

Burden of fungal infections in Algeria

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Abstract We report for the first time in Algeria and provide burden estimates. We searched for existing data and estimated the incidence and prevalence of fungal diseases based on the population at risk and available epidemiological data. Demographic data were derived from the National Office of Statistics (Office National des Statistiques: ONS), World Health Organization (WHO), The Joint Nations Programme on HIV/AIDS (UNAIDS) and national published reports. When no data existed, risk populations were used to estimate frequencies of fungal infections, using previously described methodology. Algeria has 40.4 million inhabitants, and probably at least 568,900 (1.41%) of Algerians have a serious fungal infection each year. Recurrent vulvovaginal candidiasis (485,000) and fungal asthma (72,000) are probably the commonest problems, as there are over 1 million adult asthmatics. Candidaemia is estimated in 2,020 people, invasive aspergillosis in 2,865 people, and intra-abdominal candidiasis in 303 people; these are the most common life-threatening problems. AIDS is uncommon, but cancer is not (45,000 new cases of cancer including 1,500 in children), nor is COPD (an estimated 317,762 patients, of whom 20.3% are admitted to hospital each year). A focus on improving the diagnosis and epidemiological data related to fungal infection is necessary in Algeria.

Introduction

Algeria is Africa's biggest country by land area, and is the world's 10th largest. The health system in Algeria is designed to take care of the health needs of the population for all problems with free access to care. It is delivered by the State, at national and regional levels [1]. The life expectancy in men is 72 years and in women 75 years. Twenty-eight percent of Algeria's population is under 16 years old [2] and health policy focuses on preventative health care, including immunization [3]. There are issues around sanitation and clean water for all, and communicable and waterborne diseases are relatively common.

There has been very little focus on fungal diseases, with the notable exception of cutaneous infections. More recently, increased focus on hospital-acquired fungal disease has emerged with cases and series of *Candida* biofilm formation [4] as well as some deep mycoses [5] aspergillosis [6], cryptococcosis [7], candidemia [8], mycetoma [9] and sporotrichosis; given this poverty of data, we have attempted to estimate the burden of fungal diseases in Algeria, using previously published methodology based on populations at risk and local incidence and prevalence data (Table 1).

Methods

We searched for existing data, and estimated the incidence and prevalence of fungal diseases based on the population at risk and available epidemiological data. Demographic data were derived from the National Office of Statistics (ONS), World Health Organization (WHO), The United Nations Programme on HIV/AIDS

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Table 1 Prevalence rates presented used to estimate the burden of serious fungal diseases in Algeria

		Number	Source
Population	Population data		[10]
	Population (M)	40,400,000	[10]
	% children	28	[10]
	Number of children	11,312,000	[10]
	Adults	29,088,000	[10]
	% women over 60	7	[10]
Respiratory diseases	Pulmonary tuberculosis annual incidence total	5,418	[11]
	Population over 40 years	11,312,522	[11]
	COPD prevalence all GOLD stages	9.20%	[12]
	Asthma rate in adults	3.10%	[13]
	Asthma numbers in adults	1,252,400	[13]
HIV/AIDS patients	Current total HIV/AIDS	9,103	[14]
	Proportion of diagnosed cases on ARVs	1,561	[14]
	Number of diagnosed cases not receiving ARVs	7,542	[14]
	Annual new AIDS cases (at risk of OIs)	1,077	[14]
	AIDS-related deaths in 2014	843	[14]
AML patients per year		300	[15]
Renal Tx per year		200	[16]

(UNAIDS) and national published reports. Estimated HIV patient numbers were derived from the UNAIDS 2014 data. Patients with acute myeloid leukaemia were assumed to be about 300 annually [15]. We identified 170 to 200 renal transplantation procedures annually [16], and no other transplant procedures. The prevalence of chronic obstructive pulmonary disease (COPD) is 9.2% in the over-40-year-old population [12], and we have assumed that 10.5% are admitted to hospital each year [17]. The proportion of adults and children with clinical asthma is 3.1% and 4.1% respectively, and we have used only the adult figure for estimates (<http://www.liberte-algerie.com/radar/un-million-dasthmatiques-recenses-en-algerie-201363>) [13]. There are at least 100 cases of cystic fibrosis cases in Algeria [18] but we have not included these in our estimates. Pulmonary tuberculosis (TB) burden was taken from the Société Algérienne de Pneumo-Phtisiologie (SAPP) [11], and 10% are assumed to have died.

Amongst cutaneous infections, tinea capitis comes second after onychomycosis in frequency in dermatology practice [19]. We found one published estimate of annual incidence; in the Constantine area, ~100 new cases were seen to be diagnosed annually (2007–2011) [20]. In estimating the minimal national burden, we have assumed that all cases are seen at the University Hospital for the entire region, and that this frequency is reflected nationwide. When no data existed, risk populations were used to estimate frequencies of fungal infections, using methodology described by LIFE. We have summarized all recent published papers about mycoses in Algeria.

Results and discussion

Superficial mycoses and dermatophytic infection

In Algeria, onychomycosis and tinea capitis dominate the superficial mycoses [21]. *Trichophyton rubrum* is the predominant pathogen of feet and the inguinal folds [21]. Tinea capitis represents a public health problem in Algeria, despite improvement of living conditions and affects mostly children of school age [22]. Ectothrix tinea is the most observed form of tinea capitis. *T. mentagrophytes* is primarily responsible for inflammatory disease (kerion celsi and related conditions) [23]. There has been a rise in *Microsporum audouinii* anthropophilic species, especially in the north [24].

Using the published example of Constantine which has a population of 950,000, and assuming that tinea capitis only occurs in children (95%) [20, 25] then the rate would be 37.7/100,000. Nationally, this equates to 4,265 cases annually. This is almost certainly a significant underestimate, as local surveys of school children indicate higher frequencies, but are not systematic and so not extrapolatable. Published studies found variable prevalence from region to region: Algiers (24.6%) [23], Constantine (37.2%) [21], Tipaza (62.4%) [23, 26], and Blida (66.4%) [27]. We note that tinea capitis is more important in these last Wilayas (localities), possibly explained by their more rural populations.

Our data are similar to other countries in north Africa including Tunisia and Morocco, where *M. canis* and

T.violaceum are the commonest agents of tinea capitis [26, 28]. While favus (definitive tinea capitis usually caused by *Trichophyton schoenleinii*) is rarely diagnosed in Algeria [29] (in the south only) [30], this pathology is still frequent in Tunisia and Morocco [26, 28].

Dermatophytes are also often isolated from ear infections, with the predominant species being *M.canis*, *T.rubrum*, *T.violaceum*, and *T.mentagrophytes* [31]. In Algeria, *Aspergillus* otitis is more often caused by *A. niger*, *A. flavus*, and *A. terreus* [30, 32].

Vulvovaginal candidiasis (VVC) is common in women, but there are no published data from Algeria. *Candida albicans* is commonly seen microscopically in vaginal smears and cultured. We have attempted an estimate of the prevalence of recurrent VVC (≥ 4 episodes annually), based on data from five countries in Europe (including France) and the USA [33]. Women over-diagnose VVC themselves, as other problems are common mimics, notably bacterial vaginosis. We have therefore reduced the self-reported rate of recurrent VVC (rVVC) obtained by an internet survey from 9% to 6% in 15- to 50-year-old women [33, 34]. However a remarkable 485,188 women probably suffer with rVVC in any given year, a population rate of 2,402/100,000 among females (Table 2). This fungal problem dwarfs all others.

Fungal keratitis is rarely diagnosed in Algeria, and may be missed. The causative agents are *Candida albicans*, followed by filamentous fungi [35]. There are no population estimates in Algeria, but in Egypt, with a population about twice that of Algeria, there are an estimated 11,550 cases annually. In

Egypt, fungi are responsible for 28–55% of cases of microbial keratitis [36].

Invasive mycoses

Invasive aspergillosis

In the lung, the incidence of invasive aspergillosis in the neutropenic patient in the north of the country is 7.7%, diagnosed by antigen detection with ELISA [6]; sixteen of 208 neutropenic patients were positive, and all 16 died from progressive leukemia. No special environmental precautions were in place. *Aspergillus flavus* and *Aspergillus niger* were more frequent than *Aspergillus fumigatus* in the local environment of the patient [6]. In Tunisia, *A.flavus* also is more often isolated than *A. fumigatus* [37, 38]. Therefore, we anticipate 47 cases of IA in haematological patients and renal transplant recipients annually.

COPD is relatively common in Algeria, with an estimated prevalence of 1,040,000 patients [39]. Of these, 20.3% are admitted to hospital each year [40]. Assuming the rate of invasive aspergillosis is the same as in Madrid [41] based on culture alone at 1.3%, an estimated 2,747 patients with COPD will develop invasive aspergillosis each year.

There are an estimated 2,707 cases of lung cancer diagnosed each year in Algeria, 7.1% of all cancers [42]. The rate of invasive aspergillosis in such patients was documented by Yan et al. [40], in Chengdu in China at 2.6%, and if this rate also pertains to Algeria, then 71 IA cases are likely. Clearly this needs local confirmation.

Table 2 Estimated burden of invasive (annual incidence) and chronic and allergic (prevalence) fungal diseases in Algeria

Infection	Number of infections per underlying disorder /year					Total burden	Rate /100 K
	None	HIV/AIDS	Respiratory	Cancer/Tx	ICU		
Oesophageal candidiasis		832				832	2.1
Candidaemia				1,414	606	2,020	5.0
Intra-abdominal candidiasis					303	303	0.75
Recurrent vaginal candidiasis >4 times/year	485,188					485,188	2,402
Allergic broncho-pulmonary aspergillosis (ABPA)			31,310			31,310	77
Severe asthma with fungal sensitisation (SAFS)			41,329			41,329	102
Chronic pulmonary aspergillosis (CPA)			897			897	2.2
Invasive aspergillosis			2,818	47		2,865	7.1
Mucormycosis				79		79	0.2
Cryptococcal meningitis		28		7		36	0.09
<i>Pneumocystis</i> pneumonia		74				74	0.18
Tinea capitis	4,265					4,265	10.6
Total burden estimated						568,942	

Cryptococcal meningitis

In a recent retrospective laboratory study, 24 of 425 HIV patients had cryptococcosis from January 2002 to March 2015. The incidence was 5.6%, translating into one to four cases per year [43]. Of the 24 patients, 18 (75%) were HIV seropositive, and so we have assumed that 25% of cryptococcosis cases in Algeria are not HIV-related, as also described in four patients. This high proportion was also found in another study, where 60 of 77 (78%) patients with cryptococcosis were HIV positive [44]. Cryptococcosis may be sometimes seen in non-HIV patients, but this is probably rare [7].

To estimate burden, we have assumed a 7-year linear decline in CD4 count to $<200 \times 10^6/l$ and therefore anticipate the risk population for opportunistic infections to be about 500 patients. Assuming a 5.6% cryptococcal rate and a 15% PCP rate (mean of many international studies) [45], we estimate about 28 HIV-associated cases of cryptococcosis, seven non-HIV cases, and about 74 patients with PCP and AIDS each year.

Candidemia

Yeasts in blood are a major cause of morbidity and mortality, and are frequently associated with the implantation of vascular catheters, especially in immunocompromised patients. We have estimated a 5/100,000 rate in accord with other European countries, in the absence of local epidemiology data, a total of 2,020 cases. *Candida* spp. are most frequent, but species distribution is variable from one study to another. In Algiers, 65 of 463 positive blood cultures (14.1%) grew *Candida*, primarily *Candida parapsilosis* (36.6%), then *C. albicans* (31.6%), *C. tropicalis* (23.3%), *C. krusei* (3.3%), and finally *C. lusitanae* (1.6%) [5]. In the University Hospital of Tlemcen (in the west of Algeria), the rate of yeast colonization of vascular catheters was 19%, of which 60% were *C. parapsilosis*, 20% *C. albicans*, 14.3% *Candida glabrata*, and 5.7% *Candida famata* [8]. In Oran in the west of Algeria, catheter colonization revealed *C. parapsilosis* in 64% of cases, followed by *C. albicans* with 12%, and 8% for *C. glabrata* and *C. krusei* [15]. Antifungal resistance to Amphotericin B and fluconazole in *C. albicans* has been found in biofilms in Algeria [46, 47].

Intrabdominal candidiasis is a relatively common complication of complex intestinal surgery, and perforation [48]. Using the French multicenter estimate of the ratio of intrabdominal candidiasis to candidaemia in intensive care, we estimate 303 cases, or 0.75/100,000 [49].

Chronic and allergic mycoses

There were 39 cases of aspergilloma diagnosed by serology and radiology over 10 years (1999 to 2009) [50]. The incidence was 3.9 cases per year, and the mean age was 49.5 years.

Tuberculosis was the most common underlying diagnosis (79.4%) [11]. Based on the 5,418 survivors of pulmonary TB in 2014 in Algeria, we estimate that 228 new patients will develop CPA annually (incidence) and that the 5-year prevalence is about 717 cases, assuming a 15% annual mortality or surgical resection. Assuming that 80% of the cases follow tuberculosis based on the series above, there are about 900 patients with CPA in Algeria (2.2/100,000).

Among adults in Algeria, 3.1% have clinical asthma, or 1,252,400 patients [51]. If we assume that the rate of allergic broncho-pulmonary aspergillosis (ABPA) is the same as in Saudi Arabia at 2.5%, and that this rate pertains to the whole population, not just those seen in secondary care, we estimate 31,310 people have ABPA. Taking only the most severe group of asthmatics (10%), fungal sensitisation is likely to be similar to other countries with rising rates as asthma severity increases. If we assume that this is 33%, then 3% of the adult asthmatics have severe asthma with fungal sensitisation (SAFS), or 41,329 people. They may be some duplication between ABPA and SAFS, because sensitization to *Aspergillus* is universal in ABPA, and some of these patients have severe asthma.

Conclusion

In Algeria, there are many superficial mycoses, especially onychomycosis and tinea capitis. Under-recognised problems include recurrent VVC in women, fungal keratitis, chronic pulmonary and allergic aspergillosis, and all serious deep mycoses. There are extremely few data on Invasive filamentous fungal infections, yet they are likely to be frequent in immunocompromised patients.

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