REVISED ABSTRACT

Background: Cryptococcal disease (CD) can be missed by medical providers and can be difficult to recognize. However, delayed diagnosis can lead to increased morbidity and mortality. 


Results: We found 5,351 patients with CD, 2,441 (45.6%) were HIV-positive and 2,910 (54.4%) were HIV-negative. Of those HIV-positive, 604 (24.6%) had a statistically significant higher risk of a missed diagnosis of CD compared to HIV-negative patients (p<0.001) (Figure 1). The most common codes associated with missed diagnosis of CD were SIRS, pneumonia and others in both groups (Table 2). 

Conclusion: A high clinical suspicion especially among people with severe underlying comorbid conditions is crucial to guide prevention strategies (e.g. early initiation of therapy) to lower morbidity.

BACKGROUND
-Cryptococcosis is a deadly disease that affects patients with both competent and incompetent immune systems. Missed opportunities for CD diagnosis are relatively common and may contribute to worse outcomes.

-CD often has an insidious presentation and a long latency period making difficult to recognize especially in apparently immunocompetent patients.

-Delayed diagnosis can lead to increased morbidity and mortality.

-This study aimed to estimate the potential number of missed opportunities for CD diagnoses and to compare the CD-associated mortality among HIV-positive and HIV-negative patients.

METHODS
-Descriptive retrospective cohort study.


-These states and years were selected based on their population diversity and their availability or linkage of patient-level encoded information across hospitalizations over time.

-Potent population: We included subject ≥15 year of age, who died in the state where hospitalization occurred, and had any discharge CD-9-CM diagnosis code for cryptococcosis (117.5) or cryptococcosis meningitis (292.13).

-Admissions before the index hospitalization were identified using the encoded patient-level identifier.

-Definitions: Missed opportunity for CD diagnosis is a hospitalization for a respiratory, central nervous system or inflammatory conditions suggestive of CD during the 90 days hospitalization prior to the index admission (Table 1).

-Deep-seated cause mortality was based on the ICD-9-CM codes (290-292).

-Statistical analysis: A generalized estimating equations model was used to evaluate the relative risk of a missed diagnosis of CD during the 90 days prior stratified by HIV status. Backward selection was used with a cut-off of p = 0.1 among factors with a p<0.1 in univariate analysis. All data management and analyses were performed using SAS v9.3.

RESULTS

ANALYSIS AND RESULTS
-In total, 3,501 subjects were diagnosed with CD during their index hospitalization, 2,441 (45.6%) were HIV-positive and 2,910 (54.4%) were HIV-negative (Figure 1).

-Of those HIV-positive, 604 (24.6%) had a statistically significant higher risk of a missed diagnosis of CD compared to HIV-negative patients (p<0.001) (Figure 1). The most common codes associated with missed diagnosis of CD were SIRS, pneumonia and others in both groups (Table 2).

-CD patients had a significantly higher number of admissions before the index hospitalization compared to the general population, with increased number of admissions before the index hospitalization.

-Cryptococcosis is a deadly disease that affects patients with both competent and incompetent immune systems. Missed opportunities for CD diagnosis are relatively common and may contribute to worse outcomes.

CONCLUSIONS

Missed Opportunities for Diagnosis of Cryptococcal Disease

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Table 1: Most Common Diagnosis and Procedure Codes Associated with Missed Diagnosis of Cryptococcal Disease by HIV Status

<table>
<thead>
<tr>
<th>HIV Status</th>
<th>Diagnosis Code</th>
<th>N (%)</th>
<th>HIV Status</th>
<th>Diagnosis Code</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-Positive</td>
<td>305.20:20</td>
<td>138 (3.1)</td>
<td>Non-HIV</td>
<td>305.20:20</td>
<td>200 (4.7)</td>
</tr>
<tr>
<td>HIV-Positive</td>
<td>305.21:20</td>
<td>45 (1.0)</td>
<td>Non-HIV</td>
<td>305.21:20</td>
<td>66 (1.5)</td>
</tr>
<tr>
<td>HIV-Positive</td>
<td>312.00:20</td>
<td>129 (2.9)</td>
<td>Non-HIV</td>
<td>312.00:20</td>
<td>118 (2.7)</td>
</tr>
</tbody>
</table>

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