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### ORIGINAL RESEARCH

## Adult Patients Living with Human Immunodeficiency Virus Hospitalized for Community-Acquired Pneumonia in the United States: Incidence and Outcomes

\*Leslie A. Beavin<sup>1</sup>, Stephen Furmanek<sup>1</sup>, Paula Peyrani<sup>1</sup>, Anupama Raghuram<sup>1</sup>, Forest Arnold<sup>1</sup>, Mark Burns<sup>1</sup>, Julio Ramirez<sup>1</sup>

### Abstract

**Background:** Community-acquired pneumonia (CAP) is a common infectious reason for hospitalization of adults in the United States (US), including those with Human Immunodeficiency Virus (HIV). While there are studies detailing the incidence and outcomes for all adults with CAP we are not aware of a recent study detailing incidence and outcomes in adult HIV patients hospitalized with CAP. The objectives of this study were (1) to define the current incidence and outcomes of adult HIV patients hospitalized with CAP in Louisville, Kentucky, and (2) to estimate the burden of CAP in the US HIV adult population.

**Methods:** This was a secondary analysis of The University of Louisville Pneumonia Study; a prospective population-based cohort study of all hospitalized adults with CAP who were residents of Louisville, Kentucky, from 1 June 2014 to 31 May 2016.

**Results:** A total of 110 unique patients living with HIV were hospitalized with CAP during our two-year study. The annual incidence of adults living with HIV hospitalized with CAP is estimated to be 1,950 per 100,000. Of the estimated 1.1 million adults living with HIV in the US currently we predict that 21,450 will be hospitalized with CAP annually. The median time to clinical stability in adult patients living with HIV hospitalized with CAP was 2 (IQR: [1, 3]) days. The median length of stay for adult patients living with HIV hospitalized with CAP was 4 (IQR: [3, 7]) days. Mortality occurred as follows; in-hospital: 1.8%, 30-day 6.8%, 6-month 15.5%, and 1 year 20.2%.

**Conclusion:** The estimated annual incidence of adult patients living with HIV and hospitalized with CAP was found to be 1,950 per 100,000 suggesting that 21,450 adults living with HIV will be admitted with CAP yearly across the US. This is a similar incidence to that recently predicted for the elderly. Mortality occurred as follows; in-hospital: 1.8%, 30-day 6.8%, 6-month 15.5%, and 1 year 20.2%. Our 30-day mortality rate for adult patients living with HIV hospitalized for CAP was similar to other figures in the literature.

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Affiliations:

<sup>1</sup>University of Louisville Division of Infectious Diseases, Louisville, KY 40202

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### Introduction

Community-acquired pneumonia (CAP) is a common infectious reason for hospitalization of adults in the United States (US), including those with Human Immunodeficiency Virus (HIV) [1-3]. Some articles have suggested that HIV patients are actually more likely to be hospitalized with CAP, regardless of their pneumonia severity index (PSI) score, than other adult populations secondary to their immunosuppressed status [4]. Current assessment of the incidence and outcomes of HIV patients hospitalized with CAP is important to guide ongoing prevention and management [5].

While there are studies detailing the incidence and outcomes for all adults with CAP we are not aware of a recent study detailing incidence and outcomes in adult HIV patients hospitalized with CAP.

\*Correspondence To: Leslie Beavin, MD  
Assistant Professor of Medicine  
Division of Infectious Diseases, University of Louisville  
Work Address: 501 E Broadway, Suite 120 Louisville, KY 40202  
Work Email: [labeav03@louisville.edu](mailto:labeav03@louisville.edu)

The objectives of this study were (1) to define the current incidence and outcomes of adult HIV patients hospitalized with CAP in Louisville, Kentucky, and (2) to estimate the burden of CAP in the US HIV adult population.

### Methods

#### Study Design

This was a secondary analysis of The University of Louisville Pneumonia Study; a prospective population-based cohort study of all hospitalized adults with CAP who were residents of Louisville, Kentucky, from 1 June 2014 to 31 May 2016 (IRB number 11.0613). All hospitalized adult patients in Louisville underwent screening for participation in the study during that time. Patients without a permanent or valid Louisville address based on US Census Bureau data, without a valid Social Security

number (SSN), or who were in the correctional system were not included. Data was collected on participants from the medical record including; age, sex, race, body mass index (BMI), HIV status, presence of malignancy, presence of renal disease, presence of heart disease, presence of chronic obstructive pulmonary disease (COPD), history of cerebrovascular event (CVA), smoking status, presence of diabetes, temperature, respiratory rate, blood pressure, heart rate, serum bicarbonate, blood urea nitrogen, serum glucose, serum hematocrit, serum sodium, admission location, presence of altered mental status (AMS), vasopressor requirements, ventilator requirements, and PSI score.

### Study Design

A patient was defined as having CAP when the following 3 criteria were met:

1. Presence of a new pulmonary infiltrate on chest radiograph and/or chest computed tomography scan at the time of hospitalization, defined by a board certified radiologist's reading
2. At least 1 of the following:
  - a. New cough or increased cough or sputum production,
  - b. Fever  $>37.8^{\circ}\text{C}$  ( $100.0^{\circ}\text{F}$ ) or hypothermia  $<35.6^{\circ}\text{C}$  ( $96.0^{\circ}\text{F}$ ),
  - c. Changes in leukocyte count (leukocytosis:  $>11,000$  cells/ $\mu\text{L}$ ; left shift:  $>10\%$  band forms/ $\mu\text{L}$ ; or leukopenia:  $<4,000$  cells/ $\mu\text{L}$ )
3. No alternative diagnosis at the time of hospital discharge that justified the presence of criteria 1 and 2.

A patient was determined to have HIV based on either prior diagnosis noted in past medical history on chart review or new diagnosis (performed at the discretion of the hospital physician) made via the fourth generation HIV screening test in combination with viral load and CD4 count.

A unique HIV patient hospitalized with CAP was counted as the first hospitalization during each study year.

### Study Measures

The annual CAP incidence rates in adult HIV patients per 100,000 adults were estimated for unique patients. The estimated number of CAP cases in HIV patients in the United States was calculated by multiplying the Louisville incidence rate by the estimated 2014 US adult population obtained from the US Census Bureau.

Time to clinical stability was defined as the number of days from admission up until the patient reached clinical stability, which was defined as the presence of all four criteria:

1. Improvement of cough and dyspnea
2. Absence of fever ( $<37.8^{\circ}\text{C}$ ) for at least 8 h
3. Normalization or greater than 10% improvement of white blood cell count
4. Adequate oral intake

Length of hospital stay was defined as the number of days from admission to discharge.

All-cause mortality for all hospitalized unique HIV patients with CAP was evaluated during hospitalization and at 30 days, 6 months, and 1 year after hospitalization. To ensure appropriate 1-year follow-up, mortality was evaluated for patients enrolled in the first year of the study. After discharge, mortality was evaluated by reviewing medical records and by matching patients' SSNs with mortality data obtained from the Kentucky Department for Public Health Office of Vital Statistics. Mortality data from Louisville were extrapolated to the US population hospitalized with CAP.

## Results

The patient characteristics for HIV patients hospitalized with CAP during this study are detailed in **Table 1**.

**Table 1** Patient characteristics.

<b>Demographics</b>	
Age, Median(IQR)	51 (16)
Male Sex, n(%)	72 (65.5)
Black or African American Race, n(%)	58 (52.7)
<b>Medical and Social History</b>	
Obese, n(%)	19 (17.3)
HIV disease, n(%)	110 (100)
Neoplastic disease (active or within the last year), n(%)	14 (12.7)
Renal disease, n(%)	27 (24.5)
Chronic renal failure, n(%)	10 (9.1)
Congestive heart failure, n(%)	18 (16.4)
Chronic Obstructive Pulmonary Disease (COPD), n(%)	41 (37.3)
Stroke, n(%)	5 (4.5)
Current Smoker, n(%)	65 (59.1)
Diabetes mellitus, n(%)	15 (13.6)
<b>Physical Exam Findings</b>	
Temperature (Degrees Celsius), Median(IQR)	37.6 (1.6)
Respiratory rate (Breaths/Minute), Median(IQR)	22 (8)
Systolic blood pressure (mmHg), Median(IQR)	109 (32.8)
Diastolic blood pressure (mmHg), Median(IQR)	60 (19.8)
Heart rate (Beats/Minute), Median(IQR)	112 (24.2)
<b>Laboratory Findings</b>	
Serum bicarbonate (mEq/L), Median(IQR)	25 (6)
Blood Urea Nitrogen (BUN) (mg/dL), Median(IQR)	15 (11.5)
Serum glucose (mg/dl), Median(IQR)	121 (43.8)
Hematocrit (%), Median(IQR)	34.3 (8.9)
Serum sodium (mEq/L), Median(IQR)	136 (7)
<b>Severity of Disease</b>	
ICU Admission, n(%)	15 (13.6)
Altered mental status on admission, n(%)	8 (7.3)
Vasopressors on admission, n(%)	0 (0)
Ventilatory support on admission?, n(%)	6 (5.5)
Pneumonia Severity Index, Median(IQR)	75.5 (66.8)
PSI Risk Class IV or V, n(%)	41 (37.3)

A total of 110 unique patients living with HIV were hospitalized with CAP during our two-year study. In 2016 there were 2,821 adults living with HIV in Louisville Kentucky [6]. Therefore, the annual incidence of adults living with HIV hospitalized with CAP is estimated to be 1,950 per 100,000. Of the estimated 1.1 million adults living with HIV in the US currently we predict that 21,450 will be hospitalized with CAP annually [7]. The median time to clinical stability in adult patients living with HIV hospitalized with CAP was 2 (IQR: [1, 3]) days. The median length of stay for adult patients living with HIV hospitalized with CAP was 4 (IQR: [3, 7]) days. Mortality occurred as follows; in-hospital: 1.8%, 30-day 6.8%, 6-month 15.5%, and 1 year 20.2%.

## Discussion

We estimated the annual incidence of adults living with HIV hospitalized with CAP to be 1,950 per 100,000 suggesting that 21,450 adults living with HIV will be hospitalized with CAP yearly across the US. A review of the literature did not reveal a recent study on incidence of adult patients living with HIV hospitalized with CAP in the US for comparison. However, looking at our data it is notable that there does seem to be a lower threshold for hospitalizing adult patients living with HIV for CAP than for the general adult population. Compared to a recent publication detailing the incidence, epidemiology, and mortality of all adults with CAP in the US, Ramirez et al, adults living with HIV presenting with CAP were admitted at younger ages and with lower PSI scores. That study indicated that the average age of admission for all adults with CAP was 68 whereas the average age of admission for adult patients living with HIV presenting with CAP was 51. That study also indicated that the average PSI score for adults admitted with CAP was 101 whereas the average PSI score for adults living with HIV admitted with CAP was 75.

Interestingly, when compared to the same study, the annual incidence of adults living with HIV hospitalized with CAP of 1,950 per 100,000 is very similar to that in the elderly. While the overall incidence of hospitalizations in all adult patients with CAP was 649 per 100,000 the incidence in the elderly (age greater than or equal to 65) increased drastically to 2093 per 100,000. This suggests that like the elderly, patients living with HIV are 3 times more likely to be hospitalized with CAP than the general adult population.

However, when comparing mortality from the same study, the mortality was lower for adults living with HIV hospitalized with CAP than all adults hospitalized with CAP at 1.8% vs 6.5% during hospitalization, 6.8% vs 13% at 30 days, 15.5% vs 23.4% at 6 months, and 20.2% vs 30.6% at 1 year [6]. This may reflect the lower threshold for hospital admission in adults living with HIV for CAP regardless of their severity of illness. A review of the literature on mortality in adult patients living with HIV with CAP revealed that our value for 30-day mortality of 6.8% was similar to the 30-day mortality described in a recent study by Cilloniz *et al.* that reported a 7% 30-day mortality in adults living with HIV hospitalized with CAP in Spain [8].

Our study has several limitations, the primary one being the lack of a gold diagnostic standard test for pneumonia. In our study, patients hospitalized with signs and symptoms of a respiratory infection, with a new pulmonary infiltrate, and no clear alternative diagnosis were classified as having CAP. Immunosuppressed patients may not meet the aforementioned criteria despite the presence of CAP, and the sensitivity and specificity of our definition is unknown due to the lack of a gold standard. Secondly, if a patient from Louisville living with HIV was hospitalized with CAP outside of Louisville they would not have been included in this study. This means that we have potentially underestimated the incidence of adult patients living with HIV hospitalized with CAP. Also, because we used 2010 US Census Bureau information to calculate incidence we excluded patients not included in the US Census Bureau data; those without a valid address, SSN, or who were incarcerated. While this would not affect our incidence, it could potentially introduce selection bias. Lastly, our study does not

detail the CD4 counts, viral loads, anti-retroviral therapy, or pneumococcal and influenza vaccination status of the patients living with HIV hospitalized for CAP. Therefore, it is difficult to extrapolate the overall immune status of the patients living with HIV included in the study.

Overall, we do feel that we were able to accurately capture the number of adult patients living with HIV in Louisville that were admitted with CAP during the study as all nine area hospitals were under constant surveillance for two years. We also believe that the incidence of HIV in Louisville, a medium sized city, is a good population to reflect overall HIV incidence and activity across the US opposed to larger or smaller cities which may over or under represent the presence of HIV.

In conclusion, the estimated annual incidence of adult patients living with HIV and hospitalized with CAP was found to be 1,950 per 100,000 suggesting that 21,450 adults living with HIV will be admitted with CAP yearly across the US. This is a similar incidence to that recently predicted for the elderly. Mortality occurred as follows; in-hospital: 1.8%, 30-day 6.8%, 6-month 15.5%, and 1 year 20.2%. Our 30-day mortality rate for adult patients living with HIV hospitalized for CAP was similar to other figures in the literature. Further research is needed to determine the overall immune status of and risk factors for adults living with HIV hospitalized with CAP. The incidence of pneumococcal and influenza vaccination in patients living with HIV admitted with CAP in tandem with microbiological data regarding causative pathogens needs further investigation as well. Pneumococcal and influenza vaccination may be over represented in this patient population compared to all adults. This may both explain milder disease in HIV patients and direct future vaccine development.

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