Background

Immune Reconstitution Inflammatory Syndrome (IRIS) can occur with initiation or reintroduction of antiretroviral therapy (ART) in persons living with HIV (PLWH) and manifests as an unmasking of a sub-clinical opportunistic infection or paradoxical worsening of a previously treated infection. In 2012, the Department of Health and Human Services published an update of the “Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents,” which recommended initiation of ART for all PLWH regardless of CD4 count. Severe immunodeficiency at the time of initiation or reintroduction of ART is an important consideration in identifying PLWH at risk for IRIS. The burden of IRIS may be lessened over time as PLWH are started on ART earlier in the course of infection before acquiring opportunistic infections. To date, the burden of IRIS on the healthcare system before and after the guideline update has not been described.

Objectives

1. To quantify the hospital days attributable to IRIS before and after the guideline update was published and to determine any temporal differences
2. To assess the reasons for hospitalizations of PLWH and to characterize any temporal differences

Methods

Study Design

• Setting: University of Virginia Hospital, a 604 bed tertiary care referral hospital.
• Subjects: Adults between 18 and 89 years of age who were coded by the International Classification of Diseases, Ninth Revision (ICD-9) as having a diagnosis of HIV/AIDS or had a reactive HIV screening assay and who were hospitalized between November 1, 2009 and July 31, 2014.
• Equivalent time periods of 28.5 months pre-guideline (November 1, 2009 - March 15, 2012) and post-guideline (March 16, 2012 - July 31, 2014) were considered.
• Electronic Medical Records were examined for patient clinical and demographic characteristics.
• Reasons for non IRIS were considered.

Definitions

• IRIS-attributable hospitalizations were identified by ICD9 codes and review of each hospitalization for PLWH by using the last search capacity of the electronic medical record to find “IRIS” or “Immune Reconstitution Inflammatory Syndrome.” Hospitalizations that were identified were then manually reviewed and confirmed.
• Reasons for non IRIS-attributable hospitalizations were systemically grouped by organ system and diagnosis category.

Statistical Analysis

• Chi squared analyses were performed on categorical data to determine statistically significant differences between groups.
• Continuous data was analyzed using t tests.

Results

• 278 PLWH were hospitalized 527 times throughout our study period (Table 1).
• The pre-guideline period had 9 PLWH with 12 IRIS-attributable hospitalizations.
• The post-guideline period had 6 PLWH with 9 IRIS-attributable hospitalizations.
• The most common cause for hospitalization was non-IRIS defining infection. This was followed by, in the pre-guideline period, gastrointestinal, AIDS-defining malignancy, and AIDS-defining infection, and in the post-guideline period, by AIDS-defining malignancy, gastrointestinal, and pulmonary (Table 3).
• The burden of IRIS may be lessened over time as PLWH are started on ART earlier in the course of infection before acquiring opportunistic infections. Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents, which recommended starting ART for all PLWH regardless of CD4 count. Severe immunodeficiency at the time of initiation or reintroduction of ART is an important consideration in identifying PLWH at risk for IRIS. The burden of IRIS may be lessened over time as PLWH are started on ART earlier in the course of infection before acquiring opportunistic infections. To date, the burden of IRIS on the healthcare system before and after the guideline update has not been described.

Conclusions

• IRIS continues to pose a considerable burden on the healthcare system.
• In our single center study, there was a lower number of IRIS-attributable hospital days in the post-guideline period compared with the pre-guideline period.
• The hospital burden of IRIS may decrease over time as more PLWH are started on ART earlier in the course of infection before acquiring opportunistic infections.
• Multicenter studies are needed to assess if similar trends are found.

Table 1. Hospitalized Patient Clinical and Demographic Characteristics by IRIS and Study Period

<table>
<thead>
<tr>
<th>Diagnosis Category</th>
<th>Pre-Guideline</th>
<th>Post-Guideline</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIDS</td>
<td>11 (70)</td>
<td>2 (22)</td>
<td>0.075</td>
</tr>
<tr>
<td>Chronic Infection</td>
<td>19 (12)</td>
<td>0 (0)</td>
<td>0.405</td>
</tr>
<tr>
<td>HIV Infection</td>
<td>3 (20)</td>
<td>1 (17)</td>
<td>0.472</td>
</tr>
</tbody>
</table>

Table 2. Hospital Usage by Study Period

<table>
<thead>
<tr>
<th>Diagnosis Category</th>
<th>Pre-Guideline</th>
<th>Post-Guideline</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIDS</td>
<td>134</td>
<td>73</td>
<td>0.003</td>
</tr>
<tr>
<td>Non IRIS</td>
<td>164</td>
<td>364</td>
<td></td>
</tr>
<tr>
<td>Percentage Attributable to IRIS</td>
<td>7.5%</td>
<td>4.2%</td>
<td></td>
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