

# Burden of serious fungal infections in Trinidad and Tobago

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## Summary

The information on the prevalence of fungal infections in the Caribbean region including Trinidad and Tobago (population 1 339 000 million) is scanty. Tinea capitis is common in children, being predominant in those of African descent, with no definitive estimate. Asthma is also common affecting 77 000–139 000 adults with an estimated 1927–3491 affected by allergic bronchopulmonary aspergillosis (ABPA) and 2544–4608 with severe asthma and fungal sensitisation (SAFS). An estimated 23 763 women have  $\geq 4$  attacks of vaginal candidiasis annually. Among the estimated 14 000 HIV-infected patients, 750 cases of oesophageal candidiasis, 400 cases of Pneumocystis pneumonia (PCP) and 50 cases of cryptococcal meningitis are anticipated. *Histoplasma capsulatum* is endemic in the islands with a 49% skin positivity rate in those <60 years old. Three cases of cutaneous histoplasmosis in AIDS patients have been reported. Three cases of pulmonary histoplasmosis were reported among German biologists following exposure to bats in a cave in Trinidad. Using a low mean international incidence figure for candidaemia of 5/100 000, 67 cases of candidaemia are estimated. The burden of fungal infections in Trinidad and Tobago is considerable and requires appropriate diagnostic and clinical expertise.

**Key words:** Fungus, prevalence, incidence, tinea, Pneumocystis, aspergillosis.

## Introduction

The information on the incidence and prevalence of fungal infections in developing countries is very scanty. This is particularly so in the Caribbean region including Trinidad & Tobago (T&T). This is due to several factors, namely, lack of awareness about the seriousness of some fungal infections, paucity of laboratory

facilities and lack of specialists for accurate diagnosis and treatment. The public health authorities have also not shown much interest in these infections, despite some of them being life-threatening. The incidence of tinea capitis, a fungal infection of scalp has been investigated in children.<sup>1</sup> *Histoplasma capsulatum* has been recovered from bat caves;<sup>2–4</sup> and there are reports of cases of histoplasmosis in AIDS patients and explorers of bat cave in T&T and the general population.<sup>5,6</sup> There are also reports of one case each of paracoccidioidomycosis<sup>7</sup> and mycetoma.<sup>8</sup> However, no attempt has been made to determine the extent of morbidity and mortality of fungal infections. The present study is the first of its kind and is aimed at estimating the burden of serious fungal infections in T&T (Fig. 1).

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## Methods

We extracted data from published papers on HIV infection, the WHO STOP TB program and UNAIDS. If



**Figure 1** Chest X-ray showing bilateral diffuse infiltration in a 43-year-old German biologist who developed histoplasmosis following an exposure to bats in Tamana cave in Trinidad (Jülg *et al.* 2008) [5].

no data existed, we used specific populations at risk and fungal infection frequencies in those populations to estimate national incidence or prevalence. Estimates of invasive mycoses were based on incidence rates reported in the international literature, although this proved to be impossible for histoplasmosis. Chronic pulmonary aspergillosis (CPA) prevalence used the incidence of pulmonary TB in 2012 and assumptions as reported previously,<sup>9</sup> and an estimate of the relative ratio of pulmonary TB with other underlying diseases associated with CPA. Estimates of allergic bronchopulmonary aspergillosis (ABPA) and severe asthma with fungal sensitization (SAFS) complicating asthma in adults were based on asthma rates in T&T in 10–19 year olds.<sup>10</sup> As asthma often remits in late adolescence, these rates may be an overestimate in adulthood; an alternative estimate based on the ratio of young adolescence and adult asthma rates in Jamaica (56%) was made. ABPA prevalence is assumed to be 2.5% of adult asthma rates.<sup>11</sup> SAFS is estimated by assuming that 10% of adult asthma is severe and that conservatively 33% of severe asthmatics are sensitised to fungi. The denominators included the overall and female T&T population, number of patients with HIV/AIDS and various respiratory diseases (Table 1).

## Results

The population of T&T has been estimated to be 1 339 000 million people (2009), of whom 21% are

children (0–14 years) and 10% are  $\geq 60$  years old. The gross domestic product (GDP) per person in T&T in 2013 was USD\$18,373. Asthma prevalence (wheezing in the last 12 months) is 13.2% in adolescents (11–19 years old).<sup>9</sup> Assuming this frequency is the same throughout adulthood there are an estimated 139 631 adult asthmatics or using the Jamaica ratio, the total estimate falls to 77 088. Using an ABPA rate of 2.5% based on other studies including one from South Africa,<sup>11</sup> T&T has an estimated 3491 ABPA cases and 4608 SAFS cases. The lower asthma estimate generates national prevalence estimates of 1927 and 2544 for ABPA and SAFS. In contrast, chronic pulmonary aspergillosis is uncommon with an estimated prevalence of 27 cases after TB, as few cases of TB are found on T&T. As CPA complicates several other pulmonary diseases, TB comprises an estimated 33% of the total chronic pulmonary aspergillosis (CPA) caseload, therefore 110 total CPA cases are expected nationally (8.2/100 000).

We estimate 23 763 women have  $\geq 4$  attacks of vaginal candidiasis annually (6% women  $>15$  years, based on several studies.<sup>12–14</sup>) Using a low mean international figure for candidaemia incidence of 5/100 000,<sup>15,16</sup> 67 cases of candidaemia are estimated to occur each year. If it is assumed that one-third of these cases occur in ICU, and that the ratio of peritonitis in surgical patients to candidaemia in ICU is the same as in France,<sup>17</sup> then 10 cases of *Candida* peritonitis annually could be expected in T&T.

An estimated 14 000 people are infected with HIV in T&T, an adult prevalence rate of 1%, of whom at least 5 000 are not on antiretroviral therapy ( $<350$  CD4  $\mu\text{l}^{-1}$ ).<sup>18</sup> Assuming that 50% of these patients (2250) have CD4 cell counts  $<200$   $\mu\text{l}^{-1}$ , probably 90% of them develop oral candidiasis ( $n = 2025$ )<sup>19</sup> and 20% or 750 cases develop oesophageal candidiasis.<sup>20,21</sup> Assuming that 10% of those not on antiretroviral therapies progress to a life-threatening opportunistic infection each year, an annual rate of 400 (80%) cases of *Pneumocystis pneumonia* (PCP)<sup>22</sup> and 50 (10%) of cryptococcal meningitis would be expected in AIDS patients. It was not possible to estimate the burden of histoplasmosis because of the paucity of data, but it certainly exists as several small series and case reports have been documented.<sup>5,6</sup> Based on the rates of acute myeloid leukaemia in the population,<sup>23</sup> an estimated 8 cases of invasive aspergillosis occurred in haematological patients. Mucormycosis and fungal keratitis caseload could not be estimated. One case of each paracoccidioidomycosis and mycetoma due to *Exophiala jeanselmei* has been reported.<sup>7,8</sup>

**Table 1** Estimated burden of fungal disease in Trinidad and Tobago.

Fungal condition	Number of infections per underlying disorder per year 2010					Total burden	Rate/100K
	None	HIV/AIDS	Respiratory	Cancer/Tx	ICU		
Oesophageal candidiasis	?	750	–	?	–	750	56
Candidaemia	–	–	–	67	20	67	5
Candida peritonitis	–	?	–	–	10	10	0.8
RVVC (4x/year +)	23 763	–	–	–	–	23 763	3550
ABPA	–	–	1927–3491	–	–	1927–3491	146–260
SAFS	–	–	2544–4608	–	–	1927–4608	193–344
CPA	–	–	110	–	–	110	8.2
IA	–	–	–	8+	?	8+	0.6
Mucormycosis	–	–	–	?	–	?	?
Cryptococcal meningitis	?	50	–	–	–	50	3.7
PCP	–	400	?	?	–	400	30
Histoplasmosis	?	?	?	–	–	?	?
Fungal keratitis	?	–	–	–	–	–	?
Tinea capitis	?	–	–	–	–	?	?
Total estimated burden.	23 763+	1200+	8208	75+	30+	31 887+	

–, No cases likely, so not estimable; ?, estimate not possible but some or many cases likely; ABPA, Allergic bronchopulmonary aspergillosis; CM, Cryptococcal meningitis; PCP, *Pneumocystis jirovecii* pneumonia; IA, Invasive aspergillosis; CPA, Chronic pulmonary aspergillosis; RVVC, Recurrent vulvovaginal candidiasis (rate per 100,000 in females only); SAFS, Severe asthma with fungal sensitisation.

## Discussion

HIV/AIDS in the Caribbean and the northern tip of South America is a major public health problem. In T&T, 1% of the adult population is estimated to be infected and of these 5000 with low CD4 cell counts are not on antiretroviral therapy.<sup>18</sup> Therefore, it is highly likely that cryptococcal meningitis, PCP and probably disseminated histoplasmosis are much more common than is apparent from the dearth of literature. Six cases of cryptococcal meningitis were known from Jamaica as far back as in 1980<sup>24</sup> and there is a recent report of a case of systemic cryptococcosis with cutaneous manifestations.<sup>25</sup> A very recent review recorded 97 cases of cryptococcosis in Cuba, 82 of these occurred in AIDS patients and 15 in non-AIDS patients.<sup>26</sup> The rarity of reports on cases of histoplasmosis in T&T probably does not match the reality as the fauna including species of bats overlaps that of Martinique, where disseminated histoplasmosis is the second most frequent opportunistic infection in HIV patients in Martinique and the first cause of death;<sup>27</sup> the prevalence of skin reactivity to histoplasmin in Trinidad<sup>28</sup> is also much higher (49%) than that observed (12%) in Martinique.<sup>29</sup> Also three cases of cutaneous histoplasmosis have been reported in HIV-infected patients.<sup>6</sup>

Histoplasmosis may also occur in immunocompetent patients in T&T, but is missed due to under diagnosis. Three cases of pulmonary histoplasmosis were

reported in German speleologists who visited a bat-infested cave, viz. Tamana cave in November 2006.<sup>5</sup> Histoplasmosis is also known to be endemic in some other Caribbean countries. Natural occurrence of *H. capsulatum* in soil in a bat cave has been demonstrated in Jamaica and several cases of clinical infections due to this fungus are known in this country.<sup>30</sup> A review of literature on serious fungal infections in Dominican Republic (DR) revealed two cases of AIDS-associated disseminated histoplasmosis in Dominican immigrants in USA and another two cases of histoplasmosis in immunocompetent Italian patients, the infection was acquired in DR in all these cases.<sup>31</sup> A case of histoplasmosis manifesting as renal fibro-inflammatory pseudotumour closely mimicking a malignant tumour has been reported from Surinam.<sup>32</sup> Histoplasmosis occurs in all regions of Cuba<sup>33</sup> and there is a report of three cases of pulmonary histoplasmosis that occurred in a group of 12 French cavers after a trip to Cuba.<sup>34</sup> Epidemiology studies using skin testing demonstrated histoplasmosis in the residents in Eastern Nigeria in the vicinity of a bat cave which was the focus of *H. capsulatum* var. *duboisii*.<sup>35,36</sup> Taking a cue from this study, investigation of skin reactivity in the inhabitants around the bat caves and among the frequent local visitors of these caves in Trinidad might give a more realistic estimate of asymptomatic histoplasmosis and possibly reveal a few cases of subclinical infection due to *H. capsulatum* in this island.

Asthma is also particularly common in T&T, as across the Caribbean. Therefore, it is highly likely that both ABPA and SAFS are also common. Both these conditions respond to antifungal therapy when conventional medication for asthma is inadequate.<sup>37–39</sup> Substantial health gains are possible in these patients with appropriate investigations. Little is known about ABPA in children and adolescence.

Virtually no data exist about the commonest invasive fungal infections in hospitalised patients, such as candidaemia, invasive candidiasis, *Candida* peritonitis and invasive aspergillosis. Conservative estimates of these infections were made, but usually the rates are much higher than the current diagnostics would indicate, even when regularly and frequently undertaken. Failure to diagnose invasive aspergillosis at autopsy is common.<sup>40,41</sup> Without the implementation of biomarker-based diagnostic and molecular techniques,<sup>42</sup> unrecognised deaths due to fungal infection will continue.

No attempt was made to enumerate or estimate cutaneous fungal infections in T&T. However, these are very common and usually easy to treat, if temporarily disfiguring and transmissible. We would like to have captured tinea capitis in children, especially a substantial minority of those affected develop kerion (highly inflammatory scalp ringworm with abscess formation), which often results in permanent hair loss and scarring of the scalp. However, data are lacking. Several cases of skin and nail infections caused by *Nattractia mangiferae* (*Hendersonula toruloidea*) and *Scytalidium hyalinum* have also been reported from Tobago.<sup>43</sup>

Numerous cases of chromoblastomycoses have been reported from other Caribbean countries, including Jamaica<sup>44</sup> and Cuba,<sup>45,46</sup> as well as the neighbouring continental countries Venezuela and Brazil.<sup>45</sup> Mycetoma is regularly encountered in South America as evidenced by reports of numerous cases from Mexico, Brazil and Argentina.<sup>45,47</sup> Two histologically diagnosed cases of mycetoma of indefinite aetiology were described from Cuba as early as 1919.<sup>48</sup> However, a recent systematic review of global burden of mycetoma<sup>47</sup> did not mention any case from Cuba. Possibly mycetoma caused by fungi (eumycetoma) is rare in Cuba. Numerous cases of sporotrichosis and some of phaeohyphomycosis have been reported from several countries in South America.<sup>45</sup> Comprehensive collaborative studies on the occurrence of subcutaneous mycoses in T&T will likely yield useful information about the epidemiology of mycetoma, chromoblastomycosis and possibly other infections including sporotrichosis and subcutaneous phaeohyphomycosis in these islands.

## Conclusion

Using the local data and the literature estimates of incidence or prevalence of fungal infections, over 31 000 people in T&T (2.3%) are estimated to be suffering from serious fungal infections each year. Local epidemiological studies are urgently required to validate or modify these estimates. Histoplasmosis is a serious public health issue that is relatively unknown in the Caribbean region. It poses a threat for people living with HIV/AIDS. Disseminated histoplasmosis often mimics tuberculosis and is often treated as such without success, and then falsely labelled as 'drug-resistant tuberculosis'. There is a great need for the public health authorities and medical authorities to create awareness about these serious systemic fungal infections in T&T. Also a well-equipped medical mycological laboratory should be established in T&T for definite diagnosis of serious fungal infections; this would facilitate timely rational therapy for the affected patients. It adds to the growing estimates of fungal disease burden in the Americas.<sup>30,31</sup>

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