

## Original Article

# Burden of fungal infections in Iran

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## Abstract

**Introduction:** The number of fungal infections occurring each year in Iran is not known. As the burden of fungal disease is a measure used to assess and compare the relative impact of different type of fungal diseases on populations, we have estimated the burden of fungal diseases in Iran.

**Methodology:** We estimated the burden of human fungal diseases based on the specific populations at risk, existing epidemiological data in both local and international databases, and modelling previously described by the LIFE program (<http://www.LIFE-worldwide.org>).

**Results:** Among the population of Iran (79,926,270 in 2016), 6,670,813 (8.3%) individuals are estimated to suffer from a fungal infection each year. A total of 2,791,568 women aged between 15 and 50 years are estimated to suffer from recurrent vulvovaginal candidiasis, annually. In addition, considering the 13.3% prevalence rate of tinea capitis in children, a total of 2,552,624 cases per year are estimated. The estimated burden of invasive aspergillosis in the 3 groups of patients with hematologic malignancy, lung cancer and chronic pulmonary obstructive disease was 6394 (8.0 per 100,000). The estimate for the burden of allergic disease related to fungi including allergic bronchopulmonary aspergillosis, severe asthma with fungal sensitization and allergic fungal rhinosinusitis was 272,095 (340 per 100,000). Based on the 28,663 cases of HIV infection reported, an estimated 900 and 113 cases with pneumocystosis and cryptococcal meningitis are annually anticipated, respectively.

**Conclusion:** Our estimates indicate that the importance of fungal infections is high but overlooked in Iran, which warrants further actions by health care authorities.

**Key words:** *Candida*; *Aspergillus*; vulvovaginal candidiasis; *tinea capitis*; burden of fungal infections; Iran.

*J Infect Dev Ctries* 2018; 12(10):910-918. doi:10.3855/jidc.10476

(Received 23 April 2018 – Accepted 13 August 2018)

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## Introduction

Fungi are key components of the earth's ecosystem with both beneficial and detrimental effects on plant, insect and animal life. Nevertheless, the importance of fungal disease in humans is not widely recognized, and deaths resulting from these infections are often overlooked [1]. In spite of these facts, there is presently little or no active mycological surveillance or control program on fungal infections administered by the World Health Organization and most public health agencies- with the singular exception of the U.S.

Centers for Disease Control and Prevention (CDC) and mycetoma control efforts [1]. The Global Burden of Disease estimations [2] have recently placed cutaneous fungal infections as the fourth most common health problem (dental caries, tension headaches, and migraines), with about 1 billion affected worldwide. Likewise, millions of individuals worldwide experience life-threatening invasive fungal infections (IFI) and other serious fungal infections each year. Diagnosis requires specialized testing and mortality is high without early diagnosis [1]. Antifungal therapy has

improved greatly in the last 15 years, and so survival and reduced morbidity are the norm, if these infections are treated promptly.

In the last two decades, increasing populations of patients at risk for IFI including those with solid organ and hematopoietic stem cell transplantation (HSCT), patients receiving immunosuppressive therapies, patients with chronic obstructive pulmonary disease (COPD), human immunodeficiency virus (HIV), premature birth and cancer are considered a major challenge for the health care systems and health authorities should make efforts to improve the outcomes.

Another concern is the cost of fungal infections. In two studies from the United States the overall cost of hospitalization associated with candidemia and aspergillosis were estimated to be US\$ 216-281 million and 633.1 million per year, respectively [3,4].

The incidence of two major fungal infections, aspergillosis and candidiasis, has significantly increased in patients with different underlying conditions, during the past two decades [5]. On the other hand, the mortality rate of the invasive form of these infections remains high despite improvements in diagnosis and advances in prophylaxis and treatment in IFIs [5].

Many reports have recently been published on the burden of fungal diseases from different countries [6]. In contrast to the unsightly and uncomfortable cutaneous and mucosal fungal infections, systemic mycoses are generally life-threatening with a high mortality and morbidity especially when they are not recognized and treated rapidly. Estimations of the incidence and prevalence of serious fungal infections, based on epidemiological data, are essential to inform public health priorities for diagnosis and treatment of fungal diseases, given constrained resources.

Iran is a Middle East country with a diverse range of climatic conditions in different areas. In the last few decades, Iran has made significant improvements in its healthcare system including applying advanced procedures in management and diagnostic methods as well as establishing many transplantation, cancer and intensive care unit centers. Nowadays, fungal disease diagnosis is not confined to cutaneous mycoses but includes life-threatening mycoses, as prompt and accurate diagnosis is of utmost importance for survival. However, the number of fungal infections occurring each year in Iran is not known. As the burden of fungal disease is a measure used to assess and compare the relative impact of different type of fungal diseases on populations, we have estimated the burden of fungal

disease based on populations at risk, supplemented with existing data.

## Methodology

To identify fungal infections frequencies and specific populations at risk in Iran a systematic literature review was conducted in both local and international research databases, including Medline, PubMed, Google Scholar, magiran, Irandoc and Scientific Information Database (SID), and available meeting abstracts. The case reports were excluded. The search terms used were “fungal infections and Iran”, “mycosis and Iran”, “candidaemia and Iran”, “candidiasis and Iran”, “aspergillosis and Iran”, “allergic bronchopulmonary aspergillosis (ABPA) and Iran”, “tinea and Iran”, “pneumocystis and Iran”, “mucormycosis and Iran” and “fungal infections, AIDS and Iran”.

Where no data were available, we used proportion of specific risk groups and fungal infection frequencies in each population to estimate national incidence or prevalence, depending on the condition.

Demographic data were obtained from the Statistical Center of Iran ([www.amar.org.ir](http://www.amar.org.ir)).

The prevalence of tinea capitis was derived from Bassiri Jahromi and Khaksar [7]. There are also several case reports on mycetoma [8,9] and chromoblastomycosis in Iran [10,11] both classified as neglected tropical diseases (NTD) by the World Health Organisation ([www.who.int/neglected\\_diseases/events/tenth\\_stag/en/](http://www.who.int/neglected_diseases/events/tenth_stag/en/)).

The number of adult women population (between age 15–50 years old) was obtained from the Statistical Center of Iran. Recurrent vulvovaginal candidiasis (RVVC) was defined as at least four episodes of vulvovaginal candidiasis (VVC) per year, and a 12.3% rate of RVVC in adult women (>15–50 years old) was used, based on the work by Nazeri *et al.* [12]. To estimate the incidence of systemic candidiasis (proven or probable candidiasis with the presence of mycological criteria) in Iran, a rate of 6.2% was considered among patients with hematologic malignancies [13].

According to a recent systematic review and meta-analysis, the prevalence of asthma in adults (>18 year) in Iran was 2.54 %, [14] yielding a total of 1,542,634 adult asthmatic patients. The prevalence of allergic bronchopulmonary aspergillosis (ABPA) complicating asthma was estimated at 2.5% based on a study by Denning *et al.*, 2013 [15]. The rate of severe asthma is 10% of the total asthma burden. On the other hand, the

prevalence of fungal sensitization is about 33%; [16] therefore we estimated the rate of severe asthma with fungal sensitization (SAFS) as: total asthma burden × 0.1 × 0.33.

A study from China suggested that approximately 8% of the adult population suffer from chronic rhinosinusitis (CRS) [17], and 6.7% of these patients have one of several forms of fungal rhinosinusitis (FRS) according to an endoscopic survey from Brazil [18]. We estimated the total number of adult Iranian population with FRS and the allergic fungal rhinosinusitis (AFRS) based on previous reports [17-19].

The rate of chronic pulmonary aspergillosis (CPA) following TB was estimated based on the annual incidence of pulmonary tuberculosis (PTB) in 2015, assuming 13.5% of these patients died [20]. For other conditions associated with CPA we used the studies of Smith and Denning, 2011 [21] and Denning *et al.*, 2011 [22] to estimate the overall prevalence of CPA.

The number of patients with hematologic malignancy was obtained from the 2008 National Registry Report of Iranian Ministry of Health and Medical Education ([www.registry.behdasht.gov.ir](http://www.registry.behdasht.gov.ir)).

The risk of IA development was considered in 5.5% among acute myeloid leukemia (AML) patients as reported previously in Iran [23]. Among patients with lung cancer, a 2.63% incidence of IA was considered, based on the study by Yan *et al.*, 2009 [24]. According to a recent study by Sharifi *et al.* [25] a rate of 9.2% was used to estimate the number of patients with COPD (aged 40 years or older) in Iran. We obtained the number of admitted COPD patients to hospital by use of a 7% rate of the total COPD population [26] in Iran. A 3.9% rate of IA in COPD patients was used, based on a work by Xu *et al.* 2012 [27]. The rates following transplantation and other immunocompromised and severely ill patient groups are not known.

Data on the HIV/AIDS population were derived from the Islamic Republic of Iran AIDS Progress Report [28]. There is no comprehensive study of infection rates of HIV infection in Iran so we used the data from Smith *et al.* [29] and Buchacz *et al.* [30] to estimate oesophageal candidiasis in HIV patients. Oral candidiasis was only estimated for new AIDS cases and was assumed to occur in 74.5% of them [31]. We have also assumed a rate of 60% for *Pneumocystis*

**Table 1.** Estimated burden of fungal diseases in Iran.

	Number of patients with underlying disorder						Burden (%)	Total burden	Rate /100K
	None	Diabetes	AML/HM/ lung cancer	COPD hospital admissions	Respiratory / FRS	HIV/AIDS			
ABPA	-	-	-	-	1,542,634	-	2.5	38,565	48.2
SAFS	-	-	-	-	154,263	-	33	50,907	63.7
AFRS	-	-	-	-	325,532 <sup>1</sup>	-	56.1	182,623	228
CPA after TB	-	-	-	-	10,399	-	22% of PTB with lung cavities, 2 % of those without cavities	1,248	1.6
IA in AML	-	-	432	-	-	-	5.5	24	0.03
IA in COPD	-	-	-	161,271	-	-	3.9%	6,290	7.9
IA in lung cancer	-	-	3,050	-	-	-	2.63	80	0.1
RVVC	22,695,674	-	-	-	-	-	12.3	2,791,568 <sub>2</sub>	9279.7
Oral candidiasis	-	-	-	-	-	1500	74.5	1,117	389 <sup>3</sup>
Esophageal candidiasis	-	-	-	-	-	28,663	20% of patients without ARVs 5% of patients on ARVs	4,895	6.1
Systemic candidiasis	-	-	4393	-	-	-	6.2	272	0.34
Pneumocystosis	-	-	-	-	-	1500	60	900	3140 <sup>2</sup>
Cryptococcal meningitis	-	-	-	-	-	28,663	0.44	113	0.14
Mucormycosis	-	4,500,000	4393	-	-	-	0.16% of Diabetic, 4.27% of HM	7388	9.2
<i>Tinea capitis</i>	19,192,665	-	-	-	-	-	13.3	2,552,624	3193.7
Total burden estimated								<b>5,638,614</b>	

None = the population without any underlying conditions, Acute Myeloid Leukemia = AML, Hematologic malignancy= HM, COPD= chronic pulmonary obstructive disease, FRS=Fungal rhinosinusitis, HIV= human immunodeficiency virus infected people, AIDS= acquired immunodeficiency syndrome, ABPA = allergic bronchopulmonary aspergillosis, SAFS= severe asthma with fungal sensitization, Allergic fungal rhinosinusitis = AFRS, PT= tuberculosis, CPA= chronic pulmonary aspergillosis, PTB= patients with pulmonary tuberculosis, IA= invasive aspergillosis, ARVs= Antiretroviral drugs, RVVC= Recurrent vulvovaginal candidiasis; 1Fungal rhinosinusitis prevalence in 6.7% of chronic rhinosinusitis. 2Rate of RVVC per 100 000 adult females between age 15–50 years old, not per total population. 3Rate per 100 000 AIDS patients, not per total population.

pneumonia in newly presenting patients with AIDS, based on a median for other countries [32].

To estimate the annual incidence of mucormycosis, we used a rate of 4.27 cases per 100 leukemic patients and 0.16% amongst diabetics, the recorded rates in Iran [33] and India [34], respectively. For cryptococcal meningitis, we used 0.44% of patients with their first diagnosis of HIV infection, the recorded rate in Russia, a neighboring country [35].

## Results

### *Country profile*

In 2016, the total population of Iran was 79,926,270, of whom 49.3% were women, 24.0% children under 15, and 9.3% were older than 60; 28.4% were women aged 15-50 years. The 2014 GDP was \$5,124 per capita. Table 1 shows the estimated burden of fungal diseases in Iran.

### *Dermatophytosis*

A total of 2,552,624 (3194/100,000) children are estimated to suffer from tinea capitis in Iran, using a prevalence figure of 13.3%, reported previously [7]. Other dermatophyte infections are common, but we have not estimated those, as usually less clinically significant.

### *Recurrent vulvovaginal candidiasis (RVVC)*

The number of women aged between 15–50 years old was 22,695,674 in 2016. With a 12.3% rate of RVVC [12], we estimated a total burden of 2,791,568 Iranian women suffering from RVVC in any one year.

### *Systemic candidiasis*

There were 4,393 registered patients with hematologic malignancy in 2008 in Iran. According to a reported rate from Iran [13] we estimated a total burden of 272 (0.34 per 100,000 general population) of systemic candidiasis in this Iranian population. Badiie *et al.* [36] reported a 0.7% rate of systemic candidiasis in ICU patients, but we have no data on the number of patients admitted to ICU in Iran. In most countries, the rate of candidemia is 1.25-25/100,000 including premature neonates, critical care, dialysis patients, post-surgical and other medical patients [37]. If we assumed conservatively that 5/100,000 were affected, this would amount to 3,996 cases nationally. Candidemia is detectable in ~40% of cases of disseminated candidiasis and a minority of patients with intra-abdominal candidiasis have candidemia [37], therefore the calculation based only on candidemia greatly underestimates the burden of invasive candidiasis.

### *Asthma and allergic aspergillosis*

The adult population with asthma was estimated at 1,542,634 individuals, based on the 2.54% reported rate of asthma in adults [14] in 2016. Assuming that 2.5% of asthmatic patients suffer from ABPA, 38,565 (48.2 per 100,000 general population) patients were estimated to have ABPA in Iran. According to a reported rate of fungal sensitization in adults with asthma (19.6%) [38], a total of 302,356 individuals were estimated. The rate of fungal sensitization rises with asthma severity, so assuming a higher rate of 33% being sensitized to fungi in severe asthma [16], 50,907 asthmatic patients have SAFS. There may be some overlap between ABPA and SAFS as some ABPA patients have severe asthma; assuming a 20% overlap, a total of 71,578 patients have ‘fungal asthma’.

### *Fungal rhinosinusitis*

A total number of 4,858,688 Iranians are affected by chronic rhinosinusitis (CRS), calculated using an 8% rate of CRS in the adult population. Fungal rhinosinusitis (FRS) has many forms and its burden was estimated to represent a total of 325,532 individuals, based on 6.7% reported rates of FRS in patients with CRS in China and Brazil [17,18]. Amongst these patients, allergic FRS is the most common, affecting 38.7% in Brazil [19] and 56.1% in rural India [19]. By extrapolation, we estimated a total burden of 125,980 to 182,623 (228 per 100,000 general population) AFRS in the Iranian population.

### *Chronic pulmonary aspergillosis*

In 2015, the WHO reported 10,399 cases of PTB in non-HIV infected patients in Iran [20], of which 1,400 cases had a fatal outcome. According to the study by Smith and Denning [21], an average of 12% of PTB will have residual cavitary lung lesions. It is also estimated that CPA will develop in 22% of patients with lung cavities, and 2% of those without cavities [22]. Following this assumption, we estimated a number of 396 cases of CPA in TB patients in Iran per year, and a 5-year-period prevalence of 1.6 per 100,000 population (1,248 cases). We assumed that CPA cases following PTB comprise 33% of the total, given the number of other patients with respiratory disorders, giving a total number of 3,745 CPA cases in Iran.

### *Invasive aspergillosis*

According to the report of the National Program for Disease Registries of the Ministry of Health and Medical Education ([www.registry.behdasht.gov.ir](http://www.registry.behdasht.gov.ir)), the



number of patients with hematologic malignancy was 4,393 in 2008. Of these patients, 432 suffered from AML and IA was estimated in 24 of these patients by assuming that 5.5% of AML patients develop IA [23]. Assuming that the number of IA patients with AML is 50% of the total in hematologic malignancy, as in France and Austria [39,40], the total estimate is 48 patients (0.06/100,000). The number of patients with lung cancer was 3,050. According to the reported rate by Yan *et al.* 2009 [24] we estimated a total burden of 80 IA in patients with lung cancer.

The COPD burden was estimated at 7,353,217 cases, based on the 9.2% reported rate of COPD (aged 40 years or older) in Iran [25] in 2015. Conservatively assuming that 7.0% of COPD patients are admitted to hospital each year (161,271) and a 3.9% rate of IA in these patients, 6,290 (7.9 per 100,000 population) are estimated to have IA.

We do not have precise numbers of patients receiving a transplant or of the rates of IA in this group of patients and no estimates could be made.

#### *Fungal infections in patients with AIDS*

Based on the data of a case registry, a total of 28,663 people living with HIV (PLWH) had been identified in Iran until September 2014 [28]. In September 2014, 5,585 PLWH (including 1,516 females and 4,069 males) were receiving antiretroviral therapy (*AIDS Control Office, MOHME Center for Communicable Disease Management; ART Registers, December 2014 (unpublished)*). In 2013, 1,500 new cases of AIDS were documented. According to these data and the reported estimation rate of oesophageal and oral candidiasis [29-31] we estimated a total burden of 1,117 new oral candidiasis and 4,895 oesophageal candidiasis in Iranian HIV patients. There is no comprehensive study on fungal infections especially pneumocystosis and cryptococcal meningitis in patients with AIDS in Iran, however we estimated a total burden of 900 and 113 cases in AIDS patients, respectively.

#### *Mucormycosis*

Based on the data presented by Esteghamati *et al.* [41] in 2011, approximately 4.5 million adult people were living with diabetes in Iran. We estimated a total burden of 7200 cases of mucormycosis in individuals with diabetes and 188 cases in patients with hematologic malignancy (rate 9.2/100,000 population). Overall, 98 cases of mucormycosis was reported from Iran in 55 publications between 1990 and 2015 [42], among them rhinocerebral infections were the most common clinical manifestation in diabetic patients and

*Rhizopus* spp. were the most prevalent (51.7%), followed by *Mucor* spp. (17.2%).

#### *Uncommon fungal infections*

According to a review by Khodavaisy *et al.* [8] there were 90 cases of mycetoma (including both actinomycetoma and eumycetoma) in Iran from 1972 to 2009. Most cases were reported in males (66.3%) and most patients were farmers (44.4%). Feet were the most commonly involved site (73.8%) followed by leg and arm (4.8% each). The most common agents in actinomycetoma cases were *Actinomadura madurae* (23.5%), *Nocardia asteroides* (20.6%), *Nocardia caviae* (13.2%), and those of eumycetoma were *Pseudallescheria boydii* (10.3%). There are only 2 case reports on chromoblastomycosis in Iran [10,11]. One from a 27-year-old man who showed lesions on the palate and chest and the culture result was reported as *Cladosporium* sp. [10]. The other case was reported from the north of Iran in a 23 year- old female farmer. The causative agent was *Phialophora verrucosa* and the affected site was feet [11].

There are no reliable data or official records on cystic fibrosis patients, and patients admitted in ICU, therefore the number of related diseases with these conditions is unknown in Iran.

## **Discussion**

Reporting cases of fungal disease in Iran is not mandatory. Therefore, we extracted the data on incidence of fungal infections from published cross sectional studies from different parts of Iran, separately. In cases for which no data were available, we relied upon the reported incidence and prevalence from other countries and populations.

Tinea capitis is one of the community health indices used in evaluation of the quality of diagnosis, monitoring and management approach for communicable diseases in developing countries. Therefore, in this present study we calculated the burden of tinea capitis among the different clinical presentation of dermatophytosis. According to different studies in the last decade, dermatophytosis is one of the most prevalent superficial fungal infections in Iran [7,43,44]. Among different clinical presentations of dermatophytosis, tinea capitis incidence varied considerably in different parts of Iran: 12.8% in the south of Iran [43], 32.5% in northeast of Iran (Mashhad) [44] and 13.3% in Tehran the capital of Iran [7]. According to the reported rate by Bassiri, Jahromi and Khaksar [7], we estimated an incidence of 3,194 per 100,000 children for tinea capitis in Iran, a high average

burden of tinea capitis compared with some other countries [45,46]. Based on our personal experience and observation in the referral mycology laboratory of Mazandaran Province (unpublished data) the prevalence of tinea capitis has decreased substantially, therefore this may be an overestimation, which needs to be validated. Regarding the results of different studies from Iran, the predominant etiological agents were *T. interdigitale* and *T. tonsurans* [43], and *T. violaceum* and *T. schoenleinii* [7,44].

There are only a few case reports on mycetoma in Iran. A review by Bassiri-Jahromi [9] showed that 35 out of 168 (20.8%) suspected patients had mycetoma confirmed by culture or histopathology. According to the history of mycetoma in Iran [8], the high prevalence rate of confirmed mycetoma in suspected cases emphasizes the need for a proper diagnosis of mycetoma in patients with cutaneous or subcutaneous lesions. Chromoblastomycosis was reported in only two patients but as climatic conditions are quite different in different parts of Iran, including both an arid and tropical climate in central and southern parts, to humid and moderate climatic conditions in northern parts, we would expect a higher prevalence of this mycosis in Iran.

A total of 2,791,568 women (9,280 per 100,000 females' population) aged between 15 and 50 years are estimated to suffer from RVVC, every year. This estimate is substantially higher than that of some comparable countries including Qatar [47] and Egypt [48] because these countries used a rate of 6% for RVVC derived from the results of published data from other countries, in contrast to ours which was based on the results of a cross sectional study from a central city of Iran (12.3%) [12]. However, there is a possibility of over-estimation of prevalence because it is based on patients being seen by a gynecologist and therefore symptomatic, not on a genuine community survey.

Our estimate of the incidence of systemic candidiasis was 0.34 per 100,000 general population. According to a systematic review and meta-analysis on candidemia in Iran [49], the main risk factors for candidemia were surgery and burns (23.6%), followed by malignancies (20%), use of broad-spectrum antibiotics (18.2%), and diabetes (7.3%). In that review *Candida parapsilosis* was the leading agent, followed by *C. albicans*, *C. glabrata* and *C. tropicalis*. Another report showed that *Candida albicans* and *C. glabrata* were the etiologic agents [36]. These data show the importance of non-*albicans* species of *Candida* in causing candidiasis, many isolates of which are azole resistant.

Our estimates on ABPA and SAFS are lower than those of Egypt [48] and Russia [45], countries with different climatic conditions, whereas these rates are higher than those of reported incidence from Qatar [47] and Spain [46]. The available data in Iran on AFRS are limited to single-center case series. For the purpose of our estimations, we used the reported rates from China and Brazil [17,18]. The incidence of AFRS in patients with CRS was 228 per 100,000 Iranian population. According to an endoscopic survey from Brazil [18], 6.7% of patients with CRS suffered from FRS; of these patients, 53% had a fungal ball and 39% AFRS. In contrast to the Brazilian data [17], only 3.9% of cases in India [19] had fungal balls, 56.3% had AFRS and 16.9% had chronic granulomatous, 1.4% chronic invasive and 17.3% acute invasive fungal rhinosinusitis. In Iran, the most prevalent causative agent of AFRS was *Aspergillus flavus*; as also reported by Chakrabarti *et al.* [19] from India. In Brazil the most common agent was *Aspergillus* spp. (48.3%) followed by *Candida* spp. (17.7%) [18].

In the present study, the estimated burden of CPA post TB (n=1,248) was 1.6 per 100 000. According to the only investigation on CPA in Iran by Hedayati *et al.* [50], the incidence of CPA in TB patients was 11.3%. It seems that CPA is usually under-diagnosed because of its overlapping clinical and radiological characteristics with TB; therefore, the importance of microbiological and serological testing to diagnose CPA is emphasized [50]. The morbidity and mortality of CPA remains high, even with treatment.

According to our estimation, the incidence of IA was 0.03 and 0.1 per 100,000 general population in patients with AML and lung cancer, respectively, which were less than other estimation rates from other countries. COPD is common in Iran with a 5.9% and 12.4% COPD prevalence in those aged 40-54 years and  $\geq 55$  years and 9.2% overall [25], and a remarkable 161,271 patients are likely to be admitted to hospital annually. In an unpublished systematic analysis on aspergillosis in Iran, there are 387 cases of proven, probable, and possible IA (based on the EORTC/MSG criteria) described in Iran; of which only 147 (38.0%) were patients with hematologic disorders. COPD was implicated in 5.3% of cases and therefore there is likely to be a major problem with underdiagnosis. *A. flavus* is the most common species causing IA, followed by *A. fumigatus* in Iran.

We estimated IA in patients with AML and lung cancer because of no official records on cystic fibrosis patients and patients admitted in ICU.

Our study has two limitations. First, we made our incidence or prevalence estimations of different fungal infections using all available data, which were based only on a limited number of relevant publications, as there was lack of population-based studies. Second, the estimated incidence of different fungal infections is based on traditional diagnostic methods, which may be less sensitive than molecular or serological methods. In spite of these limitations, this analysis provides a warning to the Iranian healthcare system that we need to reconsider the importance of fungal infections which have been neglected hitherto and more action to reduce their impact and burden in Iran and across the world is required. However, substantial improvements have occurred in infectious disease-related morbidity and mortality generally in Iran, and this needs to be extended to fungal disease.

## Conclusion

This study is the first report on the burden of serious fungal infections in Iran. According to obtained results in the present study, RVVC was the most common fungal infection, followed by tinea capitis. Interestingly, *A. flavus* was the most prevalent specie of *Aspergillus* in IA patients, which is different from the findings of most other studies from different countries. Our estimates also indicate that fungal infections are neglected in Iran, which warrants further actions by health care authorities. Substantial uncertainty surrounds the reported numbers and formal epidemiological and surveillance studies are urgently required to validate or modify these estimations.

## Acknowledgements

This study was supported by Invasive Fungi Research Center, Mazandaran University of Medical Sciences, Sari (Iran) (fund number: 738).

## Author contribution

All authors have contributed original content, reviewed and revised the manuscript, and approved the final version.

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**Conflict of interests:** David W Denning is President of the Global Action Fund for Fungal Infections ([www.GAFFI.org](http://www.GAFFI.org)) which aims to improve the outcome of patients with serious fungal infections across the world. Other authors declare that there is no conflict of interests.