

Community-Acquired Legionella Pneumonia in Elderly Patients: Characteristics and Outcome

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OBJECTIVES: To compare the risk factors, clinical and laboratory features, and outcome of community-acquired pneumonia (CAP) caused by *Legionella pneumophila* in elderly (aged ≥ 65) and younger patients.

DESIGN: Prospective enrollment of subjects with retrospective data analysis.

SETTING: A 630-bed tertiary center in Badalona (Barcelona), Spain.

PARTICIPANTS: A total of 158 patients diagnosed with CAP caused by *L. pneumophila* from 1994 to 2004: 104 younger than 65 and 54 aged 65 and older.

MEASUREMENTS: Epidemiological, clinical, laboratory, and radiological data and the outcome of the two groups were compared using univariate and multivariate analysis.

RESULTS: Underlying diseases, such as chronic pulmonary diseases, diabetes mellitus, neuromuscular diseases, and heart failure; risk of aspiration; and therapy with corticosteroids were significantly more frequent in patients aged 65 and older. Patients younger than 65 were more likely to be male and have toxic habits (cigarette smoking, alcoholism) and human immunodeficiency virus infection than older patients. Fever, nonrespiratory symptoms (diarrhea and headache), and some laboratory abnormalities (hyponatremia (serum sodium concentration < 130 mmol/L) and high aspartate aminotransferase and creatinine kinase levels) were significantly less frequent in patients aged 65 and older than in younger patients. No significant differences were observed between the two groups in the frequency of higher-severity risk classes and intensive care unit admission or in outcome (complications and mortality).

CONCLUSION: Elderly patients with CAP caused by *L. pneumophila* had a higher frequency of underlying comorbidities and presented less frequently with fever and

classical nonrespiratory symptoms and laboratory abnormalities of Legionnaires' disease than younger patients, although greater severity of illness at onset and higher mortality were not significantly different between the two age groups. *J Am Geriatr Soc* 55:114–119, 2007.

Key words: community-acquired pneumonia; *Legionella*; elderly.

In recent decades, there has been a progressive aging of the population in developed countries, such as in Europe, with 16.5% of the citizens being aged 65 and older in 2004.¹ Community-acquired pneumonia (CAP) is a frequent cause of morbidity and mortality in older people, in whom the incidence is three to five times as high as in the remaining adult population.^{2–4} Elderly people have a higher risk of legionnaires' disease (LD), and several studies have demonstrated that age is a risk factor for *Legionella* pneumonia.^{5,6} Thus, in four hospital-based series including severe pneumonias, *Legionella* spp. caused 4% to 12% of the CAP occurring in older patients.^{7–11} Moreover, nearly half of the people with LD reported to public authorities are aged 60 and older, and the rates of legionellosis are two times as high in this age group.¹² However, the incidence of this disease may be underestimated in older people, because it is not easy to obtain sputum samples, and urinary antigen detection is not systematically performed in all centers.

Several studies have shown that CAP in older people usually occurs in individuals with high comorbidity and with fewer symptoms than in younger adults, thereby delaying the diagnosis and worsening the prognosis.^{13,14} However, little is known about the epidemiological characteristics, the presentation, or the evolution of CAP caused by *Legionella* in older people. Knowledge of these data may aid in increasing diagnostic suspicion and improving the healthcare of these patients. Thus, the aim of our study was to compare the risk factors, the clinical presentation and the evolution of CAP caused by *L. pneumophila* in patients aged 65 and older with those of younger patients.

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METHODS

Patients

One hundred fifty-eight patients prospectively diagnosed with CAP cause by *L. pneumophila* in the University Hospital Germans Trias i Pujol in Badalona from 1994 to 2004 were included in the study. The patients were divided into two groups on the basis of age: 104 patients younger than 65 (65.9%) and 54 patients aged 65 and older (34.1%). Twenty-two patients (13.9%) were aged 70 and older, and three were aged 85 and older. Institutionalized patients were not included in the study.

Setting

Since 1994, cases of CAP caused by *Legionella* admitted to this hospital, a 630-bed tertiary center located in Badalona (Barcelona, Spain) that serves an urban area of 700,000 inhabitants and has 22,000 admissions annually, have been prospectively studied. The urinary antigen assay for *L. pneumophila* serogroup 1 was introduced in this hospital in 1994. From 1994 to 1996, this test was applied within a prospective study of CAP to cases without another etiological diagnosis or when *Legionella* pneumonia was suspected.⁸ Since 1997, the urinary antigen test has been routinely applied in the center to all adult patients with CAP admitted to the emergency department, irrespective of age or severity.

Diagnostic Methods

Diagnosis was achieved using urinary antigen detection of *L. pneumophila* serogroup 1 (using enzyme immunoassay or immunochromatography), isolation of *Legionella* spp. in sputum by culture in selective BCYE- α medium, and serology with a four times or greater increase in antibody titers to 128 or more for *L. pneumophila* serogroups 1–6 using immunofluorescence (Micro-IFA Slides, Labsystems, Spain). Some patients were diagnosed using several methods. Sputum and serology were obtained when possible.

Definitions

Risk of aspiration was defined as the presence of risk factors for aspiration, such as severely altered consciousness, abnormal gag reflex, and abnormal swallowing mechanisms. Patients included in Classes III and IV according to the pneumonia severity index developed previously are defined as having a sufficiently high risk for death and other adverse medical outcomes that physicians can consider inpatient treatment.¹⁵ Delay of treatment was defined as the number of days from the onset of illness (fever, if present) to the administration of appropriate antibiotic therapy. Time to apyrexia was defined as hours of fever after the initiation of appropriate antibiotic treatment. Antibiotic treatment was considered adequate if it included a quinolone or a macrolide. Death was considered to be attributable to *Legionella* pneumonia if the episode was the primary cause of the death or contributed to it during hospital stay.

Statistical Methods

The qualitative variables were compared using univariate analysis using the chi-square or Fisher exact test, as appropriate, and the continuous variables with the Student

t test. Significant variables according to univariate analysis were analyzed using multivariate analyses using SPSS version 12 (SPSS Inc., Chicago, IL). Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. Differences between variables were considered significant with a *P*-value < .05.

RESULTS

Epidemiological Data and Risk Factors

Patients aged 65 and older diagnosed with CAP caused by *Legionella* had a greater prevalence of underlying illnesses such as chronic pulmonary diseases, diabetes mellitus, neuromuscular disorders, and heart failure; a greater risk of aspiration; and a greater likelihood of receiving immunosuppressive therapy (mainly corticosteroids) than those younger than 65 during the same period. In contrast, adults younger than 65 were more likely to be male, smoke, be an alcoholic, and have human immunodeficiency virus (HIV) infection than older patients (Table 1).

Clinical Presentation, Laboratory and Radiological Data

Clinical presentation with fever and nonrespiratory symptoms such as diarrhea and headache were significantly less frequent in patients aged 65 and older than in younger patients. Moreover, the duration of fever before diagnosis was shorter in the older age group, although this variable was not significant according to univariate analysis (Table 2).

Laboratory abnormalities on presentation such as hyponatremia (serum sodium concentration <130 mmol/L) and elevated creatinine kinase and aspartate aminotransferase levels were significantly less frequent in patients aged 65 and older than in younger patients. However, the older patients had higher blood urea nitrogen levels (Table 2).

Finally, no significant differences were found in radiological presentation, regarding bilateral extension (14 (13.5%) vs 4 (7.7%)) and the presence of pleural effusion (12 (11.7%) vs 9 (16.7%)), between patients younger than 65 and those aged 65 and older, respectively.

Treatment and Outcome

There were no statistically significant differences between the younger patients and older patients in the frequency of adequate antibiotic treatment (98 (96.1%) vs 50 (98%)) or of treatment with a quinolone versus a macrolide (43 (43.9%) vs 19 (38%)) or in delay to adequate treatment (4.9 ± 2.3 vs 5.1 ± 2.9 days). The mean duration of treatment (excluding patients who died) was longer in the younger than the older patients (17.8 ± 5.5 vs 15.9 ± 5.4 days), although this variable did not achieve statistical significance (*P* = .72). However, time to apyrexia was significantly longer in the younger than the older patients (69.6 ± 74.6 vs 34.3 ± 26.1 hours; *P* = .003).

Regarding outcome, there were no differences in the frequency of complications (55 (52.9%) vs 30 (55.6%)) such as respiratory failure (51 (49%) vs 27 (50%)), the need for mechanical ventilation (15 (14.6%) vs 5 (9.3%)), renal failure (10 (9.6%) vs 6 (11.5%)), and septic shock (8 (7.7%) vs 3 (5.6%)) between the younger and older

Table 1. Demographics and Risk Factors of Community-Acquired Legionella Pneumonia by Age Group

Variable	Aged <65 (n = 104)	Aged ≥65 (n = 54)	P value*	Odds Ratio (95% Confidence Interval)
	n (%)			
Season (summer-autumn)	67 (64.4)	34 (63)	.85	1.06 (0.53–2.10)
Sex				
Male	92 (88.5)	38 (70.4)	.009	3.22 (1.39–7.46)
Female	12 (11.5)	16 (29.6)		
Any risk factor	92 (88.5)	45 (83.3)	.37	1.53 (0.60–3.90)
Smoking	71 (68.9)	6 (11.1)	<.001	0.05 (0.22–0.14)
Alcoholism	36 (35)	5 (9.3)	.001	0.19 (0.69–0.52)
Any underlying illness	48 (46.2)	41 (75.9)	.001	3.68 (1.76–7.66)
Chronic pulmonary disease	11 (10.6)	19 (35.2)	<.001	4.59 (1.98–10.61)
Diabetes mellitus	8 (7.7)	15 (27.8)	.002	4.61 (1.81–11.76)
Neuromuscular disease	1 (1)	11 (20.4)	<.001	26.35 (3.30–210.44)
Neoplasm	7 (6.7)	7 (13)	.19	2.06 (0.68–6.22)
Heart failure	1 (1)	8 (14.8)	.001	17.91 (2.17–147.41)
Human immunodeficiency virus infection	16 (15.4)	0	.001	1.61 (1.42–1.83)
Cirrhosis	5 (4.9)	1 (1.9)	.66	0.37 (0.04–3.31)
Chronic renal failure	3 (2.9)	1 (1.9)	1.00	0.63 (0.06–6.25)
Risk of aspiration	0	3 (5.6)	.01	3.04 (2.42–3.80)
Immunosuppression	6 (5.8)	7 (13)	.20	2.43 (0.77–7.64)
Corticosteroids	4 (3.9)	7 (13)	.048	3.68 (1.03–13.21)

P value

*:NS (Not significant) if P-value >.20; significant if P-value <.05.

patients. Finally, mortality was two times as great in the older patients as in the younger patients (6 (11.2%) vs 5 (4.8%)), although the differences were not statistically significant.

The variables that remained significant according to multivariate analysis are shown in Table 3.

Microbiological Diagnosis

Urinary antigen detection for *L. pneumophila* serogroup 1 was performed in 141 cases (89.2% of the total): 91 (87.5%) in younger patients and 50 (92.6%) older patients. This test was positive in 90 of 91 cases in the younger group and in all 50 cases in the older group, although there

Table 2. Clinical Presentation and Laboratory Data of Community-Acquired Legionella Pneumonia According to Age Group

Variable	Aged <65 (n = 104)	Aged ≥65 (n = 54)	P value	Odds Ratio (95% Confidence Interval)
Fever, n (%)	101 (97.1)	47 (87)	.03	0.20 (0.05–0.80)
Days of fever, mean ± SD	4.56 ± 2.62	3.84 ± 2.23	.09	0.72 (0.43–1.58)
Cough, n (%)	81 (77.9)	35 (64.8)	.11	0.52 (0.25–1.08)
Expectoration, n (%)	45 (43.3)	23 (42.6)	.93	0.97 (0.5–1.89)
Dyspnea, n (%)	45 (43.3)	28 (51.9)	.30	1.41 (0.73–2.73)
Thoracic pain, n (%)	27 (26)	9 (16.7)	.18	0.57 (0.24–1.32)
Diarrhea or vomiting, n (%)	33 (31.7)	9 (16.7)	.06	0.43 (0.19–0.98)
Diarrhea, n (%)	29 (27.9)	3 (5.6)	.001	0.15 (0.44–0.52)
Headache or confusion, n (%)	45 (43.3)	11 (20.4)	.007	0.33 (0.56–0.72)
Headache, n (%)	36 (34.6)	1 (1.9)	<.001	0.03 (0.005–0.27)
Confusion, n (%)	16 (15.4)	10 (18.5)	.61	1.25 (0.52–2.98)
Previous beta lactam, n (%)*	34 (33)	14 (26.9)	.44	0.74 (0.35–1.56)
Leukocytes > 12,000/mm ³ , n (%)	47 (46.1)	29 (54.7)	.31	1.41 (0.72–2.75)
Serum sodium < 130 mmol/L, n (%)	27 (27)	3 (5.7)	.001	0.16 (0.04–0.56)
Creatinine kinase > 237 U/L, n (%)	26 (28.9)	6 (12.5)	.05	0.35 (0.13–0.92)
Aspartate aminotransferase > 37 U/L, n (%)	55 (55)	16 (30.8)	.008	0.36 (0.18–0.74)
blood urea nitrogen > 13 mmol/L, n (%)	7 (7.2)	13 (26)	.004	4.51 (1.67–12.22)

P value: NS (Not significant) if P-value >.20; significant if P-value <.05.

* Amoxicillin, amoxicillin-clavulanate, cefuroxime, ceftriaxone.

Table 3. Characteristics of Legionella Pneumonia in Patients Aged 65 and Older and Younger than 65 According to Multivariate Analysis

Variable	P-value	Odds Ratio [‡]	95% Confidence Interval [‡]
Smoking*	<.001	0.12	0.04–0.35
Chronic lung disease [†]	.02	3.56	1.19–10.65
Neuromuscular disease [†]	.01	16.87	1.76–161.65
Headache*	.004	0.04	0.005–0.38
Serum sodium <130 mmol/L*	.04	0.16	0.03–0.93
Aspartate aminotransferase >37 U/L*	.01	0.28	0.10–0.80
Blood urea nitrogen >13 mmol/L [‡]	.02	5.54	1.31–23.26

P value: NS (Not significant) if P-value >.20; significant if P-value <.05.

*Significantly more frequent in patients younger than 65.

[†]Significantly more frequent in patients aged 65 and older.

[‡]Referring to older patients.

were no statistically significant differences in the frequency of application and sensitivity of this test between the two groups. Sputum culture was performed in 69 cases (43.7%): 50 cases (48.1%) in the younger group and 19 cases (35.2%) in the older group ($P = .14$). *L. pneumophila* was isolated from sputum in 11 (6.9%) cases: 10 (20% of the performed) of the older patients and one (5.2%) of the younger patients ($P = .09$). Two paired serum samples were obtained in 62 cases (39.2%), and seroconversion was detected in 31 (70.4%) older patients and 11 (61.1%) younger patients.

DISCUSSION

This study shows that patients aged 65 and older with CAP caused by *Legionella* had a significantly higher frequency of underlying comorbidities, especially chronic pulmonary diseases, diabetes mellitus, neuromuscular disorders, and heart failure, and were significantly more likely to be receiving corticosteroid therapy than younger patients, who were more likely to be male and have toxic habits (smoking, alcohol) and HIV infection.

Underlying chronic illnesses, such as pulmonary diseases and heart failure, and immunosuppressive therapy are known risk factors for CAP in older people and LD in the general population.^{4,16–18} Diabetes mellitus is a frequent condition in older people, depressing immunity and favoring infection. Moreover, it is one of the most prevalent underlying diseases in CAP and LD, although it is usually associated with other comorbid conditions.^{4,19} Finally, neurological disorders, mainly cerebrovascular diseases and dementia, increase the risk of developing pneumonia because of their association with other chronic diseases and the risk of aspiration.²⁰ Classically, aspiration has been implicated in pneumonia caused by microorganisms found in the oropharyngeal flora and anaerobes,²¹ although recently the microaspiration of contaminated water has been considered to be the mechanism of transmission of *Legionella* pneumonia in elderly hospitalized patients with swallowing difficulties.²² In the current study, 5.6% of patients with LD aged 65 and older had a risk of aspiration, and thus, this mode of transmission may not be excluded in these patients at home.

The prevalence of LD in HIV patients is lower compared with other infectious etiologies occurring in the population, possibly due to underreporting of the disease and prophylaxis with cotrimoxazole.^{8,23} This fact and the low prevalence of HIV infection in subjects aged 50 and older may explain why all the cases in the current study occurred in the younger group.

Smoking raises the risk of having *Legionella* pneumonia two to seven times and may be the only risk factor present in some young individuals.⁸ Alternatively, alcoholism is considered a risk factor for legionellosis and pneumonia because of the alterations this habit produces in immunity.^{4,16} Their having given up these habits in view of the presence of comorbidities may explain the lower prevalence of both risk factors in the older patients than in the younger patients that was observed in the present study. However, in patients in the younger group who did not have underlying comorbidities, toxic habits were a stronger predictor of infection than associating chronic diseases.

The male predominance in the two groups coincides with the twofold greater risk of LD in men, possibly due to the higher prevalence of cigarette smoking and its complications in men.⁴ However, in another study on pneumonia, the frequency of women was greater in the older age group, which may be due to the increase in the prevalence of female sex with age.²⁴

The highest rates of CAP in older people are observed in the winter, coinciding with the period during which the influenza virus may be found.¹⁷ Nonetheless, as with other studies, *Legionella* pneumonia was more prevalent during the summer and the autumn, with no differences found between the two groups.¹⁹

The presentation of *Legionella* pneumonia was less symptomatic in the older patients, as shown by the lower frequency of fever, cough, and nonrespiratory symptoms such as headache and diarrhea. This is consistent with pneumonias of other etiologies and may be explained by the physiological changes in older people and the lower tendency to report symptoms in these patients.^{13,14} Fever may be absent or blunted in older people, because they have lower baseline temperatures and because of the difficulties in measuring temperatures.²⁵ These changes may explain, in part, the delayed onset of fever and the shorter time to apyrexia in the older patients observed in this study.

Moreover, as stated previously, this tendency not to report symptoms in older patients may delay the diagnosis of pneumonia and worsen the prognosis.²⁶

Some clinical data (headache, diarrhea) and laboratory alterations such as severe hyponatremia and high aspartate aminotransferase and creatinine kinase levels were observed more often in CAP caused by *Legionella* than by other etiologies, although they were not specific.^{27,28} However, the frequency of these classical manifestations of LD would be even lower in elderly people, making it necessary to routinely apply specific diagnostic tests. The lower prevalence of these laboratory abnormalities observed in the older patients may be due to the lesser severity, earlier hospital admission, and the lower inflammatory response than in younger patients. However, the greater frequency of high blood urea nitrogen levels found in the older age group may be due to the greater risk of renal failure in these patients.¹⁰

With regard to diagnosis, most of the cases were detected using urinary antigen testing, with no differences found in the sensitivity of this test between the two age groups. Consequently, the routine use of this sensitive and highly specific test for CAP may increase the rate of *Legionella* diagnosis in older people.¹¹ Alternatively, difficulties with expectoration and collection of good-quality samples that occur in older people may explain the lower frequency of isolation of *Legionella* in sputum in older than in younger subjects (5.2% vs 20%).⁴

The prognosis with CAP in older persons is usually worse than in the remaining adult population because of higher mortality, which ranged from 11% to 35% in the hospital-based series.^{9,10} The most important prognostic factors are older age, degree of comorbidity, functional limitations, alterations in vital signs, and high creatinine levels.²⁹ However, the effect of etiology on mortality from CAP in older people has been little studied, being higher for gram-negative enteric bacilli and *Pseudomonas*, followed by *Streptococcus pneumoniae* and then *Legionella* and other atypical pathogens.⁷ The mortality from CAP caused by *Legionella* in the older patients (11%) was lower in this study than in other investigations on CAP in this age population, although it was 2.2 times as great as in the younger group.^{9,10} This coincides with the decrease in mortality of community-acquired LD in the last decade and may be explained by the early diagnosis achieved as a result of urinary antigen detection and the high rate of appropriate treatment administered.³⁰ Moreover, no significant differences were observed in the rate of higher severity risk class (despite the weight of age in that score), complications, and intensive care unit admission between the two groups.

This study had some limitations. It was performed in a series of patients with CAP caused by *Legionella* who had been hospitalized, and thus, the mildest cases may not have been seen. Likewise, institutionalized patients were not included, because the characteristics of pneumonia in these patients are more related to those factors occurring in such health-care centers (e.g., lower staffing ratio, lack of onsite laboratory, etc.). The results of this study can therefore not be extrapolated to patients with characteristics that are different from the individuals studied.

CONCLUSION

Taking into account the progressive aging of the population, the higher incidence of CAP in elderly patients, and the increase in the risk of *Legionella* infection with age, a progressive increase can be foreseen in cases of legionellosis in older persons. Better knowledge of the characteristics of LD in senior citizens may aid in increasing diagnostic suspicion and improving the health care of these patients. Patients aged 65 and older with CAP caused by *Legionella* have a higher frequency of comorbidity, of less-symptomatic presentation (lower frequency of fever), of classical nonrespiratory symptoms, and of laboratory abnormalities of LD than younger patients. Consequently, a high index of suspicion and the routine application of urinary antigen detection is necessary to diagnose *Legionella* pneumonia in elderly patients. Finally, greater severity of illness at onset and higher mortality did not significantly differ between the two age groups.

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