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Burden of serious fungal infections in Honduras

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Abstract

Background: The burden of serious fungal infections in Honduras is unknown. The diagnosis of fungal diseases relies on almost exclusively on microscopy and culture limiting an accurate estimate of the burden of disease.

Objectives: The primary objective of the study was to estimate the burden of serious fungal infections in Honduras using previously described methods.

Methods: National and international demographic data on population, HIV, tuberculosis, asthma, COPD and cancer were obtained. A thorough literature search was done for all epidemiological studies and case series of serious fungal diseases. Using these risk populations and whatever incidence and prevalence could be found that was most pertinent to Honduras, a burden estimate was derived.

Results: The estimated number of serious fungal infection was estimated to be between 178,772 and 179,624 with nearly 2300 cases of these representing opportunistic infections in people living with HIV. The incidence of histoplasmosis and cryptococcosis in people living with HIV is high and estimated to be 4.3 and 4.6 cases per 100,000 population respectively. Approximately 12,247–13,099 cases of aspergillosis and 164,227 of other serious fungal infections were estimated to occur each year.

Conclusion: An accurate estimate of the burden of serious fungal infections in Honduras is unknown but based on our results, likely significant. Serious fungal infections represent an important public health problem in Honduras affecting approximately 1.8% of the population. There is a clear need for better access to diagnostic tools and antifungals to conduct research to better understand the impact of fungal diseases in Honduras.

KEYWORDS
aspergillosis, burden, cryptococcus, fungal infection, histoplasmosis, HIV, Honduras

1 | INTRODUCTION

Honduras is a small country with an area of 112,492 km^2 located in the heart of Central America. The country has a population of 9,512,342 persons, a gross national income (GNI) per capita of $2200 and is, after Haiti and Nicaragua, the poorest country in the Western Hemisphere.[1,2]

The life expectancy in Honduras is of about 75 years with cardiovascular diseases and stroke being the major causes of death.[1,3] Communicable diseases such as respiratory infections and diarrheal illnesses continue to be major drivers of mortality, especially in those younger than 5 years of age.[3] The burden of serious fungal infections (SFIs) in Honduras is unknown and likely important given the high burden of SFIs in neighbouring Guatemala, a country with similar geography, climate, demographics, social and healthcare infrastructure to Honduras.[4]

The Honduran health system comprises a private and public sector. The public sector includes the Ministry of Health and The

Honduran Institute of Social Security (IHSS). There is also a private sector that includes both non-profit and for-profit organisations. Approximately 60% of the population relies on a healthcare system provided by the Ministry of Health since 9 out of 10 people have no insurance and 18% of the population has limited to no access to care.[5] Honduras has the lowest health investment in Central America ($101 per person), a limited number of hospitals and hospital beds (ie 9.5 hospital beds per 10,000 habitants, a coverage of 0.4 hospitals per 100,000 population) and 0.37 physicians per 1000 population.[5,6]

The available assays for the diagnosis of communicable diseases such as fungal infections are thus basic, limited, and usually restricted to regional and reference hospitals in the public sector and to private entities in the major cities of the country. Regional and reference hospitals can perform routine fungal cultures of specimens such as blood, urine, sputum, cerebrospinal fluid and bone marrow but there is no government-sponsored facility able to perform lysis centrifugation blood cultures. Non-culture methods such as immunoassays and nucleic amplification tests are restricted to donations from international public health and academic organisations. Phenotypic and genotypic antifungal susceptibility testing is not widely accessible and restricted to *Candida* spp. isolated from urine and blood cultures. Available systemic antifungals are limited to fluconazole, ketoconazole, itraconazole, voriconazole amphotericin deoxycholate and occasionally liposomal amphotericin. There is very limited to no availability of posaconazole, isavuconazole and flucytosine. The echinocandins are not available in the public sector.

In this study, we summarise the available literature of SFIs endemic to Honduras. In addition, we provide estimates of the burden of SFIs in Honduras by identification of rates in populations at risk based on previously described methods.[7] The data used for the estimates are based on published local reports. Information from neighbouring countries or based in other published literature was used when local data were not available. We hope for these findings to ignite further research in this area and to institute interventions to address the unrecognised morbidity and mortality attributed to serious fungal infections.

2 | METHODS

We searched the MEDLINE, Scielo, Lilacs and Google Scholar databases as well as the Revista Medica Hondureña's website and included all articles until 30 September 2021. The search terms were “Honduras” associated with “histoplasmosis,” “blastomycosis,” “coccidioidomycosis,” “cryptococcosis,” “paracoccidioidomycosis,” “candida,” “pneumocystis,” “mucormycosis,” “mycetoma,” “sporotrichosis,” “fungal keratitis,” “chromoblastomycosis,” “human immunodeficiency syndrome (HIV),” “acquired immunodeficiency syndrome (AIDS),” “tuberculosis,” “asthma,” “invasive aspergillosis,” “chronic pulmonary aspergillosis (CPA),” “severe asthma with fungal sensitization (SAFS),” “allergic bronchopulmonary aspergillosis (ABPA),” “chronic obstructive pulmonary disease (COPD),” “diabetes mellitus” and “leukemia.” We also reviewed the references of the selected articles and searched and revised those that provided information about Honduras and fungal infections. All types of articles in English and Spanish were included. We selected studies describing epidemiological data, case reports or case series.

The country demographics for 2021 were obtained from the National Institute of Statistics and the United Nations Population Fund.[2,8] The data regarding the HIV epidemic in Honduras were obtained from the United Nations Program on HIV/AIDS (UNAIDS) for 2020[9] and tuberculosis data from the World Health Organization (WHO) for 2020.[10]

The expected cases of histoplasmosis, pneumocystosis, cryptococcosis and invasive candidiasis in people living with HIV (PLHIV) were obtained from publications by the Central and South America Network for HIV Epidemiology (CCASAnet), case reports or series and deduced from other recent reports describing incidence and/or prevalence for these diseases.

Other SFIs analysed included chronic pulmonary aspergillosis (CPA), allergic bronchopulmonary aspergillosis (ABPA), severe asthma with fungal sensitisation (SAFS), mucormycosis, fungal keratitis, invasive candida infections (ie candidaemia, oesophageal candidiasis and candida peritonitis) and recurrent vulvovaginal candidiasis. A thorough search of the literature for reports of these fungal diseases in Honduras was undertaken, and unfortunately, none were available. Estimates were therefore extrapolated from calculations of rates of these SFIs available in the literature.

Analysis of predisposing conditions for SFIs that affect the lung included pulmonary tuberculosis with emphasis on cavitary disease as a complication, asthma and chronic obstructive pulmonary disease (COPD). Rates of pulmonary tuberculosis were obtained from the World Health Statistics for 2020.[11]

Chronic pulmonary aspergillosis was determined based on previously described methods.[12] In this model, approximately 22% of survivors from pulmonary tuberculosis develop cavities as a sequalae. The incidence of CPA in patients with pulmonary cavities is 22% compared to 2% in those patients who do not develop pulmonary cavities. The 5-year prevalence of CAP assumed an unchanged incidence of pulmonary tuberculosis over the previous years and a 15% annual loss due to death or surgical cure.[13] The model also attributed pulmonary tuberculosis to be the predisposing condition for 67% of all cases of CPA.[14]

Estimates for ABPA assumed a 2.5% rate in adults with asthma[13,15] while the estimate of SAFS in adults was assessed based on a 33% rate in those with the most severe form of asthma (10% of patients with asthma).[16]

Leukaemia and lung cancer rates were obtained from the 2020 International Cancer Control Partnership report for Honduras.[17] Additional data were obtained from a recent report that examined the leukaemia incidence trends at the national, regional and global level.[18]

The prevalence and incidence rates of SFIs in Honduras were calculated based on methods previously described.[7] The burden for each SFI was estimated and reported as absolute numbers of cases per year and/or annual rates. The absolute number of cases

is presented as incidence or prevalence rates, but we were unable to calculate these rates for each disease given the paucity of data. The incidence and prevalence rates were calculated as the absolute number of cases over the total population in Honduras.

3 | RESULTS AND DISCUSSION

According to the National Institute of Statistics and the United Nations Population Fund, Honduras has a population of approximately 9.5 million inhabitants (see Table 1).[2,8] Estimates of key underlying conditions for serious fungal infections (ie HIV, cancer, COPD and asthma) are also shown in Table 1.

3.1 | HIV and HIV-related SFIs

Honduras has 54 'Centers for the Integral Attention of people living with HIV (PLHIV)' in the 20 health regions of the country. Since 1985 and up to July 2021, a total of 39,212 people have been diagnosed with HIV with an average of 1100 new cases every year (ie approximately 80 new cases per month). Each centre is responsible for the provision of evidence-based HIV care including uninterrupted access to antiretroviral therapy and prevention of opportunistic infections (OIs) through primary or secondary prophylaxis. Access to free testing such a CD4 cell count and viral load are also an important aspect of the services provided. Patients failing therapy are referred to infectious diseases experts in either San Pedro Sula or Tegucigalpa.

TABLE 1 Demographics—Population and population at risk for invasive fungal infections

Population	*N*
Total	9.9 million
Adult women	3,570,000
Total children (0–14 years)	3,030,000
Population living with HIV/AIDS (PLHIV)	25,000
Proportion of PLHIV on ARVs	12,000
ARV failure rate	3480
New cases of AIDS per year	1857
PLHIV at risk for OIs	5337
AIDS related death 2019 per UNAIDS	500
Cancer	
Acute lymphoblastic leukaemia	379
Acute myeloid leukaemia	297
Lung cancer	386 (3.8% incidence)
Structural lung disease	
Asthma	166,375
COPD	312,008
Pulmonary tuberculosis	2730 (91% of all TB cases/year)

Abbreviations: AIDS, acquired immunodeficiency syndrome; ARVs, antiretrovirals; COPD, chronic obstructive pulmonary disease; HIV, human immunodeficiency virus; OI, opportunistic infections; PLHIV, people living with HIV; UNAIDS, Joint United Nations Program on HIV/AIDS.

The UNAIDS report for 2020 estimated the number of PLHIV in Honduras to be 25,000 with 13,000 not on antiretroviral therapy (ARV) (Table 1).[9] Of those not on ARV, a total of 1857 progress to acquire immunodeficiency syndrome (AIDS) every year, assuming a 7-year linear decline to a CD4 cell count of <200 cells/mm^3.[19] HIV resistant to ARVs was extrapolated from a recent survey conducted between 2016 and 2017 that showed a 29% prevalence of acquired resistance among PLHIV on therapy for 48 months.[20] Based on these data, approximately 3480 PLHIV are failing therapy in Honduras. A total of 5337 PLHIV are therefore at risk for opportunistic infections.

3.1.1 | Pneumocystosis

There is limited information about the burden of *Pneumocystis jirovecii* pneumonia (PJP) in Honduras. A study conducted between 2001 and 2012 in a referral centre in Tegucigalpa identified PJP as one of the most common AIDS defining illnesses accounting for 8.4% of all OIs which would translate to approximately 450 cases every year.[21] The estimated annual rate is of 4.5 cases of PJP per 100,000 population (Table 2). The burden of PJP is likely underappreciated given the limitation of diagnostic methods in the country, in both PLHIV and other immunocompromised individuals.

3.1.2 | Candidiasis and aspergillosis

Gastrointestinal candidiasis is a common infection in people with AIDS. Approximately 20% of patients with advanced HIV disease and 0.5% of those on ARV treatment develop oesophageal candidiasis.[22,23] Based on these data, approximately 971 cases of oesophageal candidiasis are expected each year translating to an annual rate of 9.8 cases per 100,000 population (Table 2). According to data from UNAIDS, there were 500 AIDS-related deaths in 2019[9] of which 4% (ie 20 deaths) are attributed to invasive aspergillosis.[24]

3.1.3 | Histoplasmosis

Histoplasmosis is a relatively new disease in the literature with the first case described by Samuel Darling while stationed in Panamá in December 1905.[25] The fourth case of histoplasmosis in the literature corresponds to a man from Trujillo, Honduras, who worked for the United Fruit Company. The patient died secondary to hepatocellular carcinoma in Panamá in 1926 with the diagnosis of pulmonary histoplasmosis made postmortem.[26] The first signal of the burden of disease in Honduras came in the early 1950s when investigators from the United Fruit Company Hospital in La Lima,

TABLE 2 Estimated burden of fungal opportunistic infections in people living with HIV in Honduras

Fungal opportunistic infection in PLHIV at risk	Prevalence in PLHIV at risk	Annual incidence per 100,000 population	Total number of cases per year	Deaths per year
Pneumocystis pneumonia	8.4%	4.5	448	
Cryptococcal meningitis	12.7%	4.6	452	52
Disseminated progressive histoplasmosis	8%	4.3	427	26–255
Oesophageal candidiasis	20%	9.8	971	
Invasive aspergillosis				20
Total			2298	98–327

Abbreviation: PLHIV, people living with HIV.

Cortés found a histoplasmin skin reactivity of 40.2% among 300 male inpatients who were born and raised in Honduras and had never travelled outside the country.[27] The hyperendemicity of histoplasmosis in Honduras was confirmed by a national histoplasmin skin reactivity study conducted in 8 of the 18 departments between 1962 and 1965.[28] The study found that 38.8% of 74,897 individuals were positive and that infection occurred early in life with 17% of those younger than 1 year of age having a positive test. The histoplasmin skin sensitivity was as high as 60.7% in the Northwestern region of the country and around 45% in the two most populated departments (ie Francisco Morazán and Cortés). By 1970, a total of 10 patients from Honduras with histoplasmosis were described in the literature with 4 cases presenting with the chronic progressive disseminated form.[29]

The arrival of HIV/AIDS in Honduras in 1985 with the subsequent establishment of an immunosuppressed pool of patients served as a thermometer of the real burden of the disease.[30] For example, a study enrolled 38 patients with AIDS that presented with a syndrome compatible with a disseminated fungal infection in two major referral centres in Tegucigalpa between May and October of 1998. In that study, histoplasmosis was the third most common fungal OI representing 8% of all cases. The study also showed a high percentage of intercurrent OIs such as tuberculosis and cryptosporidiosis.[31] In another study conducted between 2002 and 2003, a total of 35 patients with HIV/AIDS (median CD4 of 109.52 cells/mm^3 $\pm$ 16.17) who had been admitted to two of the three major centres in Tegucigalpa with fever, hepatosplenomegaly, pulmonary symptoms and anaemia were evaluated for histoplasmosis by buffy coat, blood and bone marrow cultures. A total of 20 patients (57%) were diagnosed with disseminated histoplasmosis with bone marrow culture (35.1%) and buffy coat (20%) having the highest diagnostic yield. Disseminated histoplasmosis was the most common OI, surpassing tuberculosis (22.8%), with an overall mortality of 11%.[32]

Another study conducted by the Caribbean, Central and South America Network for HIV Epidemiology (CCASAnet) included patients of at least 18 years of age from 2001 to 2012 who had an OI before ARV initiation. Histoplasmosis was one of the most common AIDS defining illnesses in Honduras representing 5% of all OIs.[21] It is important to mention that the burden of disease is not truly appreciated in these studies given the limited diagnostic capabilities available at that time (eg lack of lysis centrifugation blood cultures or urine and serum *Histoplasma* antigen assays). This is exemplified by a recent study done in 3 Central American countries that included Honduras, Guatemala and Panamá and used rapid diagnostic assays for histoplasmosis according to predefined clinical criteria. Honduras had the highest histoplasma antigen positivity rate at 23%.[33] This is important as the magnitude of the problem is at least comparable to the frequency by which histoplasmosis is encountered in neighbouring Guatemala. In a recently published study in Guatemala, the overall incidence of disseminated histoplasmosis in people living with HIV and a CD4 of <350 cells/mm^3 was 7.9% and as high as 19.7% with a CD4 cell count of <50 cells/mm^3.[34]

Finally, a recent modelling study that estimated the burden of histoplasmosis in people living with HIV in Latin America calculated an annual incidence of histoplasmosis of approximately 1.97 (1.95–1.99) per 100 people living with HIV in Honduras.[35] This would translate to 430–500 cases of disseminated histoplasmosis in patients living with HIV with 26 to 255 deaths per year considering different modelling scenarios for symptomatic disease and case fatality.[35] If the proportion of the PLHIV at risk for OIs is assumed to be 8%, approximately 430 cases of histoplasmosis occur in Honduras every year translating to an annual rate of 4.3 per 100,000 population (Table 2).

3.1.4 | Cryptococcosis

There are scant epidemiological data about cryptococcosis in Honduras in PLHIV and practically none in the non-immunosuppressed population. In the study mentioned above in two major referral centres in Tegucigalpa in 1998, cryptococcosis accounted for 29% of fungal OIs and was the most common systemic fungal infection identified.[31] The study conducted by CCASAnet detailed above identified 8 cases of cryptococcosis in PLHIV accounting for 6.7% of OIs and being the 5th most common AIDS defining illness.[21]

Another study conducted by CCASAnet examined the outcomes of cryptococcal meningitis in PLHIV in the participating Latin American sites between 1985 and 2014. Honduras included 27 patients with cryptococcal meningoencephalitis with a median CD4 cell count at time of diagnosis of 50 cells/mm^3 (45–100 cells/mm^3)

and with a mortality rate of 33%.[36] The most comprehensive study to date examined the prevalence of cryptococcal antigenemia in PLHIV in 2 large referral centres in Honduras. A total of 220 patients with CD4 of <100 cells/mm^3 were screened and followed for 1 year. The overall prevalence was of 12.7% and was 40% among hospitalised patients. The 12-month mortality rate was 11.4%.[37] Based on information from this recent study, approximately 452 cases and 52 deaths per year are assumed to occur in PLHIV at risk for OIs assuming that 66% of the PLHIV population at risk for OIs had a CD4 of <100 cells/mm^3. This translates to an annual rate of 4.6 per 100,000 population (Table 2).

Finally, the genetic population diversity of *Cryptococcus* spp. in Honduras is poorly understood. Dr Acevedo Almendarez described the genetic diversity of 13 clinical isolates from PLHIV (12 from cerebrospinal fluid and 1 from sputum). A total of 9 were *C neoformans* var. *grubii* (7 VNI and 2 VNII), 2 were *C gattii* (1 VGI and 2 VGII) and one *C laurentii* isolated from cerebrospinal fluid.[38]

3.2 | Non-HIV-related SFIs

3.2.1 | Coccidioidomycosis

The first study to examine the existence of coccidioidomycosis in Honduras was realised by North American physicians of the United Fruit Company in La Lima, Cortés finding a 4.1% positive skin reaction rate to coccidioidin among 300 male inpatients.[27] Scott found a 1% rate of coccidioidin positive skin tests in Tela, Atlántida.[39] The first Central American case of coccidioidomycosis was described in 1955 in a patient that resided in the Valley of Comayagua in the central region of Honduras.[40,41] Between 1962 and 65, 4.5% of a total of 8052 individuals had a positive skin test in the department of Francisco Morazán.[28] The valley of Comayagua is considered an endemic area in Honduras with prevalence of skin positivity ranging between 8.7% and 17.5% and as high as 26% in the city of Comayagua.[40,42] There are only sporadic cases of coccidioidomycosis originating from Honduras reported in the literature and likely related to lack of awareness and the unavailability of mycology diagnostics in the endemic areas of the country.[43]

3.2.2 | Paracoccidioidomycosis

The first case of paracoccidioidomycosis in Honduras published in 1963 describes a 32-year-old male patient from Talanga, Francisco Morazán with oral and pulmonary involvement.[44] In 1965, 4 additional cases were described among males from different regions of the country, indicative of endemicity. All had cervical lymph node involvement, 3 had laryngeal or oral mucosa lesions, and 3 also had pulmonary involvement.[45] Although the disease is not uncommonly seen in the inpatient setting in the major referral centres of the country, only a few cases are reported in the literature.[46–49]

3.2.3 | Blastomycosis

Although blastomycosis is not considered endemic in Central America,[50] there a few cases reported from Honduras. The first case published in 1942 describes a woman with cutaneous fistulas on her back from which *Blastomyces dermatitidis* was eventually isolated.[51] In 1951, Hoenka et al described a male patient with pulmonary and oral involvement due to blastomycosis. The patient succumbed 3 years after development of symptoms. The patient had been born in Missouri, USA, but had lived in Honduras for the last 30 years before symptom onset. The authors conclude that the patient acquired the disease most likely in Honduras.[52]

3.2.4 | Aspergillosis

The clinical presentation of pulmonary aspergillosis is diverse. Invasive pulmonary aspergillosis is typically seen in immunosuppressed patients that have a quantitative or qualitative defect in neutrophil function. Chronic pulmonary aspergillosis is seen in patients with previous structural lung disease due to COPD, mycobacterial disease or sarcoidosis. Allergic bronchopulmonary aspergillosis affects patients with obstructive lung disease attributed to asthma or cystic fibrosis which is often associated with bronchiectasis.[53] In Honduras, there are sporadic case reports of invasive pulmonary aspergillosis in the setting of both neutropenia and structural lung disease.[54,55]

Leukaemia and lung cancer rates were obtained from the 2020 International Cancer Control Partnership report for Honduras that demonstrated an incidence of 5.4% and 3.9% respectively (total population 9,746,115).[17] According to a recent report that examined the leukaemia incidence trends at the national, regional and global level, Honduras had the highest incidence of acute lymphoblastic leukaemia (ALL) at 3.83 per 100,000 population (total of 379 cases per year) and the second highest incidence of chronic myelocytic leukaemia (CML) in the world after Ethiopia. The age-standardised incidence rate for acute myeloid leukaemia (AML) in 2017 was over 3 per 100,000 population which would translate to 297 cases per year (Table 3).[18] The risk of invasive aspergillosis in the setting of AML and ALL without mould prophylaxis is estimated to be 13.7 and 11.3 per 100 patient-years, respectively, which would translate to 41 and 43 cases per year respectively.[56] Stem cell transplantation is not performed in Honduras, and very few kidney transplants are performed in Honduras to include in the analysis.[57] For lung cancer, the risk for the development of invasive aspergillosis is estimated to be 2.6%, and it can be mistaken for lung cancer progression.[58,59]

Honduras has the highest age-standardised death rate attributed to COPD in the Western Hemisphere with 58.7 deaths per 100,000 population, and one of the highest age-standardised death rates attributed to asthma.[60] The prevalence of asthma and COPD in Honduras is not known. The prevalence for asthma was extrapolated from that found in Guatemala (2.42%)[61] and for COPD from that found in Mexico (3.1%) for GOLD stages II-IV.[62] This will translate to

TABLE 3 Estimated burden of the different clinical forms of aspergillosis in Honduras

Condition	Incidence	Prevalence	Total number of cases per year
Invasive aspergillosis in acute leukaemia	Risk in AML and ALL without mould prophylaxis is 13.7 and 11.3 per 100 patient-years		84
Invasive aspergillosis in severe COPD	1.3–3.9 incidence in hospitalised patients		426–1278
Allergic bronchopulmonary aspergillosis in adults with asthma		42	4160
Severe asthma with fungal sensitisation in adults		55.4	5490
Chronic pulmonary aspergillosis after tuberculosis	1.5		153
Chronic pulmonary aspergillosis after tuberculosis		4.9	484
Chronic pulmonary aspergillosis (all)		14.6	1451
Total			12,247–13,099

Abbreviations: ALL, acute lymphocytic leukaemia; AML, acute myeloid leukaemia; COPD, chronic obstructive pulmonary disease.

166,375 and 312,008 adults living with asthma and COPD respectively. Considering a 10.5% hospitalisation rate for COPD per year, approximately 32,761 adults are admitted to the hospital per annum. The percentage of invasive aspergillosis in patients hospitalized due to COPD is 1.3%–3.9%, translating to 426 to 1278 cases annually (Table 3).[62] The annual mortality attributed to invasive aspergillosis in the setting of COPD was estimated to be between 43% and 72% or 307 to 550 deaths.[63]

We have not attempted any additional estimates of invasive aspergillosis, notably in severely ill patients with influenza or coronavirus diseases 2019 (COVID-19). Numerous risk groups exist,[64] but denominators are not available for Honduras.

Chronic pulmonary aspergillosis, including aspergilloma, complicates many chest disorders, and the initial estimate was made using tuberculosis data from Honduras and international estimates of subsequent prevalence. With 2290 pulmonary tuberculosis survivors in 2020, and an assumption that 4.84% of those with cavities post-treatment and 1.6% of those without cavities develop CPA, we estimate an incidence of 153 patients annually and a 5-year period prevalence of 484 patients. Given relatively low pulmonary tuberculosis numbers and moderate numbers of people with asthma, lung cancer and COPD, our total CPA prevalence estimate is 1450 patients or 14.6 per 100,000 (Table 3). There are no reports of CPA from Honduras, but of note the mortality of unproven pulmonary tuberculosis was higher in unconfirmed tuberculosis at 19%, compared with confirmed tuberculosis (11%) in 759 patients from Latin America.[65] This higher mortality is most likely attributable to misdiagnosis, and CPA is probably the most common mimic of tuberculosis that is often fatal.

Asthma is moderately prevalent in Honduras, although direct estimates are lacking. Experts from Honduras participated in a forum on severe asthma, indicative of country concern.[66] There are no reports of ABPA or SAFS from Honduras, or the common complication of bronchiectasis in ABPA *Aspergillus* sensitisation is relatively common in children receiving immunotherapy.[67] We have therefore tentatively estimated an ABPA and SAFS prevalence of 4160 and 5490 cases per year (Table 3), with likely some duplication between these entities. There are no data about cystic fibrosis in Honduras, and this is therefore not included in the estimate.

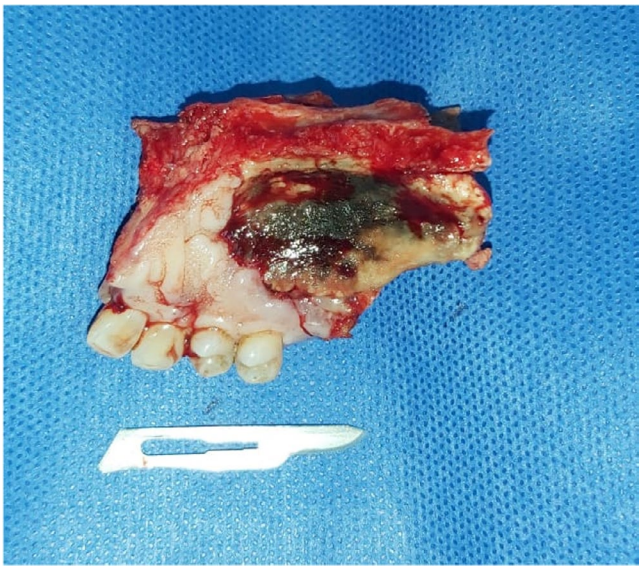

FIGURE 1 Mucormycosis affecting the hard palate of a patient with COVID-19 and diabetes mellitus treated with steroids. COVID-19: coronavirus disease 2019. Photo courtesy of Dr Diana Varela

3.2.5 | Mucormycosis

Mucormycosis is a rare invasive and life-threatening mould infection that characteristically affects individuals with a weakened immune system and poorly controlled diabetes. The disease has been sporadically reported in Honduras in association with prolonged neutropenia due to leukaemia and most recently with COVID-19.[68–70]

There are no available incidence data of mucormycosis in Honduras although we think that its occurrence is not rare. Undiagnosed and poorly controlled diabetes mellitus is an important risk factor for the disease in low-income countries such as Honduras where the prevalence is 7.2%.[71] The prevalence of undiagnosed diabetes mellitus in adults living with diabetes is in the range of 31.9%–53.7%.[72] There are no published reports of mucormycosis in the setting of poorly controlled diabetes mellitus that we could find in Honduras although one of the authors has taken care of three individuals with diabetes complicated by the rhino-orbital-cerebral (ROC) form in the last 3 months and in the setting of worsening glucose control following steroid administration for the treatment of COVID-19 (Figure 1). It is important to mention that the recognition of ROC mucormycosis in diabetics is usually delayed and therefore associated with an unfavourable outcome.[73]

An estimated rate of 0.2 cases of mucormycosis per 100,000 was extrapolated from the literature.[74] Based on such report, we calculate a burden of approximately 20 cases per year although as mentioned previously, with the pool of poorly controlled diabetics in the country incidence is likely to be higher (Table 4).

3.2.6 | *Candida* infections

Candidaemia is the most important invasive fungal infection in hospitalised patients.[75] The Latin America Invasive Mycosis Network published the first report of the epidemiology of candidaemia in Latin America from data collected between November 2008 and October 2010 in 21 tertiary hospitals in 7 countries.[76] In Honduras, the incidence of candidaemia per 1000 admissions was of 0.90 (0.88–0.98) and an incidence per 1000 patients/day of 0.25 (0.24–0.30). The most common species was *C. albicans* representing 27.4% of all isolates, followed by *C. tropicalis* (14.1%) and *C. guillermondi* (20.7%). Other identified species included *C. parapsilosis*, *C. glabrata*, *C. krusei* and C. *lusitinae*.[76] Another study performed by the same group that examined the paediatric population showed that the proportion of species causing candidaemia in this patient population was similar between *C. albicans* (28.9%), *C. tropicalis* (22.7%) and *C. guilliermondii* (22.7%). The median incidence for all countries was 0.81/1000 admissions (0.47–1.64) and 0.17/1000 patient-days (0.16–0.25).[77] The particularly high frequency of *C. guilliermondii* (which typically has higher minimum inhibitory concentrations to echinocandins) compared with other countries has not been explained.

Another study examined the different species from 167 clinical samples (63 urine, 45 sputum, 18 vaginal swabs, 12 blood, 9 catheters, 5 stool/rectal swabs, 2 cutaneous secretion, 2 otic secretion, 4 oral swabs, 2 cerebrospinal fluid and 5 abscesses) from a tertiary hospital in Tegucigalpa. *Candida albicans* was the most frequently reported species causing human infection but other species such as *C. glabrata*, *C. parapsilosis*, *C. tropicalis* and *C. krusei* were also identified.[78] Finally, a study that evaluated the frequency of different *Candida* species as a cause of candiduria by PCR-RFLP found that *Candida albicans/dubliniensis* was the most frequent species accounting for 30% of all isolated followed by *Candida glabrata* (28.8%).[79]

Taking a conservative mean of the literature, the rate of candidaemia is about 5 cases per 100,000 population with 30% occurring in critical-ill or post-surgical patients and 70% in the setting of cancer or other immunosuppressive condition.[80] The rate of peritonitis due to *Candida* spp. was assumed to be 50% the rate of that seen in the intensive care unit setting.[81] Based on these data, there are approximately 495 cases of candidaemia every year in Honduras (rate of 5 per 100,000 population) with 347 occurring in the immunocompromised population and 149 cases in post-surgical and critically ill patients. Approximately 74 cases of peritonitis due to *Candida* spp. are anticipated translating to an annual rate of 0.8 cases per 100,000 population (Table 4).

There are no data about the burden of recurrent vulvovaginal candidiasis in Honduras, but it is estimated to affect between 3700 and 4000 cases per 100,000 women, considering a 6% flat rate for women 15–50 years of age (Table 4).[82]

3.2.7 | Sporotrichosis

Sporotrichosis is a frequent fungal infection seen in Honduras with 10 cultured confirmed lymphocutaneous cases reported in the literature by 1941.[83] A study that examined the aetiology of subcutaneous and deep fungal infection in 52 patients admitted in Hospital Escuela between 1998 and 1999 found sporotrichosis to be the most common mycosis. A total of 19 cases of sporotrichosis were identified with 14

TABLE 4 Estimated burden of other serious fungal infections in Honduras

Condition	Annual incidence per 100,000 population	Total number of cases per year
Candidaemia	5	495
Candida peritonitis	0.8	74
Recurrent Candida vulvovaginitis	3294[a]	163,140
Mucormycosis	0.2	20
Fungal keratitis	5	495
Chromoblastomycosis	0.16–0.3/1,000,000	2–3
Total		164,227

[a]Per 100,000 females.

with a lymphocutaneous and 5 with a verrucose plaque presentation and representing 36.5% of all mycotic infections. Most patients were from Olancho and El Paraiso, and there was a statistically significant association with trauma.[49] The prevalence and incidence of sporotrichosis in Honduras are not known but the disease is likely a common cause of morbidity throughout the country.[84,85]

3.2.8 | Chromoblastomycosis

Chromoblastomycosis is endemic in Honduras with the first cases described in the early 1950s by Dr Corrales Padilla and with 7 cases reported by 1956.[86,87] An additional 32 cases were reported between 1957 and 1969, with most affected individuals being male famers living in poor conditions in rural areas of the country and labelled by the author as a medical-social problem given delays in diagnosis that in some cases required amputation.[88] Another study performed between September 1998 and 1999, identified an additional 9 patients in Hospital Escuela for a total of 48 cases in the literature (although totalling 52 in another report) translating to a prevalence of 0.16–0.30 cases per million inhabitants (Table 4).[49,89]

3.2.9 | Mycetoma

Although there are very few published reports of eumycetoma in Honduras, the deep fungal infection is likely common. For example, in just 1 year, 11 cases were described in one of the major referral centres of the country. Eumycetoma was the second most common deep fungal infection in that series being more common than actinomycetomas and chromoblastomycosis and only surpassed by sporotrichosis.[49]

3.2.10 | Fungal keratitis

One of the few studies done in Hospital San Felipe, the referral eye centre in Honduras, examined the aetiology of a corneal ulcer in 43 out of 70 patients that presented for evaluation between October 2002 and August 2004. Based on culture data, fungal keratitis was the most common aetiology accounting for 59.5% of all cases. *Fusarium* spp. accounted for 60% of cases followed by *Aspergillus* spp. and *Mucor* spp. with 20% each. Farmers or construction workers accounted for 72% of all cases.[90]

A recent report that evaluated the global burden of this entity concluded that the incidence per 100,000 people in Central America is of approximately 5%.[91] Based on this estimate, 495 cases of fungal keratitis are expected to occur every year in Honduras (Table 4).

4 | CONCLUSION

This is the first systematic approach to estimating the burden of SFI in Honduras. The estimation is challenging due to limitations inherent to the lack of a national surveillance system for prevalent fungal infections such as candida vulvovaginitis. There is also limited access to non-culture diagnostic tests for diseases such as cryptococcosis, histoplasmosis and aspergillosis. The burden of SFIs in Honduras is therefore unknown and likely underappreciated.

We estimate that between 178,772 and 179,624 people in Honduras (1.8% of the population) suffer from a SFI every year. We have been unable to estimate the prevalence of tinea capitis, in the absence of any data, a condition usually included among serious fungal infections. This high burden estimate is driven by recurrent candida vulvovaginitis and the different forms of aspergillosis. In PLHIV, oropharyngeal candidiasis is the most frequently encountered opportunistic infection. The absolute number of cases of pneumocystosis, cryptococcosis and histoplasmosis is very similar, and further studies to determine the true incidence and mortality rates are urgently needed.

Evidence-based care for the management of SFIs for the vast majority of the population is challenging due to the limited access to refined and rapid fungal diagnostics and to life-saving antifungals included in the WHO's Essential Medicine List such as flucytosine. There is also a pressing and overdue need for governmental and non-governmental institutions to better define the disability-adjusted life year (DALY) attributable to SFIs. Investment in education, water and sanitation, clean energy, infrastructure and health must surpass investment in other sectors. For example, Honduras military spending as percentage of the GDP has had a linear increase since 2000 from 0.7% to 1.7% in 2020. In comparison, the healthcare expenditure as percentage of the GDP has decreased from 8.9% in 2009 to 7.05% in 2018.[92,93]

In conclusion, SFIs represent a formidable public health problem in Honduras that needs to be better defined. There is a clear need for research to better understand the impact of fungal diseases in Honduras. Such research can be only accomplished with better access to diagnostic tools and antifungals throughout the country and by considering the social, political and economical situation of the affected communities.

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CONFLICT OF INTEREST

All the authors have no conflicts of interest and nothing to declare.

AUTHOR CONTRIBUTION

Nelson Iván Agudelo Higuita: Data curation (equal); Formal analysis (equal); Methodology (supporting); Writing – original draft (lead); Writing – review & editing (equal). **Diana Varela Bustillo :** Data curation (supporting); Writing – review & editing (equal). **David Denning:** Conceptualization (lead); Data curation (equal); Formal analysis (equal); Methodology (lead); Writing – review & editing (equal).

TRANSPARENCY DECLARATION

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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REFERENCES

1. Centers for Diseases Control and Prevention. Honduras country profile. https://www.cdc.gov/globalhivtb/where-we-work/region/westernhemisphere/honduras/honduras.html. Accessed November 9, 2021.
2. Instituto Nacional de Estadistica. https://www.ine.gob.hn/V3/. Accessed November 9, 2021.
3. Institute for Health Metrics and Evaluation. Honduras. http://www.healthdata.org/honduras. Accessed November 9, 2021.
4. Medina N, Samayoa B, Lau-Bonilla D, et al. Burden of serious fungal infections in Guatemala. *Eur J Clin Microbiol Infect Dis*. 2017;36(6):965-969. doi:10.1007/s10096-017-2920-0
5. Carmenate-Milián LH-RA, Ramos-Cáceres D, Lagos- Ordoñez K, et al. Situation of the health system in Honduras and the new proposed health model. *Arch Med*. 2017;9(4):1. doi:10.21767/1989-5216.1000222
6. Central American (Guatemalan, Honduran, Salvadoran) Minor Refugees. Immigrant, refugee and migrant health. Centers for disease control and prevention. https://www.cdc.gov/immigrantrefugeehealth/profiles/central-american/index.html#ref-14. Accessed December 12, 2021.
7. Longini IM Jr, Clark WS, Gardner LI, Brundage JF. The dynamics of CD4+ T-lymphocyte decline in HIV-infected individuals: a Markov modeling approach. *J Acquir Immune Defic Syndr (1988)*. 1991;4(11):1141-1147.
8. United nations population fund. https://www.unfpa.org/data/world-population/HN. Accessed November 23, 2021.
9. Federspiel F, Skovmand S, Skarphedinsson S. Eosinophilic meningitis due to *Angiostrongylus cantonensis* in Europe. *Int J Infect Dis*. 2020;93:28-39. doi:10.1016/j.ijid.2020.01.012
10. Global tuberculosis report 2021. Geneva: World Health Organization; 2021. Licence: CC BY-NC-SA 3.0 IGO.
11. World Health Organization. World health statistics. 2021. https://worldhealthorg.shinyapps.io/tb_profiles/?_inputs_&entity_type=%22country%22&lan=%22EN%22&iso2=%22HN%22. Accessed November 9, 2021.
12. Denning DW, Pleuvry A, Cole DC. Global burden of chronic pulmonary aspergillosis as a sequel to pulmonary tuberculosis. *Bull World Health Organ*. 2011;89(12):864-872. doi:10.2471/BLT.11.089441
13. Denning DW, Pleuvry A, Cole DC. Global burden of allergic bronchopulmonary aspergillosis with asthma and its complication chronic pulmonary aspergillosis in adults. *Med Mycol*. 2013;51(4):361-370. doi:10.3109/13693786.2012.738312
14. Smith NL, Denning DW. Underlying conditions in chronic pulmonary aspergillosis including simple aspergilloma. *Eur Respir J*. 2011;37(4):865-872. doi:10.1183/09031936.00054810
15. Benatar SR, Keen GA, Du Toit NW. Aspergillus hypersensitivity in asthmatics in Cape Town. *Clin Allergy*. 1980;10(3):285-291. doi:10.1111/j.1365-2222.1980.tb02109.x
16. Denning DW, Pashley C, Hartl D, et al. Fungal allergy in asthma-state of the art and research needs. *Clin Transl Allergy*. 2014;4:14. doi:10.1186/2045-7022-4-14
17. International Cancer Control Partnership. WHO - Cancer Country Profiles Honduras 2020. https://www.iccp-portal.org/who-cancer-country-profiles-honduras-2020. Accessed November 9, 2021.
18. Dong Y, Shi O, Zeng Q, et al. Leukemia incidence trends at the global, regional, and national level between 1990 and 2017. *Exp Hematol Oncol*. 2020;9:14. doi:10.1186/s40164-020-00170-6
19. Ewings FM, Bhaskaran K, McLean K, et al. Survival following HIV infection of a cohort followed up from seroconversion in the UK. *AIDS*. 2008;22(1):89-95. doi:10.1097/QAD.0b013e3282f3915e
20. Giron-Callejas A, Garcia-Morales C, Mendizabal-Burastero R, et al. High level of pre-treatment and acquired HIV drug resistance in Honduras: a nationally representative survey, 2016–17. *J Antimicrob Chemother*. 2020;75(7):1932-1942. doi:10.1093/jac/dkaa100
21. Crabtree-Ramirez B, Caro-Vega Y, Shepherd BE, et al. Time to HAART initiation after diagnosis and treatment of opportunistic infections in patients with AIDS in Latin America. *PLoS One*. 2016;11(6):e0153921. doi:10.1371/journal.pone.0153921
22. Smith E, Orholm M. Trends and patterns of opportunistic diseases in Danish AIDS patients 1980–1990. *Scand J Infect Dis*. 1990;22(6):665-672. doi:10.3109/00365549009027119
23. Buchacz K, Baker RK, Palella FJ Jr, et al. AIDS-defining opportunistic illnesses in US patients, 1994–2007: a cohort study. *AIDS*. 2010;24(10):1549-1559. doi:10.1097/QAD.0b013e32833a3967
24. Antinori S, Nebuloni M, Magni C, et al. Trends in the postmortem diagnosis of opportunistic invasive fungal infections in patients with AIDS: a retrospective study of 1,630 autopsies performed between 1984 and 2002. *Am J Clin Pathol*. 2009;132(2):221-227. doi:10.1309/AJCPRAAE8LZ7DTNE
25. Darling ST. A protozoön general infection producing pseudotubercles in the lungs and focal necroses in the liver, spleen and lymphnodes. *JAMA*. 1906;XLVI(17):1283-1285. doi:10.1001/jama.1906.62510440037003
26. Phelps BM, Mallory FB. *Toxic cirrhosis and primary liver cell carcinoma complicated by histoplasmosis of the lung, Fifteenth Annual Report of the Medical*. Department of the United Fruit Co. NY, United Fruit Co.; 1926:11.
27. Hoekenga MT, Tucker HA. [Sensitivity to histoplasmin and coccidioidin in Honduras; report on 300 cases]. *Bol Oficina Sanit Panam*. 1950;29(11):1135-1138. Sensibilidad a la histoplasmina y a la coccidioidina en Honduras; informe sobre 300 enfermos.
28. Alvarado R. Resultado del estudio epidemiológico de la histoplasmósis y coccidioidomicosis realizados en la república de Honduras, C. A. 1962 -1965. *Rev Med Hondur*. 1966;34(4):250-258.
29. Cardona Lopez V, Aguilar-Paz E. Histoplasmosis en Honduras. *Rev Med Hondur*. 1970;38(3):109-125.
30. EL Figueroa M. SIDA en los homosexuales de Honduras. *Rev Med Hondur*. 1988;56(3):194-198.
31. Flores-Martinez L, Lopez-Lutz E. Comportamiento clinico y epidemiologico de enfermedades oportunistas por hongos en pacientes infectados con VIH del instituto nacional del torax y hospital escuela. *Rev Med Post UNAH*. 1999;4(4):224-231.
32. Canales-Beltran M, Palou EY. Histoplasmosis diseminada en pacientes HIV/SIDA. *Rev Méd De Los Post Grados De Medicina UNAH*. 2006;9(1):58-64.
33. Caceres DH, Arauz AB, Flores C, et al. Implementation of rapid diagnostics assays for detection of histoplasmosis and cryptococcosis in central American people living with HIV. *Mycoses*. 2021;64(11):1396-1401. doi:10.1111/myc.13303
34. Medina N, Alastruey-Izquierdo A, Bonilla O, et al. A rapid screening program for histoplasmosis, tuberculosis, and cryptococcosis reduces mortality in HIV patients from Guatemala. *J Fungi (Basel)*. 2021;7(4):268. doi:10.3390/jof7040268
35. Adenis AA, Valdes A, Cropet C, et al. Burden of HIV-associated histoplasmosis compared with tuberculosis in Latin America:

a modelling study. *Lancet Infect Dis*. 2018;18(10):1150-1159. doi:10.1016/S1473-3099(18)30354-2
36. Crabtree Ramirez B, Caro Vega Y, Shepherd BE, et al. Outcomes of HIV-positive patients with cryptococcal meningitis in the Americas. *Int J Infect Dis*. 2017;63:57-63. doi:10.1016/j.ijid.2017.08.004
37. Zuniga-Moya JC, Romero-Reyes LE, Saavedra EB, et al. Prevalence of Cryptococcal antigen and outcomes in people with human immunodeficiency virus in Honduras: a cohort study. *Open Forum Infect Dis*. 2021;8(1):ofaa557. doi:10.1093/ofid/ofaa557
38. Acevedo Almendarez LM. Genotipos de aislamientos de Cryptococcus de pacientes y muestras ambientales del Instituto Nacional Cardiopulmonar, utilizando PCR-RFLP URA5- Tegucigalpa, Honduras, 2015. Universidad Nacional del Nordeste Facultad de Medicina; 2015. https://repositorio.unne.edu.ar/bitstream/handle/123456789/1540/RIUNNE_TM_Acevedo%20Almendarez_L.pdf?sequence=1&isAllowed=y. Accessed November 6,2021.
39. Scott V. Histoplasm, coccidioidin and tuberculin sensitivity in Honduras. *Am J Trop Med Hyg*. 1951;31(1):27-32. doi:10.4269/ajtmh.1951.s1-31.27
40. Poujol ER, Javier CA. Estudio epidemiológico de la coccidioidomicosis en el valle de comayagua. *Rev Med Hondur*. 1971;39(3):274-285.
41. Javier Zepeda CA. Sinopsis de la evolucion de la infectologia en Honduras. *Rev Med Hondur*. 2011;79(3):146-152.
42. Negroni R. [Historical evolution of some clinical and epidemiological knowledge of coccidioidomycosis in the Americas]. *Rev Argent Microbiol*. 2008;40(4):246-256. Evolucion de los conocimientos sobre aspectos clinico-epidemiologicos de la coccidioidomycosis en las Americas.
43. Laniado-Laborin R, Arathoon EG, Canteros C, Muniz-Salazar R, Rendon A. Coccidioidomycosis in Latin America. *Med Mycol*. 2019;57(Supplement_1):S46-S55. doi:10.1093/mmy/myy037
44. Fernandez E. South American blastomycosis (Futz-Splendore de Almeida disease). Report of the first case in Honduras. *Rev Med Hondur*. 1963;31:41-49.
45. Fernandez E, Lainez H. Incidencia de la blastomicosis Sur Americana en Honduras. *Rev Med Hondur*. 1965;33(3):61-76.
46. Raudales O. Blastomicosis sudamericana. Informe de dos casos. *Rev Med Hondur*. 1967;35(3):168-170.
47. Castejón Cruz ÓA, Luxely Toledo M, Cerrato LL. Paracoccidioidomicosis en cavidad oral: a propósito de un caso. *CIMEL Cien E Invest Méd Estudiantil Latinoam*. 2010;15(2):82-84.
48. Toledo ML, Plata Espinal JA. Paracoccidioidomycosis of the upper lip. *Rev Med Hondur*. 2012;80(2):57.
49. Velásquez-Montoya X, Herrera-Guzmán M, Wilkinson-Oberti O, Jeremías-Soto R, Alger J. Subcutaneous and deep fungal infections in hospital escuela tegucigalpa. *Rev Med Post UNAH*. 2001;6(1):61-65.
50. McBride JA, Gauthier GM, Klein BS. Clinical manifestations and treatment of blastomycosis. *Clin Chest Med*. 2017;38(3):435-449. doi:10.1016/j.ccm.2017.04.006
51. Vidal A. Blastomicosis en Honduras. *Rev Med Hondur*. 1942;12(1):55-62.
52. Hoenka MT, Rodríguez SG. Blastomicosis norteamericana-ageneralizada.- comunicación de un caso. *Rev Med Hondur*. 1951;21(5):464-467.
53. Kosmidis C, Denning DW. The clinical spectrum of pulmonary aspergillosis. *Thorax*. 2015;70(3):270-277. doi:10.1136/thoraxjnl-2014-206291
54. Sabillón VN, Santiago Antúnez H, Martín BR. Aspergilosis invasiva: reporte de un caso y revisión de literatura. *Rev Med Hondur*. 2006;76(6):201-204.
55. Varela-Martínez C. Aspergiloma en un pulmon con secuelas de tuberculosis. *Rev Med Hondur*. 2010;78(1):20.
56. Chen CY, Sheng WH, Tien FM, et al. Clinical characteristics and treatment outcomes of pulmonary invasive fungal infection among adult patients with hematological malignancy in a medical centre in Taiwan, 2008–2013. *J Microbiol Immunol Infect*. 2020;53(1):106-114. doi:10.1016/j.jmii.2018.01.002
57. Castellanos AL, Valladares E, Strup S, Bautista B, Bendeck S, Gedaly R. Planting a seed: joining efforts to establish a successful, self-sustained kidney transplant program in Honduras. *Clin Nephrol*. 2020;94(2):103-104. doi:10.5414/CN110118
58. Yan X, Li M, Jiang M, Zou LQ, Luo F, Jiang Y. Clinical characteristics of 45 patients with invasive pulmonary aspergillosis: retrospective analysis of 1711 lung cancer cases. *Cancer*. 2009;115(21):5018-5025. doi:10.1002/cncr.24559
59. Park M, Ho DY, Wakelee HA, Neal JW. Opportunistic invasive fungal infections mimicking progression of non-small-cell lung cancer. *Clin Lung Cancer*. 2021;22(2):e193-e200. doi:10.1016/j.cllc.2020.10.001
60. PAHO. *The burden of chronic respiratory diseases in the Region of the Americas, 2000-2019*. Pan American Health Organization; 2021. https://www.paho.org/en/noncommunicable-diseases-and-mental-health/noncommunicable-diseases-and-mental-health-data-20.
61. To T, Stanojevic S, Moores G, et al. Global asthma prevalence in adults: findings from the cross-sectional world health survey. *BMC Public Health*. 2012;12:204. doi:10.1186/1471-2458-12-204
62. Hammond EE, McDonald CS, Vestbo J, Denning DW. The global impact of aspergillus infection on COPD. *BMC Pulm Med*. 2020;20(1):241. doi:10.1186/s12890-020-01259-8
63. Guinea J, Torres-Narbona M, Gijon P, et al. Pulmonary aspergillosis in patients with chronic obstructive pulmonary disease: incidence, risk factors, and outcome. *Clin Microbiol Infect*. 2010;16(7):870-877. doi:10.1111/j.1469-0691.2009.03015.x
64. Denning DW. Diagnosing pulmonary aspergillosis is much easier than it used to be: a new diagnostic landscape. *Int J Tuberc Lung Dis*. 2021;25(7):525-536. doi:10.5588/ijtld.21.0053
65. Crabtree-Ramirez B, Jenkins C, Jayathilake K, et al. HIV-related tuberculosis: mortality risk in persons without vs. with culture-confirmed disease. *Int J Tuberc Lung Dis*. 2019;23(3):306-314. doi:10.5588/ijtld.18.0111
66. Garcia G, Bergna M, Vasquez JC, et al. Severe asthma: adding new evidence - Latin American thoracic society. *ERJ Open Res*. 2021;7(1). doi:10.1183/23120541.00318-2020
67. Gonzales-Gonzalez VA, Diaz-Flores AM, Fernandez-Zelaya KZ, Rivera-Reyes MF. [Prevalence of sensitization to inhalant allergens in the immunology department from Hospital de Especialidades Pediatricas Maria, Honduras, 2016]. *Rev Alerg Mex*. 2017;64(1):24-33. Prevalencia de sensibilidad a aeroalergenos en el servicio de inmunologia del Hospital de Especialidades Pediatricas Maria, Honduras, 2016. doi:10.29262/ram.v64i1.229
68. Mandegari E, Fu L, Arambu C, et al. Mucormycosis rhinosinusitis at diagnosis of acute lymphoblastic leukemia: diagnostics and management challenges in a low-middle-income country. *J Pediatr Hematol Oncol*. 2015;37(3):e173-e177. doi:10.1097/MPH.0000000000000198
69. Palou EY, Ramos MA, Cherenfant E, et al. COVID-19 associated rhino-orbital mucormycosis complicated by gangrenous and bone necrosis-A case report from Honduras. *Vaccines (Basel)*. 2021;9(8):826. doi:10.3390/vaccines9080826
70. PAHO. Epidemiological alert COVID-19 associated mucormycosis (11 June 2021). https://www.paho.org/en/documents/epidemiological-alert-covid-19-associated-mucormycosis-11-june-2021. Accessed November 23, 2021.
71. World Health Organization - Diabetes Country Profiles, 2016. https://www.who.int/diabetes/country-profiles/hnd_en.pdf. Accessed November 30, 2021.
72. Aviles-Santa ML, Monroig-Rivera A, Soto-Soto A, Lindberg NM. Current state of diabetes mellitus prevalence, awareness, treatment, and control in Latin America: challenges and innovative solutions to improve health outcomes across the continent. *Curr Diab Rep*. 2020;20(11):62. doi:10.1007/s11892-020-01341-9

73. Corzo-Leon DE, Chora-Hernandez LD, Rodriguez-Zulueta AP, Walsh TJ. Diabetes mellitus as the major risk factor for mucormycosis in Mexico: epidemiology, diagnosis, and outcomes of reported cases. *Med Mycol*. 2018;56(1):29-43. doi:10.1093/mmy/myx017
74. Prakash H, Chakrabarti A. Global epidemiology of mucormycosis. *J Fungi (Basel)*. 2019;5(1):26. doi:10.3390/jof5010026
75. Kullberg BJ, Arendrup MC. Invasive candidiasis. *N Engl J Med*. 2015;373(15):1445-1456. doi:10.1056/NEJMra1315399
76. Nucci M, Queiroz-Telles F, Alvarado-Matute T, et al. Epidemiology of candidemia in Latin America: a laboratory-based survey. *PLoS One*. 2013;8(3):e59373. doi:10.1371/journal.pone.0059373
77. Santolaya ME, Alvarado T, Queiroz-Telles F, et al. Active surveillance of candidemia in children from Latin America: a key requirement for improving disease outcome. *Pediatr Infect Dis J*. 2014;33(2):e40-e44. doi:10.1097/INF.0000000000000039
78. Montes K, Ortiz B, Galindo C, Figueroa I, Braham S, Fontecha G. Identification of Candida species from clinical samples in a Honduran tertiary hospital. *Pathogens*. 2019;8(4):237. doi:10.3390/pathogens8040237
79. Ortiz B, Perez-Aleman E, Galo C, Fontecha G. Molecular identification of Candida species from urinary infections in Honduras. *Rev Iberoam Micol*. 2018;35(2):73-77. doi:10.1016/j.riam.2017.07.003
80. Arendrup MC. Epidemiology of invasive candidiasis. *Curr Opin Crit Care*. 2010;16(5):445-452. doi:10.1097/MCC.0b013e32833e84d2
81. Montravers P, Mira JP, Gangneux JP, Leroy O, Lortholary O, AmarCand study g. A multicentre study of antifungal strategies and outcome of Candida spp. peritonitis in intensive-care units. *Clin Microbiol Infect*. 2011;17(7):1061-1067. doi:10.1111/j.1469-0691.2010.03360.x
82. Denning DW, Kneale M, Sobel JD, Rautemaa-Richardson R. Global burden of recurrent vulvovaginal candidiasis: a systematic review. *Lancet Infect Dis*. 2018;18(11):e339-e347. doi:10.1016/S1473-3099(18)30103-8
83. Anonymous. Un nuevo caso de esporotricosis en honduras. *Rev Med Hondur*. 1941;11(3):153-157.
84. Lizardo Castro GA, Zúniga MP. Esporotrichosis linfocutanea en niños: a proposito de un caso. *Rev Med Hondur*. 2011;79(2):81-84.
85. Chakrabarti A, Bonifaz A, Gutierrez-Galhardo MC, Mochizuki T, Li S. Global epidemiology of sporotrichosis. *Med Mycol*. 2014;53(1):3-14.
86. Cueva JA. Cromoblastomicosis en Honduras. *Rev Med Hondur*. 1956;24(4):112-117.
87. Corrales PH. Cromomicosis. *Rev Med Hondur*. 1970;38(2):48-54.
88. Corrales PH. Cromomicosis. *Rev Med Hondur*. 1970;38(2):55-63.
89. Santos D, de Azevedo C, Vicente VA, et al. The global burden of chromoblastomycosis. *PLoS Negl Trop Dis*. 2021;15(8):e0009611. doi:10.1371/journal.pntd.0009611
90. Lagos-Bulnes LA, Zúñiga S. Corneal ulcers: etiology and therapeutics. *Rev Med Post UNAH*. 2006;9(2):249-254.
91. Brown L, Leck AK, Gichangi M, Burton MJ, Denning DW. The global incidence and diagnosis of fungal keratitis. *Lancet Infect Dis*. 2021;21(3):e49-e57. doi:10.1016/S1473-3099(20)30448-5
92. Military expenditure (% of GDP) - Honduras. https://data.worldbank.org/indicator/MS.MIL.XPND.GD.ZS?locations=HN. Accessed December 5, 2021.
93. Current health expenditure (% of GDP) - Honduras. https://data.worldbank.org/indicator/SH.XPD.CHEX.GD.ZS?locations=HN. Accessed December 5, 2021.

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