

Serious fungal infections in Egypt

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Abstract We aimed to estimate the burden of serious fungal infections in Egypt, currently unknown, based on the size of the populations at risk and available epidemiological data. Data were obtained from the World Health Organization (WHO), the Joint United Nations Programme on HIV/AIDS (UNAIDS), and published reports with clearcut denominators. When no data existed, risk populations were used to estimate frequencies of fungal infections, using previously described methodology. The population of Egypt in 2011 was ~82,500,000; 31% children, and 8% women >60 years of age. Amongst about 21.8 million women aged 15–50 years, recurrent vulvovaginal candidiasis (≥ 4 episodes/year) is estimated to occur in 1.3 million (3,169/100,000 females). Using a low international average rate of 5/100,000, we estimate 4,127 cases of candidaemia, and 619 patients with intra-abdominal candidiasis. Amongst the survivors of pulmonary tuberculosis (TB) in Egypt in 2012, 319 new cases of chronic pulmonary aspergillosis (CPA) are likely, a prevalence of 1,005 post-TB and a total prevalence estimate of 3,015 CPA patients in all. Asthma is common in Egypt, affecting 9.4% of adults, 5.35 million, and so ABPA and SAFS were estimated in around 162/100,000 and 214/100,000 respectively. Invasive aspergillosis is estimated to affect 495 patients following leukaemia therapy, there are an estimated 37 cases in renal and liver

transplant recipients, and an estimated 132 patients develop IA in the context of lung cancer. Amongst 641,000 COPD admissions to hospital each year, 8,337 patients develop IA. The total HIV-infected population is small, with an estimated 6,500 patients, 2,500 not on antiretroviral therapy. Amongst HIV-infected patients, 38 (0.6%) cases of cryptococcal meningitis and 125 (1.9%) cases of *Pneumocystis* pneumonia are estimated each year. Fungal keratitis is common, with 28–55% (mean 40%) of corneal infections being fungal, an estimated total of 11,550 cases. The present study indicates that 2% of the Egyptian population is affected by fungal infections. The estimates are certainly incomplete, and need further epidemiological and diagnostic studies.

Introduction

The substantial burden of fungal diseases has only recently been estimated as 1,500,000 worldwide deaths every year [1]. Cutaneous fungal diseases are estimated to affect nearly a billion people [2]. Despite this, patients have received little attention from governments and public health authorities. Complete global estimation of the burden of fungal diseases is of great importance for worldwide public health measures, in order to understand and determine impact of these diseases on human populations. Country estimates aid prioritization of diagnostic and treatment resources within each country, and may assist in identifying gaps in care.

Egypt is a transcontinental country that lies in the north-east corner of Africa and in the southwest corner of Asia. The two continents are connected to each other by the land bridge “The Sinai Peninsula”. Egypt is a Mediterranean country. It has an unusually hot, sunny, and dry climate with rain falls in the winter months. Most of Egypt’s territory of 1,010,408 km² lies within the Nile Valley. Egypt is

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categorized as a middle-income country with a per capita gross domestic product (GDP) in 2013 of \$5,370. It has a relatively low rate of both tuberculosis (TB) and HIV infection, but a high rate of hepatitis.

Egypt has the largest population among the Middle East and North African countries, but fungal diseases are hardly addressed. No multicenter epidemiology studies have been reported, but the incidence of some fungal diseases in Egyptian population at risk has been reported previously from single centers; mucormycosis [3], dermatophytosis [4], mycotic keratitis [5, 6], cryptococcosis [7], and candidiasis [8]. Antifungal susceptibility testing of Egyptian fungal pathogens has been reported [9, 10]. The aim of this study is to estimate the burden of serious fungal diseases in Egypt, which has not previously been attempted.

Materials and methods

Published papers reported for incidence and prevalence of fungal diseases from Egypt were identified using the PubMed website and Google search. Populations at risk and frequencies of fungal diseases in those populations were used to estimate the burden of fungal diseases in Egypt. Country population data were taken from The World Health Organization report [11]. Data on the HIV population were extracted from the joint United Nations programme on HIV/AIDS (UNAIDS) 2013 Global report [12]. The number of pulmonary tuberculosis (PTB) cases was obtained from the WHO report [13]. We used the data presented in the 2012 report of the Egyptian Ministry of Health to determine the annual number of renal and liver transplants and cancer (especially leukaemia) patients.

Estimates of invasive candidiasis, *Candida* peritonitis, oral candidiasis, oesophageal candidiasis in HIV infection, and recurrent *Candida* vulvovaginitis (rVVC) were obtained from multiple studies [14–19].

Prevalence of chronic pulmonary aspergillosis (CPA) following (PTB) was estimated according to Denning et al. [20]. The estimated number of people and the number hospitalized with chronic obstructive pulmonary disease (COPD) were taken from Polatali et al. [21]. The rate of IA amongst COPD admissions, based on culture was 1.3% in Madrid [22] or 3.9% in Guangzhou [23] — we have taken a median figure of 2.6%. Asthma rates in adults were obtained from Ben Abdallah et al. [24], while estimates of allergic bronchopulmonary aspergillosis (ABPA) were made using a 2.5% rate of ABPA derived from Al-Mobeireek et al. [25]. Severe asthma with fungal sensitization (SAFS) was estimated by assuming that 10% of adult asthmatics have severe asthma and 33% have fungal sensitization [26]. We have assumed that 10% of patients with acute myeloid leukaemia develop invasive

aspergillosis (IA), and an equal number of all other predisposing haematological malignancies. We also assumed a rate of 1% of IA in renal transplantation and 4% among liver transplantation; there are 5,017 reported cases of lung cancer in Egypt (2012, Globocan data), and we have assumed that 2.63% develop IA [27].

We estimated the incidence of all reported keratitis cases per year in Egypt by assuming that there is a referral eye hospital for 2 million people and all keratitis goes there. Shabrawy et al. [5] collected 350 cases in 6 months, so it is assumed to be 700 in 1 year. Of these, 28–55% were fungal (overall 40%) [5, 6]. This suggests 280 cases for 2 million people, and this enabled us to estimate the number of cases presented annually in Egypt.

Results & discussion

Egypt is the most populous country in the Middle East and North Africa. The inhabitants are concentrated on the sides of the Nile Valley. Egyptians are divided demographically into those who live in the major urban centers and farmers who live in rural villages. The population of Egypt in 2011 was ~82.5 million people; 31% children, 69% adults and 8% women >60 years of age. The estimated number of HIV-infected patients is 6,500, with an estimated 2,500 not on antiretroviral therapy. In 2012, the Egyptian Ministry of Health recorded 1,675 kidney transplantations, 495 liver transplantations, 108,611 cases of cancer in adults, 306 cases of cancer in children, and a total of 93,863 cases of nosocomial respiratory infectious diseases. Using these basic data, an estimation of the total burden of serious fungal diseases in Egypt and the rate per 100,000 inhabitants indicated that about 1,649,686 (2%) Egyptians suffer from serious fungal diseases annually (Table 1).

Amongst about 21.8 million women aged 15–50 years, recurrent vulvovaginal candidiasis (≥ 4 episodes/year) (rVVC) is estimated to occur in 1,307,766 million (3,169/100,000 females), nearly 6% of adult women. Unfortunately, despite its likely high frequency, no study has addressed the problem of VVC or rVVC in Egypt. Using a low international average rate of 5/100,000, we estimate 4,127 cases of candidaemia, and 806 patients with intra-abdominal candidiasis (0.98/100,000), assuming that 39.1% of cases of candidaemia occur in intensive care units [14]. A three-fold higher rate (15.4/100,000) of candidaemia was reported in Qatar (53.5%) [28], possibly suggesting that our estimate is too low. This implies that our estimate of intra-abdominal candidiasis (806 cases or nearly 1/100,000) is also too low. We have not included *Candida* peritonitis attributable to chronic ambulatory peritoneal dialysis through lack of data, but if the same rate

Table 1 The estimated burden of serious fungal diseases in Egypt

| Serious fungal infection | Number of fungal diseases per underlying disorder per year | | | | | Total burden | Rate/100,000 |
|--|--|----------|----------------------|-----------|-------|--------------|--------------|
| | None | HIV/AIDS | Respiratory diseases | Cancer/Tx | ICU | | |
| Cryptococcal meningitis | | 38 | | | | 38 | 0.00 |
| <i>Pneumocystis pneumonia</i> | | 125 | | | | 125 | 0.15 |
| Invasive aspergillosis | | | | 664 | 8,337 | 9,001 | 10.7 |
| Chronic pulmonary aspergillosis — all | | | 3,015 | | | 3,015 | 13.8 |
| Allergic bronchopulmonary aspergillosis (ABPA) | | | 133,834 | | | 133,834 | 162 |
| Severe asthma with fungal sensitization (SAFS) | | | 176,661 | | | 176,661 | 214 |
| Candidaemia | | | | 2,889 | 1,238 | 4,127 | 5.00 |
| Candida peritonitis | | | | | 619 | 619 | 0.75 |
| Oral candidiasis | | 2,250 | | | | 2,250 | 2.73 |
| Oesophageal candidiasis | | 700 | | | | 700 | 0.85 |
| Recurrent candida vaginitis ($\geq 4 \times$ /year) | 1,307,766 | | | | | 1,307,766 | 3169 |
| Fungal keratitis | 11,550 | | | | | 11,550 | 14 |
| Total serious fungal diseases burden | | | | | | 1,649,686 | |

is used as for Hungary [29], this might constitute another 320 intra-abdominal cases. In HIV patients, 2,250 cases of oral candidiasis and 700 cases of oesophageal candidiasis are expected annually. The rates of oral and oesophageal candidiasis were low, as the HIV-infected population is 6,500 patients only; oral candidiasis is reported in 34.6%, while 10.7% is the reported percentage of oesophageal candidiasis in HIV patients.

Egypt has a very high prevalence of chronic respiratory diseases, notably asthma and COPD. These patients are at risk of allergic, chronic, and invasive fungal disease. Asthma is common in Egypt, affecting 9.4% of adults or 5.35 million people. ABPA is therefore estimated to affect 133,834 (162/100,000). SAFS is estimated in around 176,661 people (214/100,000). The total number of allergic pulmonary fungal disease is probably less than the total of ABPA and SAFS (310,495) because of duplication. If the assumption of a 20% overlap between these entities is assumed, then nearly 250,000 have asthma exacerbated by fungal allergy which is potentially responsive to antifungal therapy [30]. There are about 6,500 deaths from asthma in Egypt each year, and many of these are potentially avoidable if antifungal therapy were given. The rate of COPD is moderately high at 3.5% of the over-40-year-old age group, with a high rate of hospitalization of 20.3% [31]. COPD is an important underlying cause of CPA and IA, as is pulmonary TB. We have a total prevalence estimate of 3,015 CPA patients in all, with 319 new cases of CPA reported per year. Amongst the survivors of pulmonary TB in Egypt in 2012, we have conservatively estimated that one-third of the CPA cases are TB-related, a prevalence of 1,005 post-TB. Invasive aspergillosis is estimated to affect 495 patients following leukaemia therapy, but is probably more common in COPD. Our estimates for IA is 8,337 cases

annually in hospitalized COPD patients. In addition, there are an estimated 37 cases in renal and liver transplant recipients, and an estimated 132 patients develop IA in the context of lung cancer. The overall number of CPA patients, estimated at 3,015, is still a significant public health issue at 14/100,000. Part of the reason why it is problematic is that it is frequently mistaken for pulmonary TB, and inappropriate treatment may be given [32].

Amongst 6,500 HIV-infected patients, 38 cases (0.6%) of cryptococcal meningitis and 125 cases (1.9%) of *Pneumocystis pneumonia* are estimated each year. We have not been able to estimate non-HIV incidence of cryptococcal meningitis or *Pneumocystis pneumonia*, so both are likely to be underestimates.

Fungal keratitis is common with 28–55% (mean 40%) of corneal infections being fungal; we used an estimated total of 11,550 cases (14/100,000) reported annually in Egypt, and this has not been estimated in any other Middle Eastern country previously.

Conclusion

It was possible to estimate the burden of serious fungal diseases in this preliminary report but, unfortunately, cutaneous fungal diseases couldn't be estimated. Egypt, the highest populated country in the Middle East and North Africa region, needs to establish at least a few medical mycology reference laboratories [1], support multicenter epidemiology studies on fungal diseases especially the cutaneous fungal diseases, and increase the availability of antifungal drugs for treatment and management.

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