



# Clinical outcomes of HIV-infected patients hospitalized with bacterial community-acquired pneumonia

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## KEYWORDS

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## Summary

**Background:** There are limited and conflicting data on clinical outcomes of community-acquired pneumonia (CAP) among HIV-infected patients.

**Methods:** Secondary analyses of clinical outcomes of CAP were performed for 118 patients with HIV infection and 2790 patients without HIV infection enrolled in the Community-Acquired Pneumonia Organization (CAPO) international study. After adjustment for significant confounders, the effect of HIV infection on length of stay (LOS) and time to clinical stability (TCS) were examined by survival analyses and overall mortality and CAP-related mortality by logistic regression methods.

**Results:** After adjusting for significant confounders, hospitalized HIV-infected patients with CAP did not have longer times to reach clinical stability (HR 1.126; 95% CI 0.917–1.391;  $p = 0.251$ ) or longer stays in the hospital (HR 1.191, 95% CI 0.979–1.449;  $p = 0.080$ ). In addition, HIV infection did not significantly influence overall mortality rates (OR 1.205, 95% CI 0.686–2.116;  $p = 0.517$ ) or CAP-related mortality rates (OR 1.338; 95% CI 0.623–3.725;  $p = 0.355$ ).

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**Conclusion:** The presence of HIV infection did not influence the clinical outcomes of CAP among patients assessed at CAPO centers. It is not intended that our results be extrapolated to populations receiving limited healthcare for advanced HIV disease, malnourishment and parasitic diseases.

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## Introduction

Pulmonary infections are a major cause of morbidity and mortality in persons infected with HIV.<sup>1</sup> Pneumonia due to unspecified organisms has been reported to be the leading cause of death among HIV-infected individuals in the USA during 1990–1999.<sup>2</sup> The introduction of highly active anti-retroviral therapy (HAART) has led to a notable decline in opportunistic infections (OI), however bacterial pneumonia remains prevalent.<sup>3</sup> In addition, bacterial community-acquired pneumonia (CAP) has been reported to be a common cause of hospitalization among HIV-infected patients.<sup>4,5</sup>

The etiology, risk and prognostic factors of CAP among hospitalized HIV-infected patients have been examined. However, studies comparing clinical outcomes of CAP in patients with and without HIV infection are limited and results are conflicting. To date, five studies have evaluated the outcomes of mortality in HIV-infected patients hospitalized with CAP.<sup>6–10</sup> Higher mortality rates among HIV-infected subjects were found in three studies.<sup>5–7</sup> Four of these five studies evaluated length of stay (LOS) and one study found longer LOS among HIV-infected patients. Time to clinical stability (TCS), as a measurable outcome of CAP, was defined in a case–control study of 58 HIV patients done by our group using the Community Acquired Pneumonia Organization (CAPO) database. Similar outcomes were found between HIV-infected patients and those without HIV infection. These five studies did only univariate analyses of clinical outcomes of CAP.

Because of these conflicting results, we performed a study with the objective of evaluating clinical outcomes of bacterial CAP among hospitalized HIV-infected patients using a cohort design and multivariate analyses that made adjustment for confounders.

## Materials and methods

### Study design

A secondary analysis was performed of the Community-Acquired Pneumonia Organization (CAPO) database.<sup>11</sup> CAPO is an international, retrospective, observational study of adult patients hospitalized with CAP. Data were analyzed from hospitals in seven countries (USA, Canada, Spain, South Africa, Argentina, Venezuela, Chile), between June 2001 and March 2006. In each participating center, random medical records of hospitalized patients with the diagnosis of CAP were reviewed. The presence of HIV infection was obtained from medical history. Each investigator filled out a case report form that was transferred via the Internet to the CAPO study center at the University of Louisville, KY, USA. A sample of the data collection form is available at the study website ([www.caposite.com](http://www.caposite.com)). Validation of data quality was performed at the study center before the case was entered in

the CAPO database. Antibiotic therapy for CAP was examined following each country's guidelines and categorized as: (1) compliance if empirical therapy covered expected CAP bacteria, and (2) non-compliance if antibiotic treatment did not cover expected CAP bacteria.

### Inclusion criteria

Patients who were included in the study met the following criteria for the diagnosis of CAP: (1) new pulmonary infiltrate on a chest radiograph, and (2) at least one of the following: (a) a new or worse cough, (b) an abnormal body temperature ( $<35.6^{\circ}\text{C}$  or  $>37.8^{\circ}\text{C}$ ), and/or (c) an abnormal serum leukocyte count.

### Exclusion criteria

In an attempt to limit our investigation to bacterial CAP, patients with a presumptive or definitive diagnosis of Pneumocystis pneumonia (PCP), mycobacterial and fungal pneumonia were excluded from this study. Furthermore, patients were excluded if they were treated for a suspected PCP, mycobacterial or fungal etiology.

### Study groups

Two study groups were established, the group of CAP patients with HIV infection based on the presence of positive serology for HIV antibody and a second group categorized as CAP patients without HIV infection based on the presence of negative HIV antibody or unknown HIV status.

### Study outcomes

#### Time to clinical stability (TCS)

A patient was defined as clinically stable and ready to be switched to an oral antibiotic the day that the following four criteria were met: (1) improved cough and shortness of breath, (2) lack of fever for at least 8 hours, (3) improving leukocytosis (decreased at least 10% from the previous day), and (4) tolerating oral intake with adequate gastrointestinal absorption.<sup>12</sup> Patients were evaluated daily within the first seven 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.

#### All-cause mortality

The sum of all patients with a final clinical outcome classified as dead. The final clinical outcome 'death or alive' was

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