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Nosocomial and community-acquired Legionella pneumonia: clinical comparative analysis

M.L. Pedro-Botet*, M. Sabria-Leal*, M. Haro**, C. Rubio*, G. Gimenez*, N. Sopena*, J. Tor

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ABSTRACT: Previous reports have suggested that nosocomial and community Legionella pneumonia cases are similar. However, community and hospital characteristics, such as aquatic environment, antibiotic pressure (usage) and populations, are quite different, leading to the suspicion that Legionella infection may differ in the two settings.

Univariate and multivariate analyses were performed to compare demographic data, risk factors, clinical, radiological and outcome data between 125 nosocomial and 33 community-acquired cases of *Legionella pneumophila* infection.

Patients in the nosocomially acquired Legionella pneumonia (NALP) group were older than those in the community-acquired Legionella pneumonia (CALP) group. Univariate analysis showed that smoking habit, cough, thoracic pain, and extrapulmonary manifestations were more prevalent in the CALP group, whilst chronic lung disease and cancer were more prevalent in the NALP group. Moreover, patients in the NALP group were more likely to have received oxygen and corticosteroid therapy and also to have altered creatinine values than patients in the CALP group, whilst more patients in the latter group had altered alanine aminotransferase values. However, multivariate analysis failed to confirm most of these differences. Smoking habit and blood creatinine levels were the only variables remaining significant.

In conclusion, demographic, clinical, laboratory, radiological and outcome data in nosocomial and community-acquired Legionella pneumonia are quite similar.
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*Unitat de Malalties Infeccioses and **Servei de Pneumologia, Hospital Universitario Germans Trias i Pujol, Badalona, Universitat Autonoma de Barcelona, Spain.

Correspondence: M. Sabria-Leal
Can Domenech 10-12
08193-Bellaterra
Barcelona
Spain

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Legionella pneumophila has been recognized as an important cause of community and nosocomial pneumonia. Experience accumulated since its first description in 1976 [1] has led to a good understanding of this infection both in the hospital and community environment. Despite the large number of reports of Legionella pneumonia infection [2–9], information concerning differences in clinical, radiological, and outcome aspects between nosocomial and community-acquired cases are very scarce. Previous reports have suggested that clinical aspects of nosocomial and community cases are similar [10]. The community and hospital characteristics, such as aquatic environment, antibiotic pressure (usage) and populations, are quite different and Legionella infection might differ in the two settings. The aquatic environment and antibiotic pressure may contribute to the selection of more virulent strains of *L. pneumophila* within the hospital.

The purpose of the present study was to compare by univariate and multivariate analysis the demographic data, risk factors, clinical and radiological data, and outcome of 125 nosocomial and 33 community-acquired cases of *Legionella pneumophila* pneumonia.

Materials and methods

Setting

The Hospital Universitario Germans Trias i Pujol is a 600 bed teaching institution, that operates as the reference hospital for a population of 700,000 inhabitants. It has an active Medicine and Surgery Department, Obstetric and Paediatric Services, Dialysis and Kidney Transplant Unit, and Intensive Care Unit. Legionella infection was detected as early as 1983 in the hospital. Despite the measures adopted, legionellosis has persisted as an endemic situation (5–15 cases·year^{-1}), with two epidemic outbreaks during the summer of 1988 and 1989 (26 and 18 cases, respectively).

Patient selection and study design

One hundred and thirty six patients with nosocomially-acquired Legionella pneumonia (NALP), and 34 patients

with community-acquired Legionella pneumonia (CALP) were included in the study. We applied the Centers for Disease Control (CDC) [11] and World Health Organization (WHO) [12] criteria for diagnosis both of nosocomial infection and Legionella pneumonia One hundred and twenty two patients were diagnosed exclusively by a fourfold or greater rise in titre of indirect fluorescent antibody (IFA) (*Legionella pneumophila* serogroups 1–6; Labsystems 6109401) and 38 patients by direct fluorescent antibody (DFA) (*Legionella pneumophila* serogroups 1–10; Genetic Systems 0149-04) in respiratory specimens.

Legionella pneumophila serogroup 1 was isolated in 28 cases. Whilst nosocomial isolates showed a single chromosomal pattern, those for community isolates were quite different [13].

A retrospective review of all medical records from patients diagnosed as NALP and CALP was made from 1983 to 1985 (18 patients). From January 1985 to December 1992, the study was conducted prospectively (140 patients). Complete records were available in 125 nosocomial cases and in 33 community cases.

The cards of selected patients included demographic information, extrinsic and intrinsic risk factors, clinical and radiological manifestations, and evolution. We also registered analytical determinations corresponding to the first week after diagnosis was made. The clinical course was assessed for the development of respiratory or renal failure and shock. Case-fatality rates were determined for death directly attributable to Legionella pneumonia infection.

Statistical analysis

Data were analyzed by means of a statistical program for personal computer. Discrete variables were analysed by univariate analysis using Chi-squared. Comparison of groups with continuous variable distribution was performed by means of the Student's t-test. Multivariate analysis was performed by logistic regression. In all analyses, the level of significance was set at a p-value equal to 0.05.

Results

Demographic data

Univariate analysis showed that patients in the NALP group were older than those in the CALP group (NALP group mean age 64±13 yrs), and CALP group mean age 48±15 yrs; p>0,001). The male:female ratio was 2:1 in the NALP group, and 4:1 in the CALP group, but the difference was not statistically significant, either in the univariate or in the multivariate analysis (table 1).

Table 1. – Univariate and multivariate analysis of demographic data and risk factors for Legionella infection

Demographic data	NALP (n=125)	CALP (n=33)	p-value^{+}	p-value^{++}
Age yrs (Mean±SD)	64±13	48±15	0.001*	0.09
Sex M/F	84/41	26/7	0.19	-
Risk factors$^{\#}$				
Smoking habit	66/121	25/33	0.02*	0.01*
Chronic lung disease	67/122	11/32	0.03*	0.31
Cardiopathies	20/122	2/33	0.21	-
Chronic renal failure	19/122	2/33	0.25	-
Diabetes mellitus	24/123	5/33	0.56	-
Cancer	22/123	0/33	0.01*	0.87
Alcoholism	40/120	16/33	0.10	-
Hepatic cirrhosis	6/122	0/32	0.44	-
Intravenous drug abuser	2/122	0/33	1.00	-
AIDS	2/122	0/33	1.00	-
Oxygen therapy	59/123	5/33	0.001*	0.6
Corticosteroid therapy	38/123	0/33	0.0002*	0.8

$^{\#}$: positive data/data available; $^{+}$: univariate analysis; $^{++}$: multivariate analysis; *: statistically significant. NALP nosocomially-acquired Legionella pneumonia; CALP: community-acquired Legionella pneumonia; AIDS: acquired immune deficiency syndrome; M: male; F: female.

Risk factors

Among the intrinsic risk factors, smoking habit was more prevalent in the CALP group than in NALP group (76 *versus* 53%; p=0.02), whilst chronic lung disease and cancer were more common in the NALP group than in the CALP group (54 and 18% *versus* 3 and 0%; p= 0.03 and p=0.01, respectively). NALP patients were also more likely to have received oxygen and corticosteroid therapy than CALP patients (47 and 30% *versus* 15 and 0%; p=0.001 and p=0.0002, respectively). The difference for other risk factors, such as cardiopathies, chronic renal failure, diabetes, alcoholism, hepatic cirrhosis, acquired immune deficiency syndrome (AIDS) or intravenous drug abuse (IDA) was not statistically significant. Nevertheless, the logistic regression analysis indicated smoking as the only significant independent variable (p=0.01) (table 1).

Clinical and radiological manifestations

Common clinical manifestations are shown in table 2. Univariate analysis showed that cough (p=0.001), thoracic pain (p=0.04) and neurological (p=0.0002) and gastrointestinal (p=0.03) manifestations were more common in the CALP group than in NALP group. However, the logistic regression analysis failed to demonstrate a significant independent association for any variable (table 2).

The radiological features at presentation and during the evolution were similar in both groups (table 3).

Table 2. – Univariate and multivariate analysis of clinical data of 125 NALP and 33 CALP patients

	NALP# (n=125)	CALP# (n=33)	p-value+	p-value++
Fever	122/123	33/33	1.00	-
Cough	65/123	27/32	0.001*	0.45
Expectoration	44/123	15/33	0.30	-
Chest pain	30/123	14/33	0.04*	0.12
Initial absence of respiratory symptoms	70/123	15/33	0.24	-
Neurological symptomatology	23/123	15/33	0.0002*	0.08
Headache	10	12		
Confusion	13	3		
Gastrointestinal symptomatology	19/123	8/33	0.03*	0.06
Abdominal pain	9	0		
Vomiting	3	3		
Diarrhoea	7	5		

#: positive data/data available; *: statistically significant; +: univariate analysis; ++: multivariate analysis. For abbreviations see legend to table 1.

Table 3. – Univariate and multivariate analysis of radiological manifestation of 125 NALP and 33 CALP patients

	NALP# (n=125)	CALP# (n=33)	p-value+	p-value++
Unilateral infiltrates	88/121	22/33	0.65	-
Unilobar infiltrates	96/121	24/33	0.58	-
Pleural effusion	23/121	9/31	0.22	-
Development of empyema	2/122	3/32	0.10	-
Development of lung abscess	7/122	2/32	1.00	-

#:positive data/data available; +: univariate analysis; ++: multivariate analysis. For abbreviations see legend to table 1.

Laboratory findings

Common laboratory findings are shown in table 4. Neither peripheral white blood cell count, natraemia, aspartate aminotransferase (AST), alkaline phosphatase, gammaglutamyl transpeptidase (GGT), bilirubin, or arterial oxygen tension (P_{a,O_2}), discriminated between the NALP and CALP groups. Univariate analysis showed that creatinine and alanine aminotransferase (ALT) were more commonly altered in the NALP group that in CALP group (p=0.001 and p=0.02, respectively). However, only creatinine persisted as a significant independent variable in the multivariate analysis.

Clinical course and outcome

The clinical course and outcome of the 125 NALP and 33 CALP patients are shown in table 5. Respiratory failure was the most common complication in both groups (58% in the NALP group *versus* 73% in the CALP group), followed by renal failure (15% in the NALP group *versus* 9% in the CALP group) and shock (11% in the NALP group *versus* 6% in the CALP group). No neurological sequelae were observed.

Table 4. – Univariate and multivariate analysis of laboratory findings of 125 NALP and 33 CALP patients

	NALP# (n=125)	CALP# (n=33)	p-value+	p-value++
Leucocyte count 10×10^9 cells·L^{-1}	84/21	24/33	0.71	-
Blood urea nitrogen (>8.6 mmol·L^{-1})	44/112	7/32	0.07	-
Blood creatinine (>106 umol·L^{-1})	51/107	5/31	0.001*	0.002*
Sodium (<135 mEq·L^{-1})	62/111	16/31	0.67	-
Chloride (>100 mEq·L^{-1})	68/98	18/27	0.78	-
AST (>43 U·L^{-1})	39/106	17/30	0.051	-
ALT (>53 U·L^{-1})	35/105	17/30	0.021*	0.52
Alkaline phosphatase (>121 U·L^{-1})	30/104	9/30	0.90	-
GGT (>66 U·L^{-1})	13/93	13/28	0.29	-
Bilirubin (>20 mmol·L^{-1})	13/95	3/28	0.90	-
P_{a,O_2} (<8.0 kPa)	57/90	21/27	0.16	-

#: positive data/data available; +: univariate analysis; ++: multivariate analysis; *: significant. AST: aspartate aminotransferase; ALT: alanine aminotransferase; GGT: gammaglutamyl transpeptidase; P_{a,O_2}: arterial oxygen tension. For further abbreviations see legend to table 1.

Table 5. – Univariate and multivariate analysis of clinical outcome of 125 NALP and 33 CALP patients

	NALP# (n=125)	CALP# (n=33)	p-value+	p-value++
Development of respiratory failure	71/122	24/33	0.12	-
Development of renal failure	18/121	3/32	0.6	-
Development of shock	13/122	2/32	0.67	-
Death directly attributable to Legionella infection	22/123	2/33	0.09	-
Death not attributable to Legionella infection	6/123	1/33	1.00	-
Case-fatality rate %	18	6		

#: positive data/data available; +: univariate analysis; ++: multivariate analysis. For abbreviations see legend to table 1.

Twenty eight patients (22%) died in the NALP group *versus* three patients (9%) in the CALP group. However, considering deaths directly attributable to Legionella infection, the case-fatality rate was 18% in the NALP group and 6% in the CALP group.

No difference concerning course and outcome between the groups was significant, either using univariate or multivariate analysis.

Discussion

The demographic characteristics of our patients are similar to those reported previously [6, 8, 10, 14]. Both in NALP and CALP groups, the risk of acquiring legionellosis was increased in males. Whilst in the NALP group, old age and intrinsic and extrinsic risk factors were common in many patients, reflecting the hospital population

characteristics, the typical patient in the CALP group was a smoking and drinking middle-aged man, with a low frequency of pre-existing chronic diseases, except for chronic lung disease. These observations are similar to those of WOODHEAD and MACFARLANE [9], suggesting that pre-existing chronic diseases in CALP are not an essential condition to acquire Legionella pneumonia. Our study suggests that the clinical findings of nosocomial and community-acquired *Legionella pneumophila* pneumonias are quite similar. Fever was the most common finding. The absence of respiratory symptomatology during the first 24 h of illness was common in both groups, thus making the early diagnosis of pneumonia difficult, especially in the NALP group and when extrapulmonary symptoms were present. However, either cough, chest pain, dyspnoea or respiratory insufficiency generally develops in most patients after the first 72 h of illness.

The extrapulmonary findings in Legionella pneumonia are common [6, 9, 15–20], the pathogenesis of which may be diverse [15, 16, 21, 22]. The incidence of neurological and gastrointestinal manifestations was lower in our series than in other published studies [6, 9, 10, 20, 23]. However, vomiting and diarrhoea were more common in the CALP (9 and 15%, respectively) than in NALP group (2 and 6%, respectively). Furthermore, headache was more frequent in the CALP (36%) than in NALP group (8%). When considered globally, the differences observed in the neurological and gastrointestinal manifestations were significant in the univariate analysis. Two reasons account for these differences in our series. The CALP patients enter the hospital late because of the lack of specifity in initial symptomatology, allowing the extrapulmonary symptomatology to develop. In our hospital and in hospitals with endemic legionellosis, the diagnosis and the onset of treatment for nosocomial Legionella pneumonia is immediate because of the high level of suspicion. This makes the extrapulmonary manifestations of Legionella infection less likely to be observed in this context.

The frequency of laboratory abnormalities in our patients was similar to that noted in other published studies [6, 9]. Abnormal liver function was observed in 1 out of 3 of the patients in both groups. Interestingly, the patients in the CALP group presented higher levels of ALT than the patients in the NALP group, a difference that was statistically significant in the univariate analysis. Furthermore, the NALP patients more frequently presented altered renal parameters than the CALP patients. The fact that many patients in the NALP group had previous nephropathies and the older age in this group accounted for these differences.

Unilobar infiltrate was the usual finding on admission chest radiographs in both groups, as noted in other published studies [10, 24–26]. Development of empyema or pulmonary abscess were uncommon accounting for 5% of the whole series. No significant difference was observed in any radiological variable between the patients groups.

As in other series, the most common complication was respiratory failure [9]. The fact that 51% of our patients had chronic lung disease and 59% were heavy smokers partially explains this finding.

The case fatality rate was 18 and 6% for the NALP and CALP groups, respectively. Despite the lower percentage of patients who died in the CALP group this difference was not statistically significant in either the univariate analysis or multivariate analysis, probably due to the few cases included in the CALP group. The CALP group has been observed in many series as having a lower mortality rate than NALP [9, 10]. Our case fatality rate in both groups was lower than the reported mortality for nosocomial and community-acquired cases in other series [6, 10, 27]. The inclusion of erythromycin in the initial combined therapy for all nosocomial pneumonia in our hospital, and the routine use of this antibiotic for the community pneumonias in our country accounted for this low rate.

We emphasize that 70% of the patients in the NALP group who died were under corticosteroid therapy. In our NALP group, corticosteroid therapy and shock were associated with a higher mortality rate in one logistic regression analysis model [23].

In conclusion, demographic, clinical, laboratory and radiological data of Legionella pneumonia in our hospitalized and community patients were quite similar and it did not justify separation of these entities. Many of the distinctions between the groups observed in the univariate analysis probably reflect differences in the hospital and community population characteristics rather than in virulence of the Legionella infection. Moreover, multivariate analysis failed to confirm almost all of them.

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