

## ABSTRACT

**Introduction:** Legionella pneumophila (Lp) is considered one of the primary etiologies of “atypical pneumonia”. On the other hand, Streptococcus pneumoniae (Sp) is considered the primary etiology of “typical pneumonia”. The traditional thought that patients with typical and atypical pneumonia have different underlying conditions and different clinical outcomes has been challenged recently.

**Objective:** The objective of this study was to define if hospitalized patients with CAP due to Lp have different underlying conditions and outcomes compared to patients with Sp.

**Methods:** This was a secondary data analysis of the Community-Acquired Pneumonia Organization (CAPO) International Cohort Study database. Hospitalized patients with CAP with positive Lp or Sp urinary antigen tests were included in the analysis. Underlying conditions and clinical outcomes were compared using the Chi-Squared test or Mann-Whitney U-test.

**Results:** A total of 95 patients with Lp and 339 patients with Sp were analyzed. There were no clinically significant differences in underlying conditions or laboratory values for both etiologies. There was no clinically significant difference between the groups in regard to clinical outcomes.

**Conclusions:** This study indicates that Lp and Sp infect similar patients and produce similar clinical outcomes. Since patients infected with these two primary atypical and typical pathogens have similar clinical characteristics, the initial empiric antibiotic therapy for all hospitalized patients with CAP should cover for the possibility of Lp or Sp.

## INTRODUCTION

Legionella species commonly causes 2 clinical symptoms, Legionnaires’ disease and Pontiac fever. Legionnaires’ disease is an acute and lethal pneumonia whereas Pontiac fever is flu-like, self-limiting illness. According to the CDC, Legionnaires’ disease has increased 217% in incidence from 2000 to 2009. (Lee M. Hampton, et al.)

Bacterial pneumonia is divided into typical and atypical pneumonia. Legionella pneumophila (Lp) is considered one of the primary etiologies of “atypical pneumonia”. On the other hand, Streptococcus pneumoniae (Sp) is considered the primary etiology of “typical pneumonia”. The traditional thought that patients with typical and atypical pneumonia have different underlying conditions and different clinical outcomes has been challenged recently.

The objective of this study was to define if hospitalized patients with CAP due to Legionella pneumoniae have different underlying conditions and clinical outcomes compared to patients with Streptococcus pneumoniae.

## OBJECTIVES

The objective of this study was to define if hospitalized patients with CAP due to Lp have different underlying conditions and outcomes compared to patients with Sp.

## MATERIALS AND METHODS

### Study Design

This was a secondary analysis of patients enrolled in the Community-Acquired Pneumonia Organization (CAPO) international cohort study. Data were collected between 2001 and 2015. In each participating center, non-consecutive medical records of hospitalized patients with the diagnosis of CAP were reviewed. A sample of the data collection form is available at the study website (www.caposite.com). Validation of data quality was performed at the study center before the case was entered in to the CAPO database. Institutional Review Board approval was obtained by each participating center.

### Study Definitions

CAP: Diagnosis of CAP required the presence of criterion A, B, and C:

A. New pulmonary infiltrate on imaging (CT scan or chest x-ray) at the time of admission to the hospital.

B. Signs and Symptoms of CAP (at least one of the following)

1. New or increased cough (per the patient)
2. Fever >37.8°C (100.0°F) or hypothermia <35.6°C (96.0°F).
3. Changes in WBC (leukocytosis >11,000 cells/mm<sup>3</sup>, left shift > 10% band forms/microliter, or leukopenia < 4,000 cells/mm<sup>3</sup>)

C. Working diagnosis of CAP at the time of hospital admission with antimicrobial therapy given within 24 hours of admission.

### Study Groups

Group 1: patients with CAP and positive Lp urinary antigen test obtained upon admission to the hospital.

Group 2: patients with CAP and positive Sp urinary antigen test obtained upon admission to the hospital.

### Study Outcomes

**Time to clinical stability (TCS):** A patient was defined as clinically stable the day that the following four criteria were met: a) improved cough and shortness of breath, b) lack of fever for at least 8 hours, c) improving leukocytosis (decreased at least 10% from the previous day), and d) tolerating oral intake with adequate gastrointestinal absorption. Patients were evaluated daily within the first 7 days of hospitalization to determine the day when clinical stability was reached.

**Length of stay (LOS):** defined in days and calculated for each patient as the day of discharge minus the day of admission. Patients hospitalized for more than 14 days were censored at 15 days in an effort to capture LOS data related only to bacterial CAP.

**In-hospital mortality:** defined as death by any cause during hospitalization.

### Statistical Analyses

Baseline categorical explanatory variables were summarized as frequencies and percentages and differences between both groups of patients were analyzed using a chi-square test or Fisher’s exact test when appropriate and warranted. Continuous variables were summarized as frequencies and interquartile range and differences between groups were analyzed by Wilcoxon-Mann-Whitney test.

TCS and LOS were analyzed with the Kaplan-Meier method, and log-rank tests were applied to evaluate differences between both groups of patients. P-values ≤ 0.05 were considered statistically significant.

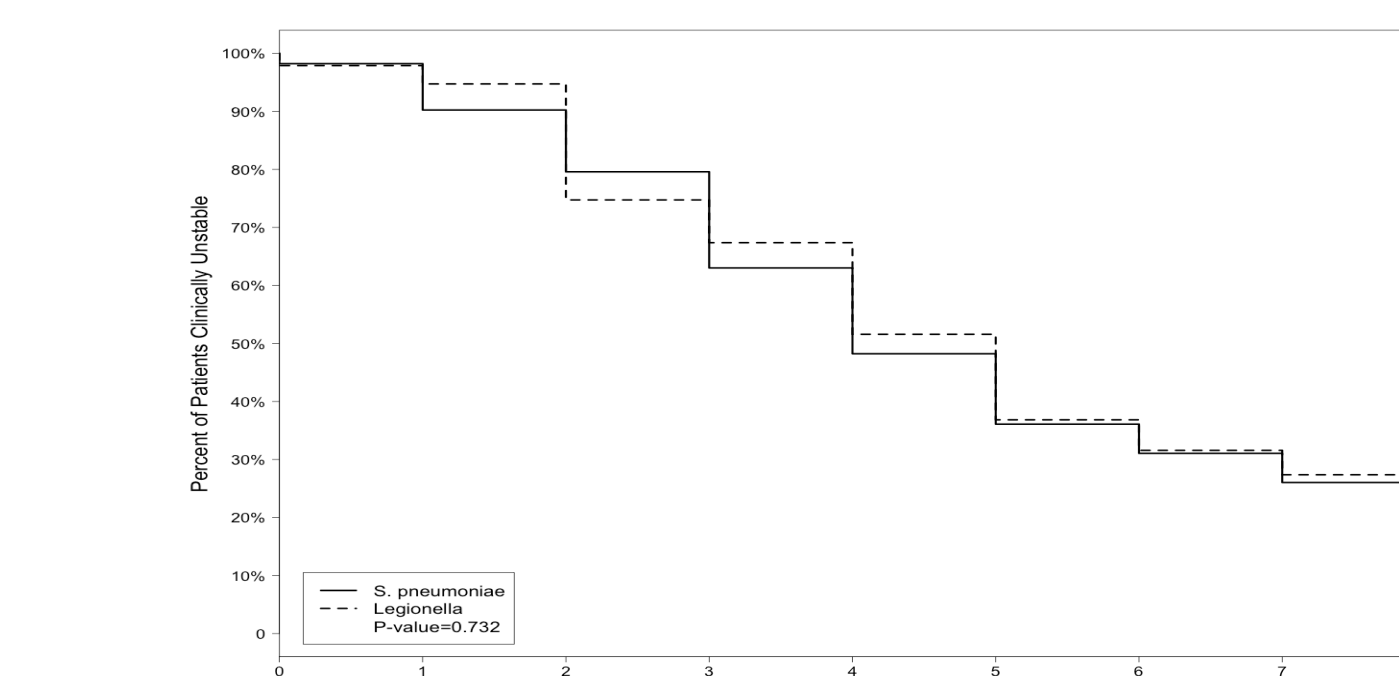
## RESULTS

A total of 95 patients with Legionella pneumoniae and 339 patients with Streptococcus pneumoniae were analyzed.

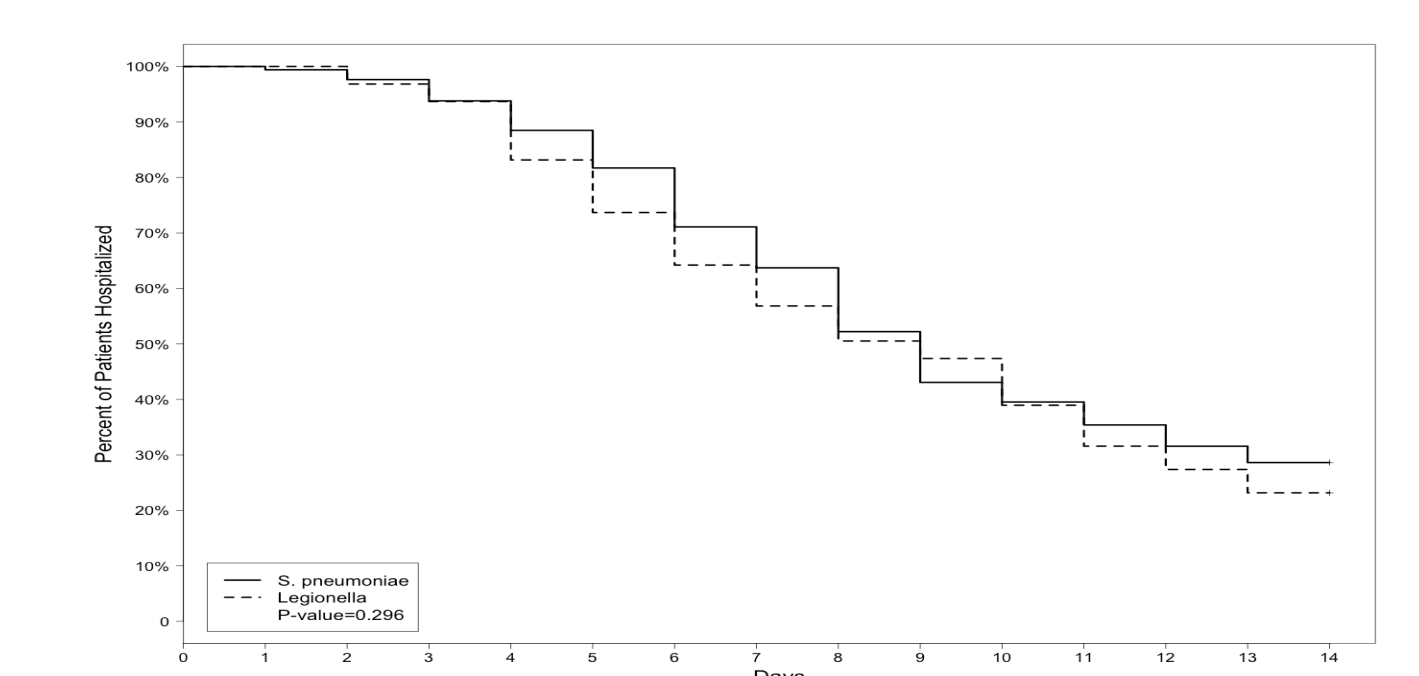
**Table 1:** Patients Demographics, Comorbid Conditions, Physical Exam, Lab/ Radiography and Severity of Disease variables.

Variable	Legionella	S.pneumoniae	P-value
<b>Demographics</b>			
Age, Median (IQR)	62 (21)	68 (27)	0.053
Male, n (%)	69 (73)	205 (60)	0.031
Nursing home resident, n (%)	2 (2)	21 (6)	0.191
<b>Comorbid Conditions</b>			
Congestive Heart Failure, n (%)	6 (6)	37 (11)	0.244
COPD, n (%)	12 (13)	64 (19)	0.172
Diabetes, n (%)	15 (16)	63 (19)	0.65
HIV, n (%)	4 (4)	13 (4)	0.772
Renal Disease, n (%)	7 (7)	25 (7)	>0.999
Liver Disease, n (%)	7 (7)	38 (11)	0.343
Neoplastic Disease, n (%)	7 (7)	51 (15)	0.06
<b>Physical Exam</b>			
Altered mental status on admission, n (%)	9 (9)	59 (17)	0.078
Respiratory Rate, Median (IQR)	20 (7)	24 (11)	0.047
Systolic blood pressure, Median (IQR)	122.5 (33.2)	120 (33)	0.241
Temperature (degrees Celsius), Median (IQR)	38.5 (1.2)	37.8 (1.6)	<0.001
Heart rate, Median (IQR)	100 (25)	102 (32)	0.616
<b>Lab/Radiography</b>			
pH, Median (IQR)	7.5 (0.1)	7.5 (0.1)	<0.001
PaO <sub>2</sub> , Median (IQR)	55.1 (13.5)	60.8 (15.8)	0.076
Blood Urea Nitrogen, Median (IQR)	35 (26)	32 (35.2)	0.609
Serum sodium, Median (IQR)	133 (8)	136 (5)	<0.001
Serum glucose, Median (IQR)	124.5 (38.8)	120 (45)	0.4
Hematocrit, Median (IQR)	39.7 (6)	38.5 (6.9)	0.255
Pleural effusion, n (%)	25 (26)	79 (23)	0.587
<b>Severity of Disease</b>			
ICU admission, n (%)	10 (11)	39 (12)	0.857
Pneumonia Severity Index, Median (IQR)	100 (40.5)	114 (46.5)	0.001

There was no clinically significant difference between the groups in regard to in-hospital mortality (RR 0.866, 95%CI 0.325-2.307, p-value=0.773).



**Figure 1:** Time to clinical stability (TCS) for both study groups



**Figure 2:** Length of Stay (LOS) in the hospital for both study groups

## CONCLUSIONS

- This study indicated that Legionella pneumoniae and Streptococcus pneumoniae infect similar patients and produce similar outcome.
- Since patients infected with these two primary atypical and typical pathogens have similar clinical characteristics, the initial empiric antibiotics therapy for all hospitalized patients with CAP should cover for the possibility of Legionella pneumoniae and Streptococcus pneumoniae.

## REFERENCES

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