National Surveillance of Legioniarnes’ Disease, China, 2014–2016

Tian Qin, Hongyu Ren, Dongke Chen, Haijian Zhou, Luxi Jiang, Duorong Wu, Jilu Shen, Fengyan Pei

Author affiliations: Chinese Center for Disease Control and Prevention, Beijing, China (T. Qin, H. Ren, H. Zhou, L. Jiang); State Key Laboratory for Infectious Disease Prevention and Control, Beijing (T. Qin, H. Zhou); Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases, Hangzhou, China (T. Qin, H. Zhou); Beijing Hospital, Beijing (D. Chen); Haikou People’s Hospital, Haikou, China (D. Wu); The Fourth Affiliate Hospital of Anhui Medical University, Hefei, China (J. Shen); Jinan Central Hospital, Jinan, China (F. Pei)

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We report national surveillance of Legioniarnes’ disease in China. Urine samples from 11 (3.85%) of 286 patients with severe pneumonia of unknown cause were positive for the Legionella pneumophila serogroup 1 antigen. We isolated Legionella strains from 7 patients. Improved diagnostic testing is needed for this underestimated disease in China.

Legioniarnes’ disease is a form of atypical pneumonia caused by bacteria of the genus Legionella. L. pneumophila serogroup 1 causes most Legioniarnes’ disease (1). Although Legioniarnes’ disease has been reported worldwide, only a few sporadic cases have been reported in China (2). Investigation of Legionella infection is urgently needed in China to describe its prevalence and epidemiology.

During 2014–2016, we conducted surveillance of Legioniarnes’ disease in 18 hospitals in China under the coordination of the Chinese Center for Disease Control and Prevention (China CDC). The Ethical Committee of the National Institute for Communicable Disease Control and Prevention, China CDC (ICDC-2014009), provided ethics approval for this study. The distribution of the 18 hospitals accounted for all regions of China (Appendix Figure 1, https://wwwnc.cdc.gov/EID/article/25/6/17-1431-App1.pdf). The hospital’s clinical diagnostic level, pneumonia pathogen detection level, and degree of cooperation with this investigation were also considered. All 18 hospitals are level 3 first-class general hospitals, representing the highest level of healthcare in their cities.

The 3,132 severe pneumonia cases were defined and detected according to the Guidelines for the Diagnosis and Treatment of Community-Acquired Pneumonia in Adults in China (2016 edition) (3) (Appendix Figure 2). Among them, 1,885 cases were diagnosed as noninfectious or nonbacterial infections, and 771 cases were diagnosed as bacterial infections other than Legionella by daily testing, including bacterial culture, viral nucleic acid detection, and immunologic detection in hospital laboratories. Patients with the remaining 476 cases of pneumonia with unknown cause were enrolled and tested for Legionella infection. Among them, 190 left the hospital, died, or were unwilling to cooperate. Thus, urine samples were collected from 286 patients and sent for urine antigen detection for L. pneumophila serogroup 1 (BinaxNow, https://www.alere.com) (Appendix Figure 2). Sputum samples were obtained from 211 of the 286 patients and sent to the laboratory of China CDC (Beijing, China) for Legionella culture, which used both buffered charcoal yeast extract agar and buffered charcoal yeast extract agar supplemented with Legionella GVPC (glycine, vancomycin, polymyxin, cycloheximide) Selective Supplement (Oxoid, https://www.thermofisher.com). Eleven (3.85%) of the 286 urine samples yielded positive results, and we isolated Legionella strains from 7 of them. All 7 L. pneumophila cultures were obtained from the same patients who tested positive by urine antigen detection. The positive rate of Legionella culture was 3.32% (7/211). All isolated Legionella strains were L. pneumophila serogroup 1.

All 11 urine antigen–positive patients were male, 23–76 years of age (average 56 years) (Table). They

<table>
<thead>
<tr>
<th>Patient</th>
<th>ID</th>
<th>Age, y</th>
<th>Date of diagnosis</th>
<th>Onset city</th>
<th>Underlying illness</th>
<th>Length of hospitalization, d</th>
<th>ICU admission</th>
<th>Outcome</th>
<th>SBT type of isolates</th>
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<td>22</td>
<td>No</td>
<td>Recovered</td>
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*All patients were male. ICU, intensive care unit; ID, identification; NS, no strain isolated; SBT, sequence-based typing; ST, sequence type.

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All 11 urine antigen–positive patients were male, 23–76 years of age (average 56 years) (Table).
resided in 7 cities, and most (9/11) cases were observed in summer (in China, July–September). All were hospitalized; length of hospitalization ranged from 7 to 93 days. Six were admitted to an intensive care unit. The case-fatality rate was 18.2% (2/11) after antimicrobial and supportive therapies.

We performed antimicrobial susceptibility testing using E-test strips (bioMérieux, https://www.biomerieux.com). According to the epidemiologic cutoff values of the European Committee on Antimicrobial Susceptibility Testing (4) or as determined by a previous study (5), all 7 strains were susceptible to fluoroquinolones, macrolides, and rifampin but not to cefuroxime (Appendix Table 1).

We subtyped the 7 strains using pulsed-field gel electrophoresis (6) and sequence-based typing (SBT) (7). All 7 strains were identified as different pulsed-field gel electrophoresis and SBT types (Appendix Figure 3). Submission to the European Working Group on Legionella Infections L. pneumophila SBT database (http://www.ewgli.org) identified 4 profiles as new; these profiles were assigned new sequence types (STs) (ST2344, ST2366, ST2368, and ST2369). Querying the European Working Group on Legionella Infections database showed that 2 STs (ST42 and ST59) contained strains that are distributed worldwide (Appendix Table 2). We also tested the 7 strains for their intracellular growth ability using previously described methods (8), and all showed high intracellular growth in J774 cells, suggesting that these strains are pathogenic (Appendix Figure 4).

Many Legionnaires’ disease cases are reported worldwide, including hundreds in the United States and Europe each year (8,9). However, no data are available on the prevalence of Legionnaires’ disease in China. In China, no Legionella urine antigen test reagent has been approved for clinical diagnosis and few hospitals conduct Legionella culture, so in clinical laboratories, Legionnaires’ disease is difficult to detect; therefore, diagnosis is based mainly on signs and symptoms. Legionnaires’ disease is usually diagnosed as unexplained pneumonia.

The results of this study showed that L. pneumophila is an important pathogen for pneumonia patients in China, and current diagnostic methods in China may misdiagnose or overlook it. We suggest establishment of a routine monitoring reporting system to investigate the prevalence and epidemiology of Legionnaires’ disease in China.

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Address for correspondence: Tian Qin, National Institute for Communicable Disease Control and Prevention, Chinese CDC, Beijing. Her research interests are surveillance of Legionnaires’ disease, and the molecular subtyping and genomic diversity of Legionella.

References