



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.e-jmii.com

Original Article

Investigation of a cluster of Legionnaires' disease during the outbreak of coronavirus disease 2019 pandemic in northeastern Taiwan, June 2021

Jung-Jr Ye ^{a,b,*}, Jun-Yuan Zheng ^a, Ya-Hsuan Chen ^c,
Ya-Ling Kao ^c, Yu-Chin Kao ^c, Shao-Wen Chao ^d

^a Division of Infectious Diseases, Department of Internal Medicine, Chang Gung Memorial Hospital at Kee-Lung, Kee-Lung, Taiwan

^b College of Medicine, Chang Gung University, Taoyuan, Taiwan

^c Hospital Infection Control Team, Chang Gung Memorial Hospital at Kee-Lung, Kee-Lung, Taiwan

^d Department of Laboratory Medicine, Chang Gung Memorial Hospital at Kee-Lung, Kee-Lung, Taiwan

Received 18 November 2021; received in revised form 25 March 2022; accepted 16 April 2022

Available online ■ ■ ■

KEYWORDS

Legionnaires' disease;
Pneumonia;
COVID-19

Abstract *Purpose:* To describe the investigation and intervention of a cluster of Legionnaires' disease detected during the outbreak of coronavirus disease 2019 (COVID-19) pandemic. *Methods:* From June 7 to 22, 2021, 15 cases in the neighborhood near our hospital were detected. Information about residence, workplace, hospital visit, and potential exposures was collected. Sampling and decontamination were performed for potential sources. *Results:* All 15 patients had pneumonia when visiting the emergency room with negative COVID-19 test results. Most patients were male (73.3%) with the mean age of 65.7 years. The most common comorbidities were diabetes mellitus (40.0%) and hypertension (40%). The most common symptom was fever (93.3%). Two (13.3%) patients needed mechanical ventilators. Fever subsided within 2 days of treatment for most cases (85.7%). Five cases had exposure history at our hospital, and the other 10 lived or worked in the area within 2 km of our hospital, mostly in buildings A and B. Water sampling was carried out for our hospital, buildings A and B; one water sample from a cooling tower in our hospital cultured positive for *Legionella* bacteria. Early testing and treatment for suspected cases were carried out for the outbreak, and all cases were discharged with pneumonia resolution.

* Corresponding author. 12F., No.222, Maijin Rd., Anle Dist., Keelung City, 204, Taiwan. Fax: +886 2 24335342.

E-mail addresses: loyalwise@gmail.com (J.-J. Ye), jercheng4@hotmail.com (J.-Y. Zheng), mllm@cgmh.org.tw (Y.-H. Chen), yalinkao@adm.cgmh.org.tw (Y.-L. Kao), yuchin@cgmh.org.tw (Y.-C. Kao), shaowen@cgmh.org.tw (S.-W. Chao).

<https://doi.org/10.1016/j.jmii.2022.04.008>

1684-1182/Copyright © 2022, Taiwan Society of Microbiology. Published by Elsevier Taiwan LLC. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Conclusion: This was a community outbreak of Legionnaires' disease near our hospital. COVID-19 tests were repeated frequently before testing for Legionnaires' disease during the COVID-19 pandemic. Early recognition of Legionnaires' disease and timely treatment improved outcome. Copyright © 2022, Taiwan Society of Microbiology. Published by Elsevier Taiwan LLC. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

Legionnaires' disease was first identified in 1976 in a pneumonia outbreak among American Legion members attending their annual meeting in Philadelphia.¹ Infection occurs through inhalation of aerosols containing *Legionella* bacteria.² The most frequently identified species isolated from patients with Legionnaires' disease was *Legionella pneumophila* serogroup 1, which has been recognized as an important cause of both hospital and community-acquired pneumonia.² A prior epidemiological study of *L. pneumophila* infection in Taiwan reported an incidence rate of 4.7% among pneumonia patients.³ In a retrospective study of Legionnaires' disease in a 1200-bed tertiary hospital in southern Taiwan, 61 cases were identified over a 9-year period. Among them, 30 (49.2%) and 20 (32.8%) had healthcare-associated and community-acquired pneumonia, respectively, including 11 (18.0%) caregivers.⁴

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first identified in Wuhan, China, in December 2019.⁵ The disease rapidly became an ongoing pandemic crisis worldwide.⁶ The pandemic had a smaller impact in Taiwan in 2020 than in most other countries; however, an outbreak in northern Taiwan occurred in May 2021, resulting in more than 15,000 confirmed cases with more than 800 deaths within the following three months.

In June 2021, we detected a cluster of Legionnaires' disease during the COVID-19 pandemic. From June 7 to 22, 2021, 15 Legionnaires' disease cases were detected in individuals living or working in the neighborhood near our hospital, including two hospital staff members. This number was three times that observed in our hospital in the previous 3 years combined, including 2 cases, 2 cases, and 1 case detected in 2018, 2019, and 2020, respectively (JJ Ye, unpublished data). This study aimed to determine whether this cluster was a nosocomial or community outbreak, investigate the potential sources, and analyze the clinical features, control measures and outcomes.

Methods

Study design, setting and patients

This retrospective study was conducted at Chang Gung Memorial Hospital (CGMH)-Keelung branch, which is a 1100-bed regional teaching hospital providing both primary and tertiary health care in northeastern Taiwan. The study protocol was approved by the Institutional Review Board of CGMH-Keelung branch (Number: 202101475B0). The ethics

committee granted a waiver for informed consent to be obtained from patients because the existing medical data and investigation reports were analyzed anonymously and maintained with confidentiality.

Legionnaires' disease was defined as a new or progressive pulmonary infiltrate on chest radiography, along with the presence of symptoms and signs of lower respiratory tract infection, and a positive result for the urinary *Legionella* antigen test.⁴ A commercial urine antigen test (Abbott BinaxNOW *Legionella* urinary antigen test kit; Abbott Laboratories, Irvine, CA, USA) was used to detect the *L. pneumophila* serogroup 1 soluble antigen. Patients' medical records were reviewed for demographic and clinical data, including comorbidities, symptoms, clinical course, laboratory data, oxygen use, treatment, and outcomes. Delayed treatment was defined as initiation of antibiotic treatment with anti-*Legionella* activity after the second day of hospitalization.

Epidemiological investigations

The epidemiological investigations were performed by the Infection Control Team of CGMH-Keelung as soon as possible after a diagnosis was confirmed. Each patient was interviewed by phone to collect information about residence, profession, workplace, and potential exposures (including travel, hospital visit, spa/pool, fountains, grocery stores, drinking water supply issues, car washes, and aerosol-generating devices or equipment) within 14 days prior to symptom onset. The data of urinary *Legionella* antigen test in the previous 5 years, and the number of confirmed COVID-19 cases with positive reverse transcription-polymerase chain reaction (RT-PCR) test based on nasopharyngeal swabs in our hospital from April to July 2021 were collected and analyzed.

Environmental investigations

Routine testing for *Legionella* bacteria with culture and free residual chlorine in water was performed in our hospital every six months for cooling towers and the water supply system in transplant wards, and annually for other water supply systems. A 300 ml water sample was collected from selected sites for culture and testing. The most recent routine testing prior to the reported Legionnaires' disease outbreak was performed in April 2020, and all water samples were negative for *Legionella* bacteria. To investigate potential sources of the reported cluster of Legionnaires' disease, water sampling was carried out by the Infection Control Team of CGMH-Keelung for our hospital and administrative office (on second floor of building A) on June 16,

2021, and by the Health Department, Keelung City, for other places on June 21, 25, and 30, 2021. Twenty samples collected in our hospital and administrative office included 8 water samples from water cooling towers, 4 from cisterns, 4 from faucets in toilets, 2 from water dispensers, and 2 swab samples from air conditioner vents. Thirty-six water samples from building A included 2 from water cooling towers, 17 from cisterns; 9 from garden ponds, fountains, and sprinklers; 5 from bathrooms and 3 from water dispensers. Four water samples from building B included 1 from a garden pond and 3 from cisterns. Each sample was cultured on the media of buffered charcoal yeast extract (BCYE) agar. Colonies suspected to be *Legionella* were incubated on BCYE agar with L-cysteine.⁷ Microscopic examination was used to verify suspect colonies. Identification of isolates was performed using Matrix-assisted laser desorption/ionization–time-of-flight mass spectrometry (MALDI-TOF MS, Autoflex II; Bruker Daltonics, Germany) and MALDI Biotyper 3.1 database system. Samples from our hospital and administrative office were also tested with RT-PCR targeting major intrinsic protein (MIP) gene.

Results

Clinical presentation and outcomes

All patients presented with pneumonia on chest radiograph when arriving at the emergency room (ER), and were then admitted to wards for treatment. Most patients were male (73.3%) with mean age 65.7 years. The most common concomitant diseases were diabetes mellitus (40.0%) and hypertension (40%). Fourteen patients had no smoking history and one had quit smoking years earlier. The most common symptom was fever (93.3%), followed by cough (66.7%) and gastrointestinal upset (26.7%) (Table 3). The days from symptom onset to hospital visit ranged from 1 to 5 days, with mean 2.3 days (Tables 1 and 3). Five (33.3%) patients had bilateral pneumonia and 13 patients had mean C-reactive protein (CRP) of 226.0 mg/L. Other abnormal laboratory data included hyponatremia (60%), elevated liver enzymes (40%) and leukocytosis (40%). Three patients used O2 masks and two used mechanical ventilators (Table 3). The days from hospitalization to diagnosis ranged from 1 to 9 days with mean 3.5 days (Tables 2 and 3). One patient with 9 days until diagnosis had end-stage renal disease with insufficient urine for urinary antigen test. Thirteen cases were treated with levofloxacin, two received azithromycin for pneumonia treatment, and four (26.7%) received delayed treatment. Fever subsided within two days of treatment for most cases (12/14, 85.7%) and all patients were discharged with resolution of pneumonia (Table 3). The hospital stays ranged from three to 58 days with mean 13.7 days (Tables 2 and 3). All cases had at least two negative COVID-19 RT-PCR test results based on nasopharyngeal swabs. Nine cases had sputum cultures and all showed growth of normal flora (Table 2).

Epidemiological investigations

Symptom onset date of cases are shown in Fig. 1. The dates of diagnosis are shown in Fig. 2. First case was

detected on June 7, 2021 and the last case on June 22, 2021. During this period, the positive rate of urinary *Legionella* antigen test was 19.2% (15/78, Fig. 2). From 2016 to 2020, 8 positive cases were detected among 372 patients who were tested for urinary *Legionella* antigen in our hospital (2.2%). Ten patients (66.7%) lived or worked in buildings A and B, located within 200 and 100 m from our hospital, respectively (Fig. 3). Among them, three patients (cases 1, 11, 12) living in building A, and five patients (cases 2, 4, 5, 9, 10) living or working in building B, had no exposure history in our hospital within 14 days prior to symptom onset. The other two patients (cases 3, 7) were our staff members working at the administrative office on the second floor of building A and in our hospital. Three patients (cases 6, 13, 14) did not live near our hospital, but had regular hemodialysis or outpatient clinic visits within 14 days in our hospital. Two patients (cases 8, 15) had no hospital visit history and lived in places within 750 m and 1800 m from our hospital. In conclusion, 5 cases had exposure history in our hospital, and the other 10 cases lived or worked within two kilometers from our hospital (Fig. 3). The numbers of confirmed COVID-19 cases were 0, 67, 45, and 8 in April, May, June, and July 2021, respectively. The COVID-19 outbreak occurred in May 2021, and the pandemic was controlled gradually within the following months.

Environmental investigations, and interventions

Three water samples from cooling towers in our hospital had positive *Legionella* PCR tests, and one had a positive culture with 130 colony-forming units/liter of *Legionella* spp. One water sample from the cooling tower in our administration office in building A had positive *Legionella* PCR test with no *Legionella* bacteria growth on culture. The screening of Legionnaires' disease with urine antigen test for all pneumonia patients in the ER or wards was performed when the outbreak of Legionnaires' disease was first observed (3 cases on June 15, 2021, Fig. 2). We also advised clinical physicians, in online conferences or meetings, to administer levofloxacin or azithromycin early for suspected cases before Legionnaires' disease was confirmed. Decontamination was carried out for the water cooling towers and cisterns in our hospital on June 17, 2021, and for water systems in other buildings later. The cooling towers were shut down and sodium hypochlorite was added to keep free residual chlorine of at least 5–15 mg/L for at least 1 h. After the disinfection period, the cooling tower water was drained into waste disposal, and all accessible system equipment was physically cleaned. Then the system was refilled with clean water, the recirculating pump was switched on, and sodium hypochlorite was added again. The system was drained after the disinfection period and refilled. Finally, we reinstated comprehensive effective water treatment, including use of biocide, and returned the control equipment to normal operation. *Legionella* testing with culture was performed for cooling towers after decontamination, and the results were uniformly negative. From June 23 to 30, 2021, 49 patients were tested for Legionnaires' disease, and all results were negative (Fig. 2).

Table 1 Demographic and clinical characteristics of each case.

Case	Age (y)	Sex	Underlying diseases	Symptoms	Onset to ER (d)	Chest radiograph findings	Other abnormal laboratory data (blood sample)	Oxygen use
1	67	Male	DM, hypertension, gout, hypothyroidism	Fever, cough, conscious change	2	RUL consolidation	Creatinine: 1.82 mg/dL Sodium: 132 meq/L Platelet count: 88000/uL	Nasal cannula
2	63	Male	Old stroke, CML, Hypertension, hyperlipidemia	Fever	2	LUL, LLL, RLL consolidation	CRP: 201 mg/L AST:108 U/L Total bilirubin: 1.4 mg/dL Sodium: 126 meq/L WBC: 15300/uL	Mechanical ventilator
3	51	Male	DM, hyperlipidemia	Fever, headache, general soreness	3	RUL, LLL consolidation	CRP: 342 mg/L Total bilirubin: 1.7 mg/dL ALT: 122 U/L WBC: 13100/uL	Nasal cannula
4	52	Male	DM, hypertension	Fever, diarrhea, vomiting	3	RUL, RLL consolidation	CRP: 272 mg/L Creatinine: 2.49 mg/dL Sodium: 132 meq/L WBC: 14500/uL	Simple mask
5	73	Male	None	Fever, cough	3	RUL, LUL consolidation	CRP: 300 mg/L Creatinine: 4.76 mg/dL Sodium: 132 meq/L WBC: 13900/uL Platelet count: 104000/uL	Mechanical ventilator
6	45	Male	DM, ESRD, Hypertension	Fever, vomiting	1	Bilateral lung infiltration	CRP: 149 mg/L Sodium: 124 meq/L WBC: 12200/uL	Simple mask
7	54	Male	Hyperlipidemia	Fever, diarrhea, vomiting	3	LLL consolidation	CRP: 229 mg/L ALT: 145 U/L Sodium: 131 meq/L	Nasal cannula
8	65	Female	None	Fever, cough	5	RLL consolidation	CRP: 338 mg/L ALT: 89 U/L	Nasal cannula
9	66	Female	DM	Cough, dyspnea	1	RUL, RLL, LLL consolidation	ALT: 86 U/L WBC: 12100/uL	Nasal cannula
10	89	Male	Hypertension	Fever, cough, sore throat	4	RUL, RLL consolidation	CRP: 170 mg/L Creatinine: 1.58 mg/dL	None
11	91	Male	Prostate cancer	Fever, cough	2	RUL consolidation	CRP: 227 mg/L Creatinine: 1.58 mg/dL Sodium: 132 meq/L Platelet count: 123000/uL	Nasal cannula
12	61	Female	Hyperlipidemia	Fever, epigastric pain,	1	RLL consolidation	CRP: 146 mg/L Sodium: 128	Nasal cannula

Table 1 (continued)

Case	Age (y)	Sex	Underlying diseases	Symptoms	Onset to ER (d)	Chest radiograph findings	Other abnormal laboratory data (blood sample)	Oxygen use
13	56	Male	DM	cough Fever, cough	2	LUL consolidation	meq/L CRP: 326 mg/L Sodium: 125 meq/L	Nasal cannula
14	81	Male	Hypertension, CAD	Fever, cough, sore throat	1	LUL consolidation	CRP: 27 mg/L	Simple mask
15	72	Female	Hand tremor	Fever, cough	1	RLL consolidation	CRP: 211 mg/L ALT: 63 U/L	Nasal cannula

Abbreviations: ER, emergency room; DM, diabetes mellitus; RUL, right upper lobe; CML, chronic myeloid leukemia; LUL, left upper lobe; LLL, left lower lobe; RLL, right lower lobe; CRP, C-reactive protein; AST, aspartate aminotransferase; WBC, white blood cell count; ESRD, end stage renal disease; CAD, coronary artery disease.

Table 2 Diagnosis, treatment, and outcome of each case.

case	Hospitalization to diagnosis (d)	Other microbiological tests	Treatment initiation	Regimens	Treatment to defervescence (d)	Days of hospitalization	Outcome	Pneumonia follow-up
1	2	COVID-19 (-) × 2 Sputum culture: normal flora	Day 1	Levofloxacin	1	21	Discharge	Resolution
2	7	COVID-19 (-) × 2 Sputum culture: normal flora Sputum PJP PCR test (-) Serum <i>Aspergillus</i> antigen (-)	Day 3	Levofloxacin	3	21	Discharge	Resolution
3	5	COVID-19 (-) × 3	Day 1	Azithromycin	1	7	Discharge	Resolution
4	5	COVID-19 (-) × 2 Influenza rapid antigen (-)	Day 4	Levofloxacin	5	14	Discharge	Resolution
5	4	COVID-19 (-) × 2 Sputum culture: normal flora	Day 2	Levofloxacin	1	58	Discharge	Resolution
6	9	COVID-19 (-) × 3 Serum Cryptococcal antigen (-)	Day 5	Levofloxacin	2	11	Discharge	Resolution
7	1	COVID-19 (-) × 3 Influenza rapid	Day 2	Levofloxacin	2	8	Discharge	Resolution

(continued on next page)

Table 2 (continued)

case	Hospitalization to diagnosis (d)	Other microbiological tests	Treatment initiation	Regimens	Treatment to defervescence (d)	Days of hospitalization	Outcome	Pneumonia follow-up
8	1	antigen (–) COVID-19 (–) × 3	Day 1	Levofloxacin	1	7	Discharge	Resolution
9	3	COVID-19 (–) × 3 Sputum culture: normal flora	Day 1	Levofloxacin	.	7	Discharge	Resolution
10	2	COVID-19 (–) × 3 Sputum culture: normal flora	Day 1	Azithromycin	1	3	Discharge	Resolution
11	5	COVID-19 (–) × 3 Sputum culture: normal flora	Day 5	Levofloxacin	1	16	Discharge	Resolution
12	2	COVID-19 (–) × 2	Day 2	Levofloxacin	1	6	Discharge	Resolution
13	4	COVID-19 (–) × 2 Sputum culture: normal flora	Day 1	Levofloxacin	1	12	Discharge	Resolution
14	2	COVID-19 (–) × 2 Sputum culture: normal flora	Day 1	Levofloxacin	1	11	Discharge	Resolution
15	1	COVID-19 (–) × 2 Sputum culture: normal flora	Day 1	Levofloxacin	1	3	Discharge	Resolution

Abbreviations: COVID-19, Coronavirus disease 2019; PJP, *Pneumocystis Jiroveci* pneumonia; PCR, polymerase chain reaction.

Discussion

This study reports a 15-case cluster of Legionnaires' disease occurring over a 16-day period in June 2021 during the COVID-19 pandemic. The case numbers and positive rate of urinary *Legionella* antigen tests significantly exceeded those noted during ordinary times. All patients diagnosed with Legionnaires' disease had pneumonia before admission. Some cases were hospital staff members or regular patients, and most patients lived or worked within 2 km of our hospital without exposure history in our hospital within 14 days prior to symptom onset. Based on the sharp surge in Legionnaires' cases, the geographic clustering, and the investigation of environmental exposures, a community outbreak was determined.

Some previous community outbreaks of Legionnaires' disease were associated with water cooling tower systems,^{8–10} which may transmit bacteria for miles¹⁰;

however, a definitive infection source is not always found.^{11–13} A water sample from a cooling tower in our hospital showed growth of *Legionella* bacteria. Although most patients had no exposure history in our hospital and had pneumonia outside the hospital, the contaminated water system was a probable source of the outbreak. The outbreak of Legionnaires' disease occurred during the COVID-19 pandemic, and the strict control policy implemented for COVID-19 made the community outbreak of Legionnaires' disease unusual. In mid-May 2021, the Taiwan government ordered that all civilians must wear face masks when in any public space, including outdoors, and all swimming pools, water parks, spas, or entertainment places were ordered to be closed. Several reports mentioned that Legionnaires' disease cases may increase in recently reopened buildings during the COVID-19 pandemic, probably due to growth of *Legionella* in low-flow water pipes

Table 3 Clinical characteristics, treatment, and outcomes of the 15 cases.

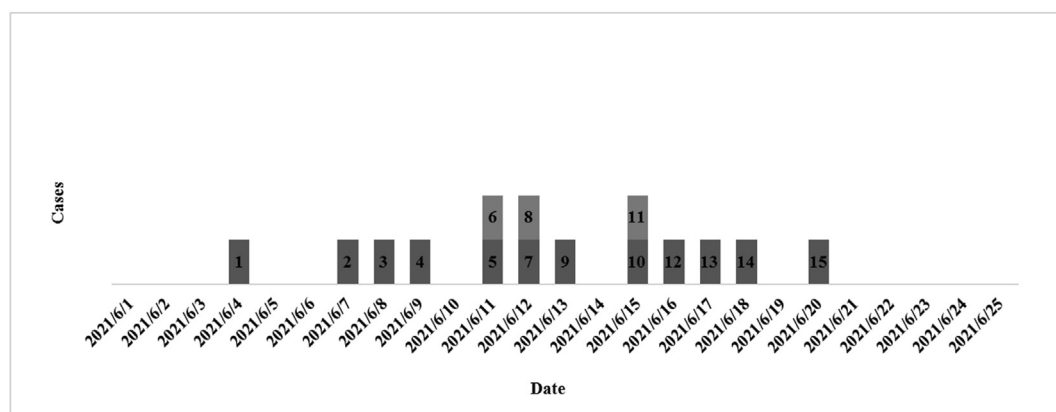
Characteristics	Value ^a
Demographic parameters	
Age, years	65.7 ± 13.6
Male/Female	11/4
Underlying diseases	
Diabetes mellitus	6 (40.0)
Hypertension	6 (40.0)
Hyperlipidemia	4 (26.7)
Malignancy	2 (13.3)
End stage renal disease	1 (6.7)
Symptoms	
Fever	14 (93.3)
Cough	10 (66.7)
Gastrointestinal upset	4 (26.7)
Onset to visit hospital, days	2.3 ± 1.2
Clinical conditions	
Bilateral pneumonia	5 (33.3)
C-reactive protein, mg/L (n = 13)	226.0 ± 91.1
Leukocytosis	6 (40.0)
Thrombocytopenia	3 (20.0)
Hyponatremia	9 (60.0)
Acute renal insufficiency	5 (33.3)
Increasing liver enzymes	6 (40.0)
Oxygen use	
Nasal cannula	9 (60.0)
Simple mask	3 (20.0)
Mechanical ventilator	2 (13.3)
Hospitalization to diagnosis, days	3.5 ± 2.4
Treatment	
Delayed treatment	4 (26.7)
Levofloxacin treatment	13 (86.7)
Treatment to defervescence >2 days	2 (13.3)
Days of hospitalization	13.7 ± 13.5
Outcomes	
Discharge	15 (100.0)
Resolution of pneumonia	15 (100.0)

^a Categorical data are no. (%) of subject, continuous data are expressed as means ± standard deviations.

with inadequate disinfection.^{14–16} However, this was not the situation of our cluster. After decontamination of the water cooling towers and cisterns in the potential sources, no additional cases were reported.

Clinical manifestations may be indistinguishable between COVID-19 and Legionnaires' disease. During the COVID-19 pandemic, all pneumonia patients must be admitted via ER to isolated wards, and tested for COVID-19 repeatedly. The American Thoracic Society (ATS) and the Infectious Diseases Society of America (IDSA) guidelines for community-acquired pneumonia recommend that only severe cases be tested with *Legionella* urinary antigen test or those with epidemiological indications,¹⁷ and our first six cases required more days for diagnosis and initiation of treatment for Legionnaires' disease than the cases that followed. Cases 2 and 5 needed mechanical ventilator use, and Legionnaires' disease was tested and confirmed after respiratory failure. When the outbreak was observed, we informed clinicians at ER and wards to perform *Legionella* urinary antigen tests for all pneumonia patients, and this helped to shorten the time for diagnosis. Early empiric use of fluoroquinolones or macrolides to cover suspected Legionnaires' cases was also carried out based on ATS/IDSA guidelines,¹⁷ and most cases detected later had adequate regimens on the first or second hospital days. Finally, all 15 cases were discharged with pneumonia resolution.

In prior studies of community-acquired Legionnaires' disease in Taiwan, the mortality rates ranged from 9.8% to 24.1%, and ventilator use rates ranged from 18.4% to 50%.^{4,18–21} The characteristics, comorbidities, and initial presentations of our cases were similar to those reported in previous studies. Most patients were older adult males with underlying diseases, including diabetes mellitus, hypertension, or malignancy. Fever, cough, and gastrointestinal upset were common, with abnormal laboratory findings, including leukocytosis, hyponatremia, increasing liver enzymes, and high CRP levels. Smoking history was common in prior studies^{4,18–21}; however, only one case among those in the present study had smoking history. Among studies in Taiwan, about 70% of patients had bilateral pneumonia,^{20,21} but other studies showed that the most common pattern was patchy, unilobar infiltrate progressing to consolidation of the lung tissue.^{22,23}

**Figure 1.** Symptom onset date of the 15 cases of Legionnaires' disease.

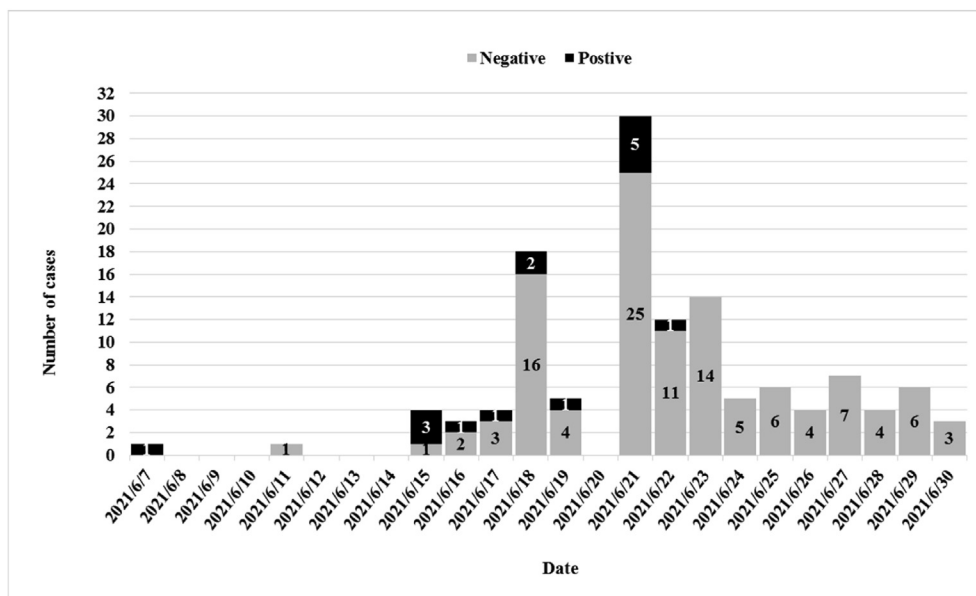


Figure 2. Cases tested with urinary *Legionella* antigen test from 7 to 30 June 2021, and the results.

Compared with other studies in Taiwan, patients in the present study had lower rates of mortality and ventilator use, and most cases (10/15, 66.7%) had unilateral pneumonia. With proactive screening for Legionnaires' disease during the outbreak, more cases may be detected with minor severity or at an early stage than prior studies in Taiwan. Besides, most of our cases (11/15, 73.3%) received azithromycin or levofloxacin on the first or second hospital day, and a prior study had a 24-h delayed treatment rate of 50% (16/32), which was associated with a higher proportion (11/16 [68.7%]) of intensive care unit admission and mechanical ventilation than among patients with adequate initiation of treatment (5/16 [31.2%]).²¹

Legionnaires' disease accounts for 2%–9% of pneumonia patients^{3,24}; however, the exact incidence worldwide may be underestimated mainly because of underdiagnosis and under-reporting.^{2,25} Detection of clusters of Legionnaires'

disease needs clinicians' awareness and understanding of the clinical characteristics of Legionnaires' disease, sound disease reporting, notification and investigation systems. Severe *L. pneumophila* pneumonia is associated with high rates of mortality and intensive care unit admission.^{4,18–21,26} Early, targeted therapy improves outcomes,^{21,27} and timely investigation and intervention for potential sources limit the scale and recurrence of outbreaks.

This study has several limitations. First, blood and respiratory samples were not collected from these cases for culture and isolation, and serogroup or sequence-based typing was not performed. Therefore, we do not know if these cases were caused by the same strain, or whether the strain detected in the cooling tower in our hospital was at cause. Another important challenge was the lack of comprehensive investigation of potential sources. Water samples were only collected from our hospital and buildings A and B, and other public and private construction sites or water systems in this area were not investigated. As a result, some potential sources may have been overlooked.

Conclusions

In conclusion, this study examined and reported a community outbreak of Legionnaires' disease in the neighborhood around our hospital. COVID-19 testing was repeated frequently before testing for Legionnaires' disease during the COVID-19 pandemic. Early recognition of Legionnaires' disease, detecting the outbreak, and providing timely treatment and intervention improved the individual and overall outcomes.

Declaration of competing interest

The authors declare that they have no competing interests. No funding sources had any role in the design or conduct of the study; collection, management, analysis, or

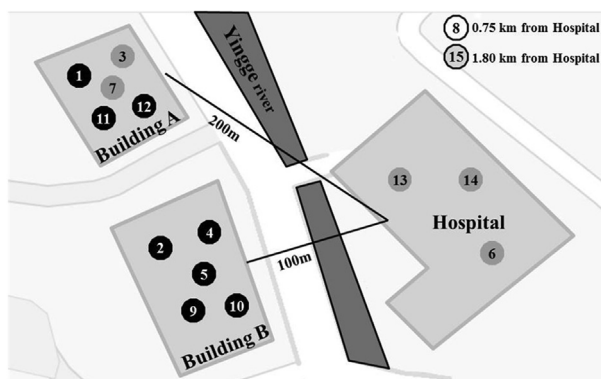


Figure 3. The cases of Legionnaires' disease and their locations. a Case 3, 7 were our staff members and case 6, 13, 14 were our regular patients. b Case 1, 11, 12 lived or worked in building A and case 2, 4, 5, 9, 10 in build B, with no visit history of our hospital in prior 14 days. c Case 8, 15 had no visit history of our hospital in prior 14 days.

interpretation of the data; or preparation, review, or approval of the manuscript.

Acknowledgements

None.

References

- Fraser DW, Tsai TR, Orenstein W, Parkin WE, Beecham HJ, Sharrar RG, et al. Legionnaires' disease: description of an epidemic of pneumonia. *N Engl J Med* 1977;297(22):1189–97.
- Cunha BA, Burillo A, Bouza E. Legionnaires' disease. *Lancet* 2016;387(10016):376–85.
- Su HP, Tseng LR, Chou CY, Chung TC, Pan TM. Legionella pneumophila infection in the Taiwan area. *J Infect Chemother* 2005;11(5):244–9.
- Hung T-L, Li M-C, Wang L-R, Liu C-C, Li C-W, Chen P-L, et al. Legionnaires' disease at a medical center in southern Taiwan. *J Microbiol Immunol Infect* 2018;51(3):352–8.
- Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395(10223):497–506.
- Pollard CA, Morran MP, Nestor-Kalinowski AL. The COVID-19 pandemic: a global health crisis. *Physiol Genom* 2020;52(11):549–57.
- Feeley JC, Gibson RJ, Gorman GW, Langford NC, Rasheed JK, Mackel DC, et al. Charcoal-yeast extract agar: primary isolation medium for Legionella pneumophila. *J Clin Microbiol* 1979;10(4):437–41.
- Weiss D, Boyd C, Rakeman JL, Greene SK, Fitzhenry R, McProud T, et al. A large community outbreak of Legionnaires' disease associated with a cooling tower in New York City. *Publ Health Rep* 2017;132(2):241–50. 2015.
- Sabria M, Alvarez J, Dominguez A, Pedrol A, Sauca G, Salleras L, et al. A community outbreak of Legionnaires' disease: evidence of a cooling tower as the source. *Clin Microbiol Infect* 2006;12(7):642–7.
- Addiss DG, Davis JP, Laventure M, Wand PJ, Hutchmson MA, McKINNEY RM. COMMUNITY-ACQUIRED legionnaires' disease associated with a cooling tower: evidence for longer-distance transport OF LEGIONELLA pneumophila. *Am J Epidemiol* 1989;130(3):557–68.
- McClung RP, Roth DM, Vigar M, Roberts VA, Kahler AM, Cooley LA, et al. Waterborne disease outbreaks associated with environmental and undetermined exposures to water—United States, 2013–2014. *MMWR Morb Mortal Wkly Rep* 2017;66(44):1222.
- Lock K, Millett C, Heathcock R, Joseph C, Harrison T, Lee J, et al. Public health and economic costs of investigating a suspected outbreak of Legionnaires' disease. *Epidemiol Infect* 2008;136(10):1306–14.
- Lee S, Lee J. *Outbreak investigations and identification of Legionella in contaminated water*. Legionella: Springer; 2013. p. 87–118.
- Proctor CR, Rhoads WJ, Keane T, Salehi M, Hamilton K, Pieper KJ, et al. Considerations for large building water quality after extended stagnation. *AWWA water science* 2020;2(4):e1186.
- Garrison LE, Kunz JM, Cooley LA, Moore MR, Lucas C, Schrag S, et al. *Vital signs: deficiencies in environmental control identified in outbreaks of Legionnaires' disease—north America, 2000–2014*. Wiley Online Library; 2016.
- Cassell K, Davis JL, Berkelman R. Legionnaires' disease in the time of COVID-19. *Pneumonia (Nathan)* 2021;13(1):2.
- Metlay JP, Waterer GW, Long AC, Anzueto A, Brozek J, Crothers K, et al. Diagnosis and treatment of adults with community-acquired pneumonia. An official clinical practice guideline of the American Thoracic Society and Infectious Diseases Society of America. *Am J Respir Crit Care Med* 2019;200(7):e45–67.
- Lin S, Chang S, Yea C, Pan T, Hsieh W. Clinical features of Legionellosis: experience of 21 cases at a teaching hospital in Taiwan. *J Infect Dis Soc ROC* 1996;(7):29–35.
- Lay C-J, Yu K-W, Chi C-Y, Lai C-H, Wong W-W, Liu C-Y. Impact of the 1997 revised Centers for Disease Control criteria on case rates of legionellosis in Taiwan: review of 38 cases at a teaching hospital, 1998-2002. *Journal of microbiology, immunology, and infection = Wei mian yu gan ran za zhi*. 2005;38(3):211–7.
- Yeh K, Lin J, Wang N, Chang F. Legionnaires' disease in community-acquired pneumonia requiring hospitalization in Taiwan. *J Med Sci-TAIPEI* 2007;27(2):63.
- Kao W-F, Wang J-T, Sheng W-H, Chen Y-C. Community-acquired Legionnaires' disease at a medical center in northern Taiwan. *J Microbiol Immunol Infect* 2019;52(3):465–70.
- Tan MJ, Tan JS, File Jr TM, Hamor RH, Breiman RF. The radiologic manifestations of Legionnaire's disease. *Chest* 2000;117(2):398–403.
- Cunha BA, Pherez FM, Nouri Y. Legionella community-acquired pneumonia (CAP) presenting with spontaneous bilateral pneumothoraces. *Heart Lung* 2008;37(3):238–41.
- Stout JE, Yu VL. Legionellosis. *N Eng J Med* 1997;337(10):682–7.
- Bartlett J. Legionnaires' disease: overtreated, underdiagnosed. *J Crit Illness* 1993;8:755–68.
- Falcó V, de Sevilla TF, Alegre J, Ferrer A, Vázquez JMM. Legionella pneumophila: a cause of severe community-acquired pneumonia. *Chest* 1991;100(4):1007–11.
- Heath C, Grove D, Looke D. Delay in appropriate therapy of Legionella pneumonia associated with increased mortality. *Eur J Clin Microbiol Infect Dis* 1996;15(4):286–90.