The burden of severe human fungal infections in Brazil

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Introduction

• Serious human fungal infections (SHFI) are worldwide associated with high morbidity and mortality rates despite some effective treatment options;
• Patients with SHFI often require hospital care, as a consequence of a difficult diagnosis and treatment – almost all fungal diseases occurs as a consequence of other health problems. Despite this, it is an internationally neglected health topic;
• This situation is also a problem in Brazil where none of the SHFI are official reportable disease (except for cryptococcal meningitis). This situation hampers epidemiological survey data and masks the tragic reality of the many fungal diseases in our country.

Purpose

• To estimate the total burden (incidence and/or prevalence) of SHFIs in Brazil so that new decision making for monitoring, prevention and fungal disease control becomes possible.

Methods

• Historical data was collected from the Ministry of Health Informatics Department System (DATASUS), from year 2011, for hospitalization admissions and/or notification cases of: cryptococcal meningitis, mucormycosis, histoplasmosis, coccidioidomycosis, paracoccidioidomycosis and blastomycosis;
• Official country data was considered consistent only for fungal diseases for which there was a surveillance program in place;
• Cases of cryptococcal meningitis and PCP (for AIDS patients) were obtained from the Information System of Notifiable Diseases (SINAN);
• For aspergillosis, candidosis and fungal keratitis we conducted multiple electronic bibliographic database searches. Assumptions were derived using the frequency of these diseases from the literature and as denominator we used official data (population, respiratory diseases, cancer and immunocompromised, and critical care beds) as reported in official governmental publications;
• All data were entered into a Microsoft Excel spreadsheet for statistical analysis.

Assumptions

• Invasive aspergillosis: 13.4% of AML + 2.3% allo HSCT + 0.5% renal Tx (Nucci, 2012); + 13.3% lung Tx (Pasquato, 2010). Not available data for aspergillosis in renal, heart and liver Tx in Brazil. World: 6% Heart Tx and 1.3% liver Tx, Other steroid patients ignored. Added to: COPD admissions to hospital per year 0.103;
• Chronic pulmonary aspergillosis (CPA) post tuberculosis: 64,825 TB pulmonary cases, and 59,639 alive pulmonary cases (WHO, 2006);
• Allergic bronchopulmonary aspergillosis (ABPA) in cystic fibrosis patients: frequencies ranging from 22-23% (Carneiro, 2008; Paschoal, 2007). ABPA affects 2.15% of asthmatics;
• Candidaemia in hospitalized patients: 2.49% Critical care + surgery (2,491,000 hospital admissions (Nucci, 2010; Colombo, 2011);
• Candidaemia in outpatients: 3% of all cases (Colombo, 2006) - conservative assumption, since another publication (Pasquato, 2005) revealed 9%;
• Oral candidosis: 90% of patients with HIV not on ARVs (possible over-estimation if a large % not on ARVs have CD4 >200 cells);
• Oesophageal candidosis: 20% of patients not on ARVs, and 0.5% of those on ARVs;
• Recurrent Candida vaginitis (>4x/year): 5% of woman (childbearing age) (75% of woman 10-49 years). Literature estimate is 5-8%;
• Fungal keratitis: 0.91/million of inhabitants per year (based on sales distribution of antifungal eye drops; Ibrahim, 2012);

Brazilian scenario: Brazil has ~194 million inhabitants (76% adults, 47% women, 30% are >40 years old). Knowing that almost all fungal diseases occurs as a consequence of other health problems; we used official Ministry Health as follows:
• HIV/AIDS: the current total of HIV/AIDS cases is 608,230 which 30% are not receiving antiretroviral (ARVs). Each year are reported 34,218 annual new AIDS cases (at risk of opportunistic infections). In 2010, about 12,000 deaths were related to AIDS;
• Respiratory diseases: pulmonary TB annual incidence is estimated in 5/100,000 with 25,244 AML patients reported per year. In 2011, about 700 patients had undergone allogeneic hematopoietic stem cell transplantation (HSCT) and 6,658 were submitted to solid organ Tx (renal, heart and liver);
• Critical care and surgery cases: Brazil has 35,400 critical care beds and ~11.6 million (M) of hospital admissions per year. A total of 5,609 peritoneal dialysis were done in 2011.

Results

• The official hospitalization data for aspergillosis presented 442 cases while in our estimative we have more than 400,000 aspergillosis cases. Most are in the community – allergic and chronic, but there are an estimated 8,664 invasive cases;
• For all kinds of Candida infections the official data in 2011 were 1,242 hospitalizations, differing absurdly of our estimation study that we should have almost 30,000 hospitalizations;
• It is important to note that we exclude for our analysis all cases of severe asthma with fungal sensitization (SAFS), that could be as many as 600,000 cases.
• The dermatomycoses were excluded for our study since the majority of the cases are treated in public health centers in private clinics, making the official data collection unreliable.

Table 1. Estimated burden of serious fungal diseases in Brazil.

<table>
<thead>
<tr>
<th>Fungal disease</th>
<th>Total</th>
<th>Respiratory + cancer</th>
<th>Other</th>
<th>Total serious fungal</th>
<th>Critical care + surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspergillosis</td>
<td>392</td>
<td>864</td>
<td>0.103</td>
<td>3,226</td>
<td>0.87</td>
</tr>
<tr>
<td>CPA post TB</td>
<td>10,000</td>
<td>35,400</td>
<td>9,897</td>
<td>27,642</td>
<td>9,211</td>
</tr>
<tr>
<td>ABPA</td>
<td>114,222</td>
<td>28,991</td>
<td>1,761</td>
<td>2,193</td>
<td>2,092</td>
</tr>
</tbody>
</table>

Contrast with official data

• No underlying disease/other HIV/AIDS Respiratory disease Cancer + Immunocompromised Respiratory diseaseients

Discussion

• Based on local data and literature estimates the frequency of mycoses in susceptible populations, 1.7% of Brazilians presents some form of serious fungal disease;
• Knowing that the mycoses are an internationally neglected health topic, we believe that if all fungal diseases could be officially notified the real number should be much higher than the estimated by this study;
• Additional epidemiological estimates are required to validate the modelling estimates presented above.

References

Graph 2. Candida infections estimated cases