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Brief Report

Leptospirosis in the Tel Aviv District, Israel, 2016-2022

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Abstract

Background: Leptospirosis is a bacterial zoonosis with a wide range of presentation, from unspecific and mild symptoms, to a more severe form of disease, which can sometimes be fatal. In Israel, leptospirosis is endemic with occasional outbreaks, including a nationwide outbreak in 2018 of approximately 600 cases. The aim of this study is to describe the epidemiologic, clinical and laboratory characteristics of leptospirosis in the Tel Aviv (TA) District, Israel between 2016-2022. **Methods:** We retrospectively analyzed all leptospirosis cases among residents of the TA District, Israel, during 2016-2022. Leptospirosis is a notifiable disease by law. An epidemiologic investigation is effectuated for each notified case by a trained nurse. Clinical data were obtained from patients' clinical files. **Results:** A total 130 patients with leptospirosis were reported in the TA district between 2016-2022 (rates from 0-7.3 per 100,000 population per year). Most cases were men (n=109, 84%). Hospitalization was required for 40 (31%) cases; no deaths were reported. Among all cases, 78 (60%) were from the Ultra-orthodox city of Bnei Brak, 6 (5%) were workers without legal residency. Common sources of exposure included freshwater recreational activities (85% cases) and exposure to rodents (8% cases) Leptospira serovars were found to be associated with different sources of exposures: L. pomona was associated with exposures to freshwater recreational activities; L. Icterohemorrhagie, L. Sejreo Bratislava and L. Burgas were associated with exposure to rodents. **Conclusion:** More accessible diagnostic methods should be developed to better recognize the prevalence of leptospirosis and its burden, taking into account clinical symptoms as well as sources of exposures. This should enable adequate treatment and better control of potential reservoirs of leptospirosis and reduce the impact on vulnerable populations, such as residents of areas of lower socio-economic status.

Introduction

Leptospirosis is one of the most widespread zoonosis worldwide, caused by bacteria of the *Leptospira* genus. Leptospires can survive for weeks to months in water and mud, especially in warm and humid conditions.

Transmission mainly occurs through contact of abraded skin or mucous membranes with water or soil contaminated by the urine of infected animals [1]. A wide range of wild, domestic and marine animals have been found to be carriers of pathogenic *Leptospira* spp.

In urban settings, rodents are a common host of pathogenic *Leptospira* spp. In rural settings, most common exposures include water sources contamined by the urine of infected animals [2-4].

The incubation period for leptospirosis among humans ranges from two to twenty-eight days after exposure. Symptoms vary widely, from asymptomatic or mildly symptomatic, self-limited to severe and rarely fatal disease. Most patients (approximately 90%) suffer from mild symptoms such as fever, flu-like and/or gastro-intestinal illness [5]. Severe forms of disease occur in about 5-15% of cases and can involve multiple organs, causing hepatic and renal failure, pulmonary involment such as acute respiratory distress syndrome (ARDS) or pulmonary hemorrhage as well as meningitis [1]. Death has been reported in approximately 5-15% of cases with severe disease [2].

In Israel, leptospirosis is endemic with occasional outbreaks, including a nationwide outbreak in 2018, with approximately cases 600 [4].

The aim of this study was to describe the epidemiologic, clinical and laboratory characteristics of leptospirosis in the Tel Aviv (TA) District, Israel, from 2016 to 2022.

Methods

Study population and data collection

Our study population consisted of residents of the TA District, Israel, diagnosed with leptospirosis by physicians, during 2016-2022.

The TA District is comprised of 12 cities located on the western coastline of Israel and has a population of approximately 1.5 million people, including 398,857 (27%) < 18 years of age. The district is known for its diverse ethnic population, which is largely defined by city of residence. The city of TA is the economic and cultural epicenter of Israel. It offers a wide range of employment opportunities, and as a result harbors a large community of undocumented African immigrants seeking work, who live in very crowded settings in the south of the city.

The city of Bnei Brak is the most densely populated city in the district (and in the country), with a predominantly Ultra-Orthodox Jewish population (92% of its residents), with high birth rates (crude birth rate of 38.4 per 1,000 population) and low socio-economic status.

Population estimates were extracted from the Israeli Central Bureau of Statistics [6].

Epidemiologic and clinical investigation

Leptospirosis is a notifiable disease by law in Israel. Cases are diagnosed by attending physicians, either in medical clinics or hospitals. Each case is reported to its corresponding district health office. Once a case is identified, a nurse contacts the case or a close relative in order to detail clinical and epidemiologic aspects of the disease and identify possible exposure sources in a timeframe of one month prior to symptom onset. Cases were surveyed regarding their potential occupational exposure, which includes veterinary occupations, plumbing jobs and healthcare work. Patients were also queried about fod and beverage consumption. In addition, patients were questioned about their exposure to water sources for recreational purposes. Furthermore, they were asked about any international travel they had undertaken within the month prior to the onset of symptoms.

Case definitions:

Confirmed cases were defined as having clinical symptoms of leptospirosis, including fever, flu-like illness, gastro-intestinal symptoms, respitatory symptoms and/or acute renal failure and/or liver failure and/or meningitis as well as laboratory evidence of infections, either serological and/or molecular.

Suspected cases were defined as having compatible symptoms of leptospirosis as well as history of exposure to a suspected source of leptospirosis, without laboratory evidence of infection as they did not have the opportunity to undergo testing.

Clinical data was extracted from patients› physician or hospital files and were entered in a database which was subsequently de-identified. Clinical data extracted included date of symptom onset, length of disease, clinical presentation, underlying medical conditions and laboratory results.

Laboratory investigation of clinical cases

Laboratory evidence of infection included one or more of the following criteria:

1. Positive polymerase chain reaction (PCR) test of a clinical sample (urine or blood) for pathogenic *Leptospira* spp within 10 days of symptom onset.
2. Microscopic Agglutination Test (MAT) of serum sample with a titre above (threshold) 1/200.

MAT was performed using 24 *Leptospira* antigens to identify the serogroup of the infecting strain with the following threshold titres: <1:50 negative test; between 1:50-200 borderline test; >1:200 positive test.

3. Evidence of seroconversion from at least two clinical serum samples by a MAT test, with at least a four fould increase in titer between the sample tested during the acute phase and the one tested during the convalescent phase.

Results

Epidemiologic and clinical characteristics

Between 2016 and 2022, a total of 130 patients were diagnosed with leptospirosis in the TA District. Annual rates of leptospirosis ranged from 0 to 7.3 per 100,000 population in the TA district between 2016-2022 (national rates ranged from 0.1 to 5.6 per 100,000 population) (Figure 1). Among all cases, 78 (60%) were residents of the city of Bnei Brak; 6 (5%) were workers without legal residency. Hospitalization was required for 40 (31%) cases, among them 35 (88%) were men; 73 (52%) were admitted to the emergency service without requiring hospitalization; 15 (12%) were diagnosed by their general practitioners. Among 21 female cases, median age was 22 years (range: 3-74 years). Among them, 5 (23%) required hospitalization.

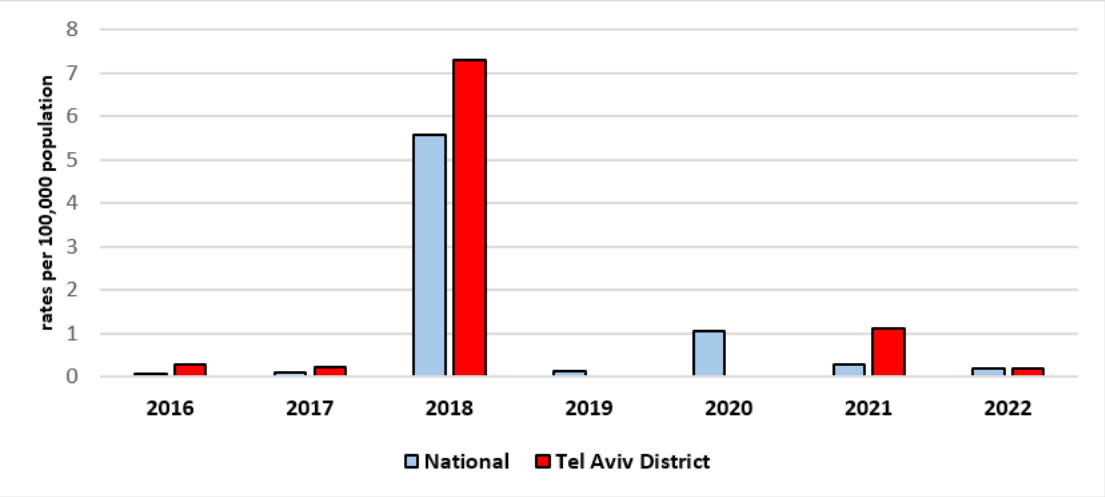

Figure 1: Rates of Leptospirosis in Israel and in the Tel Aviv District, 2016-2022.

No deaths were reported. Median length of hospital stay was 3 days (range: 2-15 days). Hospitalization in the Intensive Care Unit (ICU) was required for three (2%) cases. Overall, among 23 cases aged above the age of 40, 12 (52%) necessitated hospitalization due to their infection with leptospirosis. Among them, four (17%) patients suffered from underlying medical conditions.

Among all cases, 35 were laboratory confirmed. Among them, 32 (91%) were men and the median age was 20 years (range:5-74 years) (Table 1).

Table 1: Epidemiologic and clinical characteristics of leptospirosis patients in the Tel Aviv District, 2016-2022.

	Confirmed cases N=35	Suspected cases N=95	Total N=130
Gender			
Male	32 (91%)	77 (%)	109(84%)
Female	3 (9%)	18 (%)	21 (16%)
Age (years)			
0-5	2 (6%)	9 (9%)	11 (8%)
6-14	5 (14%)	25 (26%)	30 (23%)
15-24	14 (40%)	36 (38%)	50 (38%)
25-39	4 (11%)	12 (13%)	16 (12%)
40-59	7 (20%)	10 (11%)	17 (13%)
>60	3 (9%)	3 (3%)	6 (5%)
Median age (range)	20 (5-74)	18 (1-73)	18 (0-73)
Symptoms			
Fever	33 (94%)	82 (86%)	115 (88%)
weakness	27 (77%)	68 (72%)	95 (73%)
Headache	23 (66%)	62 (65%)	85 (65%)
Gastro-intestinal symptoms	15 (43%)	56 (59%)	71 (55%)
Myalgia	25 (71%)	40 (42%)	65 (50%)
Conjunctivitis	3 (9%)	13 (14%)	16 (12%)
Jaundice	9 (26%)	3 (3%)	12 (9%)
Acute renal failure	7 (20%)	2 (2%)	9 (7%)
Meningitis	1 (3%)	0 (%)	1 (1%)
Pneumonia	1 (3%)	1 (1%)	2 (2%)
Cholecystitis	1 (3%)	0	1 (1%)

Hospitalization	23 (66%)	17 (18%)	40 (31%)
Median length of hospital stay (d) (range)	4 (2-15)	2.5 (2-4)	3 (2-15)
ICU	3 (9%)	0	3 (2%)
Workers without legal residence	5 (14%)	1 (1%)	6 (5%)
Resident of the Ultra-Orthodox community of Bnei Brak	15 (43%)	63 (66%)	78 (60%)
Source of exposure			
Rodents	10 (29%)	1 (1%)	11 (8%)
Freshwater recreational exposure	19 (54%)	92 (97%)	111 (85%)
Exposure to sewage	2 (6%)	0	2 (2%)
Travel related	2 (6%)	0	2 (2%)
Unknown	3 (9%)	2 (2%)	5 (4%)

Most common clinical symptoms included fever (88% cases), weakness (73% cases), headache (65% cases) and gastro-intestinal symptoms (55% cases).

Among residents of the Ultra-Orthodox city of Bnei Brak, 39 (50%) cases were aged between 15-24 years and 20 (26%) cases were aged between 6-14 years.

In the rest of the Tel Aviv District, 14 (27%) cases were aged 40-59 years; 11 (21%) cases were aged between 15-24 years; 11 (21%) cases were aged between 25-39 years.

Overall, sources of exposures included recreational freshwater (111 (85%) cases), exposure to rodents (11 (8% cases), 2 cases were related to travel in other countries and two cases were due to sewage exposure, one of which was occupational (as a plumber). All freshwater exposures reported by cases were in popular water sources renowned for providing recreational activities in the Northern district of Israel. Among those cases, 65 (83%) were diagnosed in 2018, with 10 (15%) patients requiring hospitalization.

Among patients whose exposure was linked to recreational freshwater activity, 76 (68%) were from the city of Bnei Brak. Median age was 18 years. Among those cases, 27 (24%) required hospitalization. None of the cases required treatment in the ICU.

Among patients whose exposure to leptospira was linked to rodents, ten (91%) were residents of the city of Tel Aviv; six (55%) were undocumented African immigrants. Median age in this group was 37 years old; eight (73%) patients required hospitalization, three of them in the ICU, including two adults with acute renal failure and a five year old child born to undocumented African immigrant parents with acute renal failure and thrombocytopenia. None of those three patients had known underlying medical conditions.

Laboratory characteristics

Among all 130 cases, 35 (27%) were confirmed by laboratory methods. Lesptospira serovar distribution by source of exposure are demonstrated in figure 2. Among the 15 patients diagnosed by a MAT test, 12 (80%) patients had more than one leptospira serovar detected.

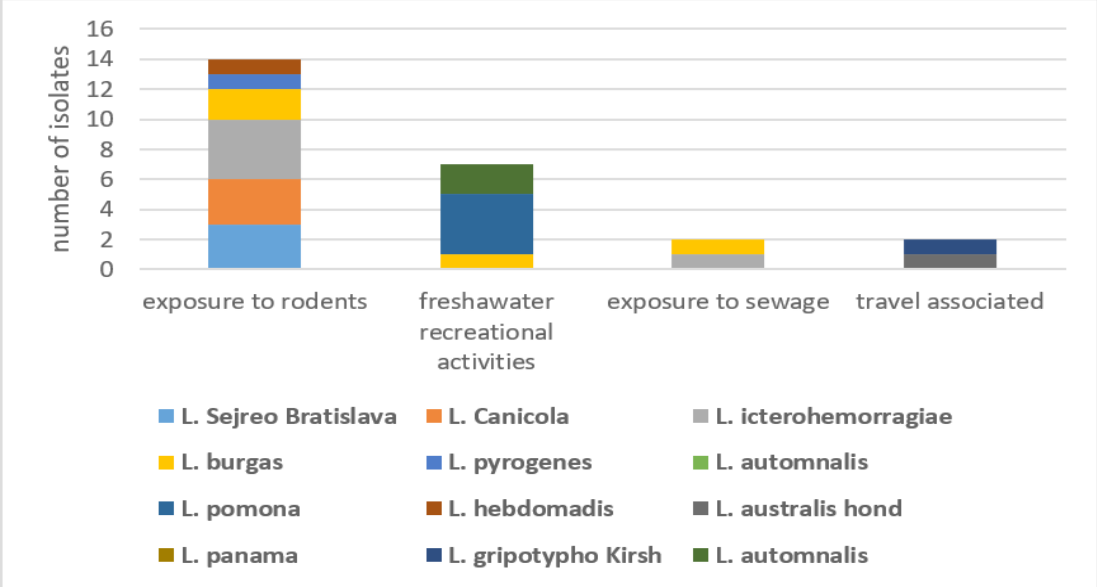

Figure 2: Leptospira serovars by type of exposure, isolated among patients in the Tel Aviv District, Israel, 2016-2022.

Among the patients whose exposure was linked to rodents, isolated leptospira serovars included L. sejreo bratislava, L. icterohemorragiae, L. burgas, L. pyrogenes and L. hebdomadis.

Among patients whose exposure was linked to recreational freshwater activities in northern Israel, isolated serovars included L. pomona, L. automnalis and L. burgas. Among patients whose exposure was linked to sewage, isolated serovars included L. icterohemorragiae and L. burgas. Two patients were exposed during travel outside of Israel. L. grypotypho kirsh was isolated in a patient who had travelled to Thailand. L. australis hond was isolated in a returning traveler from India.

Discussion

This study details the clinical and epidemiologic characteristics of leptospirosis in the Tel Aviv District, Israel, during 2016-2022. Rates of disease fluctuated during the study period, peaking at 7.3 cases per 100,000 population in 2018, during a large nationwide outbreak.

Overall, hospitalization was required for 40 (31%) cases, three of them necessitating treatment in the ICU. No deaths as a result of leptospirosis were reported in our study. Median age among all our patients was 18 years. Clinical presentation was most commonly mild, with frequent symptoms including fever, weakness and headache.

All cases in this study were symptomatic, as testing was not carried out for asymptomatic patients with relevant exposures. This might have contributed to an underestimation of the disease incidence.

Moreover, mildly symptomatic patients might not have disclosed potential exposures, that would prompt testing for leptospirosis, or sought medical advice altogether. Also, paradoxically, severe cases might not be able do disclose exposures and specific tests for leptospirosis might not be carried out, as leptospirosis symptoms are not specific.

Laboratory evidence of infection was obtained for 33 (25%) of patients. Patients that were linked to a known outbreak were more likely to have a diagnosis based on clinical and symptoms and known exposure, mostly during the 2018 outbreak. Sporadic patients whose exposure was not linked to a known outbreak were more likely to have laboratory evidence of infection and were more frequently linked to rodent exposure.

In our study, the most commonly identified exposure was recreational water activity, mostly in northern Israel. Among cases with such exposure, 76 (68%) were from the Ultra-Orthodox city of Bnei Brak. Among them, 61 (80%) were male and under the age of 30 years old. Most of these cases were diagnosed in the summer of 2018, during a nationwide outbreak of leptospirosis [4]. During this outbreak, the majority of leptospirosis cases were suspected based on clinical symptoms and exposures. This might have been due to a heightened degree of suspicion and awareness among clinicians during that period. During this outbreak, two cattle herds from northern Israel were found to be contaminated with L. Pomona. Their exposure was linked to natural water sources in the area, which were likely infected by wild boars [4,7]. As a result,

mandatory vaccination with a vaccine that includes L. Pomona of beef cattle heards was implemented in order to reduce disease burden and transmission. All the cases in our study with laboratory evidence of leptospira and exposure to recreational water activities were linked to L. Pomona. In addition, during that time, three travelers from New York were infected with leptospirosis in the course of water activities in Israel, two of which developed meningitis [8]. Health recommendations should be given to travelers to Israel concerning this risk, to minimize exposure. Also, upon symptomatic travellers' return, rapid detection of infection should be implemened, so as to provide adequate treatment and avoid potential complications.

Leptospirosis cases that occurred in urban settings were linked to exposure to rodents and took place in areas with poor sanitation and disturbed urbanization due to infrastructure changes, such as light-rail construction works in the city of TA. In particular, in 2021, a cluster of five leptospirosis cases was reported, all with exposure to rodents in the southern part of the city of TA. Among the reported cases, three patients were undocumented african immigrants, including two children, one of whom was admitted to the ICU. Two other cases were adults with underlying conditions, including HIV and syphilis among one case, and among the other diabetes mellitus, hypertension and atherosclerosis. Their isolated serotypes were L. burgas, L. canicola and L. ictero.

As seen in previous reports [9,10], women in our study were less likely to be diagnosed (109 male cases vs 21 female) and required less hospitalizations (32% among males vs 24% among females). Leptospirosis might cause a milder disease among women. In addition, women might be less prone to certain exposures (such as occupational exposure to sewage, or recreational water exposures, which are more popular among young males).

In our study, two patients were infected with leptospirosis while they were travelling outside of Israel. Their isolated leptospira serotype, L. australis hond and L. gripotypho kirsh, differed from those commonly isolated in Israel and were not isolated in other patients with local exposure.

Enhanced awareness regarding the disease and its diagnostic methods is crucial to accurately comprehend its impact. This entails considering clinical symptoms and sources of exposure. Conversely, it is equally important to uncover potential sources of exposure by obtaining a diagnosis confirmed by laboratory methods.

We found different leptospira genotypes linked to different sources of exposure, which could help at identifying the potential source of exposure. This should enable adequate treatment and better control of potential reservoirs of leptospira (such as implementing sanitary measures to address rodent infestation or considering vaccination of wild animals, when they are linked to outbreaks) and reduce the impact on vulnerable populations, such as residents of areas of lower socio-economic status.

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