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BRIEF REPORT

Leptospirosis in Retirees Living in Rural Areas: A Poorly Recognized Emerging Problem in Mainland France?

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Among 40 patients diagnosed with leptospirosis in 3 hospitals of western mainland France between 2014 and 2018, half were at least 60 years old and retired. Their exposure factors were mainly rural residential environment with limited remarkable risk factors. Better awareness and information on leptospirosis appear necessary in this population.

Keywords. leptospirosis; zoonotic disease; epidemiology; risk factor; elderly; differential diagnoses.

Leptospirosis is a cosmopolitan zoonosis, whose causative agent is a spirochete bacterium of the genus *Leptospira* [1]. Leptospirosis can occur in humans directly through a contact with a *Leptospira*-shedding animal—mainly rodents—or indirectly through a contaminated environment—mainly by *Leptospira*-shedding rodent urine [1]. The annual incidence of leptospirosis in mainland France has increased recently to 1/100 000, the highest level ever reported [2, 3]. *Leptospira* exposure factors can be either recreational or professional activities. Regarding professional exposure, in the last 2 decades, agriculture and the building sector accounted for more than half of the cases reported to the National Reference Centre for Leptospirosis [4]. Recreational activities reported in studies previously conducted in mainland France were mostly classical freshwater exposures through canoeing, fishing, and swimming [5–7]. However, human activities and demographics may have evolved and modified classic epidemiological patterns of leptospirosis as previously suggested [8]. This hypothesis is currently difficult to test given the absence of recent epidemiological data on adult leptospirosis in mainland France, especially in regions with increasing incidence, such as the Pays de la Loire region (western France) [3]. We therefore conducted a study to describe the epidemiology of recent adult cases of leptospirosis in 2 counties of the Pays de la Loire and identify their exposure factors.

METHODS

Study Design

We conducted a multicenter cross-sectional study of patients aged ≥18 years with suspected leptospirosis managed in 3 western French hospitals (Nantes university hospital, La Roche sur Yon hospital, and Saint Nazaire hospital) between January 2014 and December 2018. These hospitals (2 in Loire Atlantique county and 1 in Vendée county) served a population catchment area of around 2 100 000 people in 2018.

Inclusion Criteria

We screened for adult patients with suspected leptospirosis by assessing the leptospirosis diagnostic tests performed in the 3 hospitals cross-referenced with the French hospital discharge database (PMSI). Among suspected patients, we applied the Centers for Disease Control and Prevention criteria to classify the patients as confirmed or probable cases [9].

Briefly, confirmed cases were defined by positive polymerase chain reaction (PCR) in blood, urine, or cerebrospinal fluid (CSF). Probable cases were defined by the association of (i) a positive serum anti-*Leptospira* immunoglobulin M (IgM), (ii) an evocative epidemiological context and clinico-biological picture, and (iii) the absence of a differential diagnosis.

After the descriptive study was undertaken, a secondary data analysis was conducted to explore the characteristics of younger and older patients.

Biological Diagnosis of Leptospirosis

Serologic screening of IgM against *Leptospira* was performed by Laboratoire Biomnis and Laboratoire Cerba with an enzyme immuno-assay technique (SERION ELISA classic Leptospira IgM, Serion, Germany).

Real-time PCR was performed in both laboratories to detect *Leptospira*.

Microscopic agglutination testing was performed at the National Reference Center for leptospirosis to determine the presumptive infecting serogroup [10].

Collection of Data and Definitions

Demographics, exposure factors, and clinical, biological, and outcome data were collected from medical charts and reported in anonymized forms.

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Initial management was defined as ambulatory, emergency department, and ward admission management.

Initial suspicion of leptospirosis and differential diagnoses were reported if mentioned in the medical chart or if the diagnostic tests were done during initial management.

Autochthonous cases were defined as cases without any report of travels outside mainland France within the 3 weeks before symptoms onset.

Quantitative variables were described with median and interquartile range, and qualitative variables were described with number and percentage.

Patient Consent

The study protocol conformed to standards currently applied in France and was consistent with the MR004 reference methodology. All study participants received an information letter that offered the possibility of not participating in the study.

RESULTS

After excluding duplicates and patients with missing data (8 patients), we included 40 patients: 27 confirmed cases (68%) and 13 probable cases (33%). During the study period, the mean number (range) was 8 (4–16) cases per year for the 3 hospitals. The median age (interquartile range [IQR], min–max) was 57.5 (34–70, 19–85) years. Twenty patients (50%) were at least 60 years old at diagnosis, all of them being retired (1 missing data). The characteristics of the study population classified by age are presented in Table 1.

Circumstances of Diagnosis

Clinical symptoms are detailed in Table 1. Of note, 10 (50%) elderly patients developed icterus, including 5 after their hospital admission. Twenty-three patients (59%) first consulted a primary physician, and 14 (35%) directly consulted at the emergency department. Diagnosis of leptospirosis was initially made in 15/40 (38%): 4/23 (17%) cases by primary physician and 11/40 (28%) cases upon hospital admission, mostly by an infectious disease specialist. The differential diagnoses made during initial management are presented in Table 1.

Biological Diagnosis

PCR was performed in 35 patients (88%) after a median delay (IQR) of 6 (4–7) days since the onset of symptoms. Of these, 16 patients had blood and urine PCR, 17 had blood PCR alone, 1 had urine PCR alone, and 1 had blood and CSF PCR.

IgM testing (enzyme-linked immunosorbent assay [ELISA]) was performed at least once in 25 patients (63%) with a median delay (IQR) of 8 (7–11) days since the onset of symptoms. ELISA testing was repeated in 6 patients (twice in 1), and seroconversion was observed in 3 of them. A microscopic agglutination test was obtained for 2 patients with 1 available result showing a Louisiana serogroup.

Table 1. Characteristics of the Study Population

	<60 Years (n = 20)	≥ 60 Years (n = 20)
Age, y	33 (29–42)	70 (66–75)
Male gender	17 (85)	17 (85)
Tobacco use	10 (50)	2 (10)
Chronic alcohol use	2 (10)	4 (20)
Comorbidity		
Hypertension	2 (10)	5 (25)
Diabetes mellitus	2 (10)	3 (15)
Cardiopathy	1 (5)	5 (25)
Immunosuppression	0 (–)	1 (5)
None	14 (70)	8 (40)
Confirmed case	12 (60)	16 (80)
1st consultation at emergency department	10 (50)	11 (55)
Symptoms on hospital admission		
Fever	19 (95)	19 (95)
Nausea/vomiting	12 (60)	8 (40)
Abdominal pain	6 (30)	7 (35)
Muscle pains	17 (85)	10 (50)
Headache	10 (50)	5 (25)
Cough	3 (15)	5 (25)
Dyspnea	1 (5)	5 (25)
Auscultation abnormalities	1 (–)	8 (40)
Icterus	5 (25)	5 (25)
Hemorrhagic syndrome	2 (10)	1 (5)
Initial suspicion of leptospirosis	6 (30)	5 (25)
Delay between symptom onset and suspicion, d	5 (4–6)	4.5 (3.75–6)
Suspected differential diagnoses[a]		
Sepsis	5	5
Pneumonia	2	6
Intraabdominal infection	2	6
Meningitis	3	3
Urinary tract infection	2	3
Arbovirus infection	5	0
ICU admission	11 (55)	10 (50)
ICU admission on hospital admission	8	8
Vasopressor agents	7	9
Hemodialysis	2	3
Mechanical ventilation	3	4
Death	1 (5)	3 (15)
Hospital stay, d	7 (3.5–11.5)	9 (6–13.25)
Antibiotic treatment	16 (80)	18 (90)
Prehospital antibiotics	4 (20)	3 (15)

Variables are represented by median with interquartile range; qualitative variables are represented by number with percentage, as appropriate.

[a]Differential diagnoses were missing for 4 patients in each group.

Thirty-five patients (86%) received antibiotics: third-generation cephalosporin (30/35), amoxicillin (13/35), aminoglycosides (12/35), and macrolides (11/35). Only 4 received cyclins. One reaction of Jarisch Herxheimer was noted. The median duration of antibiotic treatment (IQR) was 10 (8–10) days.

Outcome

Overall, 21 patients (53%) were admitted to the intensive care unit (ICU) with a median length of stay (IQR) of 4 (3–10)

Table 2. Exposure Factors

	<60 Years (n = 20) No. (%)	≥60 Years (n = 20) No. (%)
Autochthonous cases	16 (80)	20 (100)
Professional exposure[a]	7 (35)	0 (–)
Agriculture[b]	1 (5)	5 (25)
Building sector[b]	3 (15)	1 (5)
Veterinary	1 (5)	0 (–)
Landscaper	1 (5)	0 (–)
Sports instructor	1 (5)	0 (–)
Nonprofessional exposure		
Freshwater immersion	10 (50)	2 (10)
Canyoning	3 (15)	0 (–)
Canoeing/kayaking	0 (–)	0 (–)
Walking or running	4 (20)	2 (10)
Maintenance work	1 (5)	6 (30)
Gardening	2 (10)	6 (30)
Fishing	3 (15)	4 (20)
Hunting	1 (5)	4 (20)
Animal proximity[c]	9 (45)	13 (65)
Rodent proximity	2 (10)	7 (35)
Stagnant freshwater near the home	2 (10)	6 (30)

[a]Eight patients <60 years old had unexposed occupation, 6 had unknown occupation, 1 had no occupation.

[b]Former profession was reported for retirees.

[c]Including rodent. Some patients had several exposure factors; percentages do not account for missing data.

days. Sixteen patients (40%) required administration of vasoactive drugs, 5 (13%) hemodialysis, and 7 (18%) mechanical ventilation. Four patients died (10%) during their stay in the ICU. The median hospital stay for the whole population (IQR, range) was 8 (5–12, 2–39) days. Among the 36 discharged patients, 21 (58%) were followed up by an infectious disease specialist in consultation. Outcomes of younger and elderly groups are detailed in Table 2.

Exposure Factors

Cases were mostly autochthonous (37/40, 93%), except for 3 who reported freshwater exposure abroad: 1 from the West Indies, 1 from Central America, and 1 from Southeast Asia. Most of the autochthonous cases occurred during summer (26/37, 70%). The probable circumstances of infection were documented in 84% of autochthonous cases. Exposure factor was collected during follow-up for 6/20 (30%) elderly patients.

Exposure factors of younger and elderly groups are detailed in Table 2.

DISCUSSION

In the present study, half of the leptospirosis cases were aged at least 60 years and were retired. The main exposure factors were the proximity of animals (including rodents), gardening activities, maintenance work, and the presence of stagnant fresh water near the home.

With a median age 10 years older than previous studies [5–7], our study suggests that older subjects seem to be overrepresented. A recruitment bias may have occurred due to the fact that most of the elderly study patients lived in Vendée county, where the population age >60 years represented 31% of the population in 2018, vs 23.8% in Loire Atlantique county. However, this bias alone does not seem sufficient to explain the age difference between our study and previous ones. Such a large proportion of patients age >60 should be of particular interest for clinicians: Older age has been associated with specific misleading clinical aspects: A possible lower incidence of myalgia, vomiting, and dyspnea has been suggested in a Brazilian study [11]; older age may increase the likelihood of hemodialysis requirement and worsen the prognosis of leptospirosis [11, 12].

In more economically developed countries, leptospirosis is classically associated with specific professional [4, 13] or nonprofessional exposures, especially recreational activities with freshwater immersion in young male subjects [14–16]. In the present study, the usual risk factors such as hunting, fishing, and freshwater immersion were not commonly reported in elderly patients.

Most studies on leptospirosis in the elderly have been performed in Brazil [11, 17]. Watrin and colleagues reported that retired patients accounted for a third of leptospirosis cases diagnosed in Normandy (northwestern France) between 2010 and 2014 (unpublished study) [18]. More than half of the study patients reported the presence of fresh water near the home, although <20% reported water sports activity and immersion.

The apparent triviality of *Leptospira* risk factors in the elderly was also noted in a previous study conducted in Germany. Residential exposure factors were 3–4 times as frequent as recreational and professional exposures in people >60 years of age [19].

This study has some limitations: (i) the number of cases was limited and probably underestimated because we included only cases managed in the 3 hospitals, (ii) the small number of cases was insufficient for robust statistical comparisons between elderly and younger patients, and (iii) no standardized survey was followed to collect exposure factors by physicians. However, we can hypothesize that the gathering of exposure factors during the infectious disease follow-up consultation was satisfying.

CONCLUSIONS

This study highlighted that the elderly may represent a significant proportion of leptospirosis cases diagnosed in rural areas of a temperate country with relatively unremarkable epidemiological risk factors. Our results are limited by small case

numbers but somewhat emphasize that we should perhaps reconsider the definition of exposed patients and thus have a greater index of clinical suspicion in such patients.

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