

Leptospirosis in Hawai'i: A Retrospective Study within a Health Care System, 2010-2021

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Abstract

Leptospirosis is a worldwide zoonotic disease with diverse clinical manifestations, ranging from mild flu-like symptoms to a life-threatening illness. It is often misdiagnosed or underreported due to the non-specific and overlapping clinical presentations with other febrile illnesses. Hawai'i has the highest incidence of leptospirosis in the United States, but there is a paucity of data regarding recent incidence and the current leptospirosis trends in Hawai'i. The objective of this study was to determine the epidemiology of patients with leptospirosis at one of the largest health care systems in Hawai'i and to identify risk factors associated with the severe illness. A retrospective study was conducted on patients with clinically suspected or confirmed leptospirosis diagnosis from 2010-2021. Of the 164 patients identified during the timeframe, 81 were outpatients with mild illness and 83 were inpatients exhibiting a more severe infection. Patients with the severe infection had a higher frequency of abnormal laboratory tests, including abnormal electrolytes, kidney and liver function tests. This group was more likely to suffer from acute kidney disease, sepsis, and rhabdomyolysis. More cases of leptospirosis were observed in the drier summer months of Hawai'i, and there were more cases in the areas with heavier rainfall on the island of Kaua'i. Risk factors for severe leptospirosis included being Native Hawaiian/Pacific Islander and elevated body mass index. Further studies on leptospirosis may reveal how patients with the above risk factors may benefit from early detection and treatment, potentially leading to reduced disease severity, and decreased hospitalization length.

Abbreviations

ALT = alanine transaminase
AST = aspartate aminotransferase
BMI = body mass index
CDC = Centers for Disease Control and Prevention
eGFR = estimated glomerular filtration rate
ELISA = enzyme-linked immunosorbent assay
HPH = Hawai'i Pacific Health
IgM = immunoglobulin M
ICU = intensive care unit
MAT = microscopic agglutination test
NHOPi = Native Hawaiian and Other Pacific Islanders

Introduction

Leptospirosis is a zoonotic infection endemic in Hawai'i caused by bacteria in the genus *Leptospira*. Hawai'i has one of the highest reported incidence rates of leptospirosis in the United States, with 11.51 cases per 100 000 population between 2014 and 2020.¹ *Leptospira* organisms colonize the kidney of infected animals including cattle, pigs, and rodents. The urine excreted by infected animals contains live bacteria which contaminate water and soil. Leptospirosis occurs when leptospires invade the human body through mucous membranes or skin abrasions.² Known risk factors for contracting leptospirosis include occupational activities such as farming and recreational activities in freshwater.³ Increase in leptospirosis cases is noted after periods of heavy rainfall likely due to the flushing of the bacteria in contaminated soil into streams, rivers, and fresh water bodies.^{4,5} The clinical presentation of leptospirosis can range from a mild flu-like illness to a life-threatening disease with multi-organ failure.⁶ Clinical diagnosis of this zoonotic illness is challenging due to the non-specific flu-like symptoms that overlap with other febrile illnesses.⁷ Limited information is available on risk factors for severe leptospirosis. Hawai'i specific data are also limited and current leptospirosis trends in Hawai'i may be evolving due to changes in the climate, economy, and population density. The last published epidemiological study utilized data from 1999-2008, while the preceding study covered the period from 1974-1998.^{3,8} This study aims to elucidate the epidemiological profiles of patients with leptospirosis who received care at a large multi-facility health care organization in Hawai'i during 2010-2021 and to identify risk factors associated with the more severe form of the disease.

Methods

This observational study reviewed the records of patients diagnosed with leptospirosis at health care facilities affiliated with Hawai'i Pacific Health (HPH) from January 1, 2010 to December 31, 2021. The following HPH facilities were involved in the diagnosis and care for patients with leptospirosis: 3 hospitals on O'ahu ranging from 126 to 243 beds, 1 hospital on Kaua'i with 72 beds, 15 outpatient clinics on O'ahu, and 5 on Kaua'i. Patients who were evaluated in an outpatient facility or who were hospitalized for less than 24 hours were defined as outpatient. Mild leptospirosis was defined as cases managed in the outpatient setting, whereas severe leptospirosis was defined as cases requiring

hospitalization. Patients were included if they had an inpatient or outpatient visit at an HPH facility during the indicated time period and if they fulfilled clinical diagnosis of leptospirosis. Patients not meeting the criteria of a positive diagnosis or clinical suspicion of leptospirosis at an HPH facility were excluded.

In this study, a clinical diagnosis of leptospirosis refers to signs, symptoms, and medical history consistent with leptospirosis infection, with or without supporting laboratory evidence. Confirmed patients with leptospirosis exhibited clinically compatible symptoms and tested positive or borderline positive in culture or serological tests (eg, positive microscopic agglutination test [MAT] titer > 1:100, borderline positive MAT titer = 1:100, reactive immunoglobulin M [IgM] enzyme-linked immunosorbent assay [ELISA], or indirect hemagglutination assay results). Serological tests were performed at the Hawai'i Department of Health. Patients suspected of leptospirosis demonstrated a clinically compatible illness with documented high-risk sources of exposure within 21 days prior to symptom onset and/or had leptospirosis-associated routine laboratory findings, but no serological evidence. These high-risk outdoor activities included occupational (eg, farming), recreational (eg, freshwater swimming, hunting), and habitational exposure to potentially contaminated freshwater, animals, soil, or mud.

Data were first extracted using International Classification of Diseases Version 10 (ICD-10) diagnosis code A27 for leptospirosis and/or positive test for leptospirosis and then manually reviewed for confirmation. Laboratory blood tests performed within 3 days following the initial visit at an HPH facility were considered. The following variables were extracted from the HPH electronic medical records: demographics, initial vital signs, hospitalization duration, laboratory test results, comorbidities, admission to the intensive care unit (ICU), intubation, dialysis, and use of vasopressor medications during hospitalization. This study was reviewed by the Hawai'i Pacific Health Research Institute and determined to be exempt from Institutional Review Board review.

Statistical analysis

The study population and demographic data were analyzed and described using medians with range, frequencies, and percentages. Chi-square test and Fisher's exact test were used to compare distributions of selected variables. A two-tailed *P*-value of <.05 was considered statistically significant. Multivariable logistic regression was used to evaluate the likelihood of developing severe disease after adjusting for sex, BMI, and race. Patients with missing data for any of the variables being analyzed were excluded from the analysis. All statistical analyses were performed using Stata IC, version 15.1 (StataCorp LLC, College Station, TX). Zip code shapefiles were obtained from the Hawai'i State Geoportal. These shapefiles were imported into Stata and merged with a dataset containing the number of cases per zip code. Heatmaps were then generated in Stata to visualize the ge-

ographic distribution of cases across zip codes, with color gradients representing case counts.

Results

The retrospective analysis identified 164 patients with confirmed or clinically suspected diagnosis of leptospirosis at HPH within the 12-year time frame. Among the study population, 50 patients had a confirmed diagnosis of leptospirosis, and 114 patients were considered clinically suspected cases.

The majority of the patients were White (54%), followed by Native Hawaiian or other Pacific Islander (NHOPI) (23%), Asian (17%), and others comprised of American Indian or Alaska Native, Black or African American, or unknown (6%) (Table 1). There were 85 cases reported in the summer months (May-September) and 79 cases occurred in the winter months (October-April) (Figure 1). By count, 105 cases (64%) resided on Kaua'i and 37 cases (23%) resided on O'ahu (Table 1). Cases were relatively evenly distributed across O'ahu (Figure 2). In contrast, the highest number of cases (*n* = 31) was reported on the windward side of Kaua'i (Figure 3). Potential sources of exposure were documented for 133 (81%) of identified cases. Recreational activities accounted for 102 cases (76%) that comprised mostly freshwater swimming; 21 cases (16%) were linked to occupational exposures mostly related to farming; 6 cases (5%) were connected to habitational exposures to canines and rodents; and 4 cases (3%) were associated with international travel to regions of high leptospirosis (Table 1).

The cases observed were predominately male patients (75%), and the patients' age ranged from 1-85 years with a median of 29 years. The most frequent signs and symptoms charted at the initial visit were fever (76%), headaches (45%), myalgia (39%), vomiting (35%), and chills (32%) (Table 1). The initial visit report included subjective symptoms described by the patient. Of the 164 patients, 35 (21%) were admitted to the ICU, 15 patients (9%) had hypotension and were treated with vasopressors, 10 (6%) had respiratory failure and underwent mechanical ventilation, and 7 (4%) had acute renal failure and were started on hemodialysis. Furthermore, 33 patients (20%) suffered from acute kidney disease, 25 patients (15%) had sepsis, and 8 patients (5%) experienced rhabdomyolysis (Table 1). One death was reported.

Eighty-one patients (49%) were managed as an outpatient with a mild infection and 83 patients (51%) were hospitalized. The median length of stay for the hospitalized group was 4 days, with a range of 2-41 days. There were notable differences between the initial vital signs and laboratory values of outpatient (mild) versus hospitalized (severe) patients with leptospirosis. Compared to the outpatient cases, hospitalized patients had a higher frequency of elevated temperature above 38.3°C (31% vs. 17%, *P*=.044), respiratory rate or tachypnea (35% vs. 5%, *P*<.001), and hypotension (13% vs 0%, *P*=.001). Initial laboratory abnormalities that were more common in hospitalized patients were hyponatremia (46% vs. 29%, *P*=.049), hypocalcemia (49% vs. 7%, *P*<.001), reduced estimated glomerular fil-

Table 1. Demographics, Clinical Manifestations, Hospitalization-Associated Treatments, Case Distributions, Sources of Exposure, and Susceptibility among the 164 Patients with Leptospirosis, Hawai'i Pacific Health, 2010-2021

Characteristics		Patients (N = 164)	
		Median	Range
	Age	29	26
		Frequency	%
Sex	Male	123	75%
	Female	41	25%
Race	White	89	54%
	Asian	28	17%
	NHOPI	37	23%
	Others	10	6%
Symptoms	Fever	124	76%
	Headaches	73	45%
	Myalgia	64	39%
	Vomiting	57	35%
	Chills	52	32%
	Nausea	42	26%
	Diarrhea	37	23%
	Abdominal Pain	31	19%
	Fatigue	30	18%
	Arthralgia	10	6%
	Jaundice	6	4%
	Conjunctivitis	5	3%
Hospitalization n = 83	ICU Admission	35	21%
	Intubation	10	6%
	Dialysis	7	4%
	Pressors	15	9%
Complications	Acute Kidney Disease	33	20%
	Sepsis	25	15%
	Rhabdomyolysis	8	5%
Case Distributions based on Patient's Zip codes	Kaua'i	105	64%
	O'ahu	37	23%
	Maui	3	2%
	Hawai'i	6	4%
	Outside of Hawai'i	13	8%
Sources of Exposure and Susceptibility	Recreational	102	77%
	Occupational	21	16%
	Habitational	6	5%
	International Travel	4	3%

Abbreviations: ICU, intensive care unit; NHOPI, Native Hawaiian and Other Pacific Islanders

tration rate (eGFR) (56% vs. 9%, $P<.001$), hyperbilirubine-
mia (48% vs. 14%, $P<.001$), and elevated liver functions
tests including aspartate aminotransferase (AST) (72% vs.
25%, $P<.001$) and alanine transaminase (ALT) (53% vs. 28%,
 $P=.002$). Patients who were hospitalized were more likely
to be overweight defined as a body mass index (BMI) >25
(55% v 35%, $P=.015$) (Table 2). Logistic regression to evalu-
ate disease severity, controlling for sex, BMI, and race re-

vealed that being female reduced the risk for severe disease
(aOR=0.39, 95%CI=0.017, 0.90), higher BMI increased risk
(aOR=1.07, 95%CI=1.01, 1.14), and being NHOPI increased
risk (aOR=4.91, 95%CI=1.85, 13.0) (Table 3)

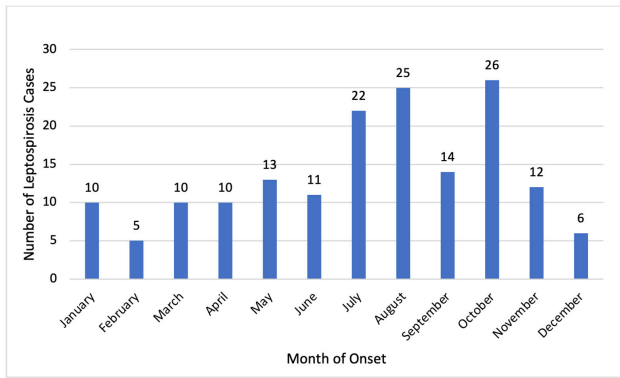


Figure 1. Monthly Distribution of Leptospirosis Cases, Hawai'i Pacific Health, 2010-2021

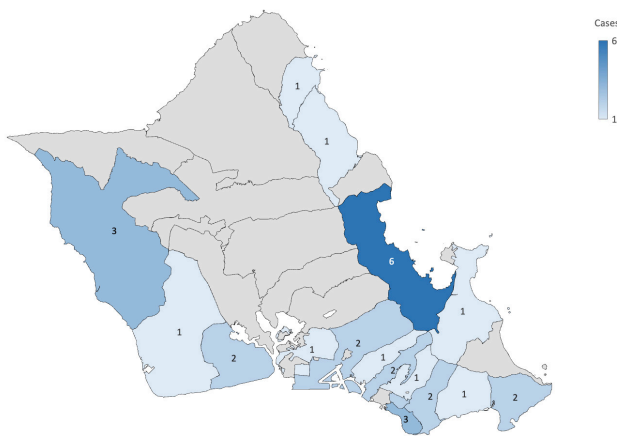


Figure 2. Distribution of Leptospirosis Cases on O'ahu, Hawai'i Pacific Health, 2010-2021

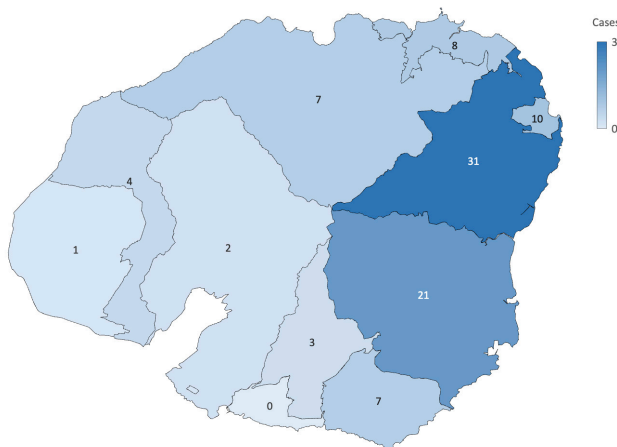


Figure 3. Distribution of Leptospirosis Cases on Kaua'i, Hawai'i Pacific Health, 2010-2021

Discussion

In this study, 164 patients met criteria for confirmed or clinically suspected leptospirosis between 2010 and 2021. For comparison, the Centers for Disease Control and Pre-

vention (CDC) reported 1053 cases of leptospirosis nationwide, including 163 confirmed and probable cases in Hawai'i from 2014 to 2020. Puerto Rico reported the highest number of cases ($n = 573$), followed by Hawai'i ($n = 163$), California ($n = 42$), and New York ($n = 38$).¹ The number of cases identified in this study aligns closely with the burden reported in high-incidence areas such as Hawai'i, despite covering 5 additional years. This similarity may be due to limited access to case reports from the Hawai'i State Department of Health. According to CDC leptospirosis data from 2014 to 2020, the majority of cases occurred among individuals who identified as Hispanic or Latino ($n = 402$) and White ($n = 280$).¹ In contrast, the fewest cases were reported among Asian individuals ($n = 7$) and NHOPI ($n = 2$). This study and CDC surveillance data both demonstrate the predominance of White individuals among cases of leptospirosis. The differences in rates among Asian and NHOPI groups are likely attributed to the high number of cases reported from Puerto Rico.

This study demonstrated that a substantial number of patients with leptospirosis required life-sustaining treatments in the ICU admission. In this study, 21% of patients with leptospirosis received ICU-level care. This represents a higher rate of critical illness compared with the historically reported 5-10% of patients who develop severe, potentially fatal multiorgan dysfunction according to the CDC.⁹ Using CDC surveillance data from 2014 to 2020 ($n = 1053$ cases), Atherstone et al in 2025 reported that among cases with available outcome data ($n = 709$), 85% (606 patients) were hospitalized and the mortality rate was 10%.¹ It is possible that patients with a milder form of the disease in this study are not presenting for care and are recovering without treatment. This would create a distorted picture of disease severity in the overall population by underestimating the mild cases. It is also possible that patients with severe symptoms may have presented at an advanced stage of the disease and therefore resulting in a higher rate of comorbid conditions and complications.

Leptospirosis is a biphasic illness with early symptoms mimicking many other acute febrile illnesses. Failure in early detection and treatment increases the risk of progression to life-threatening disease.¹⁰ Finally, it is possible that higher ICU admission rate is indicative of more virulent serovars in the community. Notably, there was only 1 death associated with leptospirosis in this study which may indicate the overall improvement in general treatment and management of critical illness.

A few interesting risk factors were identified in this study. NHOPI were at a higher risk for severe leptospirosis compared with non-NHOPI groups. Previous studies have reported that NHOPI have higher obesity and chronic health condition rates in comparison to non-Hispanic Whites and Asian Americans.^{11,12} The high prevalence of pre-existing chronic conditions could be the reason why this patient population is more susceptible to severe leptospirosis. It is also possible that this population is not accessing medical care during the early stages of the illness when symptoms are mild and more treatable. It is well-established that NHOPI patients are less likely to access

Table 2. Sex, Race, Abnormal Initial Vitals, and Laboratory Findings between Mild and Severe Leptospirosis Infections, Hawai'i Pacific Health, 2010-2021

		Mild (N = 81)		Severe (N = 83)		P-value
		Frequency	%	Frequency	%	
Sex	Male	62	70%	61	80%	.148
	Female	26	30%	15	20%	
Race	White	52	64%	37	45%	.012
	Asian	15	19%	13	16%	
	NHOPI	12	15%	25	30%	
	Others	2	3%	8	10%	
Abnormal Initial Vitals	Temperature (>38.3°C)	13	17%	25	31%	.044
	Respiratory Rate (>20)	2	5%	28	35%	<.001
	Mean Arterial Pressure (<65 mm Hg)	0	0%	11	13%	.001
	BMI (>25kg/m ²)	23	35%	44	55%	.015
Laboratory Findings	Neutrophilia	23	42%	47	57%	.147
	Lymphocytopenia	23	42%	47	41%	.115
	Anemia	8	15%	38	47%	<.001
	Thrombocytopenia	13	23%	64	78%	<.001
	Hyponatremia	16	29%	38	46%	.049
	Hypocalcemia	4	7%	40	49%	<.001
	Low eGFR	4	9%	30	56%	<.001
	Hyperbilirubinemia	7	14%	39	48%	<.001
	High AST	13	25%	60	72%	<.001
	High ALT	14	28%	44	53%	.002

Abbreviations: ALT, alanine transaminase; AST, aspartate aminotransferase; BMI, body mass index; eGFR, estimated glomerular filtration rate; NHOPI, Native Hawaiian and Other Pacific Islanders

Table 3. Adjusted Odds Ratio of Factors Predictive of Severe Leptospirosis, Hawai'i Pacific Health, 2010-2021

Variables	aOR	[95% CI]
Sex (Female)	0.39	[0.16, 0.90]
BMI	1.07	[1.01, 1.14]
Primary Race		
White	1	Reference
Asian	1.37	[0.52, 3.61]
NHOPI	4.91	[1.85, 13.04]
Other	4.03	[0.69, 23.43]

*Adjusted for sex, BMI, and race

Abbreviations: aOR, adjusted odds ratio; BMI, body mass index; CI, confidence interval; NHOPI, Native Hawaiian and Other Pacific Islanders

care due to cultural and/or socioeconomic barriers.¹⁵ Outreach directed toward NHOPI populations to disseminate leptospirosis information and provide early diagnostic testing could serve to improve outcomes. Elevated BMI was also a risk factor for more severe leptospirosis. Further studies to elaborate on these risk factors may aid in early detection and treatment, minimize leptospirosis severity, and decrease the length of stay and hospitalization costs.

Females were at reduced risk of severe leptospirosis and of leptospirosis in general. Several studies have shown that men are associated with having a higher leptospirosis incidence due to higher outdoor and occupational exposure.^{14, 15} However, occupational exposure in this study only represents a small portion of exposure sources, with recreational activities being predominant.

It is not surprising that inpatients have a more severe form of leptospirosis evidenced by a higher rate of complications and laboratory test abnormalities. Severe leptospirosis is characterized by multi-organ dysfunction that requires intensive life-saving treatments. The results are compatible with other studies detailing the severe infection of leptospirosis. A greater portion of hospitalized patients suffered from tachypnea (35% vs 5%) and hypotension (13% vs 0%) than non-hospitalized patients. Tachypnea is a common sign of respiratory distress in severe leptospirosis, and hypotension could lead to pulmonary complications and renal failure.^{16,17} The high frequency of initial laboratory test abnormalities in hospitalized patients also corroborates with other studies. Thrombocytopenia was frequently reported at the time of hospital admission for severe leptospirosis. A significant increase in total bilirubin and low level of hemoglobin was correlated with thrombocytopenia-associated hospital admission.¹⁸ A modest increase in liver enzymes, AST and ALT, and disproportion-

ately elevated total bilirubin levels were noticed at the time of hospitalization in patients with severe leptospirosis.¹⁹

There are only 2 seasons in Hawaii's climate: warm, dry summer (May-September) and cooler, wet winter (October-April). Rainfall and rainstorms are more prevalent during the winter months.²⁰ Throughout this 12-year period, the cases were about equally distributed between wet and dry seasons with slightly more cases noted in the drier months (85 cases vs 79 cases). Previous studies conducted in tropical regions similar to Hawai'i demonstrated cases of leptospirosis at its peak during the rainy seasons.^{21,22} Based on the results, the highest incidence of leptospirosis cases occurred from midsummer to early winter (July-October). Greater cases in the drier summer months may be attributed to an increase in recreational activities. This differs from the study by Katz et al in 2011 in which most cases occurred during the wetter winter months.³ However, Katz et al in 2002 reported that cases of leptospirosis were more frequent during the summer months in Hawai'i.⁸ Thus, patients and providers should remain vigilant throughout the year as seasonality does not appear to be a major factor in developing leptospirosis in Hawai'i.

In this study, most of the cases occurred in Kaua'i residents as opposed to O'ahu residents. This may be caused by the abundance of animal reservoirs, greater rural areas, popularity of freshwater recreational activities, and copious rainfall on Kaua'i compared to the other Hawaiian Islands.^{23,24} Feral swine, a widespread invasive species, and cattle tend to reside in regions with nearby water sources on Kaua'i.²⁵ The Kaua'i leptospirosis outbreak in 1987 revealed half of the cattle near the outbreak site tested positive for *Leptospira*.²³ Swine, cattle, and other animal reservoirs can contaminate water systems and as a result, leptospirosis would then be transmitted to humans who engage in freshwater recreational activities.

There are a large number of cases in the areas with heavier rainfall on Kaua'i, which differs from the equal case distributions throughout O'ahu. Most cases were reported on the wetter windward side of Kaua'i and O'ahu. Hawaii's changing climate reveals increasing temperature and declining rainfall. The observed number of hot days and warm nights increased substantially during 2015 to 2020. The precipitation rate in the winter season decreased remarkably since 2007.²⁶ Climate change may influence the maintenance host's environment such that it affects the spread of this zoonotic disease.

Limitations

This study was limited by the small sample size inherent to the design of this hospital-based investigation. Past studies analyzed the leptospirosis case investigation reports from the Hawai'i State Department of Health.^{3,8} These reports contained every leptospirosis case that was identified in the state. In this study, only patients from HPH facilities were

included, which limited the detailed analysis of the impact of comorbidities on leptospirosis severity. Since HPH facilities are located solely on the islands of O'ahu and Kaua'i, it is not possible to grasp a full understanding of leptospirosis trends on the other Hawaiian Islands. Given the retrospective nature of this study some values were missing for clinical variables. Furthermore, it is possible that patients with the subclinical or mild form of the disease never sought medical treatment and the illness was unreported. This introduces a selection bias into the study, such that the more severe illness is depicted as opposed to all cases of leptospirosis representative of the population and may have increased the rate of severe forms of illness in this report.

Conclusion

This study identified NHOPI and elevated BMI as risk factors for the severe form of leptospirosis. NHOPI may have a higher risk due to other comorbid conditions or this result may represent delays in presenting for care early, when illness is mild. It is important for patients to seek medical care early on to reduce the potential for life-threatening outcomes especially if they have one of the risk factors for severe disease. Outreach to the NHOPI community regarding leptospirosis could decrease the morbidity of the illness. Furthermore, the seasonal peak of cases has recently shifted towards the late summer and early winter, rather than that of the wetter winter months in the previous 10-year study of 2011.³ Although leptospirosis has been associated with heavy rainfall, this association may be dependent on the exposing activities. In many other countries, farming is the prevailing mode of exposure. In Hawai'i, recreational activities occur year-round due to the state's mild tropical climate and consistently favorable environmental conditions.²⁷ Future studies should analyze the difference in time from the exhibition of symptoms or presumed exposure to the initial health care visit. In addition, investigating a larger statewide and Pacific region dataset would further improve the comprehension of seasonal and geographical influences on leptospirosis and risk factors.

Conflict of Interest

None of the authors identify a conflict of interest.

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