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Current situation of fungal diseases in Eritrea

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Abstract

The epidemiology of fungal infections in Eritrea is unknown. Most cases are underreported due to a lack of diagnostics. This study estimates the burden of serious fungal infections and highlights treatment and diagnostic gaps in the country. All publications related to fungal infections were identified by searches using PubMed/Medline and Google Scholar. Where no data were available, data from neighbouring countries, then sub-Saharan African countries, then other parts of the world were considered for deriving estimates. The Eritrea population was 3,546,427 in 2020. In 2020, HIV/AIDS patients numbered 1400 and TB incidence were 2875. The five-year adult prevalence of asthma (2016–2020) was 41,390, and the total prevalence estimate of chronic obstructive pulmonary disease (COPD) was 308,328. The annual incidence of cryptococcal meningitis and *Pneumocystis jirovecii* pneumonia in AIDS patients was estimated at 96 and 205 cases. Oesophageal candidiasis incidence is 715 HIV-infected patients. Chronic pulmonary aspergillosis prevalence, including post-tuberculosis cases, was estimated at 1399 (39/100,000). Fungal asthma has a prevalence of 1035 and 1366 in adults. The estimated prevalence of recurrent vulvovaginal candidiasis and tinea capitis is 59,391 and 342,585, respectively. There are no data on candidaemia, but it is estimated at 5/100,000 (177 cases annually). Invasive aspergillosis in leukaemia, lung cancer, COPD and HIV is estimated at 540 cases and fungal keratitis in 514 cases annually. Serious fungal infections are prevalent in Eritrea with approximately 408,164 people (11.5%) affected annually. Studies on fungal diseases to improve diagnosis and treatment are required with the implementation of a national surveillance program.

KEYWORDS
aspergillus, candida, fungal infection, pneumocystis, tinea capitis

1 | INTRODUCTION

Eritrea gained independence from Ethiopia in 1993. It is located in the Horn of Africa and bounded on the east by the Red Sea, on the southeast by Djibouti, on the south and west by Ethiopia, and on the north and west by Sudan (Figure 1). The country has been self-governing since 1993.[1] Eritrea is facing a triple disease burden, with a significant increase in non-communicable diseases (NCDs) and injuries coupled with the existing communicable diseases burden. The all-cause mortality remains high at 1297/per 100,000. NCDs are responsible for 671/100,000 deaths as compared to communicable conditions (506/100,000 persons) and violence/injuries (119/100,000 persons).[2] In 2019, the infant mortality rate was 30.5 per 1000 live births.[3] NCDs have

recently outstripped communicable diseases, in terms of mortality. Eritrea is regarded as a low burden HIV and low burden TB country.[4]

The Ministry of Health (MoH) has developed a new National Health Policy (2021), in line with the Sustainable Development Goals (SDGs) and Universal Health Coverage (UHC), taking into account the current COVID-19 pandemic.[2] This new policy is based on the principles of provision of essential healthcare services for all regardless of age under the overall global directions of SDG especially SDG 3 and the principles of UHC.[4]

Currently, there are 28 hospitals, 53 health centres and 186 health stations in Eritrea. There are 5 levels of laboratories, constituting one National Health Laboratory (NHL), four National Referral Hospital Laboratories, six Regional Hospital Laboratories, 20 hospital laboratories and 43 community hospital laboratories in the country.[4] Over 60% of the population lives within 5 km of a health facility. The tertiary level of service is provided by the national referral hospitals situated in the capital city Asmara. Tertiary-level health facilities not only serve as national referral facilities but also as centres of excellence for specialised training/education, research and continuing education.[5]

Every year, over 2 million people die of fungal disease worldwide and many have significant morbidity from dermatophytosis, vulvovaginal candidiasis, allergic diseases, subcutaneous infections and life-threatening invasive systemic diseases.[6] Fungal infections are common in Africa, mainly driven by HIV/AIDS, tuberculosis, poverty and the increasing number of patients with non-communicable diseases notably, cancers, asthma and diabetes mellitus.[7] Definitive diagnosis of the fungal disease requires expertise as well as laboratory systems and equipment such as microscopy, culture, histopathology, antigen and antibody assays, and *Pneumocystis* PCR. There is a scarcity of data related to fungal disease in Eritrea although reports of Eritrean migrants who have fungal infections have been published in Europe.[8–10] However, to our knowledge, there are no epidemiological data on the burden of fungal diseases published or generated in Eritrea.

In this study, we aim to estimate the burden of serious fungal infections in Eritrea, using established deterministic modelling and data generated from countries nearby or internationally. Underdiagnosis is a global problem for fungal disease and without an estimate of likely incidence and prevalence, little action is likely to be taken to improve the situation.

2 | METHODS

This literature review was based on articles about fungal infections using Google Scholar and PubMed/Medline searches, African newspapers, health reports, epidemiological journals and WHO reports. The articles were searched in English. The keywords searched were as follows: fungal infection, opportunistic disease, HIV/AIDS, tuberculosis, chronic pulmonary, *Cryptococcus* and *Histoplasma*, all associated with Eritrea. No individual patient data were used and so there was no need for an ethical review.

FIGURE 1 Map of Africa showing Eritrea

There are a few research studies on fungal infections related to the Eritrean population; however, none of them estimated the burden of fungal infections. We considered neighbouring countries, then sub-Saharan African countries for deriving estimates. When data were not available in the African region, data were gathered from countries outside Africa.

The demography data were taken from Worldmeter, WHO reports, the Eritrean national action plan for health security 2017–2021 (NAPHS), and also from Eritrea Demographic and Health Survey 2010 (EDHS; Table 1). HIV prevalence and death were taken from the 2020 UNAIDS report. To evaluate the incidence of children at risk of developing opportunistic infections (OIs), we have assessed different factors impacting OI incidence in the literature.[18]

We estimated the people living with HIV infection (PLWHIV) at risk by assuming that PLWHIV who are not on antiretroviral therapy (ART) generally develop profound immune deficiency over 7 years for adults and 5 years for children and that the failure of ART is 11%.[19] TB rates were taken from the WHO global report 2020, and the number of survivors of pulmonary TB was derived. The prevalence of asthma was calculated from a WHO country report of five consecutive years of asthma caseload in all six regions.[2] For the prevalence of chronic obstructive pulmonary disease (COPD), a weighted average from Eastern Africa data was used and annual hospital admission percentage was estimated at 10.5%.[20] Lung cancer annual incidence was taken from Globocan,[21] and acute leukaemia was estimated at 2.5/100,000.[17] Data on transplant procedures (haematopoietic, renal, heart, liver and lung) were not available (but assumed to be none).

A number of denominators, populations and prevalence or incidence assumptions were used from multiple sources; all are described and shown in Table 2.

3 | RESULT

3.1 | Country's profile

As of 2020, the population of Eritrea was estimated to be 3,546,427 (Table 1).[11] Children aged 0–14 constitute about 42% while senior citizens (>60 years) comprise approximately 4% of the general population.[12,40] The real GDP showed an increase of 3.8% in 2019 but it is expected to drop in the following years due to the COVID-19 pandemic and locust invasion.[41] The world data atlas report states that the GDP per capita in 2020 was $588.

Despite the economic and political challenges, Eritrea has managed to achieve Millennium Development Goals (MDGs) 4, 5, 6 to reduce child mortality, improve maternal health and combat HIV/AIDS, malaria, respectively, and other diseases.[5] Significant progress has also been made in reducing TB incidence and TB-related deaths, with the estimated TB incidence having reduced from 108/100,000 in 2016 to 89/100,000 in 2018 while death reduced from 19 to 16/100,000 in the same period.[2] The annual incidence of pulmonary TB (PTB) in 2020 was 1868 (Table 1), of which 76% were laboratory confirmed.[14] Between 2005 and 2019, HIV prevalence was nearly halved, dropping from 1.1% to 0.6%.[2] In 2020, the number of PLWHIV was 14,000 (Table 1).[13] On the contrary, NCDs have been rising; we estimated 380,328 COPD cases and the 2020 Globocan report indicates the incidence of lung cancer and acute leukaemia cases as 67 and 89, respectively (Table 1), which may be underestimated. Opportunistic diseases such as fungal infections are not well addressed probably due to the low capacity for diagnostics. There are no recent data on hospital beds or annual abdominal surgeries conducted, which both influence the occurrence of invasive candidiasis.

3.2 | Fungal skin infections: Tinea capitis and neglected tropical diseases

Our estimation indicates that tinea capitis is the most common fungal infection in Eritrea. Every year, approximately 342,585 children are suffering from tinea capitis infection, at a rate of 9660/per 100,000 (Table 3).[39] Fungal neglected tropical diseases (FNTDs) consist of a diverse group of implantation mycoses, which usually present a long time after the initial infection. These diseases include sporotrichosis, mycetoma (Madura foot), chromoblastomycosis (chromomycosis), lacaziosis (lobomycosis) and entomophthoromycosis (subcutaneous zygomycosis).[42] Sporotrichosis is a neglected fungal infection caused by *Sporothrix* spp. Despite its presence almost everywhere, there are no data on sporotrichosis in Eritrea. Perhaps it is not reported or misdiagnosed. Mycetoma is not on the list of the seven

TABLE 1 Basic health demographics of Eritrea

Data	Number	Comment	Reference
Population	3,546,427	2020	11
Proportion children 0–14	1,489,499	42% of the population	12
HIV/infection	14,000	Prevalence of HIV/AIDS	13
Pulmonary tuberculosis	1868	Annual incidence 2020	14
Asthma in adults	41,390	Prevalence over 5 years	2
COPD patients	380,328	Population, 7.8%	15
Lung cancer	67	2.1/100000 incidence 2020	16
Acute leukaemia	89	2.5/100,000 incidence	17

Abbreviation: COPD, chronic obstructive pulmonary disease.

TABLE 2 Assumptions underlying the assessment of serious fungal diseases burden

Fungal Infection	Underline condition	Assumptions	Reference
Cryptococcal meningitis	HIV/AIDS	12.7% in HIV/AIDS patients with CD4 < 200/μl	22–24
Pneumocystis pneumonia	HIV/AIDS	11% of newly diagnosed HIV adults, 35% of children with HIV/AIDS	25,26
Invasive aspergillosis (IA)	HIV/AIDS respiratory diseases, cancer	10% of AML develop IA and an equal number of non-AML haematological conditions. 2.6% of lung cancer patients and 1.3% of COPD annual admissions	27
Chronic pulmonary aspergillosis (CPA) post TB	Respiratory disease	19% of HIV− and 10% of HIV+ clinically diagnosed PTB, 7% of HIV− and 3% of HIV+ proven PB and 1.5% annual rate after PTB cure	28
Chronic pulmonary aspergillosis - all	Respiratory diseases	Assumes 50% of cases occur after TB	28
Allergic bronchopulmonary aspergillosis (ABPA)	Respiratory diseases	2.5% of adult asthmatics	29,30
Severe asthma with fungal sensitisation (SAFS)	Respiratory diseases	33% of 10% adult asthmatics with severe asthma	31
Candidaemia	Cancer, surgery critical care	5/100,000 (mean of 2–11/100,000)	32
Oesophageal candidiasis	HIV/AIDS	20% of new HIV/AIDS patients and 0.5% of those on ARVs	33
Recurrent *Candida* vaginitis (≥4x/year)		6% females aged 15–49	34
Mucormycosis		0.2/100,000	35
Fungal keratitis		14/100,000	36–38
Tinea capitis		23% of children 0–14 years	39

Abbreviations: AML, acute myeloid leukaemia; ARV, antiretroviral therapy; COPD, chronic obstructive pulmonary disease; PTB, pulmonary tuberculosis.

TABLE 3 Estimate of serious fungal infection in Eritrea

Serious Fungal Infection	Estimate	No underlying disease	HIV/AIDS	Respiratory disease	Cancer + immunocompromised	Rate /100,000	Total burden
Cryptococcal meningitis	I	-	120	-	-	3.4	120
Pneumocystis pneumonia	I	-	256	-	-	7.2	256
Invasive aspergillosis	I	-	12.4	519	19	15.5	551
Chronic pulmonary aspergillosis post TB	P	-	-	689	-	19.4	689
Chronic pulmonary aspergillosis – all	P	-	-	1379	-	39	1379
ABPA	P	-	-	1035	-	29	1035
SAFS	P	-	-	1366	-	39	1366
Candidaemia	I	-	-	-	177	5.0	177
Oesophageal candidiasis	I	-	784	-	-	22	784
Recurrent Candida vaginitis (≥4x/year)		59,391	-	-	-	1675[a]	59,391
Mucormycosis	I	7	-	-	-	0.2	7
Fungal keratitis	I	514	-	-	-	14.5	514
Tinea capitis	P	342,585	-	-	-	9660	342,585
Total serious fungal infection burden		402,497	1172	4299	196		**408,164**

The bold value refers to an overall burden of serious fungal infections.

[a]Only female population.

Abbreviations: I = incidence; P = prevalence; ABPA, Allergic bronchopulmonary aspergillosis; SAFS, severe asthma with fungal sensitisation.

prominent NTDs in Eritrea. There are publications from Switzerland of two Eritreans with mycetoma, yet this cannot confirm the existence of mycetoma in Eritrea, because most migrants from Eritrea have stopovers in other countries such as Sudan and Ethiopia where mycetoma is common.[43]

3.3 | HIV-associated fungal diseases

In 2020, the number of PLWHIV was 14,000, and about 62% were on ART ($n = 8835$). There were less than 100 deaths in children and 310 deaths in adults.[13] The number of HIV-diagnosed adults who are not on ART is 5165 and 738 of these PLWHIV have a CD4 count <200/μl based on a 7-year decline. We estimated 1710 PLWHIV who are at risk of acquiring opportunistic infections assuming an 11% ARV failure rate in those on ART.

Pneumocystis pneumonia and cryptococcal meningitis are common opportunistic diseases among PLWHIV. The estimated burden of cryptococcal meningitis is 120 at a rate of 12.7% in HIV/AIDS patients with CD4 <200/μl and *Pneumocystis* pneumonia at 256 a rate of 11% of newly diagnosed HIV adults, 35% of children with HIV/AIDS.[22–26] Data on histoplasmosis are not available in Eritrea. Hardly any histoplasmosis was reported in other countries of the horn of Africa, one case in Ethiopia and another in Somali,[44] so it may be a very rare infection.

3.4 | *Candida* infections

Recurrent vulvovaginal candidiasis (rVVC) is defined as four or more episodes per year. It is usually caused by *Candida albicans*. *Candida glabrata*, which is fluconazole resistant, and other species are implicated less often.[45] We calculated the prevalence of rVVC to be 59,391, using a 6% proportion of women between 15–49 years of age (1,147,848) at a rate of 1675/100,000 females.[34] It is thought that approximately 70% of women suffer from vulvovaginal candidiasis at least once in their lives, more often during pregnancy, but we have not estimated this incidence rate.[45]

We estimated the annual incidence of candidaemia to be 124 using the estimation of 5/100,000. There are no published data from Eritrea on candidaemia. Candidaemia underestimates invasive candidiasis as blood cultures are only 40% sensitive. The estimated incidence of oesophageal candidiasis in PLWHIV is 784 at the rate of 22/100,000.[33]

There is no peritoneal dialysis in Eritrea and very few ICU beds so an estimation of peritoneal (or intraabdominal) candidiasis is likely to be inaccurate. We have also not estimated oral candidiasis which is common in PLWHIV, newborns, those on corticosteroid inhalers and very ill patients.

3.5 | Fungal asthma and aspergillosis

According to the WHO Eritrea annual report 2020, there are 41,390 reported asthma cases over the past 5 years. We estimated the prevalence of allergic bronchopulmonary aspergillosis (ABPA) to be 1035 using the rate of 2.5% of asthmatic adults developing ABPA (estimate from Saudi Arabia) and the prevalence of severe asthma with fungal sensitivity (SAFS) is estimated to be 1366 adults.[29] There is an overlap between these conditions, but also no data on fungal sensitisation in asthma in Eritrea to support the estimate.

The incidence of TB in Eritrea in 2020 was 2900 of which 63% (1868) were assumed to be pulmonary TB. We estimated that 124 patients were misdiagnosed as PTB but had CPA and co-infection of TB and aspergillosis involved 39 cases. An additional 15 patients developed CPA as they completed treatment for TB, and 1.5% annually developed CPA in subsequent years. We assumed that 20% of patients with CPA would die in their first year and each year subsequently a 7.5% annual mortality. Therefore, we estimated the 5-year period prevalence of CPA to be 689 people or 19.4 per 100,000. Assuming that pulmonary TB comprises 50% of the cases, the total prevalence estimate for CPA is estimated at 1379.

Invasive aspergillosis incidence was estimated at 540 annually (15.5/100,000). Respiratory disease is the main contributor to IA (primarily COPD which is relatively common in Eritrea), followed by HIV/AIDS, and cancer (primarily leukaemia, lymphoma and lung cancer). There is no organ transplant service in Eritrea. The estimated number of people who suffer from mucormycosis is 7 using a rate of 0.2 per 100,000.[35]

3.6 | Fungal keratitis

In a rapid assessment of avoidable blindness conducted in Eritrea, corneal scars ranked third (9.2%) following cataracts (55.1%) and glaucoma (15.2%) as causes of bilateral blindness.[46] Fungal keratitis is not reported in Eritrea. We calculated an incidence of 514 for fungal keratitis each year based on data from Egypt at a rate of 14.5/100,000.[36]

4 | DISCUSSION

Eritrea covers an area of 124,000 km^2, and the Red Sea coast stretches for about 1200 km. It has diverse geographical and climatic features. About 80% of the population live in rural areas in approximately 2580 villages, relying on rain-fed agriculture and livestock rearing for their livelihoods.[1] Administratively, Eritrea is divided into six regions (zobas), 58 sub-regions and 704 administrative areas (Figure 2). Asmara is its capital city, and the two major seaports on the Red Sea are Massawa and Asseb.

In Eritrea, health services are delivered on three levels. The primary level of service consists of community-based health services with coverage for an estimated 2000 to 3000 people. This level provides basic healthcare package (BHCP) services by empowering communities and mobilising and maximising resources. Community hospitals provide all services available at lower-level facilities and additionally deliver obstetric and general surgical services to provide vital lifesaving surgical, medical and other interventions closest to the people (based on the Health Sector Strategic Development Plan 2012–2016).

Currently, over 60% of the population lives within 5 km of a health facility,[5] but access to specialist healthcare is a challenge for much of the population because of travel time and distance. Looking at infrastructure, current data show that there are 28 hospitals, 53 health centres and 186 health stations.[4] Intensive care capacity is limited to eight beds nationally, with a mechanical ventilation system.[48] The National Medicines and Food Administration (NMFA), a body of the Ministry of Health that regulates the quality of pharmaceuticals and medical supplies in the country, was formed to ensure that the public has access to quality, safe, efficacious, and affordable pharmaceuticals, and medical supplies.[4]

Availability of reliable means of diagnostics and skilled manpower to run the diagnostic tools is key in improving public health. The WHO recommends a list of essential in vitro diagnostics for fungal diseases encompassing direct microscopy, blood and fungal culture, histology, *Cryptococcus* antigen (2018) and recently added *Histoplasma* antigen (2019), *Aspergillus* antigen, *Aspergillus* antibody, *Pneumocystis* PCR (all 2021).[49]

In Eritrea, most fungal diseases are diagnosed by inspection and there is direct microscopy for skin, hair and nails as well as *Cryptococcus* antigen. Preliminary culture supplemented with preliminary identification tests is available. There is a BSL-3 laboratory in Eritrea but it has no protocols for handling pathogenic fungi because culture is not widely performed. Histopathology is available, yet may not be widely practised in case of fungal infections and blood culture is rarely done. Direct microscopy of bronchoscopy fluid and vaginal samples, *Histoplasma* antigen, *Aspergillus* antigen and antibody, and *Pneumocystis* PCR tests are considered to be unavailable in Eritrea. There is limited laboratory equipment and diagnostic capacity. Chest X-rays are available at the regional and national referral hospitals, but CT scans and MRIs are only available at the National referral hospital. Similarly, bronchoscopy, spirometry, corneal scraping, lumbar puncture and skin biopsy are done mostly in national and regional hospitals and rarely in other hospitals.

Access to standard treatment is also essential to mitigate mortality from diseases. Antifungal therapy in Eritrea is mostly limited to topical preparations. The WHO has listed eight essential antifungal drugs, following application since 2013 from the Global Action For Fungal Infections (GAFFI).[49] Out of those, amphotericin B, natamycin eye drops (5%) and fluconazole are the only available antifungal treatments.[50] Few pharmaceutical distributors operate in Eritrea, and there are some demands by medical professionals for additional antifungal therapies.

We estimated about 408,164 serious fungal infections each year, which is approximately 11.5% of the total population of Eritrea. Data related to fungal diseases in Eritrea were scant; therefore, incidence or prevalence from other countries was used to estimate the burden in Eritrea. The summary shown in Tables 2 and 3 is derived from the various populations at risk and the rate per 100,000 inhabitants. However, we were not able to estimate the burden of oral candidiasis, peritoneal candidiasis or histoplasmosis.

Superficial mycotic infections are common in Africa, and tinea capitis is especially prevalent among children in Africa with a pooled prevalence of 23%.[39] In a recently conducted case–control study in Eritrea, among the dermatophytes, *Trichophyton verrucosum* was the major isolate followed by *T. mentagrophytes* and tinea capitis as the most investigated clinical presentation. Intimate contact with domestic animals as well as contact with infected children and shared items such as combs, and towels were among the associated risk factors[51] There are also reports of tinea capitis from Eritrean migrants in Switzerland and other European countries, one after returning from a 4-week visit in Eritrea[52] and the other immigrants from Eritrea. In

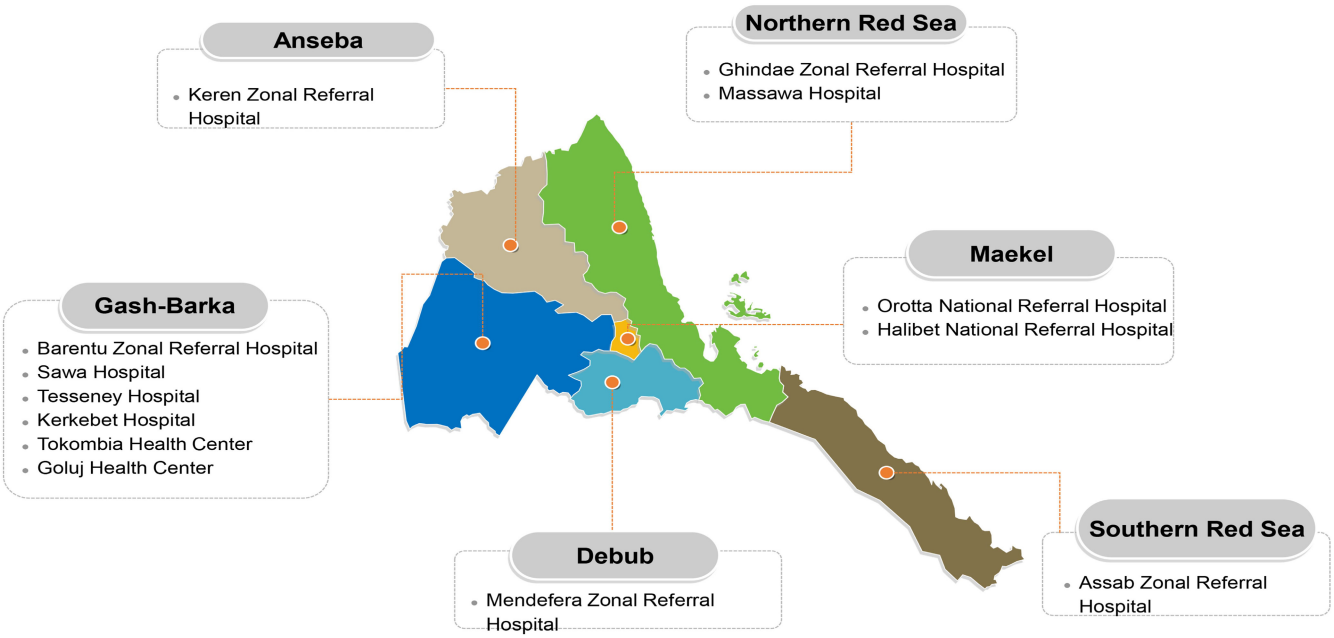

FIGURE 2 Map of Eritrea, its six administrative regions and the geographic distribution of the sampling points (health facilities in each zone) covering all of the regions of the country[47]

a similar context, a study of tinea capitis in an immigrant paediatric community showed that out of 76 cases, 64 (84%) had a positive culture. The study was conducted among children born in Israel to Eritrean parents, meaning the children did not acquire the infection primarily from Eritrea.[53] Interestingly, the probability of an Israeli child getting tinea capitis is very low.[54] Hence, the high rate of hair infection could be explained by the circulation of fungal infection in the community. Most of the immigrants live in areas of southern Tel Aviv where it is crowded and of low socioeconomic status which promotes transmission.[53] Genetic susceptibility may be a contributing factor.

Most NTDs are seen in tropical and subtropical climates and affect people from low and middle-income countries.[42] Sporotrichosis is one of the fungal NTDs, and the largest outbreak so far has been among gold miners in South Africa.[55] Sporotrichosis is omnipresent, yet the poor ventilation and darkness in mining sites can promote the growth as well as transmission of sporotrichosis. There are no data about sporotrichosis in Eritrea and with the expansion of mining practices and in particular gold mining in the country, consideration of this possible diagnosis may become important.

There are no data on fungal keratitis in Eritrea; hence, we used data from research conducted in Egypt and derived an estimated incidence of 514 annually. Given that a large proportion of the Eritrean population is engaged in traditional agriculture, the number of fungal keratitis cases might be higher. Corneal scraping is done at the national ophthalmologic hospital; however, people residing in rural areas might have difficulty accessing this service in a timely way.

With continuous efforts to extend the provision of ART in Eritrea, the burden of OIs related to HIV/AIDS is expected to fall. According to the UNAIDS 2020 report, 86% of people know their HIV status, and 62% of PLWHIV are on ART. CD4 counts are performed on nearly all HIV patients, including those with high viral load, using FACS analysis on-site.[13] Eritrea is found in the meningitis belt,[2] so there is good awareness of this diagnosis in Eritrea. Cryptococcal meningitis is still a common OI in PLHIV. Fortunately, liposomal amphotericin is among the listed medicines in the Eritrean national list; however, it is not widely used.

Pneumonia is one of the leading causes of mortality in children under 5 years;[56] this might also be true in Eritrea. Among PLWHIV, we have a conservative incidence estimate for *Pneumocystis* pneumonia of 256 annually. The burden of PCP might be higher as people who are HIV negative but immunocompromised are also susceptible. Appropriate investigations for PCP are not currently done. In 2019, in Ethiopia, the estimated number of PCP among AIDS patients was 12,700.[57] The relatively higher number of PCP compared to Eritrea might be attributed to the burden of HIV/AIDS prevalence in Ethiopia.

Histoplasmosis is a neglected disease in Africa. The symptoms of pulmonary histoplasmosis resemble pulmonary tuberculosis.[44] There are no reports of histoplasmosis in Eritrea. Histoplasma antigen test is not available, and blood culture is rarely done; thus, histoplasmosis cases might be misdiagnosed.

Oesophageal candidiasis is also a common fungal infection among PLWHIV. In addition, healthy individuals[58] and those who suffer from diabetes mellitus and other chronic diseases can have oesophageal candidiasis, but we have not been able to estimate this incidence.

Candida species are the most common cause of fungal infection in critically ill patients, accounting for 85% of fungal isolates in the National Nosocomial Infections Surveillance System study in the United States. Peritoneal (or intraabdominal) candidiasis is more common among patients in ICU, following abdominal surgery or pancreatitis.[59] Given the limited capacity of ICU with only 9 beds in Eritrea with mechanical ventilation,[48] and unavailability of reliable information about abdominal surgeries, we were not able to estimate peritoneal candidiasis.

Tuberculosis is one of the most frequently documented diseases by the Eritrean Ministry of Health, and complicated by CPA. Our estimation for total CPA over 5 years is at least 675. Among African countries, Nigeria is the leading country followed by Uganda and Kenya in terms of the burden of CPA.[60] The unavailability of *Aspergillus* IgG antibody detection means several cases might be misdiagnosed and mistreated, as respiratory fungal culture infrequently yields *Aspergillus*. Our incidence estimate of invasive aspergillosis is limited to leukaemia, lung cancer and COPD. It ignores those with influenza, COVID-19 (especially those treated with corticosteroids) and other immunocompromised patients. Currently, it is unlikely to be diagnosed in Eritrea as there is no *Aspergillus* antigen testing.

Asthma is common at all ages, and 33% of adult asthma is considered to be severe or poorly controlled asthma.[31] The highest burden of ABPA in Africa is in Algeria (310,310)[60] while our estimation for Eritrea is 1035. There is generally an increase in asthma cases with the increase in pollutants in the environment and lifestyle changes. Fungal (and especially *Aspergillus*) allergy or sensitisation is particularly common in severe asthma and is linked to hospitalisation for asthma and possibly death.

5 | CONCLUSION

Our estimates derived from available data lead us to conclude that serious fungal infections are prevalent in Eritrea. Although some means of diagnosis and treatment are in place, their sensitivity and specificity are questionable, given the limited usage of both fungal culture and most non-culture diagnostics. There is no dataset particular to fungal disease in the health registry. Therefore, it is fair to conclude little attention is given to fungal diseases despite their burden in Eritrea.

AUTHOR CONTRIBUTIONS

Sara Werkneh: Conceptualization (equal); data curation (supporting); formal analysis (supporting); funding acquisition (supporting); investigation (supporting); methodology (equal); project administration (supporting); resources (supporting); software (supporting); supervision (supporting); validation (equal); visualization (lead); writing – original draft (equal); writing – review and editing (equal). **Emma Orefuwa:** Conceptualization (equal);

data curation (supporting); formal analysis (supporting); funding acquisition (supporting); investigation (supporting); methodology (supporting); project administration (equal); resources (supporting); software (supporting); supervision (equal); validation (supporting); visualization (supporting); writing – original draft (supporting); writing – review and editing (equal). **David Denning:** Conceptualization (lead); data curation (equal); formal analysis (lead); funding acquisition (lead); investigation (supporting); methodology (lead); project administration (lead); resources (supporting); software (supporting); supervision (lead); validation (lead); visualization (supporting); writing – original draft (equal); writing – review and editing (lead).

CONFLICT OF INTEREST

We declare no competing interests.

DATA AVAILABILITY STATEMENT

All research articles and data sources are referenced, and no additional data are available for review.

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