Fungal diseases in Africa: epidemiologic, diagnostic and therapeutic advances

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The spectrum of fungal diseases that affect humans is broad, ranging from asymptomatic superficial mycoses to deep systemic diseases due to opportunistic or primary fungal pathogens.[1] Recently, the COronaVIrus Disease 2019 (COVID-19) pandemic has highlighted mucormycosis as an important opportunistic fungal disease, especially in patients with uncontrolled diabetes mellitus and prolonged, high-dose corticosteroid use.[2]

Fungal diseases substantially contribute to the burden of diseases in Africa, mainly driven by heavy affliction of poverty, tuberculosis (TB) and human immunodeficiency virus (HIV) (Figure 1).[3,4] Recent estimates of the burden of key fungal diseases are summarized in Table 1.

The overarching aim of the special collection was to provide a state-of-the-art overview of our current understanding of various aspects of fungal diseases in Africa. It was overwhelmingly successful with a total of 14 high-quality submissions summarized below.

In this issue, two articles further highlighted the burden of histoplasmosis in Africa. Kuate *et al.*[12] bring new insights into the burden of triple co-infection with histoplasmosis, TB and HIV in sub-Saharan Africa (SSA). Pulmonary histoplasmosis is often misdiagnosed as smear negative pulmonary TB due to similarities in their clinical and radiological presentations.[11] On the contrary, HIV, which is highly prevalent in SSA, is the most important risk factor for both disseminated histoplasmosis and TB. Ekeng *et al.*[13] summarized 44 cases of histoplasmosis among African children. Despite close to 55% of the cases being disseminated histoplasmosis, HIV was only reported in 6.8% of these children and most of the cases were due to *Histoplasma capsulatum var. duboisii*, the aetiologic agent of African histoplasmosis. These two articles therefore shine a light on the need for awareness among clinicians and the need to enhance laboratory diagnostic capacity for invasive fungal diseases in SSA and a need for a unified algorithm for pulmonary infections with similar presentation.

In line with the above, Osaigbovo and Bongomin[14] discussed the available point-of-care tests (POCTs) for invasive fungal infections (IFIs) which are designed to detect their respective fungal antigens or antibodies and barriers to their uptake, including cost, lack of evidence to back up policy recommendations and lack of awareness among health care providers. The authors suggested a blueprint strategy to increase availability and accessibility in SSA, including increasing awareness about IFIs and corresponding POCTs, research, integrating the diagnosis of IFIs into existing vertical disease programmes, country adoption of the World Health Organization's Essential Diagnostics List, advocacy and improving POC diagnostics and supply chains.

Bongomin and Otu[15] showed that a deterioration in the symptoms component of the St. George's Respiratory Questionnaire (SGRQ) and worsening of patients' self-assessment domain may be associated with clinical recurrence of chronic pulmonary aspergillosis (CPA). However, they recommended diagnosis of recurrent CPA using a combination of clinical history, SGRQ scores, chest imaging and a workup to exclude other causes of the patients' symptoms. Also regarding CPA, Oladele *et al.*[16] highlighted the need to standardize *Aspergillus*-specific IgG diagnostic cut-off values to enhance diagnosis of CPA among Nigerians. The authors reported a lower optimal diagnostic cut-off value (0.821) than the manufacturer's recommended cut-off value (1.0) for

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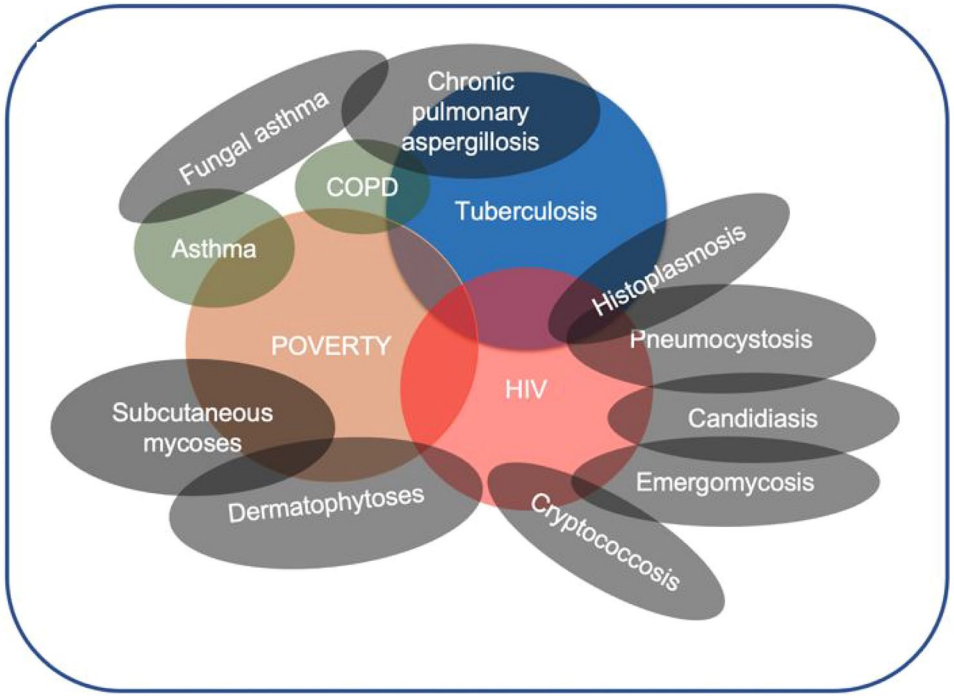

Figure 1. Major drivers of fungal diseases in Africa.
COPD, chronic obstructive pulmonary disease; HIV, human immunodeficiency virus.

the Bordier *Aspergillus* IgG antibody test, highlighting the ethnic differences in antibody response in CPA.

In Uganda, Kwizera *et al.*[17] found a high prevalence (60%) of *Aspergillus fumigatus* skin positivity in apparently healthy non-atopic individuals in Uganda with skin positivity being more in younger individuals. They proposed a revised definition of a suitable cut-off wheal size in healthy adults and not to use skin prick testing (SPT) alone to diagnose *A. fumigatus* sensitivity. Again in Uganda, Njovu *et al.*[18] established that approximately 71% of patients with clinical signs of pulmonary TB were positive for pulmonary fungal pathogens (PFPs) and about 4% had a co-infection of PFPs and *Mycobacterium tuberculosis*. PFPs and *M. tuberculosis* were isolated in people with HIV. The findings re-emphasize the need to have routine mycoses diagnostic tests in patients with suspected TB infection.

In Nigeria, Campbell *et al.*[19] found that *A. fumigatus* constituted only 4.3% of the 117 isolates of *Aspergillus* species in the 168 soil samples tested contrary to other studies done in Nigeria and in other parts of the world. Importantly, all the isolates did not exhibit triazole resistance. In Tanzania, Mushi *et al.*[20] identified *Candida albicans* as the most predominant *Candida* species isolated from 325 oral swabs from HIV-uninfected children aged between 2 and 15 months with low resistance to fluconazole. However, some *C. albicans* isolates were resistant to fluconazole, voriconazole and posaconazole; hence, continuous monitoring of susceptibility is required for effective management of oral candidiasis in children. In Senegal, Deh *et al.*[21] foregrounded the possibility of a highly inflammatory tinea capitis due to *Microsporum audouinii* as they described a case of a nine-year-old HIV negative schoolgirl who was diagnosed with a severe form of kerion celsi. The infection completely regressed after 2 months following evacuation of 50 ml of pus and treatment with oral terbinafine 125 mg per day and ketoconazole-based shampoo.

As part of the ongoing effort of the Global Action for Fungal Infections (GAFFI) to estimate the burden of serious fungal infections in each country, we received two submissions. Lakoh *et al.*[22] found that serious fungal infections affect a total

Table 1. Previous estimates of the burden of fungal diseases in Africa.

Fungal disease	Burden	Author/reference
PCP, HIV-associated	The pooled prevalence of 15.4%; highest among inpatients, 22.4%	Wasserman *et al.*[5]
Oesophageal candidiasis, HIV-associated	Pooled prevalence of 12%; 34.1% pre-ART and 8.7% in ART era	Olum *et al.*[6]
Tinea capitis in African children	Pooled prevalence of 23%; about 138 million cases annually	Bongomin *et al.*[7]
Cryptococcal meningitis, HIV-associated	In a modelling study, of 223,100 incident cases of cryptococcal meningitis globally in 2014, 73% (162,500 cases) occurred in sub-Saharan Africa; of 181,100 global death cases due to cryptococcal meningitis, 135,900 (75%) occurred in sub-Saharan Africa	Rajasingham *et al.*[8]
Fungal asthma	The prevalence of fungal sensitization was ~3–52% (pool prevalence of 28%) and ~23.3%, due to *Aspergillus* species; prevalence of allergic bronchopulmonary aspergillosis of 1.6–21.2%	Kwizera *et al.*[9]
CPA	1247 cases of CPA reported between 1976 and 2021, 61.3% had a history of active/treated TB, 2.3% had HIV and 1.5% had diabetes mellitus	Olum *et al.*[10]
Histoplasmosis	470 cases of histoplasmosis between 1952 and 2017; 38% of the cases had HIV infection	Oladele *et al.*[11]

ART, anti-retroviral therapy, CPA, chronic pulmonary aspergillosis; HIV, human immunodeficiency virus; PCP, pneumocystis pneumonia; TB, tuberculosis.

of 4.92% of the population in Sierra Leone, and the annual burden of fungal infections among people with HIV was 2.9%. This was attributable to the late-stage presentation of people with HIV to care and high burden of advanced HIV disease in the country. Second, Huseynov *et al.*[23] estimated that fungal diseases affect an estimated 2.3% of the population in Azerbaijan. The need to improve diagnostic capabilities for IFIs of Azerbaijan was highlighted. In the same vein, Diongue *et al.*[24] from Senegal pointed out that despite the low frequency of IFIs for which more than half is cryptococcosis, the risk factors for IFIs are prevalent across Senegal. However, it was reported that fluconazole is the only systemic antifungal available in the country, yet it has no activity on many fungi such as *Aspergillus* spp. responsible for IFIs in Senegal.

Finally, Otu *et al.*[25] spotlight the importance and reliability of digital platforms and the case-based learning approach in fostering clinical reasoning skills and cascading knowledge to health professionals on clinical mycology based on their experience with online clinical mycology case competition amid the COVID-19 social distance restrictions hosted by the Medical Mycology Society of Nigeria.

In conclusion, these articles provide new insights into the burden and challenges with diagnosis and treatment of fungal diseases in Africa. There is a need to put emphasis on fungal diseases and channelling of more resources towards their prevention, diagnosis and management to improve outcomes.

Author contributions

Felix Bongomin: Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources; Software; Supervision; Validation;

Visualization; Writing – original draft; Writing – review & editing.

Winnie Kibone: Writing – original draft; Writing – review & editing.

Jerom Okot: Writing – original draft; Writing – review & editing.

Lauryn Nsenga: Writing – original draft; Writing – review & editing.

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