Prevalence and Correlates of Cryptococcal Antigen Positivity among AIDS Patients, United States from 1986-2012

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Background

Cryptococcal meningitis (CM) is the most common cause of AIDS-related mortality in sub-Saharan Africa. CM accounts for between 33% and 63% of all adult meningitis within that region and is responsible for over 500,000 deaths annually; more AIDS-related deaths than tuberculosis. In sub-Saharan Africa, the World Health Organization recommends routinely screening AIDS patients with a CD4 T-cell count less than 100 cells/μl for cryptococcal infection and initiating anti-cryptococcal therapy to prevent CM. The prevalence at which routine cryptococcal infection was found to be cost-effective was 2%. In the United States however there are no such screening recommendations because there is a lack of prevalence data and thus no opportunity for a cost-effective analysis. We aimed to determine the prevalence of cryptococcal infection among advanced AIDS patients in the United States to guide potential updates in the prevention and management of CM.



Methods

Using stored sera from 1986 to 1996 the Multicenter AIDS Cohort Study and the Women's Interagency HIV Study, we screened specimens from 1,872 participants with CD4 T-cell counts less than 100 cell/μl for cryptococcal infection. We tested serum from participants using the CrAg Lateral Flow Assay (Immy, Inc. Norman, OK), a FDA-cleared test for the detection of cryptococcus antigen (CrAg). Demographic and clinical data were first compared using Chi-square and Students T tests. Univariate and multivariate logistic regression were used to examine correlates of a positive CrAg test.

Results

The overall prevalence of CrAg positivity within this population was 2.9% (CI:0.20-3.80). Women has a higher prevalence than men (3.3% (CI: 2.3-4.7%) and 2.6% (CI: 1.7-3.8%)), respectively). Bronx, NY has the highest prevalence of CrAg positivity (4.3% (CI: 2.2-8.4%)), followed by Pittsburgh, PA (4.2% (CI: 2.1-8.3%)), and District of Columbia (4.0% (CI: 1.7-9.1%). Differences in prevalence were also seen between education levels and race. Results from logistic regression show that race is a significant correlate for a CrAg positive test result.

Figure 1. Frequency of positive CrAg specimen over time

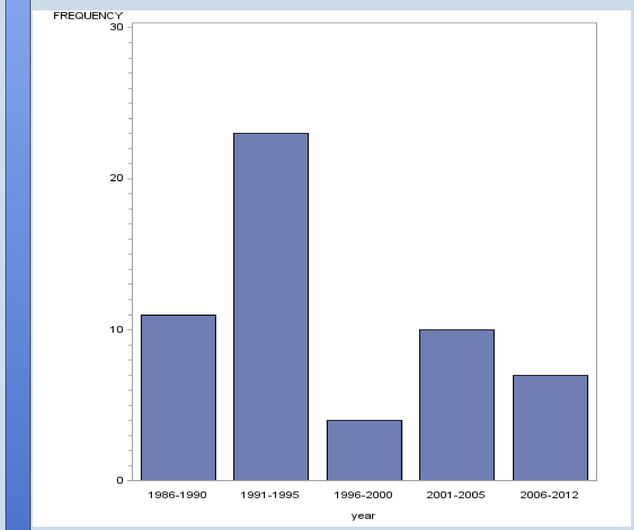


Figure 2. Range of CrAg Titers

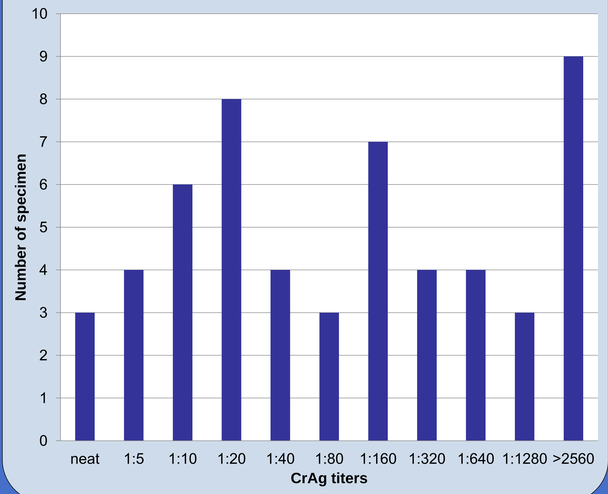


Table 1. Prevalence by Demographic Characteristics

Characteristics	Total (%) (n=1872)	Prevalence (CI)
Gender		
Male	989 (53.32)	2.6% (1.7-3.8%)
Female	866 (46.68)	3.3% (2.3-4.7%)
Study location		
Baltimore, MD	241 (12.99)	3.0% (1.5-6.0%)
Bronx, NY	183 (9.87)	4.3% (2.2-8.4%)
Brooklyn, NY	162 (8.73)	1.9% (0.6-5.3%)
Chicago, IL	342 (18.44)	0.5% (.08-2.57%)
District of Columbia	123 (6.63)	4.0% (1.7-9.1%)
Los Angeles, CA	514 (27.71)	3.3% (2.1-5.2%)
Pittsburgh, PA	187 (10.08)	4.2% (2.1-8.3%)
San Francisco, LA	103 (5.55)	3.9% (1.5-9.5%)
Race/Ethnicity		
White	849 (45.87)	2.47% (1.62-3.75%)
Black	651 (35.17)	2.46% (1.52-3.96%)
Hispanic	117 (6.32)	1.71% (.47-6.65%)
Other	234 (12.64)	6.41% (3.92-10.31%)
Education		
High school or less	790 (42.98)	3.80% (2.67-5.37%)
College	773 (42.06)	2.46% (1.58-3.81%)
Graduate school	275 (14.96)	1.46% (.56-3.93%)

Discussion

Although there have been great strides in the United States in reducing the morbidity and mortality of CM through early access to ART, CM continues to be a problem in the United States; with an incidence among those with infected with HIV/AIDS between 2 and 7 cases per 1,000 persons, and a mortality rate approximately 12%.

Implementation of screen and treat programs have begun in many countries throughout the world, including South Africa, where the prevalence and case fatality rate of CM are high. In the United States however, there is no recommendation for implementing such program, despite having similar programs for other common opportunistic infections, such as tuberculosis. In a 2013 update by the HIV Medicine Association of the Infectious Disease Society of America, routine screening for cryptococcal antigen was not recommended, "but may be considered in selected patients with CD4 cell counts <50 cells/μl."

The results from this study, coupled with the results from recent cost-benefit analyses and the development of new test, suggest the prevalence of cryptococcal infection in the United States is substantial and above the published cost-effective threshold, and may warrant updates to the prevention and management of CM among those infected with HIV.

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