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Fungal infections in Algeria

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Abstract

Introduction: Invasive and superficial fungal infections are increasingly reported in Algeria, testifying to the increase in their frequency in parallel with the increase in risk factors and the availability of diagnostic means, at least in university hospitals (CHU). The latter, located in the major northern cities, are equipped with high-performance diagnostic tools compared to hospitals in the interior of the country.

Methods: A comprehensive search of published and grey literature was undertaken. Prevalence and incidence of discrete fungal diseases were estimated using a deterministic modelling approach based on populations at risk. Population (2021) and major underlying disease risk groups were obtained from UNAIDS, WHO Tuberculosis and the international transplant registries as well as published data for asthma and COPD. The health service profile was summarised from national documentation.

Results: Among the 43.6 million, including 12.9 million children, living in Algeria, the most prevalent fungal diseases are tinea capitis (>1.5 million), recurrent vaginal candidiasis (>500,000) and allergic fungal lung and sinus disorders (>110,000) and chronic pulmonary aspergillosis (>10,000). Life-threatening invasive fungal infection incidence includes 774 *Pneumocystis* pneumonia in AIDS, 361 cryptococcal meningitis, 2272 candidaemia and 2639 invasive aspergillosis cases. Fungal keratitis probably affects >6000 eyes each year.

Conclusions: Fungal infections are underestimated in Algeria because they are sought in patients with risk factors only after bacterial infections when they should be sought in parallel. The diagnosis is only accessible in hospitals in large cities and the work carried out in mycology is rarely published, making the estimation of the burden of these conditions difficult.

KEYWORDS
aspergillosis, candida auris, fungal rhinosinusitis, mycetoma, otitis externa

1 | INTRODUCTION

The epidemiology of fungal infections is constantly changing worldwide in terms of the incidence and nature of the responsible fungi. The incidence of invasive forms has increased due to the increase in risk factors such as cancer, chemotherapy, organ transplants, immunosuppressive treatments, COPD, HIV infection. Recent publications report the occurrence of invasive mycoses in patients with severe forms of COVID-19 hospitalised in intensive care units. Extensive skin burns are also a risk factor for localised or generalised

fungal infections. In Algeria, publications on fungal infections are few, even though many medical theses, biology and pharmacy dissertations on invasive and superficial fungal infections have been carried out in recent years.

The objective of this work is to report these different works and to estimate the incidence and prevalence of invasive and superficial fungal infections in Algeria.[1] This was done about 5 years ago and since then a substantial increase in data has been published, and some presented in so-called 'grey' publications. Our study also highlights the potential factors that have favoured the emergence of particular fungal disease and the practical consequences of these epidemiological changes.

2 | METHODS

Our study is a review of the literature reporting the epidemiology of certain fungal infections that have been diagnosed in recent years and listed from thesis work in medical sciences, doctoral dissertations in pharmacy, master's degree in biology and other specialties. We also report the results published in journals and have selected some results of pertinent work presented at the last national congress of parasitology-mycology in December 2021.

We sourced 2021 data on population from the Central Intelligence Agency, USA (CIA) fact book,[2] HIV/AIDS data for 2020 from UNAIDS[3] and deaths estimated from Spectrum,[4] 2020 tuberculosis data from WHO (and assumed that the proportions of deaths for pulmonary TB mirrored overall deaths),[5] 2019 prevalence asthma in adults from country reports,[6] chronic obstructive pulmonary disease (COPD) prevalence and hospitalisations from the BREATHE study in 2012,[7,8] 2020 lung cancer incidence from the International Agency for Research in Cancer (IARC)[9] and nationally,[10] acute leukaemia incidence for 2020 from IARC and 2019 transplantation procedures from The International Registry on Organ Donation and Transplantation (Irodat).[11]

To calculate incidence and prevalence of each fungal disease we applied the country data as a numerator with the at risk population as a denominator in a straightforward deterministic model, for most conditions. Invasive aspergillosis annual incidence was composed of several underlying risk groups: acute myeloid leukaemia (13.7% risk in the absence of anti-mould prophylaxis)[12] and an equal number of cases from all other risk haematological conditions, HSCT (10%), lung cancer (2.6%),[13] deaths from AIDS (4%)[14] and 1.3% of COPD hospitalisations.[15]

Chronic pulmonary aspergillosis (CPA) incidence and prevalence was estimated using four components linked to pulmonary tuberculosis (PTB) data: Incorrect initial diagnosis – usually in smear/Xpert negative PTB cases (19% in HIV negative cases), dual PTB and CPA (3% in HIV negative patients), the development of CPA during or immediately after anti-PTB therapy (10%) and late development of CPA (1.5% annually).[16] We also assumed a 20% year 1 mortality and a 7.5% annual mortality for 5 years.[16] PTB as the underlying cause of CPA was assumed to be 50% of all CPA cases.[17] Allergic bronchopulmonary aspergillosis was assumed to affect 2.5% of adult asthmatics.[18,19] Severe asthma probably affects ~10% of and assuming at least 33% are sensitised to fungi,[20] then 3.3% of adults will likely have severe asthma with fungal sensitisation (SAFS). Mucormycosis was assumed to affect two persons per million per year.[21]

We assumed that 6% of patients with advanced HIV disease and AIDS develop cryptococcal meningitis[22] and 15% develop *Pneumocystis* pneumonia.[23] We assumed that the HIV risk group is composed of one seventh of that not on antiretroviral therapy (ARVs) (7 year decline in immune function) and 29% of those on ARVs in view of the high ARV resistance rates (Table 3). We assumed a 20% rate of oesophageal candidiasis in advanced HIV disease patients and an additional 5% (conservative) in those on ARVs.[24] To estimate the incidence of candidaemia in intensive care units, we referred to the work of Hamouda in Batna[25] who found 2.17 cases per 100 admissions. Using multicentre data from France, we assumed that there is one case of intraabdominal (or peritoneal) candidiasis per two cases of candidaemia, in intensive care.[26] Recurrent vulvovaginal candidiasis was assumed to affect 6% of women between the ages of 15 and 50 years.[27] Fungal keratitis was based on data from Egypt[28] and for fungal rhinosinusitis population data from India.[29]

The number of public and private health structures as well as human resources such as the number of university hospital doctors, public health specialists, general practitioners, dental surgeons and pharmacists were taken from the statistical directory 'health in figures 2020' at the level of the Department of Studies and Planning of the Ministry of Health, Population and Hospital Reform.

3 | RESULTS

3.1 | General framework of Algeria

3.1.1 | Geographically

Algeria is located in the northwest of Africa on the African continent, south of the Mediterranean Sea and in the centre of the Maghreb, and it constitutes, by its area (2,381,741 km2), the largest country in Africa and the ninth in the world. With 1200 km of coastline and 6343 km of land borders, Algeria is open to the Mediterranean in the North and borders the North-West, South and East with respectively seven countries: Morocco, the Sahara West, Mauritania, Mali, Niger, Libya and Tunisia.

3.1.2 | Demographically

The population of Algeria was estimated at 43.6 million on 1 January 2021 with an average density of 18.40 inhabitants per km^2. This average hides an uneven distribution on the territory with a concentration of between 250 and 3500 inhabitants per km^2 in the coastal areas for a density of less than 20 inhabitants per km^2 in the Saharan region.

The breakdown by age shows that more than half (54%) of the population is under 30 years old. Children aged 0–14 represent 29.5% of the population. For the distribution by sex, the numerical difference generally observed between men and women is not very large with a slight predominance of the male population (50.7%).

3.1.3 | Economic characteristics

Algeria is economically dominated by the oil and gas sector with 94% of product exports. With a per capita income of US$3761.1 (2021), Algeria is classified as a lower-middle-income country. It is the fourth largest economy on the African continent, and the second in the North African sub-region, after Egypt.

3.1.4 | Organisation of healthcare

Health is the fourth item of country budgetary expenditure with more than 439 billion DA (~3.1 billion USD) to be spent in 2022. The supply of care in Algeria is based on public hospital and extra-hospital structures (Table 1).

Access to care in all of these public healthcare structures is provided free for the population.

As for the private sector, in 2020 there were 407 clinics and 28,705 medical practices between specialist doctors, general practitioners and dental surgeons, and just over 10,985 pharmacies (Table 2).

3.1.5 | Human resources for health

More than a hundred specialists in parasitology-mycology work in public hospitals across the national territory.

TABLE 1 Public health structures in Algeria in 2020.

Type of establishment	Number of structures	Number of beds
Third level		
University hospital centres	15	13,125
University hospital establishment	1	1029
Second level		
Specialised hospital establishments	79	12,843
Public hospital establishments	210	39,522
Hospitals	9	1316
First level		
Local public health establishments	273	7777
Total	587	75,612

Source: Ministry of Health – General Directorate of Health Services.

3.2 | Risk factors for invasive fungal infections

3.2.1 | Cancer and transplantation

Algeria registers nearly 50,000 new cases of all types of cancer every year, according to data from the national cancer registry of the National Institute of Public Health (INSP). According to a multicentric national study, the overall incidence of lung cancer in Algeria is 3.4 cases per 100,000 inhabitants or a total of 1482 cases; with a male predominance (5.8) compared to female (1.0) (Table 3).[10]

The incidence of acute myeloid leukaemia in Algeria is 2.5/100,000 inhabitants (WHO) corresponding to 1090 cases (Table 3). Other haematological conditions including non-Hodgkin lymphoma, Hodgkin lymphoma and multiple myeloma are also factors favouring fungal infections and these conditions totalled 2531 cases in 2020.[30]

In Algeria, kidney transplants are performed only from living donors. In 2019, there were only 268 kidney transplants and 11 liver transplants (Table 3).[31] As for allogeneic transplants, 160 cases are performed annually according to the Director General of the National Transplant Agency.[32]

3.2.2 | HIV/AIDS infection

According to the 2021 national response report, the estimated number of people living with HIV (PHIV) (adults and children) is 21,000 (9000 women and more than 1000 children under 15) (Table 3). The proportion of cases diagnosed and receiving antiretroviral therapy (ARV) is 17,000 and the number of patients not receiving triple therapy is 4000. The number of new cases at the AIDS stage with risk of opportunistic infection is 5161. In 2020, given the Spectrum curve, we can deduce that the number of deaths is between 225 and 350 (average of 270 deaths).[4] Primary resistance of HIV to the three classes of antiretrovirals (NRTIs, NNRTIs and PIs) is estimated at 23.1% and secondary resistance to the same molecules was 60% in 2017.[33]

3.2.3 | Tuberculosis, asthma and COPD

Tuberculosis is endemic in Algeria. Pulmonary localisation of TB is a key background for chronic pulmonary aspergillosis (CPA). According

TABLE 2 Numbers and health coverage ratios of healthcare personnel in 2020.

Staff category	Workforce	Ratios (per inhabitants)
University hospital	4389	1/10080
General practitioners	26,680	1/1658
Specialist doctors	15,110	1/2928
Dental surgeons	6662	1/6641
Pharmacists	2164	1/20445
Paramedics	157,804	1/280

Source: Ministry of Health – General Directorate of Health Services.

TABLE 3 Total population and patient numbers at risk for serious fungal infections.

Data	Number	Comment	Reference
Population	43.6 million	2021	CIA fact book
Proportion children 0–14	12.9 million	29.6% of the population	CIA fact book
HIV/infection	21,000	Prevalence of HIV/AIDS 2021	UNAIDS
Pulmonary tuberculosis	8060	Annual incidence 2020	WHO
	5035	11.37/100,000	INSP
Asthma in adults	1,227,776	4% of adults in 2019	http://www.santemaghreb.com/actus.asp?id=26644
	1,032,000	8% of children in 2019	
COPD patients	1,613,200	3.7% of population	Tageldin[6]
COPD hospital admissions	169,386	10.5% annually	Idrees[7]
Lung cancer	4774	10.9/100,000 incidence 2020	Globocan[9]
	1482	3.9/100,000	Bounedjar[10]
Acute leukaemia	1683	2.5/100,000 incidence	Globocan[9]
Renal transplants	268	2019	IRODAT[11]. https://www.irodat.org/
Liver transplants	11	2019	IRODAT[11]. https://www.irodat.org/
Allogeneic HSCT	160	2017	https://www.agence-biomedecine.fr

Abbreviations: AIDS, acquired immunodeficiency syndrome; CIA, Central Intelligence Agency; COPD, chronic obstructive pulmonary disease; HIV, human immunodeficiency virus; HSCT, haematopoetic stem cell transplant; NISP, National Institute of Public Health.

to national institute of public health (INSP) data, the prevalence of pulmonary tuberculosis is 11.37 cases per 100,000 inhabitants, that is, a total of 5035 cases (Table 3). According to the WHO, it is estimated at 18.5/100,000 inhabitants, a total of 8060 cases.

Asthma is a frequent pathology in Algeria and its prevalence is 4% in adults, that is, 1,227,776 cases, and 8% in children, equivalent to another 1,032,000 cases (Table 3).[34] In the international BREATHE study,[7] the prevalence of COPD in Algeria was estimated at 3.7% of the population, which corresponds to a total of 1,613,200 cases (Table 3) of which 54% are classified D (high severity and high risk) and 169,386 patients (10.5%) are hospitalised each year.[8]

3.3 | Estimation of fungal infection burdens

3.3.1 | Invasive aspergillosis (IA)

Estimating that 13.7% of acute leukaemias are complicated by IA the total number of cases is 300 cases. Assuming that 2.6% of patients with lung cancer develop IA we anticipate 124 cases. In HIV-infected patients, 4% of AIDS-related deaths typically have IA, approximately 11 cases. However, the number of AI cases occurring in patients hospitalised for COPD is estimated at 1.3%, corresponding to 2202 cases. In total, the annual incidence of IA in Algeria is 2639 cases (Table 4). These estimates do not include IA cases in severe influenza or COVID-19 in intensive care.

3.3.2 | Chronic pulmonary aspergillosis (CPA)

Pulmonary tuberculosis (PTB) is probably the commonest underlying disorder for CPA but other lung conditions also predispose, including sarcoidosis, pneumothorax, asthma and others. CPA may occur during or after antituberculosis treatment, particularly if there are residual sequelae cavities. Thus 8060 cases of PTB were estimated by the WHO in 2020 (31% of all TB cases), including 68 cases in HIV-positive patients. The rate of probable (microbiologically unconfirmed) PTB was 19% (WHO): 1531 cases in non-HIV and 12 cases in HIV positive people. After treatment 22% of patients are left with residual cavities on radiography[35] corresponding to 1773 cases. The total number of TB-related deaths was 1043.

As many as 194 people have dual PTB and CPA co-infection. Towards the end of treatment for PTB and in the few months afterwards, an estimated 663 patients develop CPA (10% of survivors). Probably about 100 (20%) of these patients die with or of CPA. Following cure of PTB, another 1160 patients develop CPA over 5 years. Assuming a first year mortality of 20% and a subsequent annual mortality of 7.5%, we estimate a 5 year period prevalence

TABLE 4 Estimated incidence and prevalence of fungal diseases in Algeria.

Infection	Incidence or prevalence	Fungal disease burden by major underlying disorder category per year						
		None	HIV/ AIDS	Respiratory	Cancer/ Transplant	ICU	Rate/ 100 K	Total burden
Invasive aspergillosis	I	-	11	124	302	2202	6.1	2639
Chronic pulmonary aspergillosis	P	-	-	10,788	-	-	5.3	10,788
Allergic bronchopulmonary aspergillosis (ABPA)	P	-	-	30,721	-	-	70	30,721
Severe asthma with fungal sensitisation (SAFS)	P	-	-	40,517	-	-	93	40,517
Chronic fungal rhinosinusitis	P	47,960	-	-	-	-	110	47,960
Pneumocystis pneumonia	I	-	774	-	-	-	1.8	774
Cryptococcal meningitis	I		289	-	72	-	0.83	361
Oesophageal candidiasis	I	-	1250	-	-	-	2.9	1250
Candidaemia	I	-	-	-	1744	528	5.2	2272
Candida peritonitis	I	-	-	-	-	264	0.6	264
Recurrent vaginal candidiasis (>4 times/ year)	P	511,980	-	-	-	-	2.9*	511,980
Mucormycosis	I	-	-	-	87	-	0.20	87
Ringworm of the scalp	P	1,548,700					3552	1,548,700
Fungal keratitis	I	6104	-	-	-	-	14	6104
Total burden estimated		2,114,700	4124	82,150	2205	2994		2,204,390

of 5394 patients and an annual CPA mortality of 467 patients. If the association of CPA and PTB is only found in 50% of CPA cases in Algeria, then a total prevalence of ~10,788 patients is likely (Table 4).

3.3.3 | Fungal asthma and fungal rhinosinusitis

Poor asthma control is common in adults in Algeria with fewer than 50% of patients well controlled. Assuming that 3.3% of adults have SAFS, which is amenable to oral antifungal therapy, we estimate a SAFS prevalence of 40,517 cases (Table 4). Using the same denominator for ABPA, our prevalence estimate is 30,721 affected patients (Table 4) with some overlap between these two conditions. SAFS occurs in children, but there are not sufficient data yet to estimate its prevalence. Chronic rhinitis is common, and the proportion attributable to fungal allergy is extrapolated from an Indian study – 0.11% of the population.[29] The estimate prevalence of chronic fungal rhinosinusitis (all its manifestations) including allergic, chronic granulomatous, eosinophilic and maxillary or sphenoid fungal ball is 47,960 cases (Table 4). We could find no direct corroborative data from Algeria, despite an active allergy and ear, nose and throat community.

3.3.4 | Pulmonary pneumocystosis (PCP)

In Algeria, the diagnosis of PCP in HIV-infected patients is most often made on clinical-radiological grounds and on response to therapy. Assuming that the stage of AIDS is reached in 7 years after primary HIV infection on average, patients at risk of pneumocystosis represent approximately 1/7 of those who are not on ARVs (571 cases) and 29% of those who are treated (4930), but not controlled, because primary ARV resistance in Algeria is estimated at 29%. A total of 5501 people living with HIV are therefore at risk. Assuming an incidence of PCP of 15% in these people,[23] 825 cases are likely (Table 4). We are not able to estimate the number of patents with PCP attributable to other risk conditions, due to lack of data, but it is likely to be at least twice this number.

3.3.5 | Neuromeningeal cryptococcosis

Cryptococcal meningitis is a major opportunistic infection common in PHIV with an advanced stage of immunosuppression. It can also be seen in other conditions such as lymphoid haemopathies or inflammatory diseases but also in immunocompetent patients. In Europe, it has clearly regressed among PHIV since the advent of ARV

therapy. In Algeria, some studies report its occurrence in patients with AIDS. In Sétif, eight cases of neuromeningeal cryptococcosis were diagnosed in 10 years among PHIV.[36] In a retrospective STUDY from 1 January 1993 to 30 June 2017 conducted in an infectious disease department in Algiers found 54 of 1289 PHIV (4.2%) presented with cryptococcal meningitis.[37] Assuming that 6% of PHIV who are at the AIDS stage have cryptococcal meningitis, the annual incidence of the latter is estimated at 330 cases (Table 4).

In non-HIV immunocompromised patients, neuromeningeal cryptococcosis is rarer and can be seen exceptionally in immunocompetent patients.[38]

3.3.6 | Oesophageal candidiasis

The prevalence of oesophageal candidiasis is estimated at 20% of patients at the AIDS stage, which corresponds to 800 cases, and 5% of patients on ARVs, equivalent to 850 cases. A total of 1650 cases of oesophageal candidiasis are probably diagnosed and treated each year (Table 4). No estimation is possible in those with other risk factors.

3.3.7 | Candidemia

Several studies have been done on invasive candidiasis, in particular candidemia, in intensive care units and in onco-haematology units, but none is of national scope. Knowing that the number of intensive care beds in Algeria is ~400 and estimating that the average length of stay in intensive care is 6 days, the total number of admissions per year is 24,333 cases. Assuming that the rate of candidemia in intensive care units is 2.17 per 100 admissions, the total number of candidemia is 528 cases per year.[25] During COVID-19 the number of ICU beds increased nationally to 2500, and the number of *Candida* bloodstream infections also probably to 3300. The incidence of candidaemia rose substantially during COVID-19. Of these patients, we assume that 25% (581) occur in intensive care and 75% (1744) in medical and surgical departments. Therefore our estimate of candidaemia ranges from 528 and 3300 in intensive care and totals from 2272 (5.2/100,000) to 4516 (11.6/100,000) (Table 4).

According to French multicentre studies, the incidence of peritoneal candidiasis can be estimated at half of the candidemia found in intensive care, which corresponds to 264 cases. We have used the more conservative number here.

A study carried out in Batna showed that *C. parapsilosis* is predominant (45%) in blood culture followed by *C. albicans* (40%).[25] In Algiers a study of isolates from seven hospitals[39] revealed that *C. tropicalis* (19/66) was the main cause of candidaemia in these seven hospitals, followed by *C. parapsilosis* (18/66), *C. albicans* (18/66) and *C. glabrata* (7/66). This study noted that fluconazole resistance in *C. tropicalis* was 31.5%.

At the Tlemcen University Hospital Center in the west of the country, emerging strains of *C. auris* have been identified in patients hospitalised in intensive care units using real-time PCR.[40]

3.3.8 | Recurrent vulvovaginal candidiasis

In Algeria, women aged 15–50 number 9,581,380 people and the number of vulvovaginal candidiasis is estimated at 6% of this population[27] (therefore 591,083 cases in 2020) (Table 4).

In Algiers, a study carried out among 100 women of childbearing age including 64 pregnant in a gynaecology-obstetrics department found 62% had vulvovaginal candidiasis.[41]

3.3.9 | Fungal infections in burns

In burn victims, local or general fungal infections are often serious. The incriminated yeasts are essentially *Candida*; wound infections may be caused by *Candida*, *Aspergillus* or agents of mucormycosis.[42] At the University Hospital of Batna, 55% of patients hospitalised for burns presented with a fungal infection. *C. parapsilosis* was the most frequently isolated fungus.[43]

3.3.10 | Fungal infections and SARS CoV2 infection (COVID-19)

Invasive fungal infections are more common in patients with severe SARS CoV 2 infections hospitalised in intensive care.[44,45] Invasive aspergillosis and, to a lesser extent, candidaemia predominate, outside of India. In Algeria, only one study was reported at the last congress of the Algerian Society of Parasitology-Mycology in December 2021 which concerned 103 samples (15 blood cultures and 88 peripheral samples for culture) from 21 patients hospitalised in intensive care for infection with COVID-19. This study found 54.4% to be positive, including a blood culture for *C. tropicalis*. *C. albicans* accounted for 72% of isolates.[46] *Aspergillus* antigen testing was not done.

3.3.11 | Ringworm of the scalp

Ringworm of the scalp (tinea capitis) is found especially in children[47,48] with a male predominance (Figure 1). The same situation pertains in Algeria.[49] The incidence varies from region to region. In one study carried out in schools in Tlemcen among 1631 children aged 4–14, nearly 12% had ringworm of the scalp. Assuming this figure is mirrored across the country, the prevalence is estimated at 1,537,000 cases (Table 4). This may be conservative as in Algiers, the prevalence was 33.5%. In Tlemcen *Microsporum canis* was the most frequent species,[50] whereas in Algiers it was *Trichophyton violaceum* (59.41%).[49]

FIGURE 1 Children with microsporic ringworm caused by *Microsporum canis*. Schools of the epidemiological survey in Tlemcen.[50]

3.3.12 | Otomycosis

Otomycosis is a fungal infection mainly affecting the external auditory canal. It is often benign. *Aspergillus niger* complex are the most frequently responsible fungi. *Candida* otitis comes second in frequency. In Constantine, 59% of cases of otitis externa were mycotic with a predominance of *Aspergillus niger* (43%) followed by *C. albicans* (22%).[51] In Blida, the fungal proportion was nearly 33% ($n=267$), including *Candida* spp. (62.5%), *C. albicans* (10.2%), *A. niger* (11.4%), *A. flavus* (9.1%) and *A. fumigatus* 4.6%.[52] In hearing aid wearers the prevalence of otomycosis is 51.9% with predominance of candidal aetiology compared to *Aspergillus* otitis. *A. persii* was described for the first time as an agent of otomycosis in three patients from western Algeria.[53]

3.3.13 | Onychomycosis

Trichophyton rubrum is the predominant pathogenic fungus of onychomycosis in Algeria followed by *C. albicans*.[54] Cutaneous aspergillosis is a rare fungal disease in immunocompetent patients. *Aspergillus flavus* has been described as the causative agent of onychomycosis following traumatic plant inoculation (Figure 2).[55]

3.3.14 | Neglected tropical fungal diseases

Sporadic cases of mycetoma have been reported in Algeria. The first case was described in 1894, by Vincent who isolated an actinomycete which he named *Streptothrix madurae* (probably *Actinomadura madurae*) from an Algerian case.[56] The latest was published in France in 2020 which reported a case of *Actinomadura madurae* in a patient from Kabylie in Algeria.[57] It was identified by molecular biology. Only

FIGURE 2 *Aspergillus* onychomycosis induced by trauma in a vegetable vendor patient.[55]

two cases of chromoblastomycosis are described from Algeria,[58] and none of sporotrichosis.

Fungal keratitis is probably as common in Algeria as in other parts of North Africa, notably Egypt.[28] We have estimated an annual incidence based on population data from Egypt (14/100,000) indicating that there an estimated 6100 cases in Algeria each year (Table 4).

4 | DISCUSSION

Algeria is committed to setting up a health system accessible to all. Despite these welcome commitments, dysfunctions currently exist at all levels of the health service. On the other hand, considerable scientific and technological advances are recorded in all fields, including the diagnosis of fungal infections. Diagnosis of fungal infections is possible in some centres in Algeria but is mal-distributed. The large cities where the university hospitals are located are better equipped with specialised human resources, materials and specific reagents for the diagnosis of fungal infections. In regions lacking resources, certain private laboratories can arrange testing, sometimes in collaboration with French laboratories.

In Algeria, there are 15 reference centres (CDR) for the management of HIV infection distributed in the East, Center, West, South-East and South-West to ensure equity of access to care. These centres have a special budget allocation for universal and free care, including the diagnosis and treatment of opportunistic infections. In the field, the diagnosis of mucosal candidiasis and cryptococcosis is carried out in the 15 CDRs. For cryptococcosis, the direct examination is carried out there after staining with India ink, the search for the antigen in the blood and the cerebrospinal fluid and the culture on Sabouraud medium. Concerning pneumocystosis, the diagnosis is made by Gomori Grocot stains in Algiers at the level of the Pasteur Institute of Algeria (IPA) and the university hospitals (CHU) (Mustapha Bacha, Beni Messous and the central hospital of the army (HCA); to the east at the CHUs of Constantine, Annaba and Batna and to the west at the CHUs of Sidi Belabes and Oran, but not elsewhere).

As for polymerase chain reaction diagnostic assays (PCR), they are only carried out at IPA, HCA and the university hospital centre of Beni Messous to the west of Algiers. Despite this, the diagnosis of pneumocystosis is rarely made because of the difficulty of taking

samples, especially BAL. Diagnosis of aspergillosis by serology, galactomanan, antigen testing and culture is carried out in all the university hospitals mentioned above. Appropriate diagnostic means for emerging fungi such as *Fusarium*, sporotrichosis and mucormycosis are also available at university hospitals.

Blood culture is only rarely performed, even at university hospitals. So our estimate of *Candida* bloodstream infection can only be an estimate until such facilities are more widely introduced.

Fungal stains are not generally done as a component of histopathology. This inevitably means that some cases will be missed as standard haematoxylin and eosin staining is not sensitive enough.

On the other hand, serological methods to diagnose other common and rarer fungal infections such as aspergillosis (invasive or chronic), histoplasmosis (acute of chronic disseminated or chronic pulmonary), blastomycosis and coccidioidomycosis are not available. The diagnostic capacity of invasive fungal infections in Algeria is better provisioned in the north of the country, particularly in university hospitals.

In recent years, it has been observed that there is more interest in fungal infections as they are more and more frequent and serious with the increase in the risk factors already mentioned above. Many end-of-study dissertations and medical science theses on fungal infections have been produced, but unfortunately the studies are short-lived and not published, which makes it difficult to utilise these data to estimate incidence or prevalence of specific fungal infections. These difficulties seem to be common to all the countries of North Africa.

According to studies, the risk factors for fungal infections are often underestimated. Asthma control in Algeria is sub-optimal, partly because of lack of use of use of long-acting bronchodilators and poor medication adherence in some patients. IgE testing in patients with poorly controlled asthma is infrequently done (23%), and so ABPA is likely to be frequently missed. Very few publications and specialists have focused on this topic area, leaving many patients undiagnosed and not optimally treated.

The primary limitation of this work is the lack of high quality epidemiological data for many fungal diseases. In the absence of large-scale epidemiological studies, estimates of fungal infections in Algeria have been calculated for the most part by analogy with work carried out in other countries. Diagnostic limitations are one key factor, combined with the common practice of researchers doing small local studies only. It is likely that the large immigrant population from south of the Sahara convey some unusual fungi and complex infections, but these are not currently addressed adequately in the national health services.

5 | CONCLUSION

Around 5% of Algerians and immigrants are troubled by a serious fungal infection annually, notably tinea capitis and recurrent vulvovaginal candidiasis. Lethal fungal infections are mostly undiagnosed, as antigen testing for *Histoplasma*, *Cryptococcus* and *Aspergillus* are not done, blood cultures are rare, as is histopathology with fungal staining and *Aspergillus* IgG and IgE testing for chronic and allergic aspergillosis not available. Superficial fungal infections such as onychomycosis and otomycosis are common but underestimated because they are often treated by the general practitioner on clinical suspicion. Laboratory diagnosis is rarely carried out even if it does not require significant resources. Awareness of the importance and severity of fungal infections by the medical community would certainly make mycology an attractive specialty which will improve the diagnosis and management of these infections.

AUTHOR CONTRIBUTIONS

Fatma Zohra Aissat: Data curation; formal analysis; writing – original draft; methodology; writing – review and editing. **David W. Denning:** Conceptualization; data curation; formal analysis; writing – original draft; writing – review and editing; validation; methodology.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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