INTRODUCTION

Honduras is a small country with an area of 112,492 km² 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. 2 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.\(^6\) 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 fluconazole. 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 sequelae. 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). 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.

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). 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$^3$. 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. 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 | Pneumocystis jirovecii pneumonia (PJP)

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. 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. 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 of which 4% (ie 20 deaths) are attributed to invasive aspergillosis.

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

| Population living with HIV/AIDS (PLHIV) | 25,000 |
| Population living with HIV/AIDS (PLHIV) on ARVs | 12,000 |
| Proportion of PLHIV on ARVs | 48 |
| 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; OIs, opportunistic infections; PLHIV, people living with HIV; UNAIDS, Joint United Nations Program on HIV/AIDS.
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 Panama and used rapid diagnostic assays for histoplasmosis according to predefined clinical criteria. Honduras had the highest histoplasma antigen positivity rate at 23%.\(^{23}\) 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%. The most comprehensive study to date examined the prevalence of cryptococcal antigenemia in PLHIV in 2 large referral centers in Honduras. A total of 220 patients with CD4 of <100 cells/mm³ were screened and followed for 1 year. The overall prevalence was of 12.7% and was 40% among hospitalized patients. The 12-month mortality rate was 11.4%. 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/mm³. 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.

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. Scott found a 1% rate of coccidioidin positive skin tests in Tela, Atlántida. The first Central American case of coccidioidomycosis was described in 1955 in a patient who resided in the Valley of Comayagua in the central region of Honduras. Between 1962 and 65, 4.5% of a total of 8052 individuals had a positive skin test in the department of Francisco Morazán. 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. 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.

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. 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. Although the disease is not uncommonly seen in the inpatient setting in the major referral centers of the country, only a few cases are reported in the literature.

3.2.3 | Blastomycosis

Although blastomycosis is not considered endemic in Central America, 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. 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.

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. In Honduras, there are sporadic case reports of invasive pulmonary aspergillosis in the setting of both neutropenia and structural lung disease.

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). 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. 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. Stem cell transplantation is not performed in Honduras, and very few kidney transplants are performed in Honduras to include in the analysis. 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.

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. The prevalence of asthma and COPD in Honduras is not known. The prevalence for asthma was extrapolated from that found in Guatemala (2.4%) and for COPD from that found in Mexico (3.1%) for GOLD stages II-IV. This will translate to...
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). 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.

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, 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. 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. 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. 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.

### 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. 

![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](image-url)
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 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. guilliermondii* (20.7%). Other identified species included *C. parapsilosis*, *C. glabrata*, *C. krusei* and *C. lusitaniae*.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>
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<tr>
<th>Table 4 Estimated burden of other serious fungal infections in Honduras</th>
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<td>Condition</td>
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<td>-----------</td>
</tr>
<tr>
<td>Candidaemia</td>
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<tr>
<td>Candida peritonitis</td>
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<tr>
<td>Recurrent Candida vulvovaginitis</td>
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<td>Mucormycosis</td>
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<td>Fungal keratitis</td>
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<td>Chromoblastomycosis</td>
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aPer 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 Paraíso, and there was a statistically significant association with trauma.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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).\textsuperscript{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.\textsuperscript{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. \textit{Fusarium} spp. accounted for 60% of cases followed by \textit{Aspergillus} spp. and \textit{Mucor} spp. with 20% each. Farmers or construction workers accounted for 72% of all cases.\textsuperscript{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%.\textsuperscript{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.\textsuperscript{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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