Burden of serious fungal infections in China
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Introduction
The incidence of serious fungal infections has been increasing over the past several decades as a result of the expanding number of immunocompromised patients with risk factors such as HIV infection, transplantation, immunosuppressive therapy, corticosteroid therapy, and broad-spectrum antibiotic medication, etc. Despite the availability of newer and potent antifungal agents, the morbidity and mortality of invasive fungal infections remain high. Understanding of the burden of fungal infections is crucial to both better disease prevention and treatment. In China, with the largest population in the world, population-based surveillance on various fungal infections is still lacking. However, data from specific high risk populations and some cities has increasingly been reported. We have attempted to estimate the burden of serious fungal infection in China through literature review.

Methods
All published epidemiology papers reporting fungal infection rates from China were identified. If few data existed, we used specific populations at risk and fungal infection frequencies in those populations to estimate national incidence or prevalence. Population (2009), HIV (2011) and TB (2011) data were from WHO. Asthma, ABPA and CPA rates were from Denning, Bull WHO 2011, Med Mycol 2013 (ahead of print) and Ma, 2011. Asthma prevalence in adults is estimated at nearly 20M and assuming 2.5% of asthmatics have ABPA, 491,721 patients with ABPA are likely and 648,300 have severe asthma with fungal sensitisation (SAFS). The rate of candidemia was estimated at 5/100,000 population (68,150 cases) and Candida peritonitis at 19,982 cases. Invasive aspergillosis (IA) numbers in renal and liver transplantation and numerous other fungal diseases were not estimated.

Results
Of the 1,363M population, 20% are children (0–14 years) and 12% are >60 years old. 20M Chinese (age 15–50) women are estimated to get recurrent vaginal thrush (4+ times annually). Of the 740,000 estimated HIV positive patients in 2011, 92,227 are not on ARVs (CD4 <350). Of these an estimated 83,000 develop oral thrush, 50,000 oesophageal candidiasis, 461 CM, 16,140 PCP and 1,383 P. marneffei infection. We estimate a 5-year period prevalence of 256,534 CPA cases (assuming 15% annual mortality); 80% from 893,121 cases of pulmonary TB, 20% other conditions. Asthma prevalence in adults is estimated at nearly 20M and assuming 2.5% of asthmatics have ABPA, 491,721 patients with ABPA are likely and 648,300 have severe asthma with fungal sensitisation (SAFS). The rate of candidemia was estimated at 5/100,000 population (68,150 cases) and Candida peritonitis at 19,982 cases. Invasive aspergillosis (IA) in >100,000 haematological patients is estimated at 8,178 cases and in the COPD 154,000 cases (11.9M admissions). IA numbers in renal and liver transplantation and numerous other fungal diseases were not estimated.

Conclusion
Without any national surveys of fungal disease in China, uncertainty surrounds all these estimates. But the burden of fungal disease is almost certainly one of the greatest in the world. Epidemiological studies are urgently required to validate or modify these estimates.

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Introduction & Purpose

Fungal Infections are a growing global problem that are difficult to quantify in terms of population affected, mortality, resources used and possible methods of prevention. Currently data available on fungal infections worldwide are crude estimates that have not been standardized. This project attempts to compile data from several countries worldwide that differ in terms of economic status, health care provision and ethnicity in order to form a better overall picture of the current state of fungal infection globally.

Methods

For the purposes of creating a comparable data set for each country a template was provided that included demographic data and specific disease related information was gathered. Relevant published epidemiology describing fungal infection in Ireland was identified. Data were collected from 2010. The population living in Ireland (ROI) and that combined data is presented here. This included some specific assumptions from published data that would allow the directly observed incidence of fungal infection to be used in conjunction with surrogate markers for fungal infection to estimate the total burden nationally.

Population data were obtained from Northern Ireland Research and Statistics Agency and Central Statistics Service (NI) and the Republic of Ireland (ROI) and that combined data is presented here. This included some specific assumptions from published data that would allow the directly observed incidence of fungal infection to be used in conjunction with surrogate markers for fungal infection to estimate the total burden nationally.

Cystic fibrosis (CF) figures were extrapolated from the CF trust (NI) and CF registry (ROI). COPD information from ROI was taken from the OECD library and asthma rates were obtained from the Asthma Society of Ireland. There was insufficient direct data for Northern Ireland for COPD of Asthma but was estimated using similar ABPA (Allergic Bronchopulmonary Aspergillosis) figures are determined by assuming rates of 15% of adult CF patients and 2.5% of adult asthmatics. SAFS (Severe asthma with Fungal sensitisation) was estimated using the CFR 33% of the total population of adult asthmatics. Pulmonary tuberculosis (TB) data for ROI was obtained from WHO and Northern Ireland information was obtained directly from PHA with supporting HIV audit data. In order to assess the total number of chronic pulmonary aspergillosis (CPA) the assumption is that 25% of CPA is as a result of TB and therefore the figure for TB is multiplied by 0.25 to give the total prevalence. The prevalence of CPA in the TB population is assumed to be 20%

Some countries have high rates of hispaplasmosis, coccidiodomycosis, tinea capitis and fungal keratitis but there are few resources available in the literature to give a good estimate for this in the Irish population and since these conditions are not always clinically apparent there was no resource for direct calculation of these numbers in Ireland. There is a general assumption that the rate of mucormycosis is approximately 2 cases per million population. This and other fungal infection estimates are summarised in the table.

Acknowledgements

Abstract

Objective: India is the world’s second most populous country, with high rates of TB and HIV. Comprehensive baseline data is necessary for effective prioritization of limited public health resources. Using scoping review methodology and deterministic modelling, we have estimated the incidence and 5-year period prevalence of chronic pulmonary aspergillosis (CPA) following TB and prevalence of allergic bronchopulmonary aspergillosis (ABPA) complicating asthma in India.

Methods: The bases for the computations have been published (Denning et al, 2011; Denning et al, 2013). The estimated pulmonary TB rates were calculated using WHO statistics, with deaths excluded. Asthma rate in adults was estimated from the country-specific prevalence of asthma from the GINA report applied to population estimates (mean prevalence of current wheezing in children was 68% of adults in the countries which participated in both studies). Additional modeling was done to accommodate several ABPA studies in India.

Results: In 2011, the population of India was estimated at 1.241,000K. The number of cases of pulmonary TB in India is 8,330,000K (24/100K) and the mortality was 300K (24/100K). The annual estimated incidence of new CPA cases was 85,012 while 5-year period prevalence was 267,987. Rates of 5%, 7% and 20% are applied (Refs. 3-6), the gross numbers of ABPA patients estimated in India rises to 1,185K, 1,660K and 4,742K respectively.

Conclusions

• The total burden of antifungal-responsive chronic and allergic aspergillosis in India is likely to exceed 860,000 patients.

• Epidemiological studies are required to better categorize the burden of these diseases in India.

References

INTRODUCTION/ PURPOSE

Singapore is a cosmopolitan South East Asian country with a Gross Domestic Product of USD 240 billion and a population of 5.35 million. However, the fungal burden is poorly recognized and documented in Singapore. We aim to estimate the burden of fungal infections in the country as part of a multi-national effort to quantify worldwide fungal infections.

METHODS

Estimation of fungal disease burden was extrapolated from available epidemiological documents. Population statistics and respective disease distributions pertaining to HIV, malignancies, tuberculosis, chronic obstructive pulmonary disease (COPD) and asthma were extracted from Singapore Demographics Profile 2012 and Ministry of Health (MOH) releases. The total number with HIV/AIDS was estimated to be 5306 from the MOH statistics in 2011. The number of new AIDS patients per year was 183, with 47.7% presenting with Pneumocystis pneumonia and 9.2% presenting with cryptococcal meningitis (taken from the Communicable Disease Surveillance Report in 1997). The prevalence of moderate to severe COPD and asthma were obtained from MOH statistics. The prevalence of moderate to severe COPD and asthma were obtained from MOH statistics. The number of AML patients per year was estimated to be 161 per year, extrapolated from the data from neighbouring Asian countries with similar population demographics. The number of critical care beds was obtained via a manual count of the hospitals countrywide. In cases whereby local incidence of specific diseases was not known, this was reasonably extrapolated from data in Taiwan and China. While asthma is relatively common in adults (250,000 - 5% of population), ABPA and SAFS are rarely diagnosed. Based on 183 annual new AIDS patients in Singapore in 2011, 9.2% (17) of those with AIDS have cryptococcal meningitis, 47.7% (87) have Pneumocystis pneumonia, 460 patients per year have oral candidiasis, and 265 have esophageal candidiasis. The annual incidence of candidemia is 268 per year (5 per 100000)2-3, with two thirds of the patients being in critical care or surgical care, and one thirds being cancer or immunocompromised patients.

RESULTS

Table: Summary of fungal burden in Singapore

<table>
<thead>
<tr>
<th>Infection</th>
<th>Number of infections per underlying disorder per year</th>
<th>Total burden</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>HIV/AIDS</td>
<td>Respiratory</td>
</tr>
<tr>
<td>Oesophageal candidiasis</td>
<td>265</td>
<td>-</td>
</tr>
<tr>
<td>Candidaemia</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Recurrent</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Chronic pulmonary aspergillosis</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Invasive aspergillosis</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Mucormycosis</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cryptococcal meningitis</td>
<td>-</td>
<td>17</td>
</tr>
<tr>
<td>Pneumocystis pneumonia</td>
<td>-</td>
<td>87</td>
</tr>
<tr>
<td>Histoplasmosis</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Fungal keratitis</td>
<td>6</td>
<td>-</td>
</tr>
<tr>
<td>Tinea capitis</td>
<td>unknown</td>
<td>-</td>
</tr>
<tr>
<td>Total burden estimated</td>
<td>106,008</td>
<td>371</td>
</tr>
</tbody>
</table>

The prevalence of medically-significant fungal infections in the population is under-recognised in Singapore. Increased awareness and surveillance will serve to enhance appropriate allocation of healthcare resources in this disease spectrum.

CONCLUSIONS

The prevalence of medically-significant fungal infections in the population is under-recognised in Singapore. Increased awareness and surveillance will serve to enhance appropriate allocation of healthcare resources in this disease spectrum.

References

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Burden of serious fungal infections in Austria, Abstract Nr. 757

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Abstract

Introduction

The incidence of fungal infections in Austria has been low until recently. We have estimated these based on population size, supplemented with existing data.

Methods

All published epidemiology papers reporting fungal infection rates from Austria were identified. The number of fungal infections occurring each year in Austria is not known. We have estimated these based on populations at risk, supplemented with existing data.

Results

In 1951, 130,964 infections were reported, of which 82.9% occurred in respiratory patients. From 1999 to 2009, the number of fungal infections increased to 518,707, with 98.8% occurring in respiratory patients. The rate of infectious disease infection in Austria is 518,707/8.22M population, consistent with 209 cases, although only 165 were actually recorded. Candida infections are estimated to be 9,949 with severe asthma with fungal sensitisation (SAFS). Of the 15,000 estimated HIV positive patients, only 95 presented with AIDS in 2010 and 100% are taking antiretroviral therapy.

Discussion

From data available, most infections occur in immunocompromised patients. No nation-wide studies on candidemia have been done so far. Overall, we notice an increase of infections due to Candida sp. and Aspergillus species. Deaths occur in patients with hematological malignancies (HMA) and HCV complications. The rate of fungal infections in patients with hematological malignancies is 518,707/8.22M population, consistent with 209 cases, although only 165 were actually recorded. Candida infections are estimated to be 9,949 with severe asthma with fungal sensitisation (SAFS). Of the 15,000 estimated HIV positive patients, only 95 presented with AIDS in 2010 and 100% are taking antiretroviral therapy.

Conclusion

No data on respiratory infections are available. We estimate these based on population size, supplemented with existing data.
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 6.6 million problem.
- This situation is also a problem in Brazil where none of the SHFI Patients with SHFI often require hospital care, as a consequence of other health problems. Despite this, it is internationally neglected.

Assumptions

- Invasive aspergillosis: 13.4% of AML + 2.3% allo HSCT + 0.5% renal Tx (Nucci, 2012) + 13.3% lung Tx (Pasqualotto, 2010). Not available data for aspergillosis in renal, heart and liver Tx in Brazil. World: 6% Heart Tx and 1.3% liver Tx. Other steroids patients ignored: Added to: COPD admissions to hospital per year "0,013.
- Chronic pulmonary aspergillosis (CPA) post tuberculosis: 64,825 TB pulmonary cases, and 55,639 alive pulmonary cases (WHO, 2011).
- 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, 2006).
- Candidaemia in outpatients: 3% of all cases (Colombo, 2006) - conservative assumption, since another publication (Pasqualotto, 2005) revealed 9%.
- Oral candidiasis: 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 women (childbearing age) (75% of woman 10-49 years). Literature estimate is 5-8%;
- Fungal keratitis: 9.01 million of inhabitants per year (based on sales distribution of antifungal eye drops) (Ibrahim, 2012).

Results

Brazilian scenario: Brazil has ~194 million inhabitants (76% adults, 51% women, and 33% 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 365,000 (2010). The chronic obstructive pulmonary disease (COPD) prevalence all GOLD stages is 15.8% with 142,421 COPD admissions to hospital per year. We have an asthma rate in adults estimated in 12.4% (To, 2012). About 200 adults are reported with cystic fibrosis;
- Cancer, leukaemia, transplant and other immunocompromised patients: the AML population frequency is estimated in 51,000 cases 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, lung, heart and liver);
- Critical care and surgery cases: Brazil has 35,403 critical care beds and ~11.6 million (M) of hospital admissions per year. A total of 5.690 peritonel dialysis were done in 2011.

Contrast with official data

- The official hospitalization data for aspergillosis presented 442 cases while in our estimente we have more than 400,000 aspergillosis cases. Most are in the community – allergic and chronic, but there are an estimated 8,684 invasive cases;
- For all kinds of Candida infections the official data in 2011 were 1,242 hospitalizations, differing absurdity of our estimations 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 minority of the cases are treated in public health centers or in private clinics, making the official data collection unreliable.

Graph 1. Aspergillosis estimated cases

Graph 2. Candidiasis estimated cases

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

<table>
<thead>
<tr>
<th>Fungal disease</th>
<th>Total Prevalence</th>
<th>National hospitalization (per year)</th>
<th>Recurrent candida vaginitis (&gt;4x/year)</th>
<th>Oral candidosis</th>
<th>CPA post TB</th>
<th>Invasive aspergillosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucormycosis*</td>
<td>245</td>
<td>0.15</td>
<td>0.06</td>
<td></td>
<td></td>
<td>0.06</td>
</tr>
<tr>
<td>Histoplasmosis*</td>
<td>378</td>
<td>0.23</td>
<td>0.11</td>
<td></td>
<td></td>
<td>0.11</td>
</tr>
<tr>
<td>Thrilamycosis</td>
<td>422</td>
<td>0.29</td>
<td>0.14</td>
<td></td>
<td></td>
<td>0.14</td>
</tr>
<tr>
<td>Total Fungal diseases</td>
<td>1047</td>
<td>0.67</td>
<td>0.22</td>
<td></td>
<td></td>
<td>0.22</td>
</tr>
<tr>
<td>Oral candidosis</td>
<td>2729525</td>
<td>2729525</td>
<td>0.1</td>
<td></td>
<td></td>
<td>0.1</td>
</tr>
<tr>
<td>CPA post TB</td>
<td>12032</td>
<td>12032</td>
<td>0.15</td>
<td></td>
<td></td>
<td>0.15</td>
</tr>
<tr>
<td>Invasive aspergillosis</td>
<td>12032</td>
<td>2.49</td>
<td>0.02</td>
<td></td>
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<td>0.02</td>
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<tr>
<td>Total Candida</td>
<td>2729525</td>
<td>2729525</td>
<td>0.08</td>
<td></td>
<td></td>
<td>0.08</td>
</tr>
</tbody>
</table>

Conclusions

- Based on local data and literature estimates of 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 here.

References