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# Leptospirosis among Returned Travelers: A GeoSentinel Site Survey and Multicenter Analysis—1997–2016

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*Abstract.* Leptospirosis is a potentially fatal emerging zoonosis with worldwide distribution and a broad range of clinical presentations and exposure risks. It typically affects vulnerable populations in (sub)tropical countries but is increasingly reported in travelers as well. Diagnostic methods are cumbersome and require further improvement. Here, we describe leptospirosis among travelers presenting to the GeoSentinel Global Surveillance Network. We performed a descriptive analysis of leptospirosis cases reported in GeoSentinel from January 1997 through December 2016. We included 180 travelers with leptospirosis (mostly male; 74%; mostly tourists; 81%). The most frequent region of infection was Southeast Asia (52%); the most common source countries were Thailand ($N$ = 52), Costa Rica ($N$ = 13), Indonesia, and Laos ($N$ = 11 each). Fifty-nine percent were hospitalized; one fatality was reported. We also distributed a supplemental survey to GeoSentinel sites to assess clinical and diagnostic practices. Of 56 GeoSentinel sites, three-quarters responded to the survey. Leptospirosis was reported to have been most frequently considered in febrile travelers with hepatic and renal abnormalities and a history of freshwater exposure. Serology was the most commonly used diagnostic method, although convalescent samples were reported to have been collected infrequently. Within GeoSentinel, leptospirosis was diagnosed mostly among international tourists and caused serious illness. Clinical suspicion and diagnostic workup among surveyed GeoSentinel clinicians were mainly triggered by a classical presentation and exposure history, possibly resulting in underdiagnosis. Suboptimal usage of available diagnostic methods may have resulted in additional missed, or misdiagnosed, cases.

## INTRODUCTION

Leptospirosis is an emerging zoonotic disease, causing more than a million severe cases worldwide and around 60,000 deaths annually.[1] The disease-causing spirochetes of the *Leptospira* genus[2] display complex transmission patterns.[3] A wide range of infecting serovars exist in a broad range of host animals, most notoriously in rats.[2] Well-known major risk factors are water associated, such as recreational water activities; water exposure following floods and heavy rain; contact with animal or animal urine such as rodents and livestock; and poor sanitation.[3] Less common risk factors include exposure through open skin wounds and soil contact,[3] which might occur while gardening[4,5] or walking barefoot.[3] Moreover, leptospirosis has emerged as an important problem in urban slums in the developing world, where rat-borne transmission increasingly triggers outbreaks.[6–11] Most cases are sporadic; however, outbreaks do occur and may be increasingly frequent because of climate change.[12]

Clinical manifestations can vary from a mild self-limiting infection to life-threatening illness. However, patients seeking

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care typically present with a mild acute febrile illness including chills, headache (often with retro-orbital pain), conjunctival suffusion, photophobia, myalgia, abdominal pain, nausea, vomiting, and sometimes transient exanthema.[2,13] About 10% of patients progress to severe disease, including Weil's disease, characterized by jaundice, acute kidney failure, or (pulmonary) hemorrhage.[2,13–16] Pulmonary hemorrhage can also be a stand-alone manifestation. Aseptic meningitis may be seen in up to 25% of leptospirosis cases.[13] Cardiac involvement is likely more common than recognized.[13] The list of differential diagnoses for the evaluating clinician to consider is long, encompassing, among others, malaria, arboviral infections, rickettsial diseases, and typhoid fever,[13,17] and misdiagnosis is common.[6,18–20] Early recognition and treatment may be essential to improve patient outcomes[13,21,22] and minimize hospitalization costs.

Establishing an early, rapid, and accurate diagnosis remains a complex matter. Widely used serological tests that detect antibodies, including the microscopic agglutination test (MAT, the current reference test) and immunoglobulin M enzyme-linked immunosorbent assay (IgM ELISA), are not suitable for early diagnosis as antibodies only appear in the blood about 5–10 days after the onset of symptoms.[2] Leptospirae can be cultured from blood in the early stages of disease, but this process can take weeks or months.[2,17] Molecular detection tests, such as polymerase chain reaction (PCR), are increasingly used for routine diagnosis of the disease in the first week of illness[23–25] but are not yet available in all countries.[26,27] Commercially available multiplex panels, testing for multiple pathogens, could be a more accessible alternative.[28] For early presentations, PCR is recommended, if possible in combination with culture. For later presentations, MAT and IgM ELISA are suggested. Convalescent samples should be collected, and a combination of the previously described tests is always preferable.[24]

The disease burden of leptospirosis is highest in resource-poor, tropical countries; the highest incidence rates occur in Oceania, Southeast Asia, the Caribbean, and East Africa.[1,29] Notably, international travel to these regions now constitutes a major independent risk factor for acquisition of leptospirosis.[30,31] In 2015, almost 1.2 billion international tourist arrivals were recorded worldwide, with an ever-growing number of travelers visiting tropical and subtropical regions.[32] With travelers being increasingly engaged in high-risk recreational activities, such as white-water rafting,[33] growing numbers of travelers with leptospirosis returning from tropical countries have been reported.[4,31,33–37] In a GeoSentinel analysis (1996–2011) of acute and potentially life-threatening tropical disease among 3,666 ill travelers from higher resource areas, leptospirosis was the fourth most common diagnosis.[38]

Here, we describe the epidemiology of leptospirosis among travelers reported to the GeoSentinel Surveillance Network since its inception more than 20 years ago (January 1997 until December 31, 2016). In addition, we report our analysis of the reported diagnostic approaches used by current GeoSentinel Surveillance Network members, through a supplemental survey among GeoSentinel sites.

## METHODS

**Data source–GeoSentinel surveillance system.** GeoSentinel is a global surveillance network designed to monitor travel-related morbidity. It was established in 1995, with systematic data collection beginning in 1997.[39,40] Currently, 70 GeoSentinel travel and tropical medicine clinics, located in 31 countries on six continents, contribute anonymous clinician-based surveillance information on ill travelers with a focus on infections acquired during travel (see http://www.istm.org/geosentinel for an up-to-date site distribution map and other information). In brief, for inclusion in the GeoSentinel database, patients must have crossed an international border within 10 years of presentation and sought medical care from a GeoSentinel site for a presumed travel-associated condition. Standard data collection forms capture patient demographic characteristics, detailed recent travel itinerary, countries visited within 5 years, reason for recent travel, symptom-based grouping by affected organ system, and whether there was a reported encounter with a health-care provider before travel.[40] Final diagnoses are assigned by the attending clinician and chosen from a list of standard diagnosis codes, guided by GeoSentinel diagnostic definitions. Each patient may have more than one travel-related diagnosis, and each diagnosis is reported as confirmed, probable, or suspected, based on the strength of the diagnosis.[40] All GeoSentinel sites use the best reference diagnostic methods available in their own country. Clinical treatments and outcomes are not routinely reported.

GeoSentinel's data collection protocol is for public health surveillance and has received a determination of non-research by a Centers for Disease Control and Prevention human subjects' advisor.

**GeoSentinel surveillance data inclusion criteria and definitions.** GeoSentinel records for patients with a post-travel diagnosis of "confirmed" leptospirosis and a clinic visit date from January 1, 1997 to December 31, 2016 were included. GeoSentinel-defined criteria for "confirmed" leptospirosis diagnosis state, "a compatible clinical history (e.g., fever with associated symptoms) plus positive microscopy, culture, histopathology, nucleic acid amplification test, antigen detection, or seroconversion with a $\geq 4\times$ titer rise on serology." Furthermore, only patients presenting within 30 days after return from travel were included, based on the incubation period of leptospirosis of 2–30 days (average 7–10 days).[17] Patients seen during travel, missing travel itinerary data, or having a non-ascertainable region of exposure were excluded. The reason for travel was stratified into four categories: tourism, business, visiting friends and relatives, and others (combining small numbers of foreign aid and missionary workers or military deployment).

**Data source—supplemental GeoSentinel network survey.** A 21-question multiple-choice survey (Supplemental Material 1) aimed to assess clinical and diagnostic practices among the GeoSentinel sites. After piloting among selected sites, the survey was distributed by e-mail between December 2015 and March 2016 to 56 GeoSentinel sites active at the time of the survey, excluding the site of survey origin (Amsterdam). Reminders to complete the survey were sent twice via separate e-mails. Each site was permitted one response. In case of multiple responses, incomplete surveys or the last submitted survey were discarded.

**Data management and analysis.** A descriptive analysis of data from the GeoSentinel surveillance system, including demographics, travel characteristics, and symptoms, was performed. Simple frequency statistics were calculated for categorical variables. Analysis of symptoms only included

data from October 2015 onward, the point where revised methods for collection of symptom data were implemented. Data from before this date are known to be incomplete. Data on the method of diagnosis have been only been captured in GeoSentinel since October 2015; similar data are not available for patients seen before that time. Data were analyzed using Microsoft Excel (2010) and SAS Enterprise Guide v5.1 (SAS Institute, Inc., Cary, NC). The GeoSentinel network survey was distributed in Survey Monkey® (www.surveymonkey.com). Results were directly exported to, and descriptively analyzed in, Microsoft Excel (2010). The vector map was created using an open source vector map (https://commons.wikimedia.org/wiki/Atlas_of_the_world) and further edited using Adobe® Illustrator® CS6 (Adobe Systems Incorporated, San Jose, CA).

Further statistical analyses of GeoSentinel data, which is not population-based, are not appropriate or advised. Such methods are limited by the biases that are introduced by each site and by their distribution, and may be misleading. These data are most appropriately analyzed descriptively, except in specific circumstances, none of which apply here.

## RESULTS

Between January 1, 1997 and December 31, 2016, 227 patients with "confirmed" leptospirosis were entered into GeoSentinel; 180 met the inclusion criteria. Reasons for exclusion were as follows: seen during travel (22), clinic visit date > 30 days after return (14), missing travel itineraries (5), or other incomplete information (6). The first patient was reported in 1999; few were entered during 1999–2007 (< 5 per year), then increased to 7 per year in 2008–2009, rising to 14–29 cases yearly thereafter (Figure 1). During the same period, the number of GeoSentinel sites increased.

Table 1 provides an overview of demographic and travel characteristics. Most of the patients were male and the median age was 32 years (range 14–72 years). The most common reason for travel was tourism (81%). Many of the reported infections were acquired in Southeast Asia (*N* = 93, 52%). Common source countries of infection were Thailand (*N* = 52), Costa Rica (*N* = 13), Indonesia (*N* = 11), and Laos (*N* = 11) (Figure 2). Fifty-nine percent of patients were hospitalized; there was one death. Female patients with leptospirosis were hospitalized less frequently than male patients, and travelers to Southeast Asia were hospitalized slightly more frequently than patients infected in other regions (Table 2). For 22 patients, more than one diagnosis was registered (Supplemental Material 2).

Analysis of symptoms only included data from October 2015 onward. Figure 3 shows signs and symptoms among the 30 travelers with leptospirosis as the only diagnosis. Fever, headache, fatigue, and myalgia were reported frequently.

Data on the method of diagnosis were only available for 44 records. Twenty-two (50%) patients were diagnosed by serology (MAT, IgM ELISA, and/or a rapid test) alone, 12 (27%) by a nucleic acid amplification test (e.g., real-time PCR or loop-mediated isothermal amplification) alone, five by both methods (11%), two by microscopy (5%), one by a nucleic acid amplification test and culture (2%), and two by other methods (not specified).

**Survey results.** Of 56 sites solicited, 42 (75%) completed the survey. Eighty-eight percent of the responding sites were academic institutions; 81% of respondents diagnosed 1–10 travelers with leptospirosis per year in the past 5 years; 19% had not yet diagnosed any. Most sites (88%) were able to obtain leptospirosis diagnostic test results within 2 weeks. Key survey questions and responses, information on availability and usage of diagnostic methods, and key suspicion-raising exposures and clinical symptoms are shown in Table 3. Supplemental Material 1 shows an overview of all questions and responses.

Half of the respondents (52%) considered leptospirosis in "nonspecific febrile illness"; only 7% performed diagnostics for leptospirosis in the majority of those cases. A majority of respondents (66%) reported not testing for leptospirosis without a compelling exposure history, equating to testing of < 10% of travelers with unspecified febrile illness returning

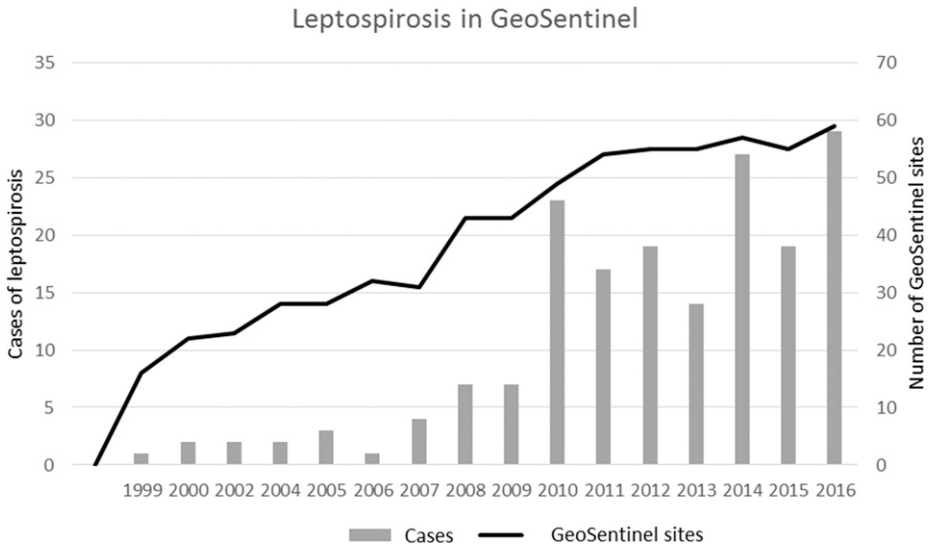


FIGURE 1. Travelers diagnosed with leptospirosis (*N* = 180) and the number of reporting sites in the GeoSentinel Network, January 1, 1999–December 31, 2016. The number of patients with leptospirosis meeting inclusion criteria in the GeoSentinel Network during 1999–2016 (grey columns) and the number of sites reporting to GeoSentinel (black line).

TABLE 1
Demographic and travel characteristics of travelers diagnosed with leptospirosis in the GeoSentinel Network, January 1, 1999–December 31, 2016, $N = 180$*

| Characteristic | Number | % |
|---|---|---|
| Male | 132 | 74% |
| Median age in years (range) | 32 (14–72) | |
| Age groups | | |
| ≤ 17 years | 4 | 2% |
| 18–34 years | 94 | 53% |
| 35–49 years | 46 | 26% |
| 50–64 years | 30 | 17% |
| ≥ 65 years | 3 | 2% |
| Pretravel advice obtained | | |
| Yes | 64 | 37% |
| No | 83 | 47% |
| Unknown | 28 | 16% |
| Travel reason | | |
| Tourism | 145 | 81% |
| Business | 15 | 8% |
| Missionary/volunteer/researcher/aid work | 9 | 5% |
| Visiting friends and relatives | 9 | 5% |
| Military | 1 | 1% |
| Travel duration in days (range)† | 21 (5–165) | |
| Time from return to presentation in days (range) | 9 (1–28) | |
| Hospitalization | 96 | 63% |
| Death | 1 | 0.7% |
| Region of exposure | | |
| Southeast Asia | 93 | 52% |
| Central America | 24 | 13% |
| South America | 15 | 8% |
| Sub-Saharan Africa | 14 | 8% |
| Caribbean | 12 | 7% |
| South Central Asia | 8 | 4% |
| Oceania | 4 | 2% |
| North Africa | 2 | 1% |
| Australia and New Zealand | 1 | 1% |
| Middle east | 1 | 1% |
| Northeast Asia | 1 | 1% |
| North America | 1 | 1% |
| Western Europe | 1 | 1% |
| Not ascertainable | 1 | 1% |

* Not all cells add to 180 because of missing data.
† Among travelers who traveled to only one country ($N = 121$).

from endemic areas. The decision to request diagnostic testing was influenced by suitable exposure histories (76%), exclusion of alternative established causes such as arboviral infections (48%), and certain laboratory abnormalities (60%). Clinical severity was reported to have no influence on testing by 69% of respondents. Most sites (63%) continued to search for a definitive diagnosis (in > 50% of patients), even when the patient was improving after empiric antibiotic therapy. Sixty percent of respondents would prescribe empiric doxycycline after exclusion of key differential diagnoses such as malaria, typhoid fever, and arboviral infections (Supplemental Material 1).

## DISCUSSION

**GeoSentinel surveillance data.** Leptospirosis was an infrequent diagnosis among febrile returning travelers in GeoSentinel, but was identified mostly among those who had traveled for tourism purposes. With increasing popularity of tourism in tropical areas,[32] including active, environmental exposures like rafting, canoeing, and triathlons, the risk of leptospirosis acquisition among travelers may be increasing, as illustrated in previous case reports.[37,41,42] Known high-risk areas, such as Southeast Asia and Central America, were the most common regions of exposure in our database. The top countries where leptospirosis was acquired, Thailand, Costa Rica and Laos, are not necessarily known to be most endemic,[1,43] but rather have higher numbers of travelers who are potentially engaged in freshwater recreational activities. The epidemiology of leptospirosis worldwide[1,43] should be considered when evaluating the ill traveler presenting with fever.

Increased risk of leptospirosis has recently been observed in more temperate regions,[34,44,45] possibly influenced by climate change or different types of risk activities.[12,45] Case series have reported significant proportions of travelers infected within Europe as well.[4,33,35,46] In the Netherlands, 318 imported cases of leptospirosis were diagnosed between 1925 and 2008; 134 (42.1%) were acquired in Asia and 132 (41.5%) in Europe. France is a major tourist destination, with one of the highest reported leptospirosis incidences in Europe.[44] Because travelers returning ill from developed temperate-zone countries may be less likely to visit GeoSentinel clinics, patients with leptospirosis acquired in those regions may be underrepresented here.

An overall increase in patients with leptospirosis reported within the GeoSentinel network was observed over time; however, this was likely associated with an increase in the number of sites reporting in the network in the same period. Alternatively, it is possible that clinicians have become more aware of the illness and that the wider introduction of PCR provided an option for more accurate diagnosis.

Only one fatality was reported to GeoSentinel, despite the potential risk of mortality associated with leptospirosis[1]; however, the GeoSentinel surveillance approach may not capture deaths efficiently.[38]

Most patients in this series were in the 18- to 49-year age group and reported nonspecific symptoms, consistent with other published reports.[33,46,47] Fever was present in almost all patients; neurologic and respiratory symptoms were present in lower proportions than found in other reports[13] but similar to a small case series in travelers.[37] It is also possible that the disease presentation was different in these travelers than is typically seen in leptospirosis in endemic areas. Other possibilities are that leptospirosis was not recognized in patients presenting with those rarer reported symptoms, that they were treated with empiric doxycycline, or that patients with these more severe forms of disease presented elsewhere. A prospective study would be needed to better address these uncertainties.

Most patients were male, although the proportion of female patients (26%) was higher than in some other large case series (reported proportions of < 10%).[33,37,46,47] A higher proportion of the reported hospitalized cases were male compared with female patients, akin to other reports.[33,48] Some possible factors that can contribute to male predominance in leptospirosis include a greater tendency to participate in high-risk outdoor activities, later presentation for medical evaluation, androgenic steroids and other biologic factors,[48,49] or a higher infectious inoculum. The relatively high percentage of female patients in our analysis could signal a shift in behavior of female travelers, increasing their risk of contracting the disease. Female travelers should be considered equally at risk as those who are male with respect to leisure exposure, and leptospirosis should be routinely considered when evaluating the febrile returned female traveler.

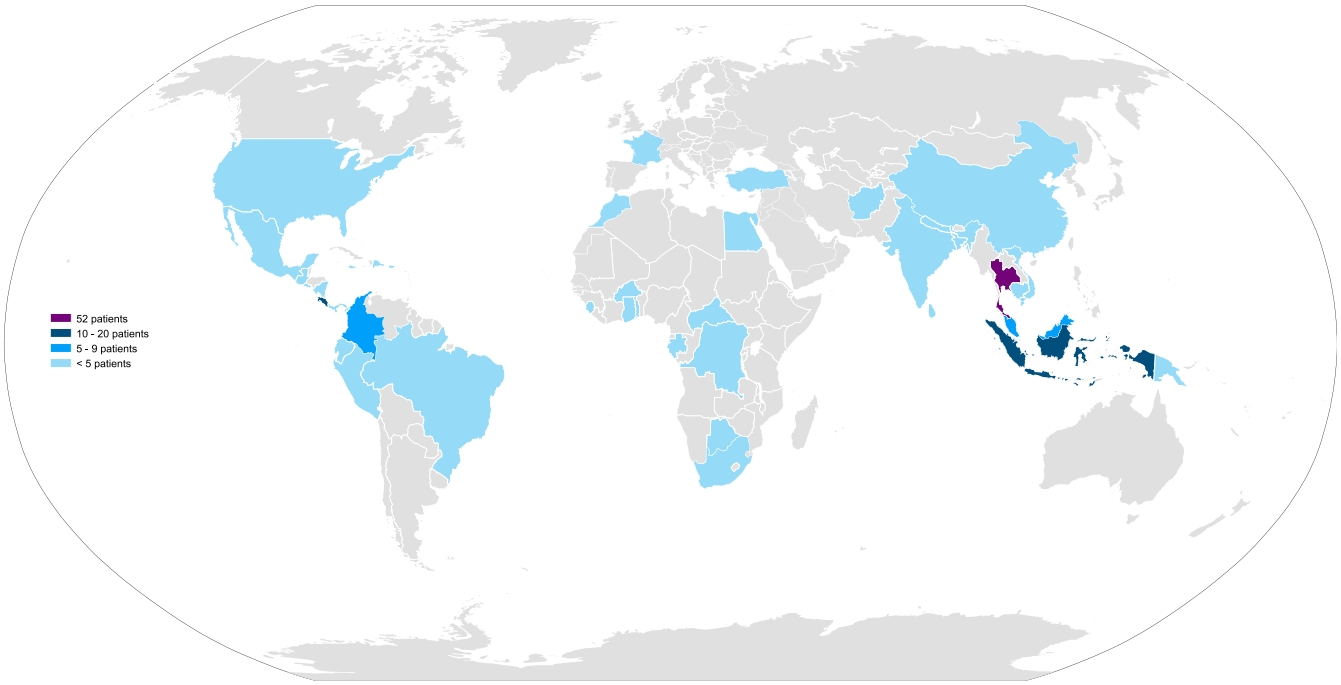


FIGURE 2. Exposure countries among travelers diagnosed with leptospirosis in the GeoSentinel Network, January 1, 1999–December 31, 2016 ($N = 167$).*† *Includes only patients for whom country of exposure data were available. †Purple represents 52 patients exposed in Thailand. Dark blue represents countries with 10–20 exposed patients (13 for Costa Rica and 11 each for Laos and Indonesia). Medium blue represents countries with 5–9 exposed patients (nine for Colombia and five for Malaysia). Light blue represents countries with < 5 patients (four for Philippines; three each for Cambodia, Gabon, Jamaica, Mexico, and Panama; two each for Brazil, Dominican Republic, Ecuador, Guadeloupe, India, Martinique, Papua New Guinea, Peru, Sri Lanka, and Trinidad and Tobago; and one each for Afghanistan, Bangladesh, Botswana, Burkina Faso, Central African Republic, China, Democratic Republic of the Congo, Egypt, El Salvador, France, Ghana, Guatemala, Mauritius, Morocco, Nepal, New Zealand, Nicaragua, Palau, Puerto Rico, Reunion, Samoa, Sierra Leone, South Africa, Togo, Turkey, United States, and Vietnam. This figure appears in color at www.ajtmh.org.

**Site survey.** Leptospirosis is an infection that is frequently underdiagnosed, especially in mild disease presentations.[17] In our survey among GeoSentinel clinicians, all reported seeing relatively few leptospirosis patients each year (< 10). The majority of respondents (75% of all sites) worked at an academic institution, where leptospirosis diagnostics are expected to be readily available. Molecular detection techniques are the cornerstone of diagnosis of leptospirosis in the acute phase,[26] but were available in only half of the clinics, and were actually used in less than a third of the clinics. In addition, convalescent samples were reported to have been collected in a minority of cases after a negative acute serology, despite the fact that antibodies only appear in the blood 5–7 days or sometimes after 10 days or longer following disease onset.[2] Possibly, patients with mild disease improved on treatment and abandoned follow-up, forgoing further testing.

TABLE 2

Distribution of gender and exposure regions with hospitalization status among travelers diagnosed with leptospirosis in the GeoSentinel Network, January 1, 1999–December 31, 2016*

| | Inpatient *n* (%) | Outpatient *n* (%) |
|---|---|---|
| Female | 21 (46) | 25 (54) |
| Median age (range) | 29 (18–56) | 28 (14–72) |
| Male | 86 (66) | 44 (34) |
| Median age (range) | 35.5 (16–66) | 33 (19–59) |
| Median age, overall (range) | 33 (16–66) | 31 (14–72) |
| Southeast Asia | 52 (63) | 31 (37) |
| Central America | 14 (58) | 10 (42) |
| South America | 9 (60) | 6 (40) |
| Sub-Saharan Africa | 6 (43) | 8 (57) |
| Caribbean | 6 (50) | 6 (50) |
| South Central Asia | 5 (63) | 3 (37) |
| Oceania | 2 (50) | 2 (50) |
| North Africa | 1 (50) | 1 (50) |
| Australia and New Zealand | 0 (0) | 1 (100) |
| North America | 1 (100) | 0 (0) |
| Northeast Asia | 1 (100) | 0 (0) |
| Western Europe | 1 (100) | 0 (0) |

* $N = 180$; 110 inpatients, 70 outpatients. Not all cells add to 180 because of missing data.

Half of the clinicians considered leptospirosis in a case of "nonspecified febrile illness," but very few actually performed diagnostics for it. Few clinicians reported testing patients without a suggestive exposure history. Classical exposures, such as freshwater contact and floods, were well known among clinicians. In the general population, the infection mechanism often remains unclear, and often there is no classical exposure history.[3] Data on travelers are scarce, but the case series that exist do report clear exposure histories.[35,37] Nevertheless, preselecting patients based only on a well-defined exposure history may result in underdiagnosis of leptospirosis among patients without a clear-cut exposure, especially when they returned from highly endemic areas.

Although the classic Weil's triad of fever, jaundice, and renal failure, with or without accompanying hemorrhagic features, was well recognized, other severe disease manifestations were less known among GeoSentinel Surveillance Network respondents. Aseptic meningitis can occur in up to 25% of cases,[13] but this manifestation was recognized by relatively few respondents (31%). Pulmonary hemorrhage is an

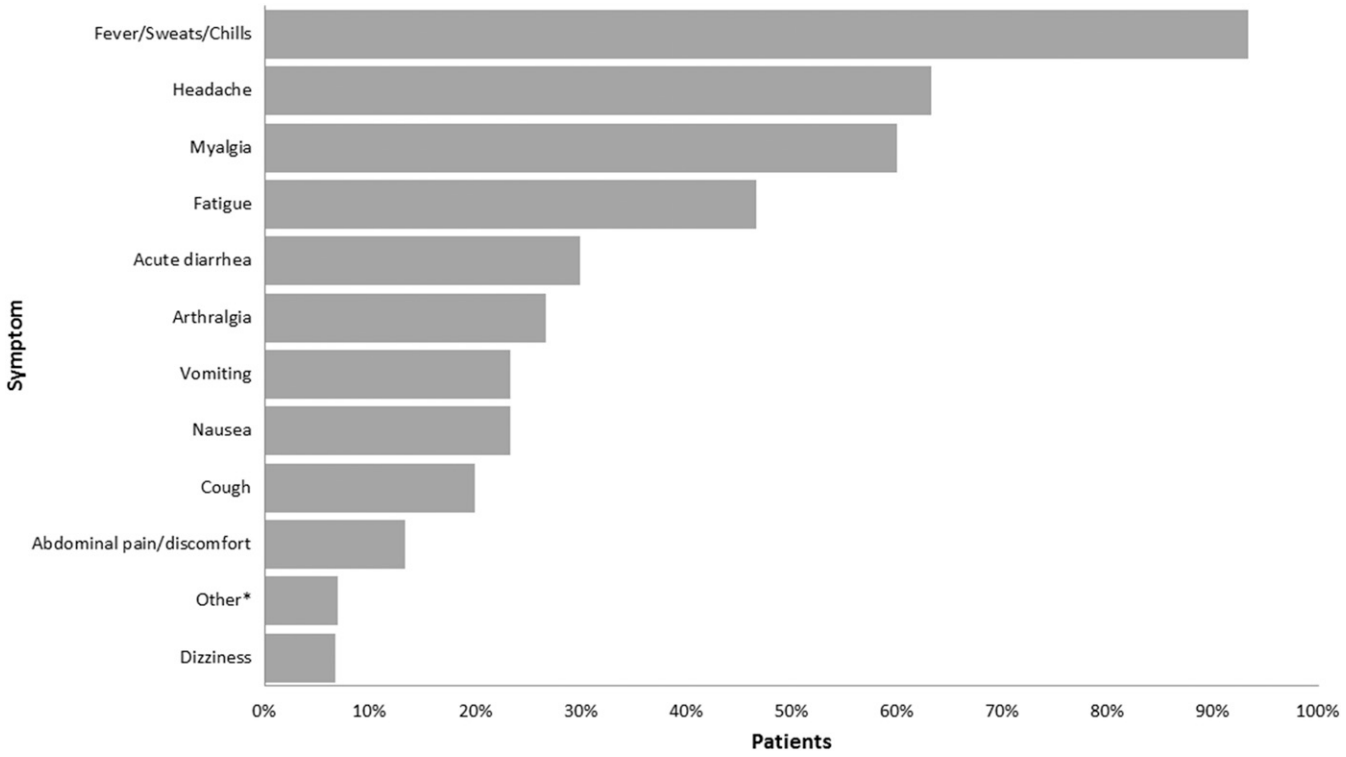


FIGURE 3. Proportion of reported signs or symptoms among patients diagnosed with leptospirosis in the GeoSentinel Network, October 31, 2015–December 31, 2016 ($N$ = 30, patients with one diagnosis only). Clinical symptoms reported in recognized disease in patients with one diagnosis, from October 31, 2015 onward, when a revised coding system of symptoms in GeoSentinel was started. Reporting may be incomplete in GeoSentinel and may not reflect the complete disease course, but rather the initial symptoms. *Other symptoms were not specified. †Less frequent reported symptoms (< 5%, or one person each) included constipation, diffuse rash, focal rash, itch, neck stiffness/photophobia, skin lesion/superficial infection, and weight loss.

important but under-recognized form of the disease, and outbreaks with only this manifestation have been described.[14,16] Almost half of the respondents did not include leptospirosis in the differential diagnosis of the febrile traveler presenting with hemorrhagic disease manifestations in the absence of the classic Weil's triad. In this analysis of returned travelers, the lesser known disease manifestations were not frequently reported, possibly because of the nature of symptom data collection in GeoSentinel, which combines specific symptoms into broad systemic categories.[40]

The results of our survey on clinical practices in specialized travel medicine settings suggest that the number of leptospirosis cases in travelers reported in the GeoSentinel Surveillance system is likely to be an underestimate. This may be due to suboptimal access to diagnostic testing at many sites, especially in the setting where acute disease is encountered. Furthermore, we found that the diagnosis of leptospirosis may not be routinely considered when clear-cut exposure histories are absent and when some rather typical clinical features are missing. Based on our site survey, there is a need for improved awareness among clinicians about the spectrum of exposures, clinical presentations, and diagnostic considerations.

**Strengths and limitations.** In addition to those already discussed, the GeoSentinel surveillance data have several other limitations and may not be generalizable to the traveler population as a whole.[38,50–52] GeoSentinel reporting may be biased toward capture of more complicated or more severe disease because most GeoSentinel sites are also academic institutions. Overall, hospitalization may be underestimated in GeoSentinel, but there are some sites that almost exclusively capture data from the inpatient setting. Therefore, the high proportion of hospitalizations should be interpreted carefully. Furthermore, leptospirosis may have been missed among travelers presenting with atypical exposures or symptoms, or presentations of milder, self-limited disease, and may have had an influence on the results. GeoSentinel preferentially captures travelers returning from tropical regions because of the nature of the clinics that make up the network; so, travelers with disease acquired in temperate regions are likely underrepresented. GeoSentinel criteria for diagnosing patients with leptospirosis may differ from the definitions used by national reference laboratories and other reporting systems, limiting direct comparison with data from those sources. Despite these limitations, this is one of the largest series of leptospirosis in travelers published to date and provides valuable information about the epidemiology of leptospirosis in international travelers.

A limitation of the network survey is that the answers were captured from clinicians specialized in travel medicine and may not be representative of all clinical practices in a particular institution. Furthermore, the data are self-reported and may therefore not be reflective of actual practice. Some questions allowed multiple answers, leading to respondents choosing incompatible answers, making the interpretation more complex. However, the relatively high response rate of 75% of GeoSentinel sites in our view accounts for a representative survey among our global network of mostly academic travel clinics.

TABLE 3

Selected results of a GeoSentinel supplemental site survey regarding clinical and diagnostic practices for leptospirosis

| What exposures raise your suspicion of leptospirosis? (multiple answers possible) | *n* | % (of 42) |
|---|---|---|
| Freshwater contact | 42 | 100 |
| Natural disasters (e.g., floods) | 36 | 86 |
| Any travel to endemic areas | 29 | 69 |
| Animal contact | 28 | 67 |
| Soil contact | 18 | 43 |
| Use of freshwater for cleaning and other activities | 12 | 29 |
| Gardening | 11 | 26 |
| Which clinical presentation makes you suspect leptospirosis (multiple answers possible) | | |
| Febrile illness with liver enzyme or renal function abnormalities | 31 | 74 |
| Febrile illness and jaundice | 29 | 69 |
| Febrile illness and conjunctival suffusion | 26 | 62 |
| Febrile illness and myalgia | 23 | 55 |
| Febrile illness with hemorrhagic manifestations | 23 | 55 |
| Nonspecific febrile illness | 22 | 52 |
| Febrile illness with headache | 17 | 41 |
| Febrile illness with clinical signs of meningitis | 13 | 31 |
| Febrile illness with exanthema | 12 | 29 |
| Febrile illness and respiratory symptoms | 12 | 29 |
| All of the above | 17 | 41 |
| How often do you perform diagnostics for leptospirosis in the first diagnostics workup in patients with unspecified febrile illness from endemic areas? | | % (of 41) |
| < 10% of cases | 25 | 61 |
| 10–30% of cases | 9 | 22 |
| 31–50% of cases | 4 | 10 |
| > 50% of cases | 3 | 7 |
| How often do you test for leptospirosis in patients without a fitting exposure history? | | |
| Never | 11 | 27 |
| In < 10% of cases | 16 | 39 |
| In 10–30% of cases | 10 | 24 |
| In 31–50% of cases | 0 | 0 |
| In > 50% of cases | 4 | 10 |
| What diagnostics for leptospirosis are available in your clinical setting? (multiple answers possible) | | |
| ELISA | 30 | 73 |
| PCR | 19 | 46 |
| MAT | 14 | 34 |
| Serological rapid test (RDT) | 13 | 32 |
| Culture | 9 | 22 |
| Do not know | 4 | 10 |
| Which diagnostic test for leptospirosis do you usually request? (multiple answers possible) | | |
| ELISA | 24 | 59 |
| PCR | 12 | 29 |
| MAT | 12 | 29 |
| Serological rapid test (RDT) | 12 | 29 |
| Determined by the laboratory | 9 | 22 |
| Determined by duration of clinical illness | 6 | 15 |
| Culture | 3 | 7 |
| Do not know | 1 | 2 |
| Approximately how often are convalescent samples collected for leptospirosis diagnostics after a negative first test? | | % of 40 |
| < 20% | 19 | 48 |
| 20–40% | 9 | 23 |
| 41–60% | 4 | 10 |
| 61–80% | 3 | 8 |
| > 80% | 5 | 13 |

ELISA = enzyme-linked immunosorbent assay; MAT = microscopic agglutination test; PCR = polymerase chain reaction; RDT = rapid diagnostic test.

## CONCLUSION

Leptospirosis may be an infrequently encountered cause of substantial morbidity among international travelers that may not be clinically suspected. Although leptospirosis was most frequently diagnosed among persons visiting highly endemic countries, it may occur elsewhere and warrants broader consideration in the differential of the ill traveler. Given the laboratory diagnostic challenges and nonspecific presentation of many clinically evident cases, the burden of reported disease is likely underestimated, as supported by other published data.[1,18–20] We recommend enhancement of awareness about leptospirosis and heightened clinical suspicion when evaluating the ill traveler. Laboratories need to have up-to-date diagnostic methods available; molecular detection techniques are key to early diagnosis, which is helpful for the early initiation of treatment that may substantially reduce morbidity and improve outcomes. Empiric treatment in cases of high suspicion is recommended. Efforts to improve knowledge among clinicians regarding (the often unclear) exposures and clinical presentations are needed.

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