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Serious fungal disease incidence and prevalence in Indonesia

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Abstract

Background: Indonesia is a tropical country, warm and humid, with numerous environmental fungi. Data on fungal disease burden help policymakers and clinicians.

Objectives: We have estimated the incidence and prevalence of serious fungal diseases.

Methods: We found all published and unpublished data and estimated the incidence and prevalence of fungal diseases based on populations at risk. HIV data were derived from UNAIDS (2017), pulmonary tuberculosis (PTB) data from 2013–2019, data on chronic pulmonary aspergillosis (CPA) were used to estimate CPA prevalence and likely deaths, COPD data from Hammond (2020), lung cancer incidence was from Globocan 2018, and fungal rhinosinusitis was estimated using community data from India.

Results: Overall ~7.7 million Indonesians (2.89%) have a serious fungal infection each year. The annual incidence of cryptococcosis in AIDS was 7,540. Pneumocystis pneumonia incidence was estimated at 15,400 in HIV and an equal number in non-HIV patients. An estimated 1% and 0.2% of new AIDS patients have disseminated histoplasmosis or *Talaromyces marneffei* infection. The incidence of candidaemia is 26,710. The annual incidence of invasive aspergillosis was estimated at 49,500 and the prevalence of CPA is at 378,700 cases. Allergic bronchopulmonary aspergillosis prevalence in adults is estimated at 336,200, severe asthma with fungal sensitisation at 443,800, and fungal rhinosinusitis at 294,000. Recurrent vulvovaginal candidiasis is estimated at 5 million/year (15–50 years old). The incidence of fungal keratitis around 40,050. Tinea capitis prevalence in schoolchildren about 729,000.

Conclusions: Indonesia has a high burden of fungal infections.

KEYWORDS
aspergillosis, candidaemia, epidemiology

1 | INTRODUCTION

Serious fungal diseases or serious mycoses are a known cause of significant morbidity and mortality worldwide. They affect more than 300 million people, with mortality exceeding 1.6 million. Apart from death, these diseases can also cause chronic disability and blindness.[1] Early diagnosis and treatment are critical to prevent these fatal consequences, which is often challenging, particularly in developing countries, due to limited reliable diagnostic measures and antifungal medication availability.

Identification of high-risk patients has become an important initial step to reduce fungal infection-related mortality. The risk of

serious fungal infection increases with the presence of certain underlying conditions, including human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS), pulmonary tuberculosis (TB), asthma, chronic obstructive pulmonary disease (COPD), particular neoplasms and among stem cell or solid organ transplant recipients. The individual risk also depends on the presence of other risk factors, such as central venous catheters, broad-spectrum antibacterials, total parenteral nutrition, prolonged intensive care unit stay, mucosal *Candida* spp. colonisation and renal failure.[1–3] Factors that contribute to poor outcomes include the number of laboratories capable of performing mycological examinations is limited[4] leading to a large number of misdiagnosed cases, lack of antimicrobial stewardship, resistance to antifungal agents (intrinsic or acquired) and poor control of underlying conditions in high-risk patients.

Indonesia is a warm and humid tropical country, which provides a good environment for growth of numerous fungi including human pathogens and allergens. This country has a huge population, approximately 270.6 million in 2019. The prevalence of HIV infection and tuberculosis in Indonesia is high. In 2018, the prevalence of asthma, cancer, and diabetes in Indonesia were 6.9%, 18 per 100,000 populations, and 10.9%, respectively.[5,6] Fungal diseases, ranging in severity from mild to invasive, affect a large proportion of these populations as they are quite common in clinical practice. Increasing numbers of patients are at risk, including COVID-19 and influenza pneumonia and more sophisticated treatment with iatrogenic risk factors all of which contribute to serious fungal infection risk. However, precise estimation regarding the annual incidence and prevalence of these infections are still lacking in Indonesia, although they have been estimated in many countries or globally.[7] In this study, we have estimated the burden of serious mycoses in Indonesia in order to provide baseline information that can help policymakers and clinicians.

2 | MATERIAL AND METHODS

The authors confirm that the ethical policies of the journal, as noted on the journal's author guidelines page, have been adhered to. No ethical approval was required as the research in this article uses secondary data from other publications and unpublished data from the repositories of universities and unpublished data from the Department of Parasitology, Universitas Indonesia, Jakarta. We searched all published and unpublished epidemiologic data and estimated the national incidence or prevalence of fungal diseases based on fungal infection frequencies in different populations at risk (Table 1). Population data for 2018 were taken from BPS-Statistics Indonesia.[6] HIV prevalence was derived from the joint United Nations programs on HIV and AIDS (UNAIDS) 2018 report.[8] Pulmonary TB incidence was extracted from the WHO 2019 TB report (Indonesia TB report).[9] We attained COPD prevalence from reports by The BOLD study,[10] with hospitalisation per year taken from Hammond et al (2020).[11] Lung cancer incidence was taken from Globocan 2018.[12] Asthma prevalence in adults was taken from an epidemiologic study by Sundaru et al[5] Renal transplant data were retrieved from Marbun et al,[13] and Supit.[14] Overseas allogeneic haematopoietic stem cell and liver transplant numbers are estimated, as there is no central register. Indonesia has nearly 8,000 ICU beds which are distributed across the country.[15]

We obtained the prevalence or incidence of fungal infections affecting particular underlying disease groups from various sources. The individual disease attack rates or prevalence are shown in Table 2. In addition, we assumed the cryptococcal meningitis incidence in non-HIV patients mirrors that in Thailand (ratio of 1–7).[16] Likewise, we have estimated the ratio of *Pneumocystis* pneumonia (PCP) in non-HIV immunocompromised patients is equal to HIV patients, which is almost certainly an underestimate as this ratio is much higher in Europe and other countries equipped with PCR detection of *Pneumocystis jirovecii*. Histoplasmosis and probably talaromycosis are endemic to the Indonesian archipelago, but rates are uncertain—we used 1% and 0.2% of advanced HIV disease to estimate annual incidence.

Invasive aspergillosis (IA) was estimated in four groups, haematologic malignancy (13% of acute myeloid leukaemia patients),[17,18] and an equal number of cases in all other lymphomas, leukaemia and multiple myeloma patients,[19] in 4% of those who died of AIDS,[20] in 1%–4% of transplant recipients, in 2.6% of lung cancer patients[21] and in 1.3% of those admitted to hospital with COPD.[22] Mucormycosis was estimated using international rates.[23] Chronic pulmonary aspergillosis (CPA) estimation is partly based on data from Indonesia and partly international. At the end of 6 months therapy for pulmonary TB, 8% of patients had CPA.[24] Pulmonary cavitation is present in 32% of those on completion of TB therapy and we assumed that 22% are at risk of CPA (ie 32%–10%) after having completed TB therapy. Using data from Uganda where 6.5% of survivors from TB who had cavitation developed CPA each year,[25] we calculated the annual incidence and 7-year period prevalence, assuming a 15% annual mortality of surgical resection rate. Fungal asthma (allergic bronchopulmonary aspergillosis [ABPA] and severe asthma with fungal sensitisation [SAFS]) prevalence is estimated from other countries. Chronic fungal rhinosinusitis was estimated based on a population study in northern India,[26] in the absence of data from Indonesia.

Given few epidemiological data on candidiasis in Indonesia, we have estimated candidaemia at 10/100,000. We have assumed that one-quarter of such cases occur in intensive care,[27] and that the number of cases of intra-abdominal candidiasis (peritoneal candidiasis) is 50% of the cases of candidaemia. The only incidence figure for oesophageal candidiasis we have estimated is that in HIV patients—20% of those with advanced HIV disease[28] and 5% in those on antiretroviral therapy.[29] Recurrent vulvovaginal candidiasis was defined as 4 or more episodes annually, and a general rate of 69% in women between the ages of 15 and 50 calculated for annual period prevalence.[30,31]

Fungal keratitis was estimated based on data from Thailand[16] and Malaysia,[32] supported by local data on the relative proportion of fungi as a cause of infectious keratitis[33,34] Tinea capitis has been found in most provinces in the country and a weighted average from

TABLE 1 Population characteristics in Indonesia

Population characteristic	No.	Source
Total population	266,795,000	BPS-Statistics Indonesia[6]
Women aged 15–50 years	74,538,700	WHO 2012 demographic proportions[75]
Population >40 years (16%)	42,687,200	Population pyramid[76]
Children (<15 years) (27%)	72,034,650	WHO 2012 demographic proportions[75]
Prevalence of HIV	0.4% (0.4%–0.5%)	Tarigan et al[77]
People living with HIV	640,000	UNAIDS, 2019[78]
Proportion of HIV patients on ARVs	17% (15%–20%)	UNAIDS, 2017[79]
Late HIV diagnosis with CD4 <350 cells/mm^3	81%	Tarigan et al[77] Siregar et al 2015[80]
Adults living with HIV & CD4 <200 cells/μl	108,240	Assumes a 5 year decline in immunity of those not on ARVs
AIDS deaths (adults)	38,000 (33,000–43,000)	UNAIDS, 2019[78]
AIDS deaths (children)	2,500 (2,100–3,000)	UNAIDS, 2019[78]
Annual cases of TB	845,000	World Health Organization 2019[9]
Annual cases of pulmonary TB who survive	650,340	World Health Organization 2018[81]
Prevalence of asthma	6,91%	Sundaru et al, 2005[5]
Adults with asthma	13,450,000	Sundaru, 2005[5]
Adults with COPD (12.5% of >40 years)	32,575,000	BOLD study, 2007[10]
Adults with COPD admitted to hospital each year (10.5%)	3,420,000	Hammond et al, 2020[11]
Renal transplants per year	100	Marbun, 2018[13]; Supit, 2019[14]
Liver transplants per year	50	Oswari et al 2020[82]
Allogeneic stem cell transplants per year	50	All international, returning home for care
Lung cancer	30,023	Globocan, 2018[83]
Acute myelogenous leukaemia (population inclidence)	0.0038%	WHO middle-income assumption[84]
Acute myelogenous leukaemia (incidence)	10,138	Supriyadi et al 2011[18] Globocan 2020[85]
Lung cancer incidence	30,023	Globocan 2018[83]
Intensive care unit beds	7,094	Ditjen Yankes, Ministry of Health, 2017[15]

Abbreviations: ARV, antiretroviral therapy; COPD, chronic obstructive pulmonary disease; TB, tuberculosis.
[a]Adjusted based on assumption that 90% of TB cases are pulmonary.

the 6 reports was used to estimate the prevalence in school-age children.[35–40] There are insufficient data to determine the prevalence of mycetoma, chromoblastomycosis and sporotrichosis, all three conditions were reported as long ago as 1984.

3 | RESULTS

3.1 | Country profile (BPS-Statistics Indonesia)

Indonesia is an emerging middle-income country with a gross domestic product per capita of USD$ 3,894 and a population of 265,015,300 in 2018. Approximately, 49.8% of this population was female. The population is distributed in 16,056 islands. Most people live in big cities, particularly in Java and Sumatera islands, where tertiary medical facilities are available. Tertiary medical service facilities are also available in capital cities of the provinces such as Makassar in South Sulawesi, Manado in North Sulawesi, Denpasar in Bali and others. Twenty-seven percent of the population was less than 15 years old (70,486,700) and 9.3% are over 60 (24,754,500).

3.2 | HIV- associated fungal infections

We estimate 28,650 cases of oesophageal candidiasis in HIV-infected people, and cannot estimate how many with other underlying conditions (Table 3).

Antigen detection in sera of HIV-infected patients showed 164 that the prevalence of antigenaemia among ambulatory patients was 6.4% in Jakarta[41] and 7.1% in Bandung.[42] While cryptococcal meningitis among HIV-infected patients is 21%.[43] Our annual incidence estimate is 7,540 cases (Table 3). Most of the cryptococcal meningitis

TABLE 2 Fungal disease assumptions

Mycosis	Assumptions	Geographic origin of data informing assumptions	Reference
Cryptococcal meningitis	Assumes a 7.1% rate in those with <200 CD4 cells	National	Muda et al. 2014,[41] Ghaniem et al 2014,[42] Sjam et al 2012,[43]
Pneumocystis pneumonia	For adults, assumed to cause 15% of all newly presenting HIV/AIDS patients	National	Rozaliyani,et al 2020[45] Data Dept. ParasitologyFKUI unpublished
Disseminated histoplasmosis	Assumed to be 1% in advanced HIV disease	National	Baker, 2019[72]
Talaromycosis	Assumed to be 0.2% in advanced HIV disease	National	Surja et al 2020[86] Widaty et al 2020[87]
Oesophageal candidiasis	20% of PLWH not on ART and 5% taking ART	International	Smith & Orholm, 1990[28]
Invasive aspergillosis	Complicates 13% of cases of AML per year and an equivalent number among all other hematologic malignancies; complicates 10% of allogeneic HSCT, 1% of kidney SOT, 4% of liver SOT, and 2.6% of cases of lung cancer; 4% of patients dying of AIDS, and 1.3% of hospitalised COPD patients.	National & International	Hammond et al, 2020[11] Chen et al 2020[17] Lortholary et al, 2011[19] Antinori et al, 2009[20] Guinea, 2010[22] Herbrecht et al, 2012[88]
Mucormycosis	2 cases per million population	International	Prakash, 2019[23]
Chronic pulmonary aspergillosis	Complicates 8% of end of therapy pulmonary TB cases and 6.5% annual rate of CPA in the remaining 24% with cavitation following TB. Pulmonary TB assumed to underlie 80% of cases of chronic pulmonary aspergillosis.	National & International	Setianingrum, 2021[24] Page, 2019[25]
Allergic bronchopulmonary aspergillosis	Assumed to affect 2.5% of asthmatic adults	International	Denning et al, 2013[89]
Severe asthma with fungal sensitisation	Assumed to affect 30% of the most severe decile of asthmatic adults	International	Denning et al, 2014[90]
Chronic fungal rhinosinusitis	Assumed to be the same as in India, based on a population survey, 0.11% of the population	International	Chakrabarti, 2015[26]
Candidaemia	No local epidemiological data, so estimated at 10/100,000; 25% in intensive care	National & International	Bongomin, 2017[1]; Tan, 2015[27]
Candida peritonitis	Post-surgical *Candida* peritonitis is 50% of the ICU-related candidaemia annual rate.	National & International	Wijayanto et al 2009[50] Kalista et al 2017[51] Rusli 2012[52] Mursinah et al 2016[53] Montravers et al, 2011[57] Hustrini et al 2019[58]
Recurrent vulvovaginal candidiasis	6%–9% of women between 15 and 54 years of age, as per references	International	Foxman et al, 2013[30] Denning et al, 2018[31]
Fungal keratitis	15/100,000	National and International	Chayakulkeeree, 2017[16] Ratnalingam et al 2017[32] Brown, 2020[33] Wahyuningsih et al 2002[34]
Tinea capitis	Multiple case series, age 22 months to 65 years, ost <14 years of age	National & Regional	See Table 4

Note: Regional implies another country in sub-Saharan Africa, while international implies outside of sub-Saharan Africa.

Abbreviations: AML: acute myelogenous leukaemia; ART: antiretroviral therapy; COPD: chronic obstructive pulmonary disease; HSCT: haematopoetic stem cell transplantation; ICU: intensive care unit; PCP: *Pneumocystis* pneumonia; PD: peritoneal dialysis; PLWH: persons living with HIV; SOT: solid organ transplantation; TB: tuberculosis.

TABLE 3 Annual incidence and prevalence of the major serious fungal diseases in Indonesia

Infection	Incidene or prevalence	Number of infections per underlying disorders per year					Rate/100K	Total burden
		None	HIV/ AIDS	Respiratory	Cancer/ Tx	ICU		
Oesophageal candidiasis	I	-	28.560	-	-	-	10	28,560
Cryptococcal meningitis	I	340	7.540	-	790	-	8.7	8,670
Pneumocystis pneumonia	I	-	15.400	-	15.400	-	11.5	30,800
Histoplasmosis	I	?	1.060	?	?	?	0.4	1,060
Talaromyces marneffei infection	I	-	210	-	?	-	0.4	210
Invasive aspergillosis	I	-	1.400	900	2,700	44,500	18.6	49,500
Mucormycosis	I	-	-	-	530	-	0.20	530
Chronic pulmonary aspergillosis	P	-	-	378,700	-	-	142	378,700
Allergic bronchopulmonary aspergillosis (ABPA)	P	-	-	336,200	-	-	126	336,200
Severe asthma with fungal sensitisation (SAFS)	P	-	-	443,800	-	-	166	443,800
Chronic fungal rhinosinutis	P	294,000	-	-	-	-	110	294,000
Candidaemia	I	-	-	-	20,030	6,680	10	26,710
Candida peritonitis	I	-	-	-	-	3,340	1.3	3,340
Recurrent vaginal candidiasis (>4 times/year)	P	5,003,000	-	-	-	-	3,747[a]	5,003,000
Tinea capitis	P	729,000					270	729,000
Fungal keratitis	I	40,050	-	-	-	-	15	40,050
Total burden estimated		6,058,050	52,263	1,186,615	39,450	54,510		7,737,413

[a]Female population only.

in HIV-infected patients is an AIDS-defining illness because many of these patients were diagnosed with advanced HIV infection.[44] We also diagnosed cryptococcosis among non-HIV patients including meningitis, pulmonary cryptococcosis, skin infection and cryptococcaemia. There is no good study of these cases, so we have use ratios from Thailand[16] to estimate 340 cryptococcal meningitis cases in non-immunocompromised patients and in immunocompromised patients.

Among 55 AIDS patients with pneumonia, PCP was found in 14.5%. Using this estimate, we have estimated 15,400 cases and an equal number in non-HIV-infected patients (Table 3). In current clinical practice in Jakarta, most PCP diagnoses are made in non-HIV patients; for example, ICU admitted patient with different underlying diseases.[45]

We have estimated 1% of new AIDS patients have disseminated histoplasmosis (1,060 cases) and 0.2% *T marneffei* infection (210), in the absence of population data, but some diagnosed cases (Table 3).

3.3 | Fungal diseases in other immunocompromised and diabetic patients

We estimate a total of 2,700 IA in leukaemia and transplant recipients, 900 cases in lung cancer, 1,480 patients who die of AIDS and 44,500 cases in COPD patients admitted to the hospital. The incidence of IA in critically ill patients Jakarta is 7.65%,[46] which is higher than in many countries, and while some of the aforementioned groups will enter intensive care, most will not with only 7,094 ICU beds in the country. So, a total of nearly 50,000 cases of IA are likely (Table 3), making this one of the highest rates in the world. One report of the outcomes of kidney transplantation: Patients found that most deaths were due to infection but there is no mention of which pathogen.[13]

Mucormycosis is reported—two cases of rhino-cerebral mucormycosis[47,48] and 13 cases of rhino-cerebral & sinusitis have been recorded at the Department of Parasitology over a 2 year period (2018–2019). These reports are surely a gross underestimate of the size of this problem, and we conservatively estimate 530 cases annually in all patient groups, including immunocompromised, trauma, burns and diabetic patients (Table 3).

3.4 | Fungal diseases associated with underlying respiratory disease

Tuberculosis incidence has been falling since 2016 according to the WHO but remains high and this complicated our estimate of CPA annual incidence and prevalence. So, in 2018, with 657,000 survivors of pulmonary TB, we estimated that 52,570 people finished their 6 months of TB therapy with CPA and over the following year

TABLE 4 Tinea capitis in Indonesia

Region and year	Prevalance	Reference
Manado, 2012	6/65 (9.23%)	Bertus et al, 2015[35]
Tangerang, 2011	3/178 (1.7%)	Octavia 2012[36]
Surabaya, 2011	5/275 (1.85%)	Putri & Astari,2017[37]
Surabaya, 2012	13/183 (7.1%)	
Surabaya, 2013	4/166 (2.4%)	
Surabaya, 2011–2013	22/624 (3.5%)	
Malang, 2017	2/19 (11%)	Pravitasari et al, 2019[38]
Bali, 2007–2010	0.21%	Karmila, 2016[39]
Jakarta, 2005–2010	2005:4/837 (0.48%)	Sari et al, 2012[40]
	2006:3/796 (0.38%)	
	2007:2/637 (0.31%)	
	2008:7/665 (1.05%)	
	2009:3/684 (0.44%)	
	2010:4/655 (0.61%)	
	Total: 23/4,274 (0.53%)	

Note: Epidemiology papers published since 2,000.

another 8,100 people would develop CPA. Using this approach between 2013 and 2019, and a 15% annual mortality or surgical removal rate, a 7-year point prevalence of ~297,570 patients with CPA after TB is estimated. Given all the other co-existing lung diseases, at least an extra 20% of other patients, we estimate a total of ~371,970 prevalence of CPA (Table 3). Overall this estimate of CPA in TB survivors is 10.1% of the TB survivors (486,000 of 4.8 million), of whom ~188,000 (38.3%) have estimated to have died (apart from a few with curative thoracic surgery).

Fungal asthma in adults was estimated based on international figures given the lack of diagnosis of these entities currently in Indonesia. Asthma prevalence is relatively high at 6.9% from 2005.[5] So ABPA prevalence may be as high as 336,200 affected (126/100,000) and SAFS 443,800 (186/100,000) (Table 3). There may some overlap between these entities as many ABPA patients also have severe asthma. The 2.5% proportion used for ABPA may underestimate the prevalence if the situation in India is mirrored in Indonesia.

3.5 | Chronic fungal rhinosinusitis

Using prevalence data from a community study from India,[26] we estimate that 293,700 people in Indonesia suffer from various manifestations of chronic fungal rhinosinusitis (FRS). These disorders do occur in Indonesia as a recent study of 20 patients with chronic fungal rhinosinusitis[49] found the level of beta-1,3-D glucan in the nasal wash to be a helpful diagnostic aid. In this study, 70% of the patients had *Aspergillus flavus* as the likely allergenic fungus, similar in frequency to the 90% found in India. The distribution of subtypes of chronic FRS patients in India was allergic rhinosinusitis (56%), chronic granulomatous rhinosinusitis (18%), eosinophilic rhinosinusitis (15%), fungal ball of the maxillary sinus (10%) and chronic invasive rhinosinusitis (1%)—this distribution of entities has yet to be studied in Indonesia. Nonetheless, we estimate nearly 300,000 people in Indonesia suffer from chronic FRS (Table 3).

3.6 | Candida infections

Candidaemia comprises a significant proportion of proven or probable causes of sepsis: 55 of 131 (39%) neonates with late-onset sepsis had candidaemia[50] and 91 of 738 (12.3%) cases of sepsis in adult admitted to the ICU (2012–2014) documented or probable invasive candidiasis.[51] In children with acute leukaemia in 2010–2011 12 of 102 (11.7%) had invasive fungal infection mostly with candidaemia or features consistent with invasive candidiasis.[52] Other series of candidaemia have been published including 117 cases over 2011–2014[53] and 72 cases over 2010–2018.[54]

Using an intermediate international figure of 10/100,000, the estimated incidence of candidaemia is 26,700 (Table 3) and invasive candidiasis 66,750 cases annually (40% only diagnosed by blood culture).[55] A study conducted in Jakarta on neonates who failed antibacterial therapy showed that the most common cause was *C. tropicalis*.[56]

Partially included within the overall tally of invasive candidiasis is intra-abdominal candidiasis. Assuming that 33% of candidaemia episodes occur in intensive care,[27] and the careful multicentre prospective study from France,[57] we have estimated a 50% proportion of intra-abdominal candidiasis to each case of candidaemia. For Indonesia, this would be about 2,000 cases annually. There is also *Candida* peritonitis complicating chronic ambulatory peritoneal dialysis (CPAD) but uncertainty about how many such patients there are in Indonesia. With 1,668 patients on CAPD currently, and the rate of *Candida* peritonitis is 2 per 100 patient/years,[58] then about 33 cases will be seen each year.

Recurrent vulvovaginal candidiasis is estimated to affect 6% of women between 15 and 50 years, a total of about 5 million in any year. We found no publications on this topic from Indonesia.

3.7 | Skin and hair fungal infections

A small number of cases of mycetoma, chromoblastomycosis and sporotrichosis have been reported in the 1980's.[59] Since then, a few case reports of chromoblastomycosis and a series of 4 cases of eumycetoma from Jakarta have been published. It is likely that these infections are grossly underdiagnosed. Only one case of human sporotrichosis is reported[60] and one case in a cat.[61] This may

be a rare infection in Indonesia. Pythiosis has not been reported in Indonesia.

Multiple case series of tinea capitis have been published with most cases in those aged <14 years (Table 4). There are wide variations in prevalence from about 0.2% in Bali[39] to 11% in Malang. The last year of survey was 2019 in Malang,[38] but the study was very small. Using a conservative national figure of 1% of children, we would anticipate about 720,000 children to have tinea capitis (Table 3).

3.8 | Ocular infections

Fungal keratitis occurs in Indonesia and a series of 366 corneal scrapings examined in Jakarta over 7 years in the mycology laboratory, 172 (47%) showed fungal hyphae and/or were culture positive. To estimate the annual incidence of fungal keratitis in Indonesia, we have used data from Thailand—15/100,000. This estimate predicts that about 40,000 people in Indonesia develop fungal keratitis each year(Table 2).[16,32–34] Most of these affected eyes will go blind, and some will need removal, preventing a later corneal transplant.

4 | DISCUSSION

The population of Indonesia is estimated to exceed 273 million in 2020, according to the United Nations, 3.5% of the global population and the fourth largest population on the planet. It is a predominantly Muslim (~80%) democracy with over 300 spoken languages and 6,000 inhabited islands. There are many ethnicities within the country, Javanese being the largest (~40%). There are over 86 medical schools graduating about 8,000 doctors annually (theasiapacificscholar.org), most of whom become specialists.[62] The health system is both private and public. Pusat Kesehatan Masyarakat (Puskesmas—Community Health Centre) is a public health facility of primary health care that is distributed all over Indonesia. Unfortunately, fungal diseases especially serious fungal diseases have not received enough attention. The government National Health Insurance Program (BPJS) and plan for universal health coverage has been developed over the last 5 years. BPJS covers all Indonesian residents and foreigners who have worked in Indonesia for at least 6 months and paid contributions to BPJS. This membership is obligatory even if people have other health insurance.[63]

Fungal infections can be broadly categorised into 5 categories: invasive and immediately life- or sight-threatening, chronic such as mycetoma and chronic pulmonary aspergillosis, allergic including fungal asthma and allergic fungal rhinosinusitis, mucosal and cutaneous (hair, nails and skin). Some infections are tough to classify in this schema, including post-operative and burn wound infections, maxillary fungal balls, diabetic foot fungal infections and others. Nonetheless, we have attempted here to estimate for the first time the burden of the most important fungal infections and termed serious in medical impact terms. The objective is to identify the approximate scale of the problem in terms of total numbers and diagnostic and awareness needs.

Due to limited mycology laboratories in the country, until recently most mycotic diseases have only been reported sporadically. A detailed study on epidemiology is limited, so magnitude of the problem is not clear.[4]

4.1 | Aspergillosis

Indonesia ranks third on the number of TB which is an important factor related to the incidence of chronic pulmonary aspergillosis. In an abstract presented in 2017, we estimated ~83,030 treated pulmonary TB patient will suffer CPA and here we estimate a prevalence of 378,700, based on recently completed studies.[24,25,64] Due to the similarity of clinical signs, usually, these patients are treated as recurrent TB. Two studies about chronic pulmonary aspergillosis were conducted in two cities, namely Jakarta (Java) and Manado (Sulawesi). In Jakarta, 10 out of 56 patients with TB were met criteria for CPA, while in Manado 72 post-TB patients were proven as CPA by radiology and antibody detection test.[64,65]

We estimated the total annual incidence of invasive aspergillosis to be 49,500 (18.6/100,000) primarily among COPD, leukaemia, lung cancer and HIV patients. This is a relatively high figure internationally. A multicentre study in 6 ICUs in Jakarta showed the prevalence of probable invasive pulmonary aspergillosis to be 7.6%[46] which is not reflected in our estimate, suggesting that our estimate could be an underestimate. Invasive *Aspergillus* rhinosinutisis has been reported as case reports[66,67] but we could not separate out these cases from the overall IA caseload.

4.2 | Candidaemia and invasive candidiasis

Candidaemia is hospital-related infection. A lack of local data prevents a very accurate estimate. Our national data are limited to the data from hospitals in Jakarta which is lower than our estimation (Table 2). Our overall estimate of the annual incidence of candidaemia is in the middle of international rates at 10/100,000, substantially lower than Pakistan, for example, at 21/1,000,000,[68] so could be an underestimate, but on the other hand, there were only 7,094 intensive care beds in 2016. Candidaemia is an insensitive means of diagnosis in invasive candidiasis at about 40%.[55]

4.3 | Cryptococcosis

With the arrival of AIDS pandemic, we saw an increase of cryptococcal meningitis in the AIDS population. Patients were only diagnosed in Jakarta & Bandung, and in a small number from other cities such as Denpasar Bali, Manado, Pontianak& Jayapura. We also diagnosed cryptococcosis in non-HIV patients. Our experience indicates that the problem of cryptococcosis is bigger than what has been

reported. The prevalence of cryptococcal meningitis in patients with HIV infection ranges from 9%–21%, depending on the method of examination whether using direct examination of India ink or by detection of *Cryptococcus* antigens. By using antigen detection, a higher diagnostic sensitivity and incidence is obtained.[42,43] Four studies on the detection of antigenaemia among ART naïve HIV patients conducted in Jakarta, Bandung, Surabaya showed the prevalence of antigenaemia varied between 6.4%–7.3%.[41,42,69] Another study conducted in Pontianak, Kalimantan (Borneo) found the prevalence of antigenaemia to be 5.6% among HIV-infected patients.[70] In our department, we recorded cases of cryptococcosis in non-HIV patients. A high index of suspicion is needed to recognise the early symptoms so that the diagnosis can be made rapidly. Outcomes may be limited as flucytosine is not available for therapy.

4.4 | Histoplasmosis

There are two important clinical manifestations of histoplasmosis—disseminated and chronic. Disseminated histoplasmosis was first reported in 1932 and since 2004, we identified histoplasmosis among AIDS patients with skin dissemination. But we do not have any data on the chronic pulmonary form which has clinical symptoms and radiological appearances to pulmonary TB. We suspect that among patients diagnosed as pulmonary TB some of them have histoplasmosis. Of 88 sera from patients with pulmonary infection 22 sera were positive for *Histoplasma* galactomannan (data are not shown). Furthermore, when considering the results of the histoplasmin skin test in three regions of Indonesia,[71,72] it is highly likely that actual cases of histoplasmosis are far more frequent than has been reported. Adrenal histoplasmosis is expected, but not reported. Case reports of various manifestations of histoplasmosis were reported from all over Indonesia from 1932 until now.[73,74]

5 | CONCLUSION

Over 6 million Indonesians probably have a serious fungal infection in any given year (2.89%). The estimates are almost certainly significant underestimates. Indonesia has a high burden of serious fungal infections, partly attributable to high TB incidence, moderate numbers of HIV patients, and many other risk factors. Additional efforts to improve diagnostic capability and undertake epidemiology studies are required.

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CONFLICT OF INTEREST

The authors report no conflict of interest.

AUTHOR CONTRIBUTION

Retno Wahyuningsih: Conceptualization (equal); Data curation (equal); Investigation (equal); Writing-review & editing (equal). **robiatul adawiyah:** Data curation (equal); Resources (equal); Validation (equal). **Ridhawati Sjam:** Project administration (equal); Validation (equal). **joedo prihartono:** Data curation (equal). **endah AT Wulandari:** Data curation (supporting); Resources (supporting). **Anna Rozaliyani:** Resources (supporting). **ronny ronny:** Data curation (supporting); Writing-review & editing (supporting). **Darma Imran:** Data curation (supporting); Resources (equal). **Mulyati Tugiran:** Resources (equal). **forman erwin siagian:** Resources (supporting). **David Denning:** Conceptualization (equal); Data curation (equal); Investigation (equal); Writing-review & editing (equal).

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REFERENCES

1. Bongomin F, Gago S, Oladele RO, Denning DW. Global and multinational prevalence of fungal diseases-estimate precision. *J Fungi (Basel)*. 2017;3(57):1–29.
2. Rüping MJGT, Vehreschild JJ, Cornely OA. Patients at high risk of invasive fungal infections: when and how to treat. *Drugs*. 2008;68(14):1941-1962.
3. Maertens J, Vrebos M, Boogaerts M. Assessing risk factors for systemic fungal infections. *Eur J Cancer Care*. 2001;10(1):56-62.
4. Chindamporn A, Chakrabarti A, Li R, et al. Survey of laboratory practices for diagnosis of fungal infection in seven Asian countries: an Asia fungal working group (AFWG) initiative. *Med Mycol*. 2018;56(4):416-425.
5. Sundaru H. Epidemiology of asthma in Indonesia. *Acta Med Indones*. 2005;37(1):51-54.
6. BPS-Statistics Indonesia. Statistical yearbook of Indonesia 2019. https://www.bps.go.id/subject/12/kependudukan.html. Accessed August 2, 2020.
7. Global Action Fund for Fungal Infections. Publications. https://www.gaffi.org/media/country-fungal-disease-burdens/. Accessed August 2, 2019.
8. Global HIV & AIDS statistics — 2020 fact sheet. 2020. https://www.unaids.org/en/resources/fact-sheetAccessed. Accessed January 4, 2021.
9. WHO Tb data. 2019. https://www.who.int/tb/data/. Accessed January 3, 2021.
10. Buist AS, McBurnie MA, Vollmer WM, et al. International variation in the prevalence of COPD (the BOLD Study): a population-based prevalence study. *Lancet*. 2007;370(9589):741-750.
11. Hammond EE, McDonald CS, Vestbo J, Denning DW. The global impact of Aspergillus infection on COPD. *BMC Pulm Med*. 2020;20(241):1–10.
12. International Agency for Globocan. https://gco.iarc.fr/today/data/factsheets/populations/360-indonesia-fact-sheets.pdf. Accessed October 5, 2020.
13. Marbun MBH, Susalit E, Umami V. Seven years' experience of living donor kidney transplantation in Indonesia: a retrospective cohort study. *Acta Med Indones - Indones J Intern Med*. 2018;50:119-124.
14. Supit T, Nugroho EA, Santosa A, Soedarso MA, Daniswara N, Addin SR. Kidney transplantation in Indonesia: an update. *Asian J Urol*. 2019;6:305-311.
15. Beds in the ICU. http://sirs.yankes.kemkes.go.id/fo/home/intensif. Accessed December 24, 2020.

16. Chayakulkeeree M, Denning DW. Serious fungal infections in Thailand. *Eur J Clin Microbiol Infect Dis*. 2017;36(6):931-935.
17. Chen L, Han X, Li Y, Zhang C, Xing X. Invasive pulmonary aspergillosis in immunocompetent patients hospitalised with influenza A-related pneumonia: a multicenter retrospective study. *BMC Pulm Med*. 2020;20(1):239.
18. Supriyadi E, Widjajanto PH, Purwanto I, Cloos J, Veerman AJ, Sutaryo S. Incidence of childhood leukemia in Yogyakarta, Indonesia, 1998–2009. *Pediatr Blood Cancer*. 2011;57(4):588-593.
19. Lortholary O, Gangneux JP, Sitbon K, et al. Epidemiological trends in invasive aspergillosis in France: the SAIF network (2005–2007). *Clin Microbiol Infect*. 2011;17(12):1882-1889.
20. 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.
21. Yan X, Li M, Jiang M, Zou LQ, Fuo F, Jiang Y. Clinical characteristics of 45 patients with invasive pulmonary aspergillosis. *Cancer*. 2009;115(21):5018-5025.
22. Guinea J, Torres-Narbona M, Gijón 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.
23. Prakash H, Chakrabarti A. Global Epidemiology of Mucormycosis. *J Fungi (Basel)*. 2019;5(1):26.
24. Setianingrum F, Rozaliyani A, Adawiyah R, et al. A prospective longitudinal study of chronic pulmonary Aspergillosis in pulmonary tuberculosis in Indonesia (APICAL). submitted to J Thorax under review.
25. Page ID, Byanyima R, Hosmane S, et al. Chronic pulmonary aspergillosis commonly complicates treated pulmonary tuberculosis with residual cavitation. *Eur Respir J*. 2019;53(3):1801184.
26. Chakrabarti A, Rudramurthy SM, Panda N, Dash A, Singh A. Epidemiology of chronic fungal rhinosinusitis in rural India. *Mycoses*. 2015;58(5):294-302.
27. Tan BH, Chakrabarti A, Li RY, et al. Incidence and species distribution of candidaemia in Asia: a laboratory-based surveillance study. *Clin Microbiol Infect*. 2015;21(10):946-953.
28. 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.
29. 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.
30. Foxman B, Muraglia R, Dietz JP, Sobel JD, Wagner J. Prevalence of recurrent vulvovaginal candidiasis in 5 European countries and the United States: Results from an internet panel survey. *J Low Genit Tract Dis*. 2013;17(3):340-345.
31. Denning DW, Kneale M, Sobel JD, Rautema RR. Global burden of recurrent vulvovaginal candidiasis: a systematic review. *Lancet Infect Dis*. 2018;18(11):e339-e347.
32. Ratnalingam V, Umapathy T, Sumugam K, Hanida H, Retnasabapathy S. Microbial keratitis in West and East Malaysia. *Int Eye Sci*. 2017;17(11):1989-1992.
33. Brown L, Leck AK, Gichangi M, Burton JM, Denning DW. The global incidence and diagnosis of fungal keratitis. *Lancet Infect Disinfect Dis*. 2020;3099(20):1-9.
34. Wahyuningsih R, Kartanegara D, Sitompul R. Jamur penyebab keratomikosis. *J Mikol Kedok Indon*. 2002;1–2:20-23.
35. Bertus NVP, Pandaleke HEJ, Kapantow GM. Profil dermatofitosis di Poliklinik Kulit dan Kelamin RSUP Prof. dr. R. D. Kandou Manado periode Januari - Desember 2012. *e-Clinic (eCl)*. 2015;3(2):731-734.
36. Oktavia A. Prevalensi dermatofitosis di poliklinik kulit dan kelamin RSUD Tangerang periode 1 Januari 2011 sampai dengan 31 Desember 2011. Universitas Islam Negeri Syarif Hidayatullah Jakarta. 2012.
37. Putri AI, Astari L. Profil dan evaluasi pasien dermatofitosis (profile and evaluation of dermatophytosis). *Periodic Dermatol Venereol*. 2017;29(2):135-141.
38. Pravitasari DN, Hidayatullah TA, Nuzula AF, Puspita R. Profil dermatofitosis superfisialis periode Januari – Desember 2017 di Rumah Sakit Islam Aisiyah Malang. *J Saint Med*. 2019;15(1):25-32.
39. Tinea kapitis tipe gray patch yang diduga disebabkan oleh Microsporum dan Trichophyton, (Program Pendidikan Dokter Spesialis Fakultas Kedokteran Universitas Udayana 2016).
40. Sari AB, Widaty S, Bramono K, Miranda E, Ganjardani M. Tinea kapitis di Poliklinik Kulit dan Kelamin RSUPN Dr Cipto Mangunkusumo Jakarta periode tahun 2005–2010. *MDVI*. 2012;39(3):113-117.
41. Muda CAK, Imran D, Herqutanto WR. Cryptococcal antigen in the serum of anti-retro viral naïve HIV infected patients. presented at: International Conference on Cryptococcus and Cryptococcosis; 15-19 May, 2014; Amsterdam.
42. Ganiem AR, Indrati AR, Wisaksana R, et al. Asymptomatic cryptococcal antigenemia is associated with mortality among HIV-positive patients in Indonesia. *J Int AIDS Soc*. 2014;17(1):.
43. Sjam R, Mulyati AR, Imran D, Wahyuningsih R. Cryptococcal meningitis among AIDS patients in Jakarta. *Majalah Kedokteran UKI*. 2012;28(4):160-166.
44. Cairns G. Indonesia: tackling HIV in one of the world's fastest-growing epidemics. Indonesia: tackling HIV in one of the world's fastest-growing epidemics. https://www.aidsmap.com/news/sep-2018/indonesia-tackling-hiv-one-worlds-fastest-growing-epidemics. Accessed January 5, 2021.
45. Rozaliyani A, Wiyono WH, Nawas MA, et al. Laboratory findings and clinical characteristics of pneumocystis pneumonia and tuberculosis infection among HIV-infected patients with pulmonary infiltrates in Jakarta, Indonesia. *Trop Biomed*. 2020;37(4):1117-1123.
46. Rozaliyani A, Sedono R, Jusuf A, et al. A novel diagnosis scoring model to predict invasive pulmonary aspergillosis in the intensive care unit. *Saudi Med J*. 2019;40(2):140-146.
47. Marpaung HG, Baso GDP, Rizka A, Nelwan EJ, Wardani RS, Wahyuningsih R. Mukormicosis rino-orbita-cerebral pada pasien diabetes melitus tipe 1: Sebuah Laporan Kasus. *J Penyakit Dalam Indones*. 2018;5(1):42-45.
48. Satari HI, Hidayati EL, Yuliarti K, et al. Mucormycoses in a child with renal tubular acidosis: a case report. presented at: The 6th Asia Pacific Society for Medical Mycology Congress; 20-22 Oktober 2016; Denpasar, Bali, Indonesia.
49. Wicaksana DA, Suheryanto R, Maharani I. Correlation between β-Glucan and neutrophil/eosinophil ratio of paranasal sinus Mucosa and blood in the diagnosis of chronic fungal rhinosinusitis. *Oman Med J*. 2018;33(5):393-400.
50. Wijayanto D, Amir I, Wahyuningsih R, Windiastuti E. Prevalens dan sebaran faktor risiko mikosis sistemik pada neonates dengan sepsis awitan lambat di RS Dr.Cipto Mangunkusumo. *Sari Pediatri*. 2009;11(4):229-237.
51. Kalista KF, Chen LK, Wahyuningsih R, Rumende CM. Karakteristik klinis dan prevalensi pasien kandidiasis invasif di rumah sakit cipto mangunkusumo. *J Peny Dal Indon*. 2017;4(2):56-61.
52. Rusli V. Prevalensi, manifestasi klinis, dan jenis infeksi jamur invasif pada anak dengan leukemia akut yang mendapat kemoterapi dan mengalami neutropenia. Universitas Indonesia; 2012.
53. Mursinah M, Ibrahim F, Wahid MH. Risk factors and scoring systems for patients with candidemia at a tertiary hospital in Jakarta, Indonesia. *Acta Med Indon*. 2016;48(3):193-199.
54. Wiwing V, Cucunawangsih C. Candidemia in an Indonesian teaching hospital: A 9-year observational study. *J Infect Public Health*. 2020;13(2):345.
55. Nguyen MH, Wissel MC, Shields RK, et al. Performance of Candida real-time polymerase chain reaction, β-D-glucan assay, and blood cultures in the diagnosis of invasive candidiasis. *Clin Infect Dis*. 2012;54(9):1240-1248.

56. Wahyuningsih R, Rozaliyani A, Jannah S, Amir I, Prihartono J. Kandidemia pada neonatus yang mengalami kegagalan terapi antibiotik. *Maj Kedokt Indones*. 2008;58:110–115.
57. Montravers P, Mira JP, Gangneux JP, Leroy O, group. LOAs. A multicentre study of antifungal strategies and outcome of Candida spp. peritonitis in intensive-care units. *Clin Microbiol Infect*. 2011;17(7):1061-1067.
58. Hustrini NM, Nugroho P, Lydia A. Continuous ambulatory peritoneal dialysis in Indonesia: A single center experience. MON 073. *Kidney Int Rep*. 2019;4:S1-S437.
59. Harahap M, Nasution MA. Dermatomycoses in Indonesia. *Int J Dermatol*. 1984;23(4):273-274.
60. Halim A, Rahaju P, Surjotomo H, Murdiyo MD. Case report: pseudocarcinomatous hyperplasia of hypopharynx due to sporothrichosis. *J Kedokt Brawi*. 2016;29(1):88-94.
61. Esfandiari A, Indriani G, Tanjung F, Matik NB, Tantina WSD. Sporotrichosis pada kucing. presented at: Musyawarah Nasional ke-3 ADHPHKI; 2016 Feb 21-23; Bali, Indonesia.
62. Konsil Kedokteran Indonesia. Data Fakultas Kedokteran. http://www.kki.go.id/index.php/informasi/index/246/1529/1543. Accessed December 20, 2020.
63. Info BPJS Kesehatan Ed 69 Menuju Kesehatan Semesta 2019. https://www.bpjs-kesehatan.go.id/. Accessed December 26, 2020.
64. Setianingrum F, Rozaliyani A, Adawiyah R, et al. Chronic pulmonary aspergillosis in active pulmonary tuberculosis patients in Jakarta, Indonesia. presented at: ISHAM meeting; 2018; Amsterdam.
65. Kurniawan I, Nugroho A, Wongkar MCP. Differences in clinical score, radiological score, and pulmonary function test as predictor of suspect chronic pulmonary aspergillosis in treated pulmonary tuberculosis patients. presented at: Petri meeting; October 2018; Bandung.
66. Wardani RS, Sinto R, Wahyuningsih R. How to deal with emerging invasive fungal rhinosinusitis. presented at: National Congress of PERHATI KL; October 24-26, 2019; Padang.
67. Setiyohadi B, Azizi MS, Yuliani IW, et al. Invasive aspergillosis in a systemic lupus erythematosus patient. *Indon J Rheumatol*. 2010;02:36-40.
68. Jabeen K, Farooqi J, Mirza S, Denning D, Zafar A. Serious fungal infections in Pakistan. *Eur J Clin Microbiol Infect Dis*. 2017;36(6):949-956.
69. Widjaja S, Triyono EA, Kawilarang AP, Rohman A. Cryptococcal antigenemia in HIV / AIDS patients using lateral flow immunoassay detection at Dr. Soetomo. *Indones J Trop Infect Dis*. 2018;7(1):11-14.
70. Febrylla S. Identifikasi kriptokokosis dengan metode dentifikasi kriptokokosis dengan metode lateral flow assay (LFA) pada pasien HIV/AIDS di Klinik Melati RSUD dr. Soedarso Pontianak periode september-desember 2014. *J Mhs PSPD FK Univ Tanjungpura*. 2015;151:10-17.
71. Baker J, Kosmidis C, Rozaliyani A, Wahyuningsih R, Denning DW. Chronic pulmonary histoplasmosis-A scoping literature review. *Open Forum Infect Dis*. 2020;7(5):ofaa119.
72. Baker J, Setianingrum F, Wahyuningsih R, Denning DW. Mapping histoplasmosis in South East Asia – implications for diagnosis in AIDS. *EmergMicrob Infect*. 2019;8(1):1139-1145.
73. Müller H. Histoplasmose in Oost Java. *Geneeskd Tijdschr Ned*. 1932;72:889-895.
74. Anggorowati N, Sulistyaningsih RC, Ghozali A, Subronto YW. Disseminated histoplasmosis in an Indonesian HIV-positive patient: a case diagnosed by fine needle aspiration cytology. *Acta Med Indones*. 2017;49(4):360-362.
75. WHO. *World health statistics 2012*. Geneva, Switzerland. World Health Organization. 2012;157-167.
76. Population Pyramids of the world. https://www.populationpyramid.net/indonesia/2019/. Accessed December 20, 2020.
77. Tarigan YN, Woodman RJ, Miller ER, Wisaksana R, Wignall FS, Ward PR. Changes in the HIV continuum of care following expanded access to HIV testing and treatment in Indonesia: a retrospective population-based cohort study. *PLoS One*. 2020;15(9):1-18.
78. UNAIDS. Country: Indonesia. https://www.unaids.org/en/regionscountries/countries/indonesia. Accessed August 20, 2019.
79. UNAIDS data. 2017 https://www.unaids.org/en/resources/documents/2017/2017databook. Accessed December 17, 2020.
80. Siregar AYM, Tromp N, Komarudin D, Wisaksana R, van Crevel R, van der Ven A, Baltussen R, et al. Costs of HIV/AIDS treatment in Indonesia by time of treatment and stage of disease. *BMC Health Serv Res*. 2015;15:440.
81. WHO Tuberculosis country profiles. Tuberculosis profile: Indonesia. 2019. https://www.who.int/tb/country/data/profiles/en/. Accessed December 20, 2020.
82. Oswari H, Rahayatri TH, Soedibyo S. Pediatric living donor liver transplant in Indonesia's national referral hospital. *Transplant*. 2020;104(7):1305-1307.
83. Globocan 2018. https://gco.iarc.fr/today/data/factsheets/populations/360-indonesia-fact-sheets.pdf. Accessed October 15, 2020.
84. Review of Cancer Medicines. Acute myelogenous leukemia and acute promyelocytic leukemia (Including Acute Promyelocytic Leukemia). 2014. https://www.who.int/selection_medicines/committees/expert/20/applications/AML_APL.pdf. Accessed November 3, 2020.
85. Globocan 2020. https://gco.iarc.fr/. Accessed January 5, 2021.
86. Surja SS, Adawiyah R, Houbraken J, et al. Talaromyces atroroseus in HIV and non-HIV patient: a first report from Indonesia. *Med Mycol*. 2020;58(4):560-563.
87. Widaty S, Santoso ID, Ricky D, Yunihastuti E, Rihatmadja R, Wahyuningsih R. Talaromycosis clinically and histopathologically mimicking histoplasmosis in an immunocompromised patient. *Dermatol Online J*. 2020;26(9):13030/qt9r49g227.
88. Herbrecht R, Bories P, Moulin JC, Ledoux MP, Letscher-Bru V. Risk stratification for invasive aspergillosis in immunocompromised patients. *Ann N Y Acad Sci*. 2012;1272:23-30.
89. 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.
90. 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.

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