospatial Health	Flood-prone areas and
7					human leptospirosis
					cases.
4	Rahman et al.	Scopus	Malaysia	Sains Malaysiana	Presence of <i>Leptospira</i> in
8	[74]				cattle farm soils after
					flooding.
4	Maric et al.		Bosnia and		Seroprevalence of
9	[75]	Scopus	Herzegovi	Acta Veterinaria	leptospirosis in dogs and
	[, 0]		na		foxes after flooding.
5	Jayaramu et al.	Pubme		International Journal	Hydrometeorological
	[76] d		Malaysia	of Biometeorology	risk factors and human
U		u			leptospirosis.
5	I I day an at al	Pubme	ne India	Indian Journal of Community Medicine	Environmental risk
1	Udayar et al.	d			factors associated with
1	[77]	u			human leptospirosis.
_	C 1 II	D. I		Tropical Medicine and Infectious Disease	Risk factors such as
5	Sohn-Hausner	Pubme	Brazil		flooding and serovars in
2	et al. [78]	d			dogs and their owners.
5	Thibeaux et al.	0	New	Science of the Total	Presence of <i>Leptospira</i> in
3	[22]	Scopus	Caledonia	Environment	soil samples after floods.
_	Rodríguez-	D 1			Risk factors for
5	Rodríguez et	Pubme	Malaysia	Zoonoses and Public	leptospirosis occurrence
4	al. [79] d		Health	in humans.	
					Positive relationship
5	Ifejube et al. Pubme [80] d	India	International Journal	between flooding and	
5		d	22.010	of Health Geographics	human cases.
					mamam cases.

The selected studies were conducted primarily on the Asian and American continents (Figure 3).

The articles were published in journals covering various thematic areas, with the most significant representation in Public Health and Epidemiology (27.3%), followed by Agriculture and Veterinary Sciences (20%) and Tropical Medicine and Neglected Diseases (20%) (Figure 4).

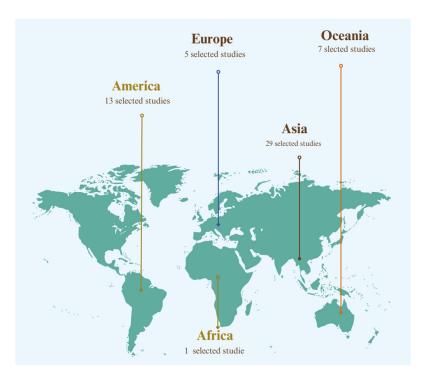


Figure 3. Illustration representing the number of articles selected for review, classified by continent of publication.

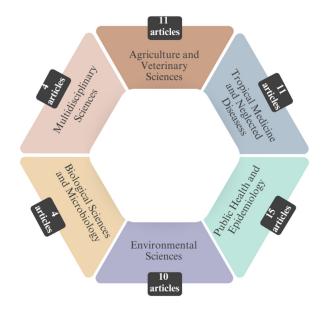


Figure 4. Illustration representing the journals of publication for the articles selected for review, categorized by related areas.

4. Discussion

The studies were conducted in 27 countries, highlighting the global public health impact of the disease, with most research conducted in Asia and America. Additionally, the publications are in journals across various thematic areas, demonstrating the interdisciplinary nature of the studies.

The main topics addressed include the relationship between leptospirosis, flooding, and precipitation, and how climatic events contribute to the spread of the disease. The influence of temperature was also discussed, demonstrating how climatic conditions can increase the incidence

of leptospirosis. Furthermore, the diversity of serovars found shows the epidemiological complexity of the disease in different regions worldwide. Finally, the studies provide important recommendations for controlling leptospirosis, especially in areas with inadequate sanitation and those vulnerable to flooding.

4.1. Leptospirosis, Flooding, and Precipitation

Floods are common natural events and are the leading cause of death in natural disasters worldwide [44]. With the increasing frequency of extreme weather events, such as floods, as a result of climate change, the risk to health is growing [57,61,64,66].

In the case of leptospirosis, the selected studies report a strong correlation with flood events in urban areas [22,29,34,36,39–42,46–48,50–57,63–65,73,77,79–81] and rural areas [31,35,37,43,45,59,60,67,68,75,78]. Only one study did not find a relationship between these factors, and its results suggest that, in the eastern region of Poland, water and soil have limited significance in the persistence and spread of *Leptospira* [28]. However, the authors mention limitations in comparing water reservoirs between areas exposed and not exposed to flooding, as well as a lack of differentiation between *Leptospira* strains.

The occurrence of leptospirosis in urban areas is directly associated with environmental and structural factors, such as poor sanitation, the accumulation of solid waste in inappropriate locations, and the proliferation of rodents [22,29,33,34,36,39–42,46–48,51–57,63–65,73,77–82]. High population density and lack of proper drainage and sewage systems worsen the situation during floods, facilitating the spread of the disease in urban environments [36,41,46]. These combined factors create favorable conditions for increased leptospirosis incidence, especially in vulnerable regions where the impact of floods is more intense and frequent [46].

In rural areas, leptospirosis is related to various environmental and occupational factors. Close contact with domestic and farm animals, which can be hosts for *Leptospira*, increases the risk of transmission [31,59]. Additionally, agricultural activities such as cattle and pig farming expose rural workers to frequent contact with contaminated soil and water through infected animals' urine [42,45]. In periods of heavy rain and floods, the inundation of agricultural areas facilitates the spread of the bacteria, contaminating water bodies and soil [67–69,75]. The lack of effective rodent control, which also acts as a reservoir, and the absence of adequate sanitation in many rural areas contribute to the persistence and spread of leptospirosis in these environments [29]. These factors, combined with favorable climatic conditions and lack of sanitary infrastructure, intensify the risk of disease outbreaks in rural areas.

There is a significant correlation between high rainfall volumes and leptospirosis outbreaks, particularly evident in areas vulnerable to flooding, where water runoff increases contamination in both urban and rural areas. In India, the peak of leptospirosis cases occurred 17 days after floods [80]. In the Philippines, increased hospital admissions were observed 15 days after increased precipitation, also associated with flooding [47]. Additionally, some studies suggest that leptospirosis incidence may increase one to three months after heavy rainfall [32,65].

Another study conducted in Puerto Rico found the presence of *Leptospira* in six public networks of surface water supply six months after a hurricane caused extensive flooding [68]. The hurricane, by causing flooding, promoted the spread of waste and urine from infected animals in water bodies, facilitating contamination of water sources, which highlights the relationship between natural disasters, such as hurricanes and subsequent flooding, and the increased risk of leptospirosis contamination in water supply networks [68].

Although floods are a relevant indicator for predicting future leptospirosis cases, floods of lesser severity do not always result in an increase in cases [80]. On the other hand, a meta-analysis on the epidemiology of canine leptospirosis did not find statistically significant evidence of an association between infection occurrence and flooding in the dog's habitat [39]. In contrast, in horses, the risk of seropositivity triples when animals are exposed to flooding [37], and among humans, exposure to flooding doubles the risk of leptospirosis infection [40,71].

In Brazil, a study found that municipalities that experienced flooding had a leptospirosis incidence rate 77% higher than municipalities that did not report flooding [64]. Studies conducted in various countries link floods to the creation of favorable environmental conditions for the proliferation of the bacteria, particularly through contact with water contaminated by the urine of rodents and other infected animals [31,34,37,48,52,55,58,66,70,77,78].

Living near water bodies is also associated with an increased risk of contracting the disease [36,48]. A study showed that pathogenic *Leptospira* remain dormant in the soil and can become active for infection under flooding conditions, when soil water content increases [70]. In other words, *Leptospira* survive at different depths in soils and surface sediments of rivers (depending on water saturation), being transferred to surface water during erosion caused by flooding [22,36]. One study suggests that pathogenic strains of *Leptospira* are widely distributed in the environment, especially in areas affected by flooding [62].

Precipitation is also a risk factor in the dynamics of leptospirosis and is discussed in several studies that associate heavy rainfall with increased disease spread [32,36,46,47,49,56,63,65,71,72,76]. In the state of Santa Catarina (Brazil), for example, it was reported that each additional day of rain in a given month increases the disease risk by an average of 6% [71]. In northeastern Australia, however, a study suggests that while heavy rainfall likely contributed to increased cases of the disease, the factor was not clearly identified as being associated with a rise in cases in this region [72].

4.2. Influence of Temperature on Leptospirosis Occurrence

Temperature variations also influence leptospirosis cases, particularly in tropical and subtropical climates, with an average 12% increase in risk for every 1°C rise in temperature [71].

An average temperature of 28°C was associated with a higher number of leptospirosis cases in Colombia [79]. In Great Britain, the annual mean temperature was the most significant variable related to the higher incidence of canine leptospirosis, with cases peaking during the autumn season [14]. According to the authors, the likelihood of the disease occurring in dogs was higher at temperatures up to 11°C, although this optimal temperature for canine leptospirosis presence varied depending on the serogroup analyzed.

In Saint Lucia, a Caribbean region, no correlation was found between temperature and disease cases [61]. Meanwhile, in two studies conducted in the state of Santa Catarina, Brazil, leptospirosis showed a seasonal pattern, peaking in summer months, which also coincide with periods of higher rainfall [57].

4.3. Diversity of Serovars Found

The pathogenicity of *Leptospira* depends on the virulence of the infecting serovar and the susceptibility of the host species, with rodents being the main carriers of *Leptospira*, followed by wild carnivores. However, all mammals have the potential to be hosts of the bacterium [9]. For instance, *L. interrogans* is the primary pathogenic species and includes 24 serogroups, such as the Icterohaemorrhagiae serogroup, which encompasses the serovars Icterohaemorrhagiae, Copenhageni, and Lai [82]. In horses, the most recurrent serovar is *L. interrogans* serovar Pomona, while in pigs, leptospirosis is commonly caused by serovars such as *L. interrogans* serovars Icterohaemorrhagiae and Copenhageni, as well as *L. pomona*, *L. canicola*, *L. tarassovi*, *L. bratislava*, and *L. muenchen* [9]. In cattle, *L. borgpetersenii* serovar Hardjo is prevalent [9]. Among dogs, the serovars Canicola and Icterohaemorrhagiae were historically the main causative agents of the disease, but vaccination against these serovars has led to the emergence of others, such as Grippotyphosa and Bratislava [8,20].

In the studies included in this review, it was found that in Australia, the most prevalent serovars in human leptospirosis cases were Australia and Zanoni [29,72], as well as Arborea and Hardjo [29]. In Indonesia, the occurrence of serovars such as Bangkinang, Grippotyphosa, Canicola, Robinsoni, Bataviae, and Mini was reported [42]. In the Philippines, the serovars Patoc, Semaranga, Grippotyphosa, Ratnapura, Copenhageni, and Poi were identified [38]. In Colombia, the most

frequent serogroups were Australis, Sejroe, Pomona, Bataviae, Pyrogenes, and Grippotyphosa [79]. In the relatively dry region of Sri Lanka, most cases during the 2011 outbreak were caused by *L. kirschneri* [30].

In dogs, the most frequent serogroups in Great Britain were Australis, Icterohaemorrhagiae, and Sejroe, the latter being absent from commercial vaccines [14]. In Malaysia, Australis, Icterohaemorrhagiae, Canicola, Bataviae, Hardjo, Lai, Grippotyphosa, Ballum, Hardjobovis, and Javanica were identified [58]. In Brazil, serovars such as Icterohaemorrhagiae, Canicola, Pyrogenes, Copenhageni, and Autumnalis were found, with three dogs testing positive for more than one serovar [78]. This study also showed an association between the presence of seropositive dogs and a higher density of human cases. In a study conducted in Bosnia and Herzegovina, the serovars Australis, Bratislava, Sejroe, and Autumnalis were found in dogs, while the highest seroprevalence in foxes was for the serovars Australis, Sejroe, Bratislava, and Bataviae [75].

In sheep, in Uruguay, the serovar isolated in two lamb herds after flooding was Pomona [59]. In cattle in Malaysia, the most frequent serovars were Pomona, Hardjo, and Hebdomadis [67]. In Paraíba State, Brazil, Hardjo was the most prevalent serovar [31,69], followed by Icterohaemorrhagiae and Australis [69]. Therefore, it is necessary to investigate the epidemiological role of domestic animals as reservoirs of leptospirosis for humans [59]. Genotyping studies suggest, for example, that multiple animal reservoirs were implicated in the leptospirosis outbreak in Western Fiji after flooding [51].

In addition to the pathogenic bacteria identified in the studies, intermediate species have also been reported in the environment. The intermediate *L. licerasiae* was isolated from the environment in Jakarta, Indonesia, and has pathogenic infection potential [52]. In Kelantan, Malaysia, following flooding, *L. wolffii*, another intermediate *Leptospira* species, was identified, which could potentially be transmitted to humans and animals [74].

The *Leptospira* serovars identified decades ago remain the causative agents of leptospirosis in humans [38]. However, the transmission of leptospirosis involves numerous factors, including the impact of climate, whose role is not yet fully understood [32]. The diversity of *Leptospira* serovars identified in humans and animals highlights the epidemiological complexity of leptospirosis and its multifactorial nature, supporting the interdependence of human, animal, plant and environmental health, a core principle of One Health. The wide serological variability suggests the presence of multiple reservoirs and transmission pathways, emphasizing the need for an integrated approach to epidemiological surveillance, control measures, and risk mitigation. Elucidating this role is essential, as it facilitates epidemic risk analysis and supports preventive efforts, which must involve intersectoral cooperation among public health authorities, promoting improvements in urban infrastructure and intensified surveillance [61,64,65].

4.4. Recommendations for Leptospirosis Control

Integrated human and animal health strategies for controlling leptospirosis in flood-prone areas should include rigorous rodent control measures both before and during the recovery period of natural disasters [51]. Prevention involves the use of personal protective equipment, such as gloves and closed footwear [29], as well as draining flooded areas and implementing sanitary controls before introducing animals [31]. A study in India reported the use of doxycycline as chemoprophylaxis in asymptomatic individuals, at variable doses based on flood exposure [28]. However, this evidence remains inconclusive because the intervention was not implemented as a controlled study, potentially leading to biased results. In contrast, rapid diagnosis, treatment, and community awareness programs are recognized methods of disease control [51].

Nevertheless, early antibiotic treatment is recommended for cases with a high suspicion of leptospirosis, even before laboratory confirmation, as it can reduce the severity and duration of the disease [17]. Therefore, leptospirosis should be included in the differential diagnosis of any patient presenting with acute febrile illness or nonspecific symptoms and a history of potential exposure to floodwaters or rodent-infested areas [83].

Given the high risk of contamination following floods, a permanent recommendation should be to avoid recreational activities in freshwater bodies [35]. Furthermore, implementing environmental interventions targeting transmission sources, such as improved waste disposal management (especially in flooded areas) and efficient basic sanitation, is crucial [41].

Definitive diagnosis of leptospirosis relies on bacterial isolation via culture, DNA detection by polymerase chain reaction (PCR), or demonstration of seroconversion in paired acute and convalescent serum samples [15,84]. The microscopic agglutination test (MAT) remains the gold standard for leptospirosis diagnosis, utilizing a panel of live antigens [1,8]. However, MAT's limitation lies in its restricted coverage of recognized serovars, potentially missing unknown serovars in specific regions [81]. Real-time PCR has been employed for early *Leptospira* detection in clinical samples during the acute, leptospiremic phase, which is critical for effective antimicrobial therapy [1]. Despite its utility, a key limitation of PCR-based diagnosis is the current inability to identify the infecting serovar, an important factor for epidemiological and public health purposes [85].

Although the disease's pathogenesis is well-documented, the cellular and molecular mechanisms remain unclear. Currently, leptospirosis research is entering a "molecular era", driven by the sequencing of both virulent and saprophytic *Leptospira* strains conducted by international research groups. This effort aims to identify key bacterial protein virulence factors [2].

Vaccines for animals are licensed worldwide, but their formulations have not significantly changed in recent decades. Vaccine-induced immunity is often restricted to related serovars and is short-lived [18]. In cattle and pigs, pentavalent vaccines typically include *L. hardjo, L. pomona, L. canicola, L. icterohaemorrhagiae*, and *L. grippotyphosa*, with some formulations also containing *L. bratislava* [9]. For dogs, bivalent vaccines (*L. icterohaemorrhagiae* and *L. canicola*) or multivalent vaccines including *L. pomona* and *L. grippotyphosa* are used. However, most dogs show negative antibody titers against all serovars one-year post-vaccination [86].

In humans, a universal leptospirosis vaccine remains unavailable, despite the testing of several recombinant vaccines that have not yet progressed to clinical trials [82]. Similar to animal bacterin vaccines, these approaches are limited by the lack of an effective cross-protective immune response [87].

5. Conclusions

The reviewed articles emphasize the importance of understanding leptospirosis in the context of climatic events, particularly highlighting the impact of floods on the disease's dissemination.

Among the main contributions to controlling leptospirosis in flood-prone areas, the review suggests strengthening basic sanitation measures e rodent control to reduce human and animal exposure to contaminated environments. Additionally, implementing early warning systems could enable the monitoring of critical climatic conditions and the anticipation of outbreaks.

Leptospirosis still faces significant underreporting, largely due to insufficient monitoring, with many cases remaining undiagnosed or not reaching healthcare services for mandatory notification. This reveals weaknesses in the surveillance system, which could operate more effectively. Furthermore, it is essential to promote more robust awareness campaigns among the population during flood periods, emphasizing the importance of preventive measures to avoid contamination and minimize the risk of disease spread.

Vaccination of dogs and production animals, particularly in high-risk regions, is also recommended to reduce the role of these animals as *Leptospira* reservoirs. However, the limited duration and serovar coverage of current animal vaccines, coupled with potential interference with serological testing, restricts their effectiveness in providing broad protection.

Addressing these multifaceted challenges necessitates a One Health approach, fostering more effective strategies for leptospirosis surveillance and control. Ultimately, preventing leptospirosis requires coordinated, interdisciplinary efforts involving physicians, veterinarians, public health specialists, and other stakeholders, particularly in the context of climate change and environmental vulnerabilities.

Author Contributions: Conceptualization, C.C.J., B.F.S. and A.E.S.; methodology, C.C.J., B.F.S. and A.E.S.; software, C.C.J., B.F.S. and A.E.S.; formal analysis, C.C.J. and B.F.S.; writing—original draft preparation, C.C.J., B.F.S. and A.E.S.; writing—review and editing, C.C.J., B.F.S., A.E.S., Á.M., C.P.B. L.A.; funding acquisition, B.F.S. and L.A. This manuscript incorporates content from the dissertation of C.C.J., submitted in partial fulfillment of the requirements for Master's degree. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by Fundação de Amparo à Pesquisa e Inovação do Estado de Santa Catarina (FAPESC) under grant numbers TO2024TR002584 (Universal 21/2024), TO2023TR001418, and TO2023TR001518 (FAPESC nº 15/2023 – Programa de Estruturação Acadêmica para Laboratórios Multiusuários).

Acknowledgments: The authors gratefully acknowledge the research financial support provided by FAPESC. Cintia Cavilha Juppa acknowledges financial support from the Programa Institucional de Bolsas de Pós-Graduação – PIBPG (CNPq N° 69/2022).

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

DNA Deoxyribonucleic acid
PCR Polymerase Chain Reaction
MAT Microscopic Agglutination Test

References

- WHO. World Health Organization. Human leptospirosis: guidance for diagnosis, surveillance and control. https://www.who.int/publications/i/item/human-leptospirosis-guidance-for-diagnosis-surveillance-and-control (accessed on 27 May 2024).
- Duarte, M. I. S..; Duarte Neto, A. N.; Pagliari, C. Doenças infecciosas: visão integrada da patologia, da clínica e dos mecanismos patogênicos; Artmed: Porto Alegre, Brasil, 2024.
- Goarant, C. Leptospirosis: risk factors and management challenges in developing countries. Res Rep Trop Med 2016, 7, 49–62. https://doi.org/10.2147/RRTM.S102543
- Brenner, D. J.; Kaufmann, A. F.; Sulzer, K. R.; Steigerwalt, A. G.; Rogers, F. C.; Weyant, R. S. Further determination of DNA relatedness between serogroups and serovars in the family Leptospiraceae with a proposal for *Leptospira alexanderi* sp. nov. and four new *Leptospira* genomospecies. *Int J Syst Evol Microbiol* 1999, 49, 839–858. https://doi.org/10.1099/00207713-49-2-839
- Marquez, A.; Djelouadji, Z.; Lattard, V.; Kodjo, A. Overview of laboratory methods to diagnose leptospirosis and to identify and to type leptospires. *Int Microbiol* 2017, 20, 184–193. https://doi.org/10.2436/20.1501.01.302
- Guernier, V.; Goarant, C.; Benschop, J.; Lau, C. L. A systematic review of human and animal leptospirosis in the Pacific Islands reveals pathogen and reservoir diversity. *PLoS Negl Trop Dis* 2018, 12, e0006503. https://doi.org/10.1371/journal.pntd.0006503
- 7. Mohammed, H.; Nozha, C.; Hakim, K.; Abdelaziz, F. *Leptospira*: morphology, classification and pathogenesis. *J Bacteriol Parasitol* **2011**, 2. https://doi.org/10.4172/2155-9597.1000120.
- 8. Quinn, P.J.; Markey, B.K.; Leonard, F.C. Microbiologia veterinária essencial, 2nd ed; Artmed, 2019.
- Mcvey, S.; Kenneddy, M.; Chengappa, M.M. Microbiologia veterinária, 3rd ed; Editora Guanabara Koogan Ltd.a, 2017.
- Baharom, M.; Ahmad, N.; Hod, R.; Ja'afar, M. H.; Arsad, F. S.; Tangang, F.; Ismail, R.; Mohamed, N.; Mohd Radi, M. F.; Osman, Y. Environmental and occupational factors associated with leptospirosis: a systematic review. *Heliyon* 2024, 10, e23473. https://doi.org/10.1016/j.heliyon.2023.e23473
- Galan, D. I.; Roess, A. A.; Pereira, S. V. C.; Schneider, M. C. Epidemiology of human leptospirosis in urban and rural areas of Brazil, 2000–2015. PLoS ONE 2021, 16, e0247763. https://doi.org/10.1371/journal.pone.0247763

- 12. Philip, N.; Ahmed, K. Leptospirosis in Malaysia: current status, insights, and future prospects. *J Physiol Anthropol* **2023**, 42, 30. https://doi.org/10.1186/s40101-023-00347-y
- 13. Rehan, S. T.; Ali, E.; Sheikh, A.; Nashwan, A. J. Urban flooding and risk of leptospirosis; Pakistan on the verge of a new disaster: a call for action. *Int J Hyg Environ Health* **2023**, 248, 114081. https://doi.org/10.1016/j.ijheh.2022.114081
- Taylor, C.; Brodbelt, D. C.; Dobson, B.; Catchpole, B.; O'Neill, D. G.; Stevens, K. B. Spatio-temporal distribution and agroecological factors associated with canine leptospirosis in Great Britain. *Prev Vet Med* 2021, 193, 105407. https://doi.org/10.1016/j.prevetmed.2021.105407
- 15. Brazil. Leptospirose. Saúde de A a Z. https://www.gov.br/saude/pt-br/assuntos/saude-de-a-a-z/l/leptospirose (accessed 03 May 2024).
- CDC. Leptospirosis. https://www.cdc.gov/leptospirosis/infection/index.html (accessed 17 May 2024).
- 17. CDC. Leptospirosis Fact Sheet for Clinicians. https://www.cdc.gov/leptospirosis/pdf/fs-leptospirosis-clinicians-eng-508.pdf (accessed 04 October 2024).
- 18. Adler, B.; Klaasen, E. Recent advances in canine leptospirosis: focus on vaccine development. *Vet Med Res Rep* **2015**, 245. https://doi.org/10.2147/VMRR.S59521
- 19. Ellis, W. A. Control of canine leptospirosis in Europe: time for a change? *Vet Rec* **2010**, *167*, 602–605. https://doi.org/10.1136/vr.c4965
- Sykes, J. E.; Hartmann, K.; Lunn, K. F.; Moore, G. E.; Stoddard, R. A.; Goldstein, R. E. 2010 ACVIM Small Animal Consensus Statement on Leptospirosis: diagnosis, epidemiology, treatment, and prevention. *J Vet Intern Med* 2011, 25, 1–13. https://doi.org/10.1111/j.1939-1676.2010.0654.x
- Costa, F.; Hagan, J. E.; Calcagno, J.; Kane, M.; Torgerson, P.; Martinez-Silveira, M. S.; Stein, C.; Abela-Ridder, B.; Ko, A. I. Global morbidity and mortality of leptospirosis: a systematic review. *PLoS Negl Trop Dis* 2015, 9, e0003898. https://doi.org/10.1371/journal.pntd.0003898
- Thibeaux, R.; Genthon, P.; Govan, R.; Selmaoui-Folcher, N.; Tramier, C.; Kainiu, M.; Soupé-Gilbert, M.-E.;
 Wijesuriya, K.; Goarant, C. Rainfall-driven resuspension of pathogenic *Leptospira* in a leptospirosis hotspot.
 Sci Total Environ 2024, 911, 168700. https://doi.org/10.1016/j.scitotenv.2023.168700
- 23. Bierque, E.; Thibeaux, R.; Girault, D.; Soupé-Gilbert, M.-E.; Goarant, C. A systematic review of *Leptospira* in water and soil environments. *PLoS One* **2020**, *15*, e0227055. https://doi.org/10.1371/journal.pone.0227055
- 24. Smith, A. M.; Stull, J. W.; Moore, G. E. Potential drivers for the re-emergence of canine leptospirosis in the United States and Canada. *Tropical Med* **2022**, *7*, 377. https://doi.org/10.3390/tropicalmed7110377
- 25. CDC. One Health. One Health. https://www.cdc.gov/one-health/about/ (accessed 24 May 2024).
- Artaxo, P. Mudanças Climáticas: caminhos para o Brasil: a construção de uma sociedade minimamente sustentável requer esforços da sociedade com colaboração entre a ciência e os formuladores de políticas públicas. Cienc Cult 2022, 74. https://doi.org/10.5935/2317-6660.20220067.
- 27. Ouzzani, M.; Hammady, H.; Fedorowicz, Z.; Elmagarmid, A. Rayyan—a web and mobile app for systematic reviews. *Syst Rev* **2016**, *5*, 210. https://doi.org/10.1186/s13643-016-0384-4
- Wójcik-Fatla, A.; Zając, V.; Wasiński, B.; Sroka, J.; Cisak, E.; Sawczyn, A.; Dutkiewicz, J. Occurrence of Leptospira DNA in water and soil samples collected in Eastern Poland. Ann Agric Environ Med 2014, 21, 730– 732. https://doi.org/10.5604/12321966.1129924
- 29. Wynwood, S.J., C., S. B.; Graham, G.C., B., B. R.; Burns, M.A., W., S. L.; Collet, T.A., M., D. B. The emergence of *Leptospira borgpetersenii* serovar Arborea as the dominant infecting serovar following the summer of natural disasters in Queensland, Australia 2011. *Trop Biomed* 2014, 31, 281–285. https://www.msptm.org/files/281_-_285_Craig_SB.pdf
- Agampodi, S. B.; Dahanayaka, N. J.; Bandaranayaka, A. K.; Perera, M.; Priyankara, S.; Weerawansa, P.;
 Matthias, M. A.; Vinetz, J. M. Regional differences of leptospirosis in Sri Lanka: observations from a flood-associated outbreak in 2011. PLoS Negl Trop Dis 2014, 8, e2626. https://doi.org/10.1371/journal.pntd.0002626
- Pimenta, C. L. R. M.; Castro, V.; Clementino, I. J.; Alves, C. J.; Fernandes, L. G.; Brasil, A. W. L.; Santos, C. S. A. B.; Azevedo, S. S. Leptospirose bovina no estado da Paraíba: prevalência e fatores de risco associados à ocorrência de propriedades positivas. *Pesq Vet Bras* 2014, 34, 332–336. https://doi.org/10.1590/S0100-736X2014000400006

- Guimarães, R. M.; Cruz, O. G.; Parreira, V. G.; Mazoto, M. L.; Vieira, J. D.; Asmus, C. I. R. F. Análise temporal da relação entre leptospirose e ocorrência de inundações por chuvas no município do Rio de Janeiro, Brasil, 2007-2012. Cien Saude Colet 2014, 19, 3683–3692. https://doi.org/10.1590/1413-81232014199.06432014
- 33. Gracie, R.; Barcellos, C.; Magalhães, M.; Souza-Santos, R.; Barrocas, P. Geographical scale effects on the analysis of leptospirosis determinants. *Int J Environ Res Public Health* **2014**, *11*, 10366–10383. https://doi.org/10.3390/ijerph111010366
- Suwanpakdee, S.; Kaewkungwal, J.; White, L. J.; Asensio, N.; Ratanakorn, P.; Singhasivanon, P.; Day, N. P. J.; Pan-Ngum, W. Spatio-temporal patterns of leptospirosis in Thailand: is flooding a risk factor? *Epidemiol Infect* 2015, 143, 2106–2115. https://doi.org/10.1017/S0950268815000205
- Matono, T.; Kutsuna, S.; Koizumi, N.; Fujiya, Y.; Takeshita, N.; Hayakawa, K.; Kanagawa, S.; Kato, Y.;
 Ohmagari, N. Imported flood-related leptospirosis from Palau: awareness of risk factors leads to early treatment. J Travel Med 2015, 22, 422–424. https://doi.org/10.1111/jtm.12241
- 36. Lau, C. L.; Watson, C. H.; Lowry, J. H.; David, M. C.; Craig, S. B.; Wynwood, S. J.; Kama, M.; Nilles, E. J. Human leptospirosis infection in Fiji: an eco-epidemiological approach to identifying risk factors and environmental drivers for transmission. *PLoS Negl Trop Dis* **2016**, *10*, e0004405. https://doi.org/10.1371/journal.pntd.0004405
- 37. Sohail, M. L.; Khan, M. S.; Avais, M.; Zahoor, M. Y.; Ijaz, M.; Ullah, A.; Fatima, Z.; Naseer, O.; Khattak, I.; Ali, S. Seroprevalence of *Leptospira* spp. in horses of distinct climatic regions of Punjab, Pakistan. *J Equine Vet Sci* 2016, 44, 82–89. https://doi.org/10.1016/j.jevs.2016.01.007
- 38. Gloriani, N.G., V., S. Y. A. M. Post-flooding surveillance of leptospirosis after the onslaught of typhoons Nesat, Nalgae and Washi in the Philippines. *Southeast Asian J Trop Med Public Health* **2016**, 47, 774–786.
- Azócar-Aedo, L.; Monti, G. Meta-analyses of factors associated with leptospirosis in domestic dogs.
 Zoonoses Public Health 2016, 63, 328–336. https://doi.org/10.1111/zph.12236
- Ledien, J.; Sorn, S.; Hem, S.; Huy, R.; Buchy, P.; Tarantola, A.; Cappelle, J. Assessing the performance of remotely-sensed flooding indicators and their potential contribution to early warning for leptospirosis in Cambodia. PLoS One 2017, 12, e0181044. https://doi.org/10.1371/journal.pone.0181044
- 41. Hayati, K.S., S. N., S. I.; Salmiah M.S., E. M. A.; Khin T.D. Hot-spot and cluster analysis on legal and illegal dumping sites as the contributors of leptospirosis in a flood hazard area in Pahang, Malaysia. *Asian J Agric Biol* **2018**, 78–82.
- 42. Syamsuar; Daud, A.; Maria, I. L.; Hatta, Muh.; Widyastuti, D. Identification of serovar leptospirosis in flood-prone areas Wajo district. *Indian J Public Health Res Dev* **2018**, *9*, 325. https://doi.org/10.5958/0976-5506.2018.01019.7
- Ijaz, M.; Abbas, S. N.; Farooqi, S. H.; Aqib, A. I.; Anwar, G. A.; Rehman, A.; Ali, M. M.; Mehmood, K.; Khan, A. Sero-epidemiology and hemato-biochemical study of bovine leptospirosis in flood affected zone of Pakistan. *Acta Trop* 2018, 177, 51–57. https://doi.org/10.1016/j.actatropica.2017.09.032
- 44. Supe, A.; Khetarpal, M.; Naik, S.; Keskar, P. Leptospirosis following heavy rains in 2017 in Mumbai: report of large-scale community chemoprophylaxis. *Natl Med J India* **2018**, *31*, 19. https://doi.org/10.4103/0970-258X.243407
- 45. Chadsuthi, S.; Chalvet-Monfray, K.; Wiratsudakul, A.; Suwancharoen, D.; Cappelle, J. A remotely sensed flooding indicator associated with cattle and buffalo leptospirosis cases in Thailand 2011–2013. *BMC Infect Dis* 2018, 18, 602. https://doi.org/10.1186/s12879-018-3537-3
- Vitale, M.; Agnello, S.; Chetta, M.; Amato, B.; Vitale, G.; Bella, C. D.; Vicari, D.; Presti, V. D. M. L. Human leptospirosis cases in Palermo Italy. The role of rodents and climate. *J Infect Public Health* 2018, 11, 209–214. https://doi.org/10.1016/j.jiph.2017.07.024
- 47. Matsushita, N.; Ng, C. F. S.; Kim, Y.; Suzuki, M.; Saito, N.; Ariyoshi, K.; Salva, E. P.; Dimaano, E. M.; Villarama, J. B.; Go, W. S.; Hashizume, M. The non-linear and lagged short-term relationship between rainfall and leptospirosis and the intermediate role of floods in the Philippines. *PLoS Negl Trop Dis* **2018**, 12, e0006331. https://doi.org/10.1371/journal.pntd.0006331

- Radi, M. F.; Hashim, J. H.; Jaafar, M. H.; Hod, R.; Ahmad, N.; Mohammed Nawi, A.; Baloch, G. M.; Ismail, R.; Farakhin Ayub, N. I. Leptospirosis outbreak after the 2014 major flooding event in Kelantan, Malaysia: a spatial-temporal analysis. *Am J Trop Med Hyg* 2018, 98, 1281–1295. https://doi.org/10.4269/ajtmh.16-0922
- Mayfield, H. J.; Lowry, J. H.; Watson, C. H.; Kama, M.; Nilles, E. J.; Lau, C. L. Use of geographically weighted logistic regression to quantify spatial variation in the environmental and sociodemographic drivers of leptospirosis in Fiji: a modelling study. *Lancet Planet Health* 2018, 2, e223–e232. https://doi.org/10.1016/S2542-5196(18)30066-4
- 50. Sohail, M. L.; Khan, M. S.; Ijaz, M.; Naseer, O.; Fatima, Z.; Ahmad, A. S.; Ahmad, W. Seroprevalence and risk factor analysis of human leptospirosis in distinct climatic regions of Pakistan. *Acta Trop* **2018**, *181*, 79–83. https://doi.org/10.1016/j.actatropica.2018.01.021
- Togami, E.; Kama, M.; Goarant, C.; Craig, S. B.; Lau, C.; Ritter, J. M.; Imrie, A.; Ko, A. I.; Nilles, E. J. A Large leptospirosis outbreak following successive severe floods in Fiji, 2012. *Am J Trop Med Hyg* 2018, 99, 849–851. https://doi.org/10.4269/ajtmh.18-0335
- 52. Widiyanti, D.; Djannatun, T.; Astuti, I. I. P.; Maharsi, E. D. Leptospira detection in flood-prone environment of Jakarta, Indonesia. *Zoonoses Public Health* **2019**, *66*, 597–602. https://doi.org/10.1111/zph.12610
- 53. Ding, G.; Li, X.; Li, X.; Zhang, B.; Jiang, B.; Li, D.; Xing, W.; Liu, Q.; Liu, X.; Hou, H. A time-trend ecological study for identifying flood-sensitive infectious diseases in Guangxi, China from 2005 to 2012. *Environ Res* 2019, 176, 108577. https://doi.org/10.1016/j.envres.2019.108577
- Sumalapao, D. P.; Del Rosario, B. M.; Suñga, L. L.; Walthern, C.; Gloriani, N. Frequency of typhoon occurrence accounts for the poisson distribution of human leptospirosis cases across the different geographic regions in the Philippines. *Asian Pac J Trop Med* 2019, 12, 38. https://doi.org/10.4103/1995-7645.250343
- 55. Naing, C.; Reid, S. A.; Aye, S. N.; Htet, N. H.; Ambu, S. Risk factors for human leptospirosis following flooding: a meta-analysis of observational studies. *PLoS One* **2019**, *14*, e0217643. https://doi.org/10.1371/journal.pone.0217643
- López, M. S.; Müller, G. V.; Lovino, M. A.; Gómez, A. A.; Sione, W. F.; Aragonés Pomares, L. Spatiotemporal analysis of leptospirosis incidence and its relationship with hydroclimatic indicators in northeastern Argentina. Sci Total Environ 2019, 694, 133651. https://doi.org/10.1016/j.scitotenv.2019.133651
- 57. Péres, E. W.; Russo, A.; Nunes, B. The association between hydro-meteorological events and leptospirosis hospitalizations in Santa Catarina, Brazil. *Water* **2019**, *11*, 1052. https://doi.org/10.3390/w11051052
- 58. Goh, S. H.; Ismail, R.; Lau, S. F.; Megat Abdul Rani, P. A.; Mohd Mohidin, T. B.; Daud, F.; Bahaman, A. R.; Khairani-Bejo, S.; Radzi, R.; Khor, K. H. Risk factors and prediction of leptospiral seropositivity among dogs and dog handlers in Malaysia. *Int J Environ Res Public Health* **2019**, *16*, 1499. https://doi.org/10.3390/ijerph16091499
- Hamond, C.; Silveira, C. S.; Buroni, F.; Suanes, A.; Nieves, C.; Salaberry, X.; Aráoz, V.; Costa, R. A.; Rivero, R.; Giannitti, F.; Zarantonelli, L. Leptospira interrogans serogroup Pomona serovar Kennewicki infection in two sheep flocks with acute leptospirosis in Uruguay. Transbound Emerg Dis 2019, 66, 1186–1194. https://doi.org/10.1111/tbed.13133
- Blagojević, J.; Šekler, M.; Rajičić, M.; Pejić, B.; Budinski, I.; Jovanović, V. M.; Adnađević, T.; Vidanović, D.; Matović, K.; Vujošević, M. The prevalence of pathogenic forms of *Leptospira* in natural populations of small wild mammals in Serbia. *Acta Vet Hung* 2019, 67, 338–346. https://doi.org/10.1556/004.2019.035
- 61. Chery, G.; Francis, L.; Hunte, S.-A.; Leon, P. Epidemiology of human leptospirosis in Saint Lucia, 2010–2017. *Rev Panam Salud Publica* 2020, 44, 1. https://doi.org/10.26633/RPSP.2020.160
- 62. Baki, N. N. A.; Ali, M. R. M.; Rahman, E. N. S. E. A.; Yusof, N. Y.; Ismail, N.; Chan, Y. Y. Detection and distribution of putative pathogenicity-associated genes among serologically important *Leptospira* strains and post-flood environmental isolates in Malaysia. *Malays J Microbiol* **2020**, *16*, 17-28. https://doi.org/10.21161/mjm.180208
- 63. Silva, A. E. P.; Chiaravalloti Neto, F.; Conceição, G. M. D. S. Leptospirosis and its spatial and temporal relations with natural disasters in six municipalities of Santa Catarina, Brazil, from 2000 to 2016. *Geospat Health* 2020, 15. https://doi.org/10.4081/gh.2020.903

- 64. Gracie, R.; Xavier, D. R.; Medronho, R. Inundações e leptospirose nos municípios brasileiros no período de 2003 a 2013: utilização de técnicas de mineração de dados. *Cad Saude Publica* 2021, 37, e00100119. https://doi.org/10.1590/0102-311x00100119
- 65. Syakbanah, N. L.; Fuad, A. Human leptospirosis outbreak: a year after the 'Cempaka' tropical cyclone. *Jurnal Kesehatan Lingkungan* **2021**, *13*, 211. https://doi.org/10.20473/jkl.v13i4.2021.211-218
- Chadsuthi, S.; Chalvet-Monfray, K.; Wiratsudakul, A.; Modchang, C. The effects of flooding and weather conditions on leptospirosis transmission in Thailand. Sci Rep 2021, 11, 1486. https://doi.org/10.1038/s41598-020-79546-x
- 67. Rahman, M.; Khairani Bejo, S.; Zakaria, Z.; Hassan, L.; Azri Roslan, M. Seroprevalence and distribution of leptospiral serovars in livestock (cattle, goats, and sheep) in flood-prone Kelantan, Malaysia. *J Vet Res* **2020**, 65, 53–58. https://doi.org/10.2478/jvetres-2021-0003
- Keenum, I.; Medina, M. C.; Garner, E.; Pieper, K. J.; Blair, M. F.; Milligan, E.; Pruden, A.; Ramirez-Toro, G.; Rhoads, W. J. Source-to-tap assessment of microbiological water quality in small rural drinking water systems in Puerto Rico six months after hurricane Maria. *Environ Sci Technol* 2021, 55, 3775–3785. https://doi.org/10.1021/acs.est.0c08814
- 69. Mgode, G. F.; Mhamphi, G. G.; Massawe, A. W.; Machang'u, R. S. Leptospira seropositivity in humans, livestock and wild animals in a semi-arid area of Tanzania. *Pathog* **2021**, *10*, 696. https://doi.org/10.3390/pathogens10060696
- Yanagihara, Y.; Villanueva, S. Y. A. M.; Nomura, N.; Ohno, M.; Sekiya, T.; Handabile, C.; Shingai, M.; Higashi, H.; Yoshida, S.; Masuzawa, T.; Gloriani, N. G.; Saito, M.; Kida, H. *Leptospira* is an environmental bacterium that grows in waterlogged soil. *Microbiol Spectr* 2022, 10, e02157-21. https://doi.org/10.1128/spectrum.02157-21
- Silva, A. E. P.; Latorre, M. D. R. D. D. O.; Chiaravalloti Neto, F.; Conceição, G. M. D. S. Tendência temporal da leptospirose e sua associação com variáveis climáticas e ambientais em Santa Catarina, Brasil. *Cien Saude Colet* 2022, 27, 849–860. https://doi.org/10.1590/1413-81232022273.45982020
- 72. Taunton, C.; Hayek, C. E.; Field, E.; Rubenach, S.; Esmonde, J.; Smith, S.; Preston-Thomas, A. Undetected serovars: leptospirosis cases in the Cairns region during the 2021 wet season. *Commun Dis Intell* **2022**, 46. https://doi.org/10.33321/cdi.2022.46.70
- 73. Nardoni Marteli, A.; Guasselli, L. A.; Diament, D.; Wink, G. O.; Vasconcelos, V. V. Spatio-temporal analysis of leptospirosis in Brazil and its relationship with flooding. *Geospat Health* **2022**, 17. https://doi.org/10.4081/gh.2022.1128
- 74. Rahman, M. S.; Bejo, S. K.; Zakaria, Z.; Hassan, L.; Roslan, M. A. Detection of *Leptospira wolffii* in water and soil on livestock farms in Kelantan after a massive flood. *Sains Malays* **2023**, *52*, 1383–1395. https://doi.org/10.17576/jsm-2023-5205-05
- Marić, J. S.; Nedić, D.; Vejnović, B.; Velić, L.; Obrenović, S. Seroprevalence of serovars of pathogenic Leptospira in dogs and red foxes (Vulpes vulpes) from Bosnia and Herzegovina. Acta Vet 2023, 73, 389–404. https://doi.org/10.2478/acve-2023-0029
- Jayaramu, V.; Zulkafli, Z.; De Stercke, S.; Buytaert, W.; Rahmat, F.; Abdul Rahman, R. Z.; Ishak, A. J.; Tahir, W.; Ab Rahman, J.; Mohd Fuzi, N. M. H. Leptospirosis modelling using hydrometeorological indices and random forest machine learning. *Int J Biometeorol* 2023, 67, 423-437. https://doi.org/10.1007/s00484-022-02422-y
- Udayar, S.; Chengalarayappa, N.; Madeshan, A.; Shivanna, M.; Marella, K. Clinico epidemiological study
 of human leptospirosis in Hilly area of South India a population-based case control study. *Indian J Community Med* 2023, 48, 316. https://doi.org/10.4103/ijcm.ijcm_316_22
- Sohn-Hausner, N.; Kmetiuk, L. B.; Biondo, A. W. One Health approach to leptospirosis: human–dog seroprevalence associated to socioeconomic and environmental risk factors in Brazil over a 20-year period (2001–2020). *Tropical Med* 2023, 8, 356. https://doi.org/10.3390/tropicalmed8070356
- Rodríguez-Rodríguez, V.; Castro-Cordero, A.; Calderón-Rangel, A.; Martínez-Ibarra, E.; Yasnot, M.;
 Agudelo-Flórez, P.; Monroy, F. P. Acute human leptospirosis in a caribbean region of Colombia: from classic to emerging risk factors. *Zoonoses Public Health* 2024, 71, 107–119. https://doi.org/10.1111/zph.13089

- Ifejube, O. J.; Kuriakose, S. L.; Anish, T. S.; Van Westen, C.; Blanford, J. I. Analysing the outbreaks of leptospirosis after floods in Kerala, India. *Int J Health Geogr* 2024, 23, 11. https://doi.org/10.1186/s12942-024-00372-9
- 81. Ramos, T. M. V.; Balassiano, I. T.; Silva, T. D. S. M. D.; Nogueira, J. M. D. R. Leptospirose: características da enfermidade em humanos e principais técnicas de diagnóstico laboratorial. *RBAC* **2022**, *53*. https://doi.org/10.21877/2448-3877.202102110
- 82. Bharti, A. R.; Nally, J. E.; Ricaldi, J. N.; Matthias, M. A.; Diaz, M. M.; Lovett, M. A.; Levett, P. N.; Gilman, R. H.; Willig, M. R.; Gotuzzo, E.; Vinetz, J. M. Leptospirosis: a zoonotic disease of global importance. *Lancet Infect Dis* 2003, 3, 757–771. https://doi.org/10.1016/S1473-3099(03)00830-2
- 83. Plank, R.; Dean, D. Overview of the epidemiology, microbiology, and pathogenesis of *Leptospira* spp. in humans. *Microbes Infect* **2000**, 2, 1265–1276. https://doi.org/10.1016/s1286-4579(00)01280-6
- 84. Cerqueira, G. M.; Picardeau, M. A century of *Leptospira* strain typing. *Infect Genet Evol* **2009**, *9*, 760–768. https://doi.org/10.1016/j.meegid.2009.06.009
- 85. Haake, D. A.; Levett, P. N. Leptospirosis in humans. In *Leptospira and leptospirosis*. *Current topics in microbiology and immunology*; Adler, B., Ed.; Springer Berlin Heidelberg: Berlin, Heidelberg, 2015; Volume 387, pp. 65–97. https://doi.org/10.1007/978-3-662-45059-8 5.
- 86. Martin, L. E. R.; Wiggans, K. T.; Jablonski Wennogle, S. A.; Curtis, K.; Chandrashekar, R.; Lappin, M. R. Vaccine-associated *Leptospira* antibodies in client-owned dogs. *J Vet Intern Med* **2014**, 28, 789–792. https://doi.org/10.1111/jvim.12337
- 87. Felix, C. R.; Siedler, B. S.; Barbosa, L. N.; Timm, G. R.; McFadden, J.; McBride, A. J. A. An overview of human leptospirosis vaccine design and future perspectives. *Expert Opin Drug Discov* **2020**, *15*, 179–188. https://doi.org/10.1080/17460441.2020.1694508.

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.