Mucormycosis in the Middle East and North Africa: Analysis of the FungiScope® registry and cases from the literature

Jannik Stemler1,2,3 | Kamal Hamed4 | Jon Salmanton-García1,2 | Ali Rezaei-Matehkolaei5 | Stefanie K. Gräfe1,2,6 | Ertan Sal1,2 | Marouan Zarrouk1,2 | Danila Seidel1,2 | Reham Abdelaziz Khedr7 | Ronen Ben-Ami8 | Eli Ben-Chetrit9 | Yehudah Roth10 | Oliver A. Cornely1,2,3,11

1Department I of Internal Medicine, Faculty of Medicine and University Hospital Cologne, Center for Integrated Oncology Aachen Bonn Cologne Duesseldorf (CIO ABCD), Excellence Center for Medical Mycology (ECMM), University of Cologne, Cologne, Germany
2Cologne Excellence Cluster on Cellular Stress Responses in Aging-Associated Diseases (CECAD), University of Cologne, Cologne, Germany
3German Centre for Infection Research, Partner Site Bonn-Cologne, Cologne, Germany
4Basilea Pharmaceutica International Ltd., Basel, Switzerland
5Infectious and Tropical Diseases Research Center, Health Research Institute, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
6Faculty of Medicine, University Medical Center Hamburg-Eppendorf, University of Hamburg, Hamburg, Germany
7Pediatric Oncology Department, National Cancer Institute, Cairo University, Egypt/Children's Cancer Hospital, Egypt
8Infectious Disease Unit, Tel Aviv Sourasky Medical Center and the Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel
9Infectious Diseases Unit, Shaare Zedek Medical Center, Hebrew University School of Medicine, Jerusalem, Israel
10Department of Otolaryngology – Head & Neck Surgery, Wolfson Medical Center, Tel Aviv University Sackler School of Medicine, Holon, Israel
11Clinical Trials Centre Cologne (ZKS Köln), University of Cologne, Cologne, Germany

Summary

Background: Regional differences in the underlying causes, manifestations and treatment of mucormycosis have been noted in studies covering Europe, Asia and South America.

Objectives: To review cases of mucormycosis across the Middle East and North Africa (MENA) region in order to identify epidemiological, treatment and outcome trends in this region.

Patients/Methods: Cases of proven or probable invasive mucormycosis from the region were identified from the FungiScope® database and the medical literature. For each case, information on underlying condition, site of infection, pathogenic species, therapeutic intervention, type of antifungal therapy and outcome were analysed.

Results: We identified 310 cases of mucormycosis in the MENA region. The number of reported cases increased by decade from 23 before 1990 to 127 in the 2010s. In this region, the most common underlying conditions associated with mucormycosis were diabetes mellitus (49.7%) and conditions associated with immunosuppression (46.5%). The majority of patients received treatment with antifungals (93.5%), with a large proportion treated with both antifungals and surgery (70.6%). Overall mortality rates decreased from 47.8% before 1990 to 32.3% in the 2010s.
Conclusions: The number of reported cases of mucormycosis in the MENA region has risen over the past few decades, in line with increases in the number of patients with underlying conditions associated with this infection. Although the majority of patients received treatment with antifungal therapies and/or surgery, the associated mortality rate remains high and there is a clear need for more effective prevention and treatment strategies in the MENA region.

Keywords
antifungal agents, fungal epidemiology, invasive fungal disease, Middle East North Africa, Mucorales

1 | INTRODUCTION

Mucormycosis is a rare opportunistic invasive fungal disease (IFD), which typically occurs in patients with a compromised immune system.1 Diabetes mellitus is a common risk factor in middle- and low-income countries, with uncontrolled diabetes posing a particular risk as the resulting ketoacidosis can suppress immune system activity.2,3 Other immunocompromised patients at risk for mucormycosis include recipients of haematopoietic stem cell or solid organ transplants, patients infected with human immunodeficiency virus and patients receiving chemotherapy for cancer.3,4 In the absence of factors affecting normal immune system function, exposure to environmental sources of fungi through penetrating injuries such as trauma or burns has also been linked to mucormycosis.3,5 In recent decades, the number of reported cases of mucormycosis has increased in both emerging and developed countries6,7 and correlates with the rapidly increasing global prevalence of diabetes and the rising number of immunocompromised patients.8,9 As the number of patients with these conditions continues to expand, a concomitant rise in the incidence of mucormycosis may perhaps be anticipated.

Mucormycosis can manifest at a variety of sites, with rhino-sinno-orbito-cerebral, pulmonary, cutaneous and gastrointestinal involvement being the most common.3 In the absence of treatment, survival rates have been reported to be as low as 3%,7 and even in the modern treatment era, day 42 mortality rates of 28%-39% have been reported with antifungal therapy and surgical debridement.10,11 Rapid initiation of treatment is critical and typically involves a combination of surgery to remove infected tissues and immediate first-line antifungal therapy.1,12,13 The most effective antifungal agents in the treatment of mucormycosis are amphotericin B, isavuconazole and posaconazole.3,11,12 Active treatment should also be combined with control of the underlying condition and/or reduction in the extent of immunosuppression.1,13

Incidence of mucormycosis is possibly related to weather conditions, with case clustering observed during periods of elevated temperatures and low precipitation.14,15 Furthermore, geographic patterns and global differences in the underlying causes, manifestations and treatment of mucormycosis have been noted in data gathered in Europe, Asia and South America.3,5,7,16,17 However, a review of cases across the Middle East and North Africa (MENA) is lacking. We have therefore collated and reviewed cases of mucormycosis from this region and herein summarise the key data from the cases identified.

2 | METHODS

We selected cases from the FungiScope® database and the medical literature. FungiScope® is a web-based registry that collects cases of rare IFDs worldwide (NCT01731353).18 The structure and management of the FungiScope® registry have been described previously.19 In brief, case enrolment requires cultural, histological or molecular evidence of infection with non-endemic fungi. Data collected for each case include demographics, underlying conditions, immunosuppressive medications, clinical signs and symptoms, sites of infection, results from diagnostic tests, pathogen identification, antifungal treatments and outcome. The authors confirm that the ethical policies of the journal, as noted on the journal’s author guidelines page, have been adhered to. FungiScope® was approved by the local institutional review board and ethics committee of the University Hospital Cologne, Germany (Study ID: 05-102). For the current review, data regarding invasive mucormycosis cases were extracted from the FungiScope® database for analysis.

Additional cases were identified from a search of the medical literature through October 2019 on PubMed and Embase using the following search terms: mucormycosis, mucor*, ficomycos*, phycomycos*, phicomites, zygomycos*, zygomyces, Absidia, Apophysomyces, Cunninghamella, Lichtheimia, Rhizomucor, Rhizopus, Saksenaea, Syncephalastrum, plus the names of the individual MENA countries (for the purposes of the current review we included Algeria, Bahrain, Egypt, Iran, Iraq, Israel, Jordan, Kuwait, Lebanon, Libya, Morocco, Oman, Palestine, Qatar, Saudi Arabia, Syria, Tunisia, United Arab Emirates and Yemen).

Relevant publications were manually selected based on their abstract and/or full text (Figure 1). We included case reports if most of the following information was described for each individual patient: underlying condition(s), site of infection, documentation of infection (histological or by culture), therapeutic intervention (presence or absence of antifungal therapy and surgery), type of antifungal therapy
Figure 1: Case selection process of patients with mucormycosis in the Middle East and North Africa. MENA, Middle East and North Africa.

Figure 2: Middle Eastern and North African countries with relative case numbers of mucormycosis.
### TABLE 1 Demographics, clinical characteristics and predisposing factors in patients with mucormycosis in the Middle East and North Africa

| Underlying condition                      | N = 310 |          |
|------------------------------------------|---------|----------|
| Sex                                      | n       | %        |
| Female                                   | 128     | 41.3     |
| Male                                     | 181     | 58.4     |
| Not stated                               | 1       | 0.3      |
| Age (years), median (IQR)                | 41 (23-59) | 76.5 |
| Year of infection                        | n       | %        |
| Before 2000                               | 73      | 23.5     |
| After 2000                                | 237     | 76.5     |
| EORTC/MSG classification                 |         |          |
| Proven IFD                               | 277     | 89.4     |
| Probable IFD                             | 33      | 10.6     |
| Underlying condition                      |         |          |
| Diabetes mellitus                        | 154     | 49.7     |
| Immunocompromised                        | 144     | 46.5     |
| Corticosteroid use                       | 63      | 20.3     |
| Solid organ transplant                   | 51      | 16.5     |
| Kidney                                   | 36      | 11.6     |
| Liver                                    | 12      | 3.5      |
| Other                                    | 4       | 1.3      |
| Haematological malignancy                | 51      | 16.5     |
| Acute leukaemia                          | 36      | 11.6     |
| Other haematological malignancy          | 15      | 4.8      |
| HSCT                                     | 9       | 2.9      |
| GvHD                                     | 3       | 1.0      |
| Long-term neutropenia                    | 36      | 11.6     |
| Other haematological disease             | 15      | 4.8      |
| Solid tumour                             | 5       | 1.6      |
| Trauma/burns                             | 24      | 7.7      |
| Renal disorder                           | 13      | 4.2      |
| Hepatic disorder                         | 12      | 3.9      |
| Chronic pulmonary disease                | 4       | 1.3      |
| Other risk factors                       | 40      | 12.9     |
| No risk factor identified                | 18      | 5.8      |

**Abbreviations:** EORTC/MSG, European Organization for Research and Treatment of Cancer (EORTC) and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (MSG); GvHD, Graft-versus-host disease; HSCT, haematopoietic stem cell transplantation; IFD, invasive fungal disease; IQR, interquartile range.

For 20 patients, the year of infection was not specified within the case reports; for these cases, the year of publication was used instead.

Patients may have more than one of the listed underlying conditions.

Cornea (n = 2), heart (n = 1) and pancreas (n = 1).

Lymphoma (n = 8), chronic leukaemia (n = 3), leukaemia type unspecified (n = 2), and myelodysplastic syndrome (n = 1).

Allogeneic HSCT (n = 8) and autologous HSCT (n = 1).

### RESULTS

The FungiScope® registry search identified seven invasive mucormycosis cases from MENA countries, one of which has already been published elsewhere. The literature searches identified a further 303 additional cases reported in 186 articles. A full reference list is provided in Appendix S1.
The distribution of the identified cases across the region is shown in Figure 2. Most of the reported cases originated from Iran (n = 74), followed by Israel (n = 63) and Tunisia (n = 49). A large proportion were also reported from Lebanon (n = 28), Saudi Arabia (n = 28), Egypt (n = 20), Iraq (n = 11) and Qatar (n = 10), with other countries reporting fewer than 10 cases. No cases were reported from Algeria, Libya, Syria or Yemen.

The detailed demographic and clinical characteristics of the identified patients are provided in Table 1. The majority of patients were male (58.4%), and the median (interquartile range) age was 41 (23-59) years. Most cases were proven (89.4%) according to the EORTC/MSG criteria. Diabetes mellitus and any immunocompromised status were by far the dominant underlying conditions (49.7% and 46.5%, respectively), with trauma/burns being the third most common (7.7%). Among patients who were immunocompromised, corticosteroid use (43.8%) was the most frequent cause.

The causative fungal pathogen was identified only to the level of the taxonomic order Mucorales for most patients (60.6%). Among all cases, the most commonly identified species were Rhizopus spp. (22.6%) followed by Mucor spp. (5.5%) (Figure 3). Coinfection occurred with Aspergillus spp. in 10 cases and with Candida spp. in 10 cases, including two patients who had coinfections with both Aspergillus and Candida spp. Species details of detected Mucorales are included in Table S1.

The most common site of infection was rhino-sino-orbito-cerebral (46.8%), followed by pulmonary (12.3%) (Table 2). Infections occurring in a single organ, across two or more neighbouring sites or tissues and disseminated infections accounted for 109 (35.2%), 142 (45.8%) and 59 (19.0%) cases, respectively. The most frequently specified and nonexclusive infected sites were paranasal sinuses (55.8%), bone/joints, including the bones of the skull involved in the rhino-sino-orbito-cerebral entity (34.2%), eye/orbital (30.0%) and deep soft tissue (28.7%). Mortality increased with the number and distance of sites involved (single organ, 33.0%; adjacent organs, 38.7%; disseminated, 61.0%).

Surgery combined with antifungal therapy was used in 219 patients (70.6%), whereas 71 patients (22.9%) received antifungal therapy only. The most commonly administered antifungal agent was amphotericin B (92.3% of cases), and in the majority of these cases the formulation used was not specified. Therapy involving two or more concomitant antifungals was administered in 55 cases (17.7%). Additional treatments details are provided in Table 3 and Figure S1.

The number of reported cases of invasive mucormycosis has increased over time, with only 23 reported prior to 1990 and 127 reported for the 10 years from 2010 to 2019 (Table 4 and Figure S1). Overall mortality rates have decreased over time (Table 4). Before the year 2000, 73 cases of mucormycosis were reported, with day 42 and day 90 mortality rates of 41.1% (30/73) and 43.8% (32/73), respectively. In the same period, mortality attributable to invasive mucormycosis was 38.4% (28/73). From 2000 onwards, 237 cases were reported, with day 42 and day 90 mortality rates of 25.7% (61/237) and 27.4% (65/237), respectively. In this period, mortality attributable to invasive mucormycosis was 17.7% (42/237).

When analysed by treatment modality, the overall mortality rate was lower for patients treated with antifungal therapy combined with surgery (32.4%, 71/219) than for patients receiving antifungal therapy only (57.7%, 41/71) or surgery only (58.3%, 7/12) (Table 3).

4 | DISCUSSION

Our study summarises 303 cases from the literature and seven cases from an international database. This first comprehensive review of mucormycosis across MENA countries shows that the number of cases reported across this region has risen steadily over the past few decades, and that the burden of mucormycosis and the associated mortality remain high despite recent improvements in treatment.
The median age of patients identified in this analysis (41 years) was in line with those reported in a global review and a review for South America (39 years and 40 years, respectively). However, higher median ages have been identified in studies covering Europe (50-60 years) and in another global study (49 years). The proportion of males (58.4%) was largely consistent with the range observed in other studies (58-70%).

The most frequent underlying condition in the MENA region was diabetes mellitus, followed by corticosteroid use, solid organ transplants, haematological malignancy and long-term neutropenia. The dominance of diabetes and conditions associated with immunosuppression broadly aligns with reports from other regions including South America and India. However, reports from Europe indicate haematological conditions as the predominant underlying pathology. Regional differences raise the concern that other factors may influence the pathogenesis, diagnosis and treatment of mucormycosis. These may include diagnostic and therapeutic resources, climate and specific patient populations. Worldwide studies to assess true geographic differences versus confounding factors are scarce. However, the European Confederation of Medical Mycology and the Mycoses Study Group (ECMM/MSG) guideline program has considered locally available resources.
The rhino-sino-orbito-cerebral location was the most frequent site for mucormycosis infection, followed by pulmonary and cutaneous sites. This is again broadly in agreement with the literature.\textsuperscript{3,16}

Of note, rhino-sino-orbito-cerebral mucormycosis infections have been associated with diabetes mellitus in particular and, to a lesser extent, immunosuppression, trends that have been observed across multiple regions.\textsuperscript{3,16} Given the worldwide increase in the number of patients who have diabetes mellitus or are immunosuppressed,\textsuperscript{8,9} such infections have growing significance in clinical practice. This may be particularly relevant for the MENA region, which had the highest comparative prevalence of diabetes in the world in 2012.\textsuperscript{28} Moreover, almost half of diabetes cases in this region are estimated to be undiagnosed,\textsuperscript{29} which may further increase the risk of mucormycosis.\textsuperscript{4}

The species involved remained unidentified in more than half of cases, and Rhizopus and Mucor species were predominant among cases where the species was identified. This aligns closely with a review of cases in South America,\textsuperscript{16} indicating that there may be difficulties in identifying pathogenic species in clinical practice in developing regions. Thus, assessment of a possible association between Mucorales species and clinical manifestations or outcome was not performed in this study. Diagnosis of mucormycosis requires the use of direct or histopathological microscopy and fungal cultures\textsuperscript{30}, the latter may be beyond the resources of many hospitals in developing regions.

Treatment in the MENA region most commonly involved antifungal therapy combined with surgery, although antifungal therapy was given alone in almost a quarter of cases. The most frequently used antifungal agent was amphotericin B, followed by triazoles. This is consistent with the recent global consensus guideline from the ECMM/MSG.\textsuperscript{1} Upon suspicion of mucormycosis, the guideline strongly recommends appropriate imaging to document the extent of disease, followed by surgical intervention. Furthermore, the guideline strongly recommends first-line treatment with high-dose liposomal amphotericin B followed by intravenous (IV) or oral isavuconazole, or IV or posaconazole delayed-release tablets. Combination antifungal treatment may be used in patients with an aggressive form of mucormycosis. To date, this approach has been mostly used as a second- or third-line treatment, with clinical success reported in 56% to > 70% of patients.\textsuperscript{31} Microbiological data based on models with Rhizopus arrhizus suggest synergism of combination antifungal therapy.\textsuperscript{31}

A prospective study where R arrhizus was the predominant causative agent did not show any impact of treatment strategy on outcome.\textsuperscript{32} However, further prospective studies to assess the benefit of combination treatment and the role of Mucorales species on outcome are required.

Surgery may not always be feasible and is generally restricted to patients with limited disease. In the opinion of the authors, antifungal prophylaxis is key to improve outcome in high-risk patients. In other immunosuppressed hosts, optimal surveillance and early treatment (whether monotherapy or combination therapy with or without surgery) is crucial to improving patient outcome.\textsuperscript{33}

It is encouraging to note the decline in the mortality rate in the MENA region over time, which may reflect improving standards of care for mucormycosis. However, the rise in the overall number of reported cases of mucormycosis and the number of deaths attributable to mucormycosis is of concern, although this may also reflect a growing awareness of such diseases and increased efforts by physicians to publish relevant cases.

This analysis has a number of limitations. The reported cases do not represent a real-world setting; in the case of mucormycosis, a disease with a relatively high mortality rate, favourable outcomes might be more frequently reported, and therefore actual mortality may be higher. Furthermore, the numbers of reports from several countries in the MENA region are very low. Two countries with relatively small populations, Lebanon and Israel, are greatly overrepresented in this analysis. Moreover, complete information was not

### Table 4: Outcome by time period and overall in patients with mucormycosis in the Middle East and North Africa

|                | Before 1990 (n = 23) | 1990-1999 (n = 40) | 2000-2009 (n = 100) | 2010-2019 (n = 127) | All patients (N = 310) |
|----------------|----------------------|-------------------|--------------------|---------------------|-----------------------|
| Day 42 mortality\textsuperscript{b} | 8 (34.8)             | 14 (35.0)         | 26 (26.0)          | 32 (25.2)           | 91 (29.4)             |
| Day 90 mortality\textsuperscript{b} | 9 (39.1)             | 15 (37.5)         | 28 (28.0)          | 33 (26.0)           | 97 (31.3)             |
| Attributable mortality\textsuperscript{c} | 6 (26.1)             | 14 (35.0)         | 14 (14.0)          | 26 (20.5)           | 70 (22.6)             |
| Overall mortality\textsuperscript{d} | 11 (47.8)            | 24 (60.0)         | 37 (37.0)          | 41 (32.3)           | 127 (41.0)            |

Note: Data are n (%);
\textsuperscript{b}For 20 patients, allocation to decade was not possible as the year was not specified in the case reports;
\textsuperscript{c}Day 42 and day 90 mortality specified only when reported as such;
\textsuperscript{d}Attributable mortality counted only when reported as such;
\textsuperscript{e}Unknown outcome: one patient in 1990-1999, nine patients in 2000-2009 and four patients in 2010-2019.
always retrievable, and the reported data were of heterogeneous quality, whereby newer reports tended to be less comprehensive. Registries typically provide a more comprehensive dataset than case reports and can help in epidemiological and clinical investigations in rare and orphan diseases. However, to date, only a small number of mucormycoses cases from the region (n = 7) have been included in the FungiScope® registry.

This study highlights the burden of mucormycosis in MENA countries and identifies trends in the cases from this region that may be of value to physicians treating this disease. Given the wide use of both antifungal therapy and surgery, and the decreasing mortality rate, the prognosis of patients with mucormycosis is improving, but the need for more effective treatment practices in the MENA region is clear. Progress towards this goal can be made through several avenues, including the use of technologies enabling earlier diagnosis, the development of new antifungal therapies and optimised use of existing therapies, as well as the implementation of policies to increase awareness of mucormycosis and to improve its regional documentation. Reducing the risk of mucormycosis in the region will also be key, for example through improved diabetes prevention and management strategies.

ACKNOWLEDGMENTS

This work was supported by Basilea Pharmaceutica International Ltd. (Work order No. 2#102273). The authors thank Morad Wattad for providing clinical details for local patients enrolled in the FungiScope® registry, Erwin Graef of Basilea Pharmaceutica International Ltd. for his support with the medical literature search, and Susann Bloßfeld from University of Cologne for technical assistance. Medical writing support was provided by Stephanie Carter of Spirit Medical Communications Group Ltd funded by Basilea Pharmaceutica International Ltd.

CONFLICT OF INTEREST

JS reports grants from Basilea Pharmaceutica International Ltd during the conduct of the study and travel grants from Meta-Alexander Foundation and from the German Society for Infectious Diseases (DGI) outside of the submitted work. KH is an employee of Basilea Pharmaceutica International Ltd. OAC has received research grants from Actelion, Amplyx, Astellas, Basilea, Cidara, Da Volterra, F2G, Gilead, Janssen Pharmaceuticals, Medicines Company, Medpace, Melinta Therapeutics, Merck/ MSD, Pfizer, and Scynexis; is a consultant to Actelion, Allecra Therapeutics, Amplyx, Astellas, Basilea, Biosys UK Limited, Cidara, Da Volterra, Entasis, F2G, Gilead, Matinas, Medpace, Menarini Ricerche, Roche Diagnostics, Merck/ MSD, Nabirwa Therapeutics, Octapharma, Paratek Pharmaceuticals, Pfizer, PSL, Rempex, Scynexis, Seres Therapeutics, Tetraphase, and Vical; and received lecture honoraria from Astellas, Basilea, Gilead, Grupo Biotoscana, Merck/ MSD, and Pfizer. JSG, ARM, SKG, ES, MZ, DS, RAK, RBA, EBC and YR have no conflicts to disclose.

AUTHOR CONTRIBUTIONS

Jannik Stemler: Conceptualization (equal); Data curation (lead); Formal analysis (lead); Funding acquisition (lead); Investigation (lead); Methodology (equal); Project administration (equal); Resources (equal); Supervision (equal); Validation (equal); Writing—original draft (supporting); Writing—review & editing (equal). Kamal Hamed: Funding acquisition (supporting); Investigation (equal); Methodology (supporting); Project administration (supporting); Resources (equal); Visualization (lead); Writing—original draft (lead); Writing—review & editing (equal). Jon Salmanton-Garcia: Formal analysis (supporting); Investigation (equal); Resources (lead); Software (equal); Validation (equal); Visualization (equal); Writing—review & editing (equal). Ali Rezaei-Matehkolaei: Data curation (equal); Investigation (equal); Writing—review & editing (equal). Stefanie K. Gräfe: Data curation (equal); Investigation (equal); Writing—review & editing (equal). Erman Sab: Data curation (equal); Investigation (equal); Writing—review & editing (equal). Marouan Zarrouk: Data curation (equal); Investigation (equal); Writing—review & editing (equal). Danila Seidel: Conceptualization (equal); Funding acquisition (equal); Methodology (equal); Project administration (equal); Supervision (equal); Writing—review & editing (equal). Reham Abdelaziz Khedr: Investigation (equal); Writing—review & editing (equal). Ronen Ben-Ami: Investigation (equal); Writing—review & editing (equal). Eli Ben-Chetrit: Investigation (equal); Writing—review & editing (equal). Yehudah Roth: Investigation (equal); Writing—review & editing (equal). Oliver A. Cornely: Conceptualization (equal); Funding acquisition (equal); Investigation (equal); Methodology (equal); Project administration (lead); Resources (lead); Supervision (lead); Writing—review & editing (equal).

ORCID

Jannik Stemler https://orcid.org/0000-0001-9152-2469
Kamal Hamed https://orcid.org/0000-0003-1896-9736
Jon Salmanton-Garcia https://orcid.org/0000-0002-6766-8297
Ali Rezaei-Matehkolaei https://orcid.org/0000-0002-3119-8342
Stefanie K. Gräfe https://orcid.org/0000-0001-7678-0179
Ertan Sab https://orcid.org/0000-0003-2761-2675
Marouan Zarrouk https://orcid.org/0000-0002-3259-6123
Danila Seidel https://orcid.org/0000-0003-4388-3117
Reham Abdelaziz Khedr https://orcid.org/0000-0001-5355-8225
Ronen Ben-Ami https://orcid.org/0000-0003-0628-0798
Eli Ben-Chetrit https://orcid.org/0000-0001-5743-1387
Oliver A. Cornely https://orcid.org/0000-0001-9599-3137

REFERENCES

1. Cornely OA,Aralstruey-Izquierdo A, Arens D, et al. Global guideline for the diagnosis and management of mucormycosis: an initiative of the European Confederation of Medical Mycology in cooperation with the Mycoses Study Group Education and Research Consortium. Lancet Infect Dis. 2019;19(12):e405-e421.

2. Jeong W, Keighley C, Wolfe R, et al. The epidemiology and clinical manifestations of mucormycosis: a systematic review and meta-analysis of case reports. Clin Microbiol Infect. 2019;25(1):26-34.

3. Prakash H, Chakrabarti A. Global epidemiology of mucormycosis. J Fungi (Basel). 2019;5(1):26.
4. Petrikos G, Skia A, Lortholary O, Roilides E, Walsh TJ, Kontoyiannis DP. Epidemiology and clinical manifestations of mucormycosis. Clin Infect Dis. 2012;54(Suppl 1):S23-S34.

5. Skia A, Pagano L, Groll A, et al. Zygomycosis in Europe: analysis of 230 cases accrued by the registry of the European Confederation of Medical Mycology (ECMM) Working Group on Zygomycosis between 2005 and 2007. Clin Microbiol Infect. 2011;17(12):1859-1867.

6. Bitar D, Lortholary O, Le Strat Y, et al. Population-based analysis of invasive fungal infections, France, 2001–2010. Emerg Infect Dis. 2014;20(7):1149-1155.

7. Roden MM, Zaoutis TE, Buchanan WL, et al. Epidemiology and outcome of zygomycosis: a review of 929 reported cases. Clin Infect Dis. 2005;41(5):634-653.

8. NCD Risk Factor Collaboration. Worldwide trends in diabetes since 1980: a pooled analysis of 751 population-based studies with 4.4 million participants. Lancet. 2016;387(10027):1513-1530.

9. Low CY, Rotstein C. Emerging fungal infections in immunocompromised patients. J Fungi (Basel). 2012(4):46.

10. Salmanton-García J, Seidel D, Koehler P, et al. Matched-paired analysis of patients treated for invasive mucormycosis: standard treatment versus posaconazole new formulations (MoveOn). J Antimicrob Chemother. 2019;74(11):3315-3327.

11. Marty FM, Ostrosky-Zeichner L, Cornely OA, et al. Isavuconazole treatment versus posaconazole new formulations (MoveOn). Antimicrob Resist Infect Control. 2019;8:14.

12. Riley TT, Muzny CA, Swiatlo E, Legendre DP. Breaking the mold: a review of mucormycosis and current pharmacological treatment options. Ann Pharmacother. 2016;50(9):747-757.

13. Spellberg B, Edwards J, Ibrahim A. Novel perspectives on mucormycosis: pathophysiology, presentation, and management. Clin Microbiol Rev. 2005;18(3):556-569.

14. Sivagnanam S, Sengupta DJ, Hoogestraat D, et al. Seasonal clustering of sinonasal mucormycosis in patients with hematologic malignancies at a large comprehensive cancer center. Antimicrob Resist Infect Control. 2017;6:123.

15. Talmi YP, Goldschmied-Reouven A, Bakon M, et al. Rhino-orbital and rhino-orbital-cerebral mucormycosis. Otolaryngol Head Neck Surg. 2002;127(1):22-31.

16. Nucci M, Engelhardt M, Hamed K. Mucormycosis in South America: a review of 143 reported cases. Mycoses. 2019;62(9):730-738.

17. Rueping MJ, Heinz WJ, Kindo AJ, et al. Forty-one recent cases of invasive zygomycosis from a global clinical registry. J Antimicrob Chemother. 2010;65(2):296-302.

18. FungiScope®. Global Emerging Fungal Infection Registry. http://www.fungiscope.net/. Accessed March 9, 2020.

19. Seidel D, Durán Graeff LA, Vehreschild M, et al. FungiScope® - Global Emerging Fungal Infection Registry. Mycoses. 2017;60(8):508-516.

20. Donnelly JP, Chen SC, Kauffman CA, et al. Revision and update of the consensus definitions of invasive fungal disease from the European Organization for Research and Treatment of Cancer and the Mycoses Study Group Education and Research Consortium. Clinical Infectious Diseases. 2019;ciiz1008. https://academic.oup.com/cid/article/doi/10.1093/cid/ciiz1008/5645434#186464855

21. Cornely OA, Hoenigl M, Lass-Flörl C, et al. Defining breakthrough invasive fungal infection–Position paper of the Mycoses Study Group Education and Research Consortium and the European Confederation of Medical Mycology. Mycoses. 2019;62(9):716-729.

22. El-Mahallawy HA, Khedr R, Taha H, Shalaby L, Mostafa A. Investigation and management of a Rhizomucor outbreak in a pediatric cancer hospital in Egypt. Pediatr Blood Cancer. 2016;63(1):171-173.

23. Pagano L, Valentini CG, Posteraro B, et al. Zygomycosis in Italy: a survey of FIMUA-ECMM (Federazione Italiana di Micopatologia Umana Animale and European Confederation of Medical Mycology). J Chemother. 2009;21(3):322-329.

SUPPORTING INFORMATION
Additional supporting information may be found in the Supporting Information section.

How to cite this article: Stemler J, Hamed K, Salmanton-García J, et al. Mucormycosis in the Middle East and North Africa: Analysis of the FungiScope® registry and cases from the literature. Mycoses. 2020;63:1060–1068. https://doi.org/10.1111/myc.13123