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Original Article

Epidemiology and burden of invasive fungal infections in the countries of the Arab League

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ABSTRACT

The burden of invasive fungal infections is alarming worldwide. The aim of this paper is to review the published literature and evaluate the knowledge gap pertaining to studies on invasive fungal infections in the countries of the Arab League. Few countries from this region have published reports. The most commonly studied invasive fungal infections is invasive candidiasis. *Candida albicans* remains overall the most common causative pathogen (33.8–60%), however, non-*albicans Candida* species are increasing. Antifungal susceptibility testing is non-standardized across the published studies. Data on aspergillosis and other fungal infections is scarce. This sheds light on the need for standardized surveillance in the region encompassing more countries of the Arab League to guide diagnostic approach and empiric therapy.

Introduction

Invasive fungal infections such as invasive candidiasis (IC) and invasive aspergillosis (IA) constitute a changing and expanding public health problem worldwide, including the Arab world [1,2]. These infections are considered to be a burden on healthcare due to their association with high morbidity, mortality, and costs of care [3].

The epidemiology of invasive fungal infections is affected by many factors including patient-related and environmental considerations, both of which differ depending on the geographic region. There is a wealth of information on the epidemiology of invasive fungal infections from developing countries [4,5] with variability among continents and countries within the same continent [6]. Knowledge of the local epidemiology is always desirable to guide diagnosis and prompt therapy. Such data from the Arab world is scarce. This review aims to summarize the published information on invasive fungal infections, mostly invasive candidiasis and invasive aspergillosis, in countries of the Arab League, including demographics, species of Candida and Aspergillus infection, susceptibility profiles, and patient outcomes.

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Method

We searched PubMed, ScienceDirect, Ovid and Scopus using the keywords Candida, Aspergillus and fungal infection and each of the countries from the Arab League (Algeria, Bahrain, Egypt, Iraq, Jordan, Kuwait, Lebanon, Libya, Morocco, Palestine, Qatar, Kingdom of Saudi Arabia (KSA), Syria, Tunisia, the United Arab Emirates (UAE), and Yemen), as well as the MeshTerms "Mycoses" and single subheadings of Arab League countries from "Middle East". Further information was gathered from abstracts presented at international meetings such as the European Congress of Clinical Microbiology and Infectious Disease (ECCMID), ID week, and Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) [7,8]. We excluded most case reports, pure molecular and phylogenetic analyses, and data from the neonatal population.

Results

Most of the published studies in this region evaluated IC infections and more specifically candidemia. Most of the studies were mainly retrospective chart reviews [9–20] while the remainder were observational epidemiological studies [21–27]. All of the investigations took place in large tertiary care centers including multiple intensive care units (ICUs), burn units, and cancer wards with pediatric, adult, and elderly patients.

KSA hosted more than half of the research projects followed by Qatar [13,21], Lebanon [14], Kuwait [18,23], UAE [15], Bahrain [17], Jordan [25], Algeria [26], Tunisia [19], Iraq [8], and Egypt [27,29].

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The different study periods ranged from 5 to 10 years extending from 1991 till 2017 with a variable number of clinical isolates, ranging from 60 to 652.

The burden of serious fungal infections in the Arab world was estimated to affect 1.41 [26], 1.9 [25], and 2.1% [7] of the population each year in Algeria, Jordan, and KSA respectively, with infections including candidemia, invasive aspergillosis, and other fungal infections. In one study from Egypt, the rate of invasive fungal infection was 8.3% in cancer patients [29].

Candida infection

Invasive candidiasis, defined mainly as positive blood [10–13,15,16,22,23] or tissue [9] culture for *Candida* spp., is the most studied fungal infection in the countries of the Arab League. Some studies included peritonitis, intraocular candidiasis [7,21,27], or *Candida* spp. cultured at any site regardless of the clinical picture [14].

The most common *Candida* species isolated was *Candida albicans*, ranging from 22.3% to 60% (Table 1). It was observed that the prevalence of non-*albicans Candida* spp. increased over the study years [9,10,14–16] except for one older study [12], where Al Hedaithy et al. found that the prevalence of non-*albicans Candida* spp. decreased from 33.3% during the first half of the study to 16.4% during the second half (1991–2000). The most commonly recovered species were *Candida tropicalis* (10.8%–37.7% of all *Candida* species), *Candida glabrata* (4.8%–19.2%), *Candida parapsilosis* (7.9%–36.6%), and *Candida krusei* (0 [13,15]–7.8%) (Fig. 1). Other less common isolated species included *Candida dubliniensis* [13], *Candida famata*, *Candida lusitaniae*, *Candida inconspicua* [15], *Candida guilliermondii*, *Candida zeylanoides, Candida pseuditropicalis*, and *Candida orthopsilosi*. Recently published reports also included *Candida auris* [30,31], an emergent resistant threat that has been detected in a single case from UAE, and in multiple cases from Kuwait, Oman and KSA [27,32].

All studies included in the table (Table 1) are from cases of IC except for the study by Araj et al. [14]. The nature of the specimen indicated in column 6 was a blood specimen for all studies except for the first study by Omrani et al. [9] where it is from “any sterile site” and the study by Araj et al. where it is from “any clinical specimen” [14].

Data concerning *in vitro* antifungal susceptibility testing were lacking in many of the available studies. When susceptibility testing was conducted, different methods were used, and sometimes they were changed within the same laboratory over the years. E-test was the most used method for susceptibility testing [9,10,14,23]. Other methods included Candifast® [10,22], disk diffusion method [10] and standard broth microdilution method [13,19]. The antifungals tested varied as well, and fluconazole, voriconazole, amphotericin B (ampho B), and caspofungin were the most commonly tested. Susceptibility of *C. albicans* to fluconazole ranged between 38.5% [10] and 96.2% [23]. It was only when tested with Candifast® that the susceptibilities were lower than 50% [10,22]. Other studies observed a susceptibility of around 90%. Susceptibility to fluconazole for the *Candida* non-*albicans* was as follows: *C. tropicalis* 11.1% [22]–100%, *C. glabrata* 50%–94.2%, and *C. parapsilosis* 66.7%–100%. Susceptibility of *C. albicans* to voriconazole ranged between 94 and 100%, and of the *C.* non-*albicans* was as follows: *C. tropicalis* 83%–100%, *C. glabrata* 74%–100%, and *C. parapsilosis* 100%. Overall susceptibility of *Candida* ranged between 81 to 100% to caspofungin and 90–100% to amphotericin [9,10,13,14,19,22,23]. The wide range of susceptibilities observed may be due to the heterogeneity of the methods used and mostly to the low number of isolates tested in some studies. For example, only 38 isolates including the different species of *Candida* were included in a study conducted by Osoba et al. [22]. *C. auris*, an emergent multidrug resistant threat, was found to be resistant to fluconazole in Kuwait [30]. Seventy three percent of the isolates in this study were also resistant to voriconazole, 23% resistant to ampho B and only 1 isolate out the 56 *C. auris* isolates was resistant to echinocandins.

The annual rates of IC infection per 1000 discharges per year did not follow a similar pattern among the different studies. Some authors reported a significant increase over the study years [9], whereas others observed that the annual incidence was constant during the study period [15]. In KSA, the median rate of IC was as low as 0.45 cases per 1000 hospital discharges per year in one study [11], and it was up to 1.65 cases per 1000 hospital discharges per year in another [9]. In UAE, however, the median rate was 0.77 cases per 1000 hospital discharges per year, and it differed between 4.51 for cancer patients and 0.33 for those with non-malignant conditions [15]. Another Saudi study reported that *Candida* spp. constituted 4% of positive blood cultures and was listed as the sixth leading cause of hospital-acquired bloodstream infections [16].

Risk factors associated with candidemia were the following: central venous catheter, ICU stay, broad-spectrum antibiotics [11,15], healthcare-associated infection [11], total parenteral nutrition [11], and age less than 1 year and more than 60 years [13]. Risk factors associated with higher mortality were cardiopulmonary diseases (20%), malignancies (17%), gastrointestinal diseases including surgery (13%), and renal diseases including kidney transplant (11%) [13].

Underlying diseases associated with candidemia were the following: hematologic malignancy [10–12,15], prematurity [12,15], surgery [11,12], renal disorders [11,12], respiratory infections [12], diabetes [12], hepatic disorders [12], neutropenia [11,15], and burns [11].

Malignancy, more specifically hematological, was significantly associated with the development of non-*albicans* candidemia compared to *C. albicans* candidemia in one study [10]. In another study, *C. albicans* and *C. glabrata* were the most frequent *Candida* spp. associated with malignancy [13]. Non-*albicans* candidemia was associated with higher numbers of antibiotics use and longer length of hospital stay prior to the development of candidemia [11].

Crude mortality rate at 30 days ranged between 40.6% [9] and 43% [11], while crude mortality rate at 90 days was found to be 51.8% in one study [9]. Crude mortality rate at 12 months reached 50% for *C. albicans* and 57.8% for *C.* non-*albicans* in another study from KSA [10], and up to 81.9% in Qatar [21]. Other authors reported an overall crude mortality of up to 56.1% [13].

While some studies found that there was no statistically significant difference between *Candida albicans* and non-*albicans* candidemia in terms of crude mortality [9,15], other studies from KSA reported that the mortality rate for *C. albicans* was 50% versus 34.8% for the non-*albicans* (43% for *C. glabrata*; 48% for *C. tropicalis* and 25% for *C. parapsilosis*) [11]. In contrast, *C.* non-*albicans* candidemia had a significantly higher mortality (68–71.4%) [13] than *C. albicans* (45.5%) in Qatar, except for *C. parapsilosis* (40.6%) [13].

Only one study from KSA compared mortality in infections caused by fluconazole-resistant *Candida* strains to those caused by fluconazole-susceptible strains and found no statistically significant difference [9].

The median time to death or length of stay ranged between 20 days [15] and 48.36 days [10].

Risk factors associated with higher mortality were the following: cardiopulmonary diseases, malignancies, gastrointestinal diseases [13], age [9], and acute renal failure [11,13].

Studies including Candida infections in other than blood were very few. Studies from Qatar [21], Jordan [25] and Egypt [27], calculated the burden of Candida infection per 100,000 inhabitants. Candida peritonitis had a rate of 8, 5 and 0.74 cases per 100,000 inhabitants respectively in Qatar, Egypt, and Jordan. In one study from Qatar, it was shown that a higher mortality from peritoneal

Table 1
The distribution of *Candida albicans* and non-*albicans* according to the different studies conducted in some of the countries of the Arab League.

Study	Year	Country	Study period	No. of isolates	Specimen	Distribution of Candida n (%)				
						C. albicans	*C. tropicalis*	*C. glabrata*	*C. parapsilosis*	*C. krusei*
Omrani et al. (SMJ) [9]	2014	SA Riyadh PSMMC	2003–2012 (10 y)	652	Any sterile site	252 (38.7%)	123 (18.9%)	106 (16.3%)	82 (12.6%)	9 (1.4%)
Thaqafi et al. (IJID) [10]	2014	SA Jeddah	8 y	252	Blood	86 (34.1%)	39 (15.5%)	23 (9.1%)	30 (11.9%)	10 (4%)
Al Tawfiq (IJID) [11]	2007	SA Armco	1996–2004 (9 y)	98	Blood	52 (53)	(19%)	(7%)	(16%)	(2%)
Al Jasser and Elkhizzi (SMJ) [16]	2004	SA Riyadh Armed Forces	1996–2002 (7 y)	294	Blood	149 (50.7%)	61 (20.7%)	21 (7.1%)	32 (10.9%)	23 (7.8%)
Al Hedaithy (Mycoses) [12]	2003	SA Riyadh KKUH	1991–2000 (10 y)	189	Blood	(50.3%)	(27%)	(7.4%)	(7.9%)	(3.2%)
Osoba et al. (SMJ) [22]	2003	SA Jeddah	1998–2002 (4 y)	83	Blood	38 (46%)	9 (10.8%)	4 (4.8%)	9 (10.8%)	5 (6%)
Taj Aldeen Mycoses [21]	2015	Qatar	2009–2014 (6 y)	288	Blood	Species distribution not specified				
Taj Aldeen et al. (Infection) [13]	2014	Qatar	2004–2010 (7 y)	187	Blood	68 (33.8%)	36 (17.9%)	38 (18.9%)	34 (26.9%)	0
Araj et al.[a] (JIDC) [14]	2015	Lebanon	9 y	247	Any clinical specimen	61 (24.7%)	(34–45%)	(25–36%)	(9–22%)	(5–11%)
Mokaddas et al. (JMM) [23]	2007	Kuwait	1996–2005 10 y	607	Blood	240 (39.5%)	75 (12.4%)	34 (5.6%)	186 (30.6%)	10 (1.6%)
Khan and Chugh (IJCDAS) [18]	2000	Kuwait	1994–1998	141	Blood	48 (34%)	15 (10.6%)	4 (2.8%)	45 (31.9%)	10 (7%)
Ellis et al. (Medical Mycology) [15]	2003	UAE	1995–2001 (6 y)	60	Blood	27 (45%)	9 (15%)	3 (5%)	3 (5%)	0
Arrache et al. (JMM) [20]	2016	Algeria	2004–2014 (10 y)	65	Blood	20 (31.6%)	15 (23.3%)	0	24 (36.6%)	2 (3.3%)
Sellami et al. (Mycoses) [19]	2010	Tunisia	2006–2009 (3 y)	130	Blood	29 (22.3%)	49 (37.7%)	25 (19.2%)	16 (12.3%)	4 (3.1%)

[a] The study by Araj et al. included non-invasive isolates.

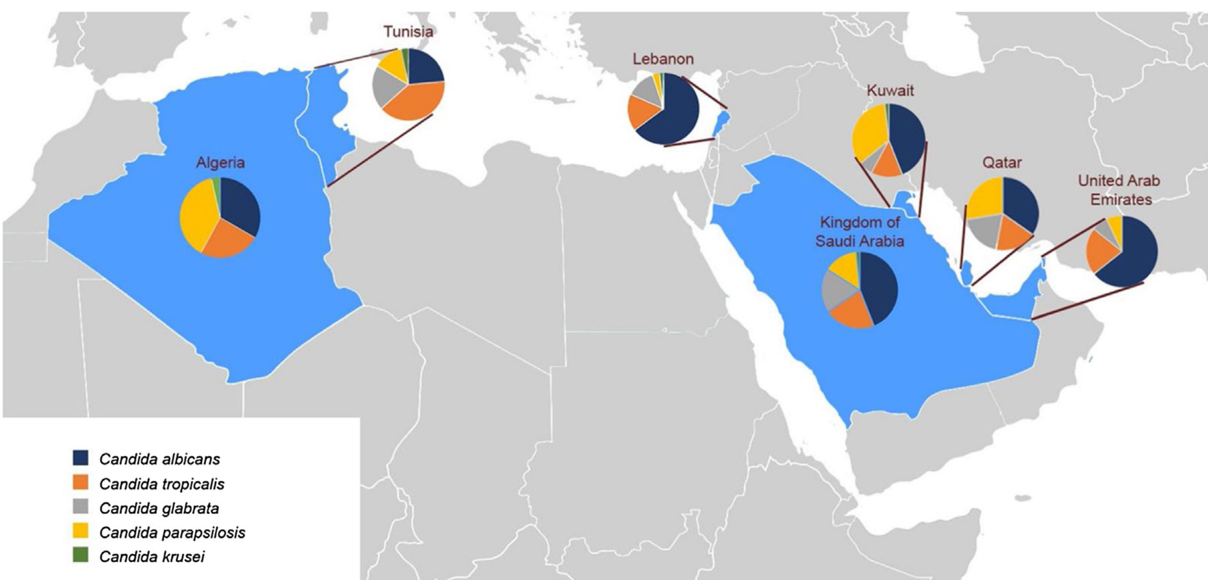

Fig. 1. The distribution of *Candida albicans* and non-*albicans* in candidemia in some countries of the Arab world.

dialysis-related peritonitis was associated with Candida infection and pseudomonal infection in comparison to other bacterial infections [33]. Intraocular candidiasis had a rate of 2.05 cases per 100,000 inhabitants in Qatar [21] compared to 14 cases per 100,000 inhabitants in Egypt [27]. Individuals at risk were patients with ICU stay, a history of malignancy, prior surgery, a history of renal transplant and immunosuppression.

In concordance with the data from the western countries, candidemia is the most investigated fungal infection in the Arab League countries. Moreover, as in studies from United States (US) hospitals [34] and multinational studies [35–37], Candida species are among the leading pathogens of healthcare-associated bloodstream infections [16].

In contrary to the United States of America (USA) and Latin American countries, where *Candida* non-*albicans* constitutes above 50% of candidemia cases [37], *C. albicans* remains the most commonly isolated species in blood in the Arab League countries. This data is similar to the ones from European and Asia-pacific studies [38,39]. This difference could be due to the different studied patient populations, such as cancer patients on prophylaxis versus ICU patients, or to the different practices of antifungal use in the regions. As in the rest of the world, a trend towards an increasing proportion of *Candida* non-*albicans* is being observed in the region.

The risk factors for candidemia in the region were similar to those found in western studies. Attributable mortality of candidemia, calculated as 47% [37] in western countries, is generally similar to the crude mortality at 30 days in the Arab League countries.

Aspergillus infection

Published regional studies on IA are very limited compared to IC. Hence, regional clinical practice guidelines for the treatment and diagnosis of aspergillosis are mostly based on international studies [21,40]. In a review on IA in developing countries, including the Middle East, sino-orbital or cerebral aspergillosis and Aspergillus endophthalmitis were reported to be emerging diseases with *Aspergillus flavus* being the predominant species. This is thought to be due to a higher prevalence of the fungus in the environment [41].

Whereas fungal asthma was reported at a rate of 60.2 cases per 100,000 inhabitants in one study from Qatar, IA was found to have a rate of only 0.6 cases per 100,000 inhabitants [21]. Another study from KSA reported a rate of 7.6 per 100,000 inhabitants [7].

In KSA, invasive aspergillus paranasal infection was found in one study to be mostly associated with *A. flavus* in immunocompetent patients and complete surgical evacuation followed by antifungal therapy was associated with relapse-free disease [42]. Another study from Bahrain found that IA was diagnosed in 16 out of 60 patients with positive Aspergillus cultures [17], where the predominant species was *Aspergillus fumigatus* (53%) and the lungs were the most common site of infection. Mortality was as high as 40%, however, adequate antifungal therapy with voriconazole was not initiated in all the cases. A retrospective study from Kuwait identified 11 cases of IA from 1994 to 1998, including 5 cases of *A. fumigatus*, 3 cases of *A. flavus* and 3 cases of *Aspergillus terreus,* mostly in renal transplant recipient patients [18].

A recent descriptive study from 5 hospitals in KSA and Lebanon reported 102 cases of invasive fungal infection due to Candida and Aspergillus species from 2011 to 2012 [1]. Among the 102 cases, only 80 cases were evidenced by culture and only 10 of which yielded *Aspergillus* spp. The overall mortality rate was found to be 42%. Mortality due to Aspergillus invasive infection alone was not calculated. In a prospective study from Egypt, in 960 patients with hematologic malignancies, invasive fungal infection was diagnosed in 8.3% of the patients, 19 (2%) of them had IA [29].

A three-year prospective study carried out in Tunisia in patients with hematologic malignancies found that among 105 neutropenic patients, 16 were diagnosed with probable and 13 with possible IA [43]. *A. flavus* was the most frequently isolated (79.2%). Environmental screening for fungal pathogens (690 samples) found that *Aspergillus* spp. was the third most frequently isolated fungal pathogen (18%). PCR sequencing of 30 *A. flavus* isolates detected from clinical and environmental samples confirmed the mycological similarity [43]. Another study from northern Algeria describes a rate of 7.7% of IA in neutropenic patients [26].

The rate of recovery of antifungal-resistant *Aspergillus* spp. is increasing in many countries, mostly in Europe [44–47]. Data on antifungal susceptibility of *Aspergillus* spp. from the Arab League countries is scarce. One study from Kuwait [30,48] analyzed 99 *A. flavus* isolates, including clinical specimens, for susceptibility testing to 6 antifungal agents by E-test and for molecular identification. The identity of all clinical and environmental isolates was confirmed as *A. flavus* species by combined analysis of β-tubulin and calmodulin genes. The mean MIC_{90} (μg/ml) values on RPMI medium for ampho B, voriconazole, posaconazole, anidulafungin, micafungin, and caspofungin were 3, 0.25, 0.25, 0.002, 0.002 and 0.032, respectively. No environmental isolate exhibited an MIC value of >2 μg/ml for ampho B. For clinical isolates, the zone of inhibition diameters for ampho B and voriconazole ranged from 7 to 16 mm and 24 to 34 mm, respectively. Linear regression analysis between E-test MIC values and disk diffusion diameters revealed a significant inverse correlation with ampho B ($p < 0.001$) and voriconazole ($p < 0.003$) [48].

Another study from KSA [7] evaluated the *in vitro* susceptibility to ampho B, itraconazole, voriconazole, posaconazole, and caspofungin of 250 clinical isolates of *Aspergillus* spp. Antifungal susceptibility testing was performed by the Clinical and Laboratory Standards Institute (CLSI) M38-A broth dilution method. From the 250 isolates, 114 were *Aspergillus niger*, 98 were *A. flavus*, 23 were *A. fumigatus*, and 15 were *A. terreus*. *A. flavus* was mainly isolated from cases of fungal rhinosinusitis. About 70% of *A. niger* was cultured from ear swabs and from nails. *A. fumigatus* was cultured more from respiratory specimens. All isolates were susceptible to itraconazole, voriconazole, posaconazole, and caspofungin. However, decreased susceptibility to ampho B was noticed with *A. flavus* and *A. terreus*. For ampho B, about 40% of *A. flavus* had an MIC of >2.0 mg/l and about 70% of *A. terreus* have an MIC of 4.0 mg/l. Voriconazole and posaconazole were the most effective agents [7].

A study from Tunisia [49] tested ampho B, itraconazole, voriconazole, posaconazole and caspofungin against 48 *Aspergillus* isolates (17 *A. niger*, 18 *A. flavus*, 9 *Aspergillus tubingensis*, 1 *Aspergillus westerdijkiae*, and 1 *Aspergillus ochraceus*) with the E-test. MICs were above the epidemiological cut-off values for ampho B in 67% of *A. flavus* strains, for caspofungin in 22% of *A. flavus* strains, and for itraconazole in 22% of *A. tubingensis* strains. Voriconazole and posaconazole MICs were below the epidemiological cut-off values for all strains.

When exposed to caspofungin, 42% of the strains exhibited trailing effect and 38% paradoxical growth. Trailing effect occurred in 61% of *A. flavus* strains and paradoxical growth in 62% of *Aspergillus* section *Nigri* strains.

Albeit there are no published data from the region on the treatment of IA, a recent international study, including a center from Lebanon where 20 patients were recruited from each center, concluded that patients with IA who received primary therapy with voriconazole-containing regimen had an improved response and survival compared with non-voriconazole containing regimens [50].

In comparison with global data, it seems that countries of the Arab League are not yet encountering the same increasing voriconazole resistance in *A. fumigatus* and other *Aspergillus* spp. The predominance of *A. flavus*, similar to other surrounding countries [51] and other studies from developing countries [41] and the relatively high frequency of ampho B resistant strains in *A. flavus*, makes voriconazole best adapted as a first-line treatment for invasive aspergillosis in countries of the Arab League.

Mucormycosis

Data on mucormycosis in countries of the Arab league is very scarce and mostly consists of individual case reports [52,53]. In one study from Qatar, mucormycosis was found to have a rate of 1.23 cases per 100,000 inhabitants [21]. In Iraq, Jordan, and Algeria, the annual rates of mucormycosis were estimated at about 0.2 cases per 100,000 [25]. KSA had an even lower rate of 0.034 cases per 100,000 [25]. A recent retrospective chart review at a tertiary care center in Lebanon identified 20 cases of mucormycosis between 2008 and 2018 [54]. In this study and an older one from Lebanon in 2006 [24], patients with mostly rhino-orbital or pulmonary involvement were found to have an underlying hematologic malignancy and/or diabetes mellitus as risk factors. Both studies observed that the number of mucormycosis cases per 10,000 hospital admissions increased significantly over the study years. All-cause mortality was found to be 60% [54]. Cause of death, however, was directly attributed to mucormycosis in only 20% of cases, despite aggressive treatment with liposomal amphotericin B, posaconazole and surgical interventions [54].

Another case series from Tunisia reported 5 cases mostly in diabetic patients. *Rhizopus arrhizus* was the most commonly isolated species followed by *Lichteimia corymbifera* [55]. All patients were treated with ampho B deoxycholate as liposomal products were not available in the country. Two of the patients died.

The scarcity of the data makes it difficult to compare the epidemiology of mucormycosis in our region to international studies. However, some of the countries of the Arab world, including Lebanon are currently participating in international registries on mucormycosis overseen by the European Confederation of Medical Mycology ECMM [56]. This registry would be of great value in comparing and contrasting epidemiological and clinical variations among regions and countries.

Other fungal infections

The annual rates of cryptococcal meningitis and pneumocystis pneumonia in Qatar was found to be respectively 0.43 and 0.8 cases per 100,000 inhabitants [21], with 125 cases of pneumocystis pneumonia detected each year [27]. There are no published reports on these infections from other countries of the Arab League. It is estimated that the annual incidence of cryptococcal meningitis is less than 500 cases annually. This is lower than the annual incidence in the United States, which ranges between 2501 and 5000 cases, and much lower than the highest incidence that is found in Sub-Saharan Africa with more than 25,000 cases annually [57]. Fungal infections due to other organisms such as *Fusarium* spp. were found to have a low rate of 1.68 cases per 100,000 inhabitants in Qatar, including few cases of Fusarium cornea infections [21]. Uncommon serious bloodstream fungal pathogens reported in one Qatari study were: *Kluyveromyces marxianus*, *Lodderomyces elongisporus*, *Lindnera fabianii*, *Meyerozyma guilliermondii*, *Pichia kudriavzevii*, *Yarrowia lipolytica*, *Clavispora lusitaniae*, and *Wickerhamomyces anomalus* [58]. Gastrointestinal basidiobolomycosis is another rare serious fungal infection with only 89 cases published worldwide since 1964 including 39 cases from countries of Arab League (KSA, Kuwait, Oman, and Qatar) [59].

Another rare fungal organism that has been described in the region to cause invasive infection is *Rhinocladiella mackenziei* (formerly *Ramichloridium mackenziei*) [60,61]. Cases of brain abscesses have been described mostly from KSA, but also from Kuwait, Qatar, and Oman among the countries of Arab League [60–62]. This is a devastating infection affecting immunocompetent patients with poor prognosis and a mortality rate of more than 80% [62].

Challenges

Many challenges remain concerning invasive fungal infections in the region. There is a vast discrepancy on the availability of the resources in the various countries. Rich countries in the region, for example, have state of the art laboratory facilities [21,23,30] and many available therapeutic options [47], whereas others lack basic laboratory tests and have only old antifungal agents (ampho B and fluconazole) available for use [47].

There is an evident lack of standardized epidemiological studies in some of the Arab countries (Table 2). Countries such as Egypt, Jordan, Lebanon, Qatar, KSA, and Tunisia generally have published data that estimates the burden of invasive fungal infections. Other countries, however, such as Libya, Morocco, Palestine, and Yemen are almost completely devoid of such studies. The emergence of new/rare *Candida* spp. in the region, the problems with proper identification methods, and the discrepancy at times between phenotypic and molecular identification remain a significant challenge. In addition, the reduced antifungal susceptibility to ampho B, the lack of routine susceptibility testing and unavailability of therapeutic drug level monitoring for azoles in many countries in the region make the management of invasive fungal infection very difficult especially in immunocompromised patients with many comorbidities.

Table 2
Availability of data on serious fungal infections in countries of the Arab League.

	Estimated burden of serious fungal infections		
	IC	IA	MM
Algeria	√	√	×
Bahrain	×	√	×
Egypt	√	√	√
Iraq	×	√	×
Jordan	√	√	√
Kuwait	√	√	×
Lebanon	√	√	√
Libya	×	×	×
Morocco	×	×	×
Palestine	×	×	×
Qatar	√	√	√
KSA	√	√	√
Syria	×	×	×
Tunisia	√	√	√
UAE	√	√	×
Yemen	×	×	×

IC: Invasive Candidiasis; IA: Invasive Aspergillosis; MM: Mucormycosis; KSA: Kingdom of Saudi Arabia; UAE: United Arab Emirates.
√: Availability of local epidemiological studies that estimate the burden of the disease.
×: Lack of studies that estimate the burden of the disease. Minor case reports that do not provide an epidemiological analysis are excluded.

Conclusion

Invasive fungal infections remain a major cause of morbidity and mortality worldwide. In light of the limited available data from the countries of the Arab League, there is a tremendous need to conduct systemic standardized surveillance in order to help establish regional guidelines for the diagnosis and management.

Studies on antifungal susceptibility are scarce, and the variety of methods used reflects the limited diagnostic resources in our region. Future studies should aim at standardizing the identification and susceptibility testing. In addition, antifungal stewardship should be practiced to curtail the potential emergence of resistance in this region.

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None declared.

Ethical approval

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