



### Burden of Serious Fungal Infection in Nigeria

*Les Fardeaux D'une Infection Mycosique Grave au Nigeria*

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#### ABSTRACT

**BACKGROUND:** Nigeria is the most populous country in Africa with a high rate of tuberculosis and a moderate HIV infection burden. Cutaneous and mucosal fungal infections are reported from Nigeria but there are few reports of serious fungal infections.

**METHODS:** A literature search was done to identify all epidemiology papers reporting fungal infection rates from Nigeria. We used specific populations at risk derived from the WHO and literature and the fungal infection frequencies were used to estimate national incidence or prevalence.

**RESULTS:** 1.5M Nigerian women get recurrent vaginal thrush. Tinea capitis occurs in >20% of school age children, translating to over 15.5M children affected. Based on the 3,459,363 cases of HIV infection; an estimated 1,449,166 (55% children) of whom are on ARV therapy; there are 281,180 new AIDS cases, and an estimated 57,866 cases of cryptococcal meningitis. 75,000 patients with AIDS cases are expected to develop *Pneumocystis pneumonia* (40% rate in children), 253,000 oral candidiasis and 144,000 oesophageal candidiasis. There were 78,032 cases of pulmonary TB in 2010, and we anticipate 19,000 new cases of chronic pulmonary aspergillosis with a 5 year period prevalence of 60,377 cases. Prevalence of asthma in adults is 15.2%, estimated at 3.7M adult asthmatics of which 94,000 (2.5%) will have ABPA and 124,000 severe asthma with fungal sensitisation (SAFS). Rates of candidaemia, *Candida peritonitis*, invasive aspergillosis and mucormycosis were estimated on a population basis, without supporting data and are probably uncommon or rare.

**CONCLUSION:** Our estimates indicate that over 11.8% of the Nigerian population is estimated to suffer from a serious fungal infection each year. If tinea capitis and recurrent vaginal thrush are excluded, over 960,000 are estimated to be affected, with substantial mortality. Epidemiological studies are urgently required to validate or modify these estimates. *WAJM* 2014; 33(2): 107–114.

**Keywords:** Nigeria, candidaemia, cryptococcal meningitis, aspergillosis, keratomycosis, PCP, candidiasis.

#### RÉSUMÉ

**CONTEXTE:** Le Nigeria est le pays le plus peuplé d'Afrique avec un taux élevé de tuberculose et une charge modérée d'infection au VIH. Les infections mycosiques cutanées et muqueuses sont rapportées au Nigéria, mais il y a peu de rapports sur les infections mycosiques graves.

**METHODES:** Une recherche dans la littérature a été effectuée afin d'identifier les papiers d'épidémiologie rapportant sur le taux d'infection mycosique au Nigeria. Nous avons utilisé des populations spécifiques à risque provenant de l'OMS et de la littérature et les fréquences d'infection mycosiques pour estimer l'incidence ou la prévalence nationale.

**RESULTATS:** 1,5 million de femmes nigérianes ont une mycose vaginale récurrente. La teigne survient dans > 20 % des enfants d'âge scolaire, traduisant une atteinte de plus de 15,5 millions d'enfants. A partir de 3.459.363 de cas d'infection au VIH; environ 1.449.166 (55%) d'enfants sont sous traitement ARV; il y a 281 180 nouveaux cas de sida, et environ 57 866 cas de méningite à Cryptocoque. 75 000 patients atteints de sida développeront une pneumonie à *Pneumocystis* (40% chez les enfants), 253 000 de candidose buccale et 144 000 de candidose œsophagienne. Il y avait 78 032 cas de tuberculose pulmonaire en 2010, et nous prévoyons 19 000 nouveaux cas d'aspergillose pulmonaire chronique avec une prévalence de 60 377 cas sur une période de 5 ans. La prévalence de l'asthme chez les adultes est de 15,2%, environ 3,7 million d'adulte asthmatiques dont 94 000 (2,5%) auront ABPA et 124000 d'asthme sévère à sensibilité fongique (SF). Le taux de candidémie, de péritonite à *Candida*, d'aspergillose invasive et de mucormycose ont été estimés sur la base d'une population, sans l'appui de données et sont probablement peu fréquentes ou rares.

**CONCLUSION:** Nos estimations indiquent que plus de 11,8% de la population nigériane sont susceptible de souffrir d'une infection mycosique grave chaque année. Si la teigne et la mycose vaginale récurrente sont exclues, plus de 960 000 selon les estimations, seront touchées, avec une mortalité importante. Les études épidémiologiques sont nécessaires de toute urgence pour valider ou modifier ces estimations. *WAJM* 2014; 33(2): 107–114.

**Mots clés:** Nigéria, candidemia, méningite à cryptococcose, aspergillose, keratomycose, PCP, candidose.

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**Abbreviations:** AJOL, African Journals Online; COPD, Chronic Obstructive Pulmonary Disease; HAART, Highly Active Antiretroviral Therapy; HIV, Human Immunodeficiency Virus; HSCT, Hematopoietic Stem Cell Transplantation; IFDs, Invasive Fungal Infections; NTM, Nontuberculous Mycobacterial; rVVC, recurrent Vulvovaginal Candidiasis; SAFS, Severe Asthma with Fungal Sensitisation.

## INTRODUCTION

Invasive fungal infections have emerged worldwide as an increasingly frequent cause of opportunistic infections.<sup>1</sup> The incidence of nosocomial fungal infections has continued to rise inexorably over the past three decades as improved therapies for previously untreatable conditions renders patients more susceptible.<sup>2,3</sup> The populations of patients at risk have expanded to include those with usually multiple underlying medical conditions, such as solid organ and hematopoietic stem cell transplantation (HSCT), chronic obstructive pulmonary disease (COPD), novel immunosuppressive therapies for rheumatoid arthritis and other inflammatory and malignant conditions, human immunodeficiency virus (HIV) infection, premature birth, advanced age, complex surgery and cancer.<sup>1</sup> The etiology of invasive mycoses has also changed; *Candida* infections were the most common in clinical practice, but have been supplemented in many patient groups by mould infections. The most frequent filamentous fungi (moulds) isolated are *Aspergillus* spp., but *Fusarium* spp., *Scedosporium* spp., *Penicillium* spp. and Zygomycetes are increasingly seen.<sup>4</sup> However the two most common organisms in all epidemiological studies of invasive fungal infections are *Candida* spp. and *Aspergillus* spp.<sup>4,5</sup>

Invasive aspergillosis complicates haematological malignancy treated with chemotherapy and stem cell transplant.<sup>6,7</sup> Chronic pulmonary aspergillosis is associated with nontuberculous mycobacterial (NTM) disease and may follow tuberculosis as well as other pulmonary conditions such as COPD and sarcoidosis.<sup>8-10</sup> Critically ill patients and neutropenic patients have been shown to be at risk of candidaemia<sup>11</sup> and invasive aspergillosis. There is a strong association between mucormycosis and uncontrolled diabetes.<sup>12</sup> The epidemic of HIV is also a major factor that has contributed to a remarkable increase in the frequency of mucosal candidiasis; before the extensive use of highly active antiretroviral therapy (HAART) in developed countries, 80% of HIV-infected patients developed oral

candidiasis and about 20% esophageal candidiasis.<sup>13</sup> Many HIV-infected patients also developed cryptococcosis, *Pneumocystis* pneumonia and other lethal mycoses, for example, penicilliosis and disseminated histoplasmosis.<sup>4,12,13</sup>

The increase in the burden of serious fungal infections has been demonstrated in some parts of the world. For instance, data from a survey of the epidemiology of sepsis conducted in the USA revealed that the incidence of fungal sepsis increased three-fold between 1979 and 2000<sup>14</sup> and most often the diagnosis was made postmortem implying a low index of suspicion and treatment.<sup>15</sup> It has been estimated that 4% of all patients who die in hospitals die of invasive aspergillosis and 2% die of invasive candidiasis.<sup>16,17</sup> Late or no treatment are independent predictors of death in both conditions.<sup>6,18</sup>

The overall incidence of cryptococcosis in the general population of South Africa was 15.6/100,000 with a 27% mortality rate in 2002–2004.<sup>19</sup> Other South African studies revealed that, the prevalence of cryptococcal antigenemia was 7%<sup>20</sup> and 48.6% for *Pneumocystis jirovecii* pneumonia (PCP).<sup>21</sup> The rate of cryptococcal infection in Uganda, (a sub-Saharan African country where about 1.1 million have HIV with an estimated 9.2% (101,000) have a CD4 count <200 cells/ $\mu$ L) was 40.4 cases per 1,000 person years and 1.5 cases per 1,000 person years in the pre-highly active antiretroviral therapy (HAART) and HAART period, respectively.<sup>22</sup>

HIV/AIDS is a huge problem in Nigeria which has a population of about 160 million people. The estimated number of HIV/AIDS infected people was 3.3 million in 2010, with 281,180 new AIDS cases and 215,130 AIDS-related deaths.<sup>23</sup> About 25% of tuberculosis cases occur in HIV positive patients (51/1,000) and 210/1,000 occur in the total population annually for HIV negative and HIV positive cases respectively.<sup>23</sup> The burden of serious fungal infections has not been properly described in Nigeria, despite these substantial underlying disease frequencies. There are very few epidemiological data on serious fungal infections in Nigeria; only few case reports of invasive fungal are available to our

knowledge.<sup>24-26</sup> We therefore estimated the burden of serious fungal infections in Nigeria based on the populations at risk to provide useful data to highlight the burden of the diseases in our country and for comparison with data from other parts of the world.

## METHODOLOGY

The literature search for publications on invasive fungal infections in Nigeria preceding 31 September 2013, was performed using Medline, Google Scholar, Pubmed website, African Journals Online (AJOL) databases and grey literature to identify all published papers reporting fungal infection rates from Nigeria. The table of contents of medical journals listed on AJOL and associated links (National Library of South Africa, Ingenta, and Quarterly Index to Periodical Literature of the Library of Congress) were also searched electronically. Articles on worldwide epidemiology of Invasive fungal infections (including World Health Organization publications) were reviewed for citations of publications (journal articles and books or monographs) from Nigeria and Africa. The references in all relevant papers were reviewed for additional publications that may not have been cited elsewhere (“snow balling”). Articles published in other languages (e.g., French and Portuguese) were considered if they were cited in any of the databases searched. The Boolean operator ‘AND’ was used to combine and narrow the searches.

During the searching, abstracts were reviewed and the relevant full text articles were selected. The next step involved a manual search of the reference lists of all the selected articles to identify other relevant articles for final selection.

Articles were selected if the following inclusion criteria were fulfilled: availability of full text article in English; studies were performed on humans and site of infection was unambiguously stated. The search terms used were “fungal infections and Nigeria,” “mycosis and Nigeria”, “candidaemia and Nigeria,” “candidiasis and Nigeria”, “aspergillosis and Nigeria,” “cryptococcosis and Nigeria,” “histoplasmosis and Nigeria,” and “fungal keratitis and Nigeria.” In

addition, specific disease conditions and “fungal infections” were searched. In each paper, study design including population base (hospital, community, and special cohorts), diagnostic criteria for invasive fungal infections, survey methods, and results were reviewed.

We used specific populations at risk and fungal infection frequencies in the population to estimate national incidence or prevalence where no relevant studies were available. WHO population statistics of 2009, the 2010 WHO HIV infection and ARV treatment rates; National Agency for the Control of AIDS child/adult HIV split 2011, WHO 2010 TB statistics, ISAAC estimate of asthma prevalence are some of the other databases used for estimating population at risk.

### Study Design

Including population based (hospital, community, and special cohorts), diagnostic criteria for fungal infections, survey methods, and results were reviewed and compared. The overall terminology used as previously listed above and diagnostic criteria for fungal infections with emphasis on serious fungal infections especially IFIs were considered in calculating estimates. Studies that were not invasive fungal infections were excluded apart from a handful of more serious superficial and cutaneous infections that were used to estimate the burden of the disease. However, for clarity purpose, this review is focused on invasive fungal infections. Due to the heterogeneity of the study methodologies in this review it was not possible to apply the conventional methods of a systematic review. A meta-analysis is only appropriate if there is satisfactory similarity in the populations studied and the measurements used. This was not the case with the studies identified in this review. Therefore, a narrative approach was taken to report the findings of the included studies.

### Data Extraction and Synthesis

Annual incidence estimates were derived as follows. 6% rate of recurrent vulvovaginal candidiasis (rVVC) in 15–50-year-old age group, based on work by Ekpenyong *et al.* 2012.<sup>27,28</sup> Oral

candidiasis was only estimated for new AIDS cases and was assumed to occur in 90% of them.<sup>29</sup> Oesophageal candidiasis was estimated to occur in 20% of new AIDS patients and 5% of those with CD4 cell counts on ARVs.<sup>13,30</sup> To estimate cryptococcal meningitis, we have assumed this occurs primarily in adults (cases do occur in children but are uncommon) and that the rate is 12.7% in screening in outpatients with HIV infection and CD4 cell counts <200/ $\mu$ L,<sup>31</sup> 45% of the 1,400,000 estimated patient not receiving ARVs. In addition, new AIDS cases presenting to the hospital develop cryptococcal meningitis (38% of all cases of meningitis in one hospital in Jos,<sup>32</sup> probably at a rate of about 10%. This ignores all occurrences after ARVs commence, which varies between 4 and 12% in the first year.<sup>33</sup> All cases occurring in other patient groups have been ignored. To estimate the frequency of PCP, we have assumed that 40% of new AIDS cases in children present with this infection and 10% of adults.<sup>33,34</sup> Again we have ignored cases that occur while on ARV therapy and non-AIDS PCP.

We estimated invasive, chronic and allergic aspergillosis in adults only. Chronic pulmonary aspergillosis estimate was taken from Denning DW (2001)<sup>10,35</sup> which was based on population data from 2005 and TB data from 2007, and allergic bronchopulmonary aspergillosis from Denning, 2013.<sup>36</sup> We have estimated the rate of severe asthma with fungal sensitization by taking the asthma rate in adults and assuming that 10% are severe and that 33% are sensitized to one or more fungi. The number of adults with asthma were estimated from Ozoh *et al.*, 2012, and Denning *et al.*, 2013.<sup>37,36</sup> Invasive aspergillosis was only estimated in haematological malignancy by assuming that 10% of acute myeloid leukaemia patients (rate 3/100,000 population) develop IA and that an equal number of cases are found in all other haematological patients, as in France and Austria.<sup>7,38</sup> Case frequency following transplantation, others on corticosteroid therapy, including COPD and other immunocompromised patient groups are not known.

Candidaemia is assumed to occur at a relatively low rate of 6 per 100,000, and

of these 33% occur in intensive care, including premature neonates.<sup>39</sup> *Candida* peritonitis complicates complex surgical cases in ICU, at a rate approximately 50% of candidaemia.<sup>40</sup> We have not estimated urinary candidiasis, which is very common, but often of uncertain significance. Mucormycosis was estimated to occur at a rate of 0.2/100,000 (a general literature estimate). Fungal keratitis was not possible to estimate. The estimate for tinea capitis was from study which documented a prevalence of 9.4% amongst school-children.<sup>41</sup>

### RESULTS

Five epidemiological or descriptive studies were included in our analysis of which only 3 were cited in Pubmed, one from AJOL database and a case report from a non-indexed online journal.. The baseline characteristics of the studies are shown in Table 1.

#### Prevalence Based Superficial Fungal Infections

There have been a handful of studies on superficial and cutaneous fungi infections in Nigeria. These studies have been mainly on Tinea capitis, oral candidiasis and vulvovaginal candidiasis. Of the 155 million Nigerian population 50% are children and 38 million are women between the age of 15 and 50 years. We estimate that ~1,500,000 Nigerian women between the ages of 15 and 50 get recurrent vaginal thrush, ie at least 4 times annually. Local estimates of tinea capitis at 9.4% of school age children, suggesting that over 15,500,000 children have tinea capitis.

#### HIV/AIDS-related Invasive Fungal Infections

Based on the 3,459,363 cases of HIV infection reported (55% children) and 1,449,166 on ARV therapy and 281,180 new AIDS cases, we estimate 57,894 cases of cryptococcal meningitis annually. This number is derived from 10% of new adult AIDS cases (12,600), 12.7% of adults with CD4 counts less than 200/ $\mu$ L (40,005 patients) and 10% additional cases in children (5,260 affected). In addition, 74,594 of the AIDS cases are expected to develop

**Table 1: Baseline Characteristics of Studies on Invasive Fungal Infections in Nigeria**

Authors (Year)	Location in Nigeria	Type of Study	Sample Size and Population Studied	Fungal Infection	Age	Rates (%)
Gugnani <i>et al</i> (1976) <sup>25</sup>	Eastern Nigeria	Case report	36 Hospital-based	Fungal Keratitis	Adults	58.3
Ekanem <i>et al</i> (2009) <sup>27</sup>	South-south Nigeria	Case report	1 Hospital-based	Histoplasmosis	Adult	
Gomerep <i>et al</i> (2010) <sup>31</sup>	North-Central Nigeria	Propective	100 Hospital-based	Cryptococcal meningitis	Mixed (adults and children)	36.0
Osazuwa <i>et al</i> (2012) <sup>30</sup>	Mid-Western Nigeria	Prospective	150 Hospital-based	Cryptococcosis	20–50 years	12.9
Fayemimo <i>et al</i> (2013) <sup>60</sup>	Western Nigeria	Retrospective	48 Hospital-based	Fungal Keratitis	Mixed (adults and children)	8.4

**Table 2: Estimated Burden of Serious Fungal Infections in Nigeria**

Infection	None	Underlying Disease				Total Burden	Rate / 100K
		HIV/AIDS	Respiratory	Cancer/Tx	ICU		
Oesophageal candidiasis	-	144,195	?	?	?	144,195	93.2
Oral candidiasis	-	253,062	?	?	?	253,062	163.6
Candidaemia	-	?	?	3,095	6,189	9,284	6.0
Candida peritonitis	-	-	-	-	2,321	2,321	1.5
Recurrent vaginal candidiasis (4x/year)	1,521,520	-	-	-	-	1,521,520	3800.0
ABPA	-	-	93,649	-	-	93,649	60.5
SAFS	-	-	123,617	-	-	123,617	79.9
Chronic pulmonary aspergillosis	-	-	120,753	-	-	120,753	78.0
Invasive aspergillosis	-	?	?	928	?	928	0.6
Mucormycosis	-	-	-	300	-	300	0.2
Cryptococcal meningitis	?	57,894	?	?	-	57,894	37.4
Oral candidiasis	253,062					253,062	163.6
Pneumocystis pneumonia	-	74,594	?	?	?	74,594	48.2
Histoplasmosis	?	?	?	-	-	?	?
Fungal keratitis	?	-	-	-	-	-	?
Tinea capitis	15,581,400	?	?	?	?	15,581,400	10,070.0
<b>Total burden estimated</b>						<b>17,983,517</b>	

*Pneumocystis pneumonia* (40% rate in children), 253,000 oral candidiasis and 144,000 esophageal candidiasis based on the WHO prevalence rate. All these estimates are likely to be underestimates because we have not factored in infections occurring after starting ARV therapy, except for esophageal

candidiasis.

There were 78,032 cases of pulmonary TB in 2010, most in HIV negative people and based on pulmonary cavity frequency and *Aspergillus* IgG serology, we expect 19,000 new cases of chronic pulmonary aspergillosis annually with a 5-year period prevalence of 60,377

cases.<sup>36</sup> This assumes a 15% annual mortality. Such post-tuberculous cases probably represent 50% (range 20–85%)<sup>9</sup> of the total chronic pulmonary aspergillosis caseload, therefore estimated at 120,754 patients affected with chronic pulmonary aspergillosis in Nigeria.

### Population Based Invasive Fungal Infections

Asthma is common in Nigeria. Prevalence studies in teenagers indicate a prevalence of 10.7–14.3% and in adults of 14–15.2%.<sup>37</sup> We have used the latest study in adults of 15.2%<sup>41</sup> and estimated 3,700,000 million adult asthmatics in Nigeria. Of these 2.5% are estimated to have ABPA (based in part on a study from South Africa by Benatar et al 1980;<sup>42</sup>) an estimated 94,600 people. And if the worse 10% of adult asthmatics are sensitized to fungi and therefore have severe asthma with fungal sensitization (SAFS), we estimated 124,000 affected, with the possibility of some duplication between the ABPA and SAFS groups.

Rates of candidaemia, invasive aspergillosis and mucormycosis were estimated on a population basis (Table 2), without supporting data from Nigeria and are probably uncommon or rare. Histoplasmosis exists in Nigeria, both caused by *H. capsulatum* var *capsulatum* and var *dubosii*,<sup>26,43</sup> but frequency is very hard to estimate based on current data.

### DISCUSSION

Our estimates indicate that over 11.8% of the Nigerian population is estimated to suffer from a serious fungal infection each year. If tinea capitis and recurrent vaginal thrush are excluded, over 960,000 are estimated to be affected, with substantial mortality. Invasive fungal infections (IFDs) are frequently life threatening infections with high morbidity and mortality rates and the groups of patients at risk are all seen and managed in Nigeria. There is however a paucity of data on IFDs in Nigeria. The question therefore is “are there no IFDs in our environment?” or is it just a case of lack of awareness (a knowledge gap which tends to lead to low clinical index of suspicion and thus management)? These questions must be answered to ensure proper management of the large numbers of patients with infection and at risk.

Our findings revealed a number of epidemiological reports on superficial and mucocutaneous fungal infections with an estimated total burden of 15,581,400 cases of tinea capitis in children.<sup>40</sup> This is comparable to the data

from Kenya which reveals a prevalence of 10.1–33.3% in rural and urban school pupils.<sup>44</sup> This problem, while not life-threatening has an impact on public health, socioeconomic and psychological wellbeing of the group at risk. In addition, at least 2% of children develop kerion or favus, inflammatory uncomfortable, unsightly and scarring complications of tinea capitis.<sup>45</sup> Assuming our estimate is adequate, over 300,000 children develop kerion, which is a substantial problem that needs addressing urgently.

Oropharyngeal candidiasis is the commonest opportunistic infection in HIV-infected individuals, and we estimate over 250,000 patients are affected annually; probably there would be many more episodes than this. Adedigba *et al.*<sup>46</sup> found it to be the commonest oral manifestation (43.1%) of HIV infection in Nigerian patients, reflecting the situation in other parts of Africa, and indeed the world.<sup>13,47</sup> The symptoms of oropharyngeal candidiasis include a sensation of burning in the mouth, oral pain, xerostomia (dry mouth), throat pain and impaired taste (dysgeusia).<sup>48</sup> Symptoms are worse if untreated, including in those with fluconazole resistance. In HIV infection, it often occurs together with oesophageal candidiasis which is a serious problem, causing nausea, vomiting and dysphagia in most patients. Our estimate in AIDS patients of 144,000 patients affected is concerning, as not all may be receiving adequate therapy. We have not estimated oral or oesophageal candidiasis in any other patient group, so our estimates will certainly be significant underestimates of the total Nigerian burden of these infections. For example, oesophageal candidiasis was endoscopically documented in Korea in non-immunocompromised well adults undergoing a health check at a prevalence rate of 0.32%,<sup>49</sup> and of course in other immunocompromised patients with some regularity.

Vulvovaginal candidiasis prevalence rates ranges between 21%–35% in Nigeria<sup>50</sup> and we have estimated that ~1.5 million Nigerian women suffer from recurrent episodes, irrespective of HIV status. An association has been demonstrated between vaginitis and

bacterial vaginosis and separately with transmissibility of HIV.<sup>51</sup> For example, a high HIV seropositivity has been noted among fertile women with symptomatic candidiasis in Cameroon, a neighbouring west African country<sup>52</sup> and the high incidence of HIV and candidiasis among youths and adolescents in Dar es Salaam, Tanzania<sup>53</sup> underlines the medical importance of vulvovaginal candidiasis in HIV infection. Recurrent VVC is an unpleasant problem for those affected, having a significant impact on quality of life with vaginal soreness, irritation, vulvar burning, dyspareunia, and external dysuria being common.

We have estimated 74,594 cases of PCP in HIV/AIDS patients only, partly using from data from other African studies. PCP is found predominantly in the paediatric age group.<sup>21,34</sup> PCP also occurs in non-HIV infected patients, and the proportion varies substantially and so it is not possible make a reliable estimate of this problem in Nigeria. Accurate diagnosis requires immunofluorescence microscopy or molecular (PCR) methodology on high quality respiratory samples, neither of which is available in Nigeria currently.

A study on cryptococcal antigen screening amongst HIV/AIDS patients in a tertiary hospital in Mid-western Nigeria revealed a prevalence of 12.7% in those with CD4 cell counts less than 200.<sup>31</sup> Given that probably 50% of the estimated 1.4M people not on ARV therapy have CD counts <200/ $\mu$ L, and that only 45% of these patients are adults, there are probably 40,000 people who could be identified by screening each year, many pre-symptomatic, before meningitis occurs. This positivity rate on screening is higher than that in Uganda at 2.9%,<sup>54</sup> in neighbouring Cameroon at 9.86%<sup>55</sup> and 8.4% in Ethiopia<sup>56</sup> but lower than that of 16.6% from a Ghanaian study.<sup>57</sup>

Long term respiratory fungal infections such as chronic pulmonary aspergillosis, ABPA and SAFS are estimated in 338,000 people, a total rate of 210/100,000 of the population, Tuberculosis is common and 78,032 cases of pulmonary TB were diagnosed in 2010, so the relatively large number of patients with chronic pulmonary aspergillosis is perhaps not a surprise. What is not

known in Nigeria is how many cases of chronic pulmonary aspergillosis occur in other at risk groups such as ABPA, sarcoidosis, COPD, following pneumothorax to name some examples. We have estimated that TB accounts for 50% of the cases. Asthma is surprisingly common in adults in Nigeria at ~15%<sup>58</sup> and the fatality rate of hospitalised cases of asthma ranges between 6–7.8%;<sup>37</sup> these deaths are preventable. One area for further research in Nigeria is the proportion of severe asthma who have SAFS and would benefit from antifungal therapy.<sup>58,59</sup> Likewise the number of patients with ABPA is uncertain but estimates of the proportion of adult asthmatics with ABPA is consistently around 2.5% in several countries including South Africa.<sup>36</sup>

Estimated cases of other immediately life threatening invasive fungal infections, (candidaemia, candida peritonitis, invasive aspergillosis and mucormycosis) is 8.2 per 100,000 of population at risk. There are very few data available in Nigeria to corroborate or otherwise these figures and no data published on histoplasmosis. There have been no proactive searches for these life threatening infections probably related to the fee for service health system in Nigeria, so most times clinicians usually prefer to commence empirical therapy rather than actively investigate the cause of the infection. Conventional diagnostic tests such as direct microscopy, histopathology and culture are available for use, but not galactomannan,  $\beta$ -D glucan, or DNA detection tests and this may have impacted on the ability to diagnose invasive fungal infections. The dearth of data makes the current situation very unsatisfactory, and it is likely that many fungal infections will be missed, and untreated.

The prevalence of blindness in Nigeria is 0.78% (~12 million) with corneal opacities accounting for 12% (~1.45 million).<sup>60</sup> However there are no epidemiological data on fungal keratitis in Nigeria, a country with a large population of rural dwellers and farmers who have no access to secondary or tertiary healthcare where this diagnosis would be made and treatment instituted. A retrospective laboratory based study

from a tertiary hospital in Nigeria showed a prevalence of fungal keratitis of 8.4% amongst cases of keratitis,<sup>61</sup> this is inconsistent with findings from a prospective study in Ghana where the prevalence rate was 37.6%.<sup>62</sup> This disparity might be due to the fact that one study proactively (prospective) looked for keratomycosis while the other was a retrospective (passive) study. A prospective Nigerian study is required to give a clearer picture.

The major limitations of our estimates and modeling are the paucity of data which has necessitated use of some data from neighbouring countries to make estimates. The studies that were available were generally hospital based frequencies which might not be representative of the whole population.

## CONCLUSION

Epidemiological data on the burden of fungal infections in Nigeria will be of substantial public health value and potentially influence the management of millions of patients at risk. In conclusion, our estimates indicate that over 960,000 of the Nigerian population suffer from life threatening fungal infections which have a high morbidity and mortality rate. Epidemiological studies are urgently required to validate or modify these estimates.

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