GAFFI - Fact Sheet

Mycetoma

Introduction

Mycetoma is an old and still neglected disease characterised by massive deformities and disabilities and enormous negative impact on patients and community. [1,2] The disease is endemic in many tropical and subtropical regions across the world with high prevalence in the "Mycetoma belt." [3,4.5] The belt stretches between 15^0S and 30^0N, and it includes the countries of Sudan, Somalia, Senegal, India, Yemen, Mexico, Venezuela, Columbia, Argentina, Iran, and others. [6,7,8]

Mycetoma is a chronic debilitating subcutaneous granulomatous inflammatory disease classified as eumycetoma (caused by fungi) and actinomycetoma (caused by bacteria). [9,10] its pathogenesis is poorly understood, probably with environmental, genetic and immunogenic factors all incriminated. [11,12,13]

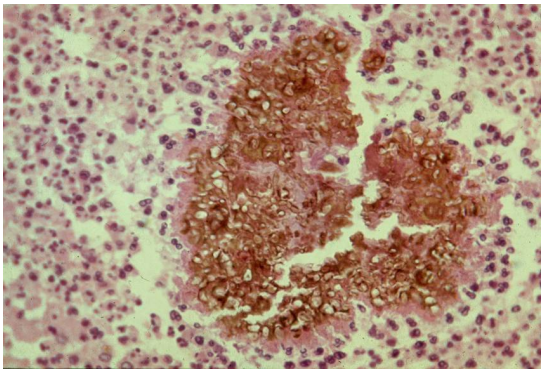


Figure 1: Typical microscopic appearance of mycetoma grain

Causative Organisms

The most common bacterial causative agents are *Nocardia brasiliensis*, *Actinomadura madurae*, *Streptomyces somaliensis*, and *Actinomadura pelletieria*.[11] The most common fungi causing disease are *Madurella mycetomatis, Madurella tropicana, Madurella fahali and Scedosporium apiopsermum*. [14,15,16,17] In general, actinomycetoma is more prevalent in Mexico and South America while eumycetoma is more frequently seen in the African continent but within a country, the mycetoma type distribution is variable and differs per region. [18,19,20,21,22,23,24] There remain many controversies on the infection entry route although traumatic inoculation of causative organisms into the skin and subcutaneous tissue is the popular theory. [25] The incubation period of mycetoma is unknown, yet, in experimental animals, a three months incubation period was reported. [26]

Epidemiology

The true annual incidence and prevalence of mycetoma globally are not well documented as it is a badly neglected and not a reportable disease. [26,27] There are probably between 20,000 and 50,000 cases worldwide, based on literature reports. Most cases are reported from Sudan, Mexico and India. Population prevalence data are available for Mauritania (3.5/100,000) and Sudan (1.8/100,000). High rates are also found in Mexico, Senegal, Niger and Somalia. The few published reports on the epidemiology of mycetoma are mostly hospital-

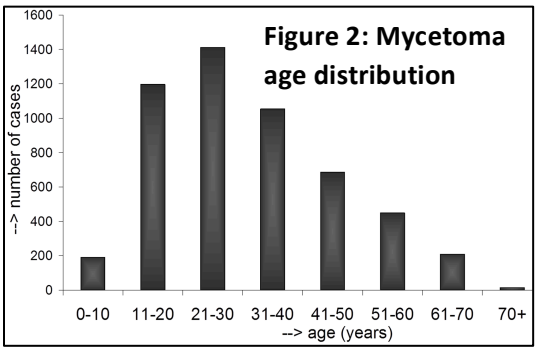
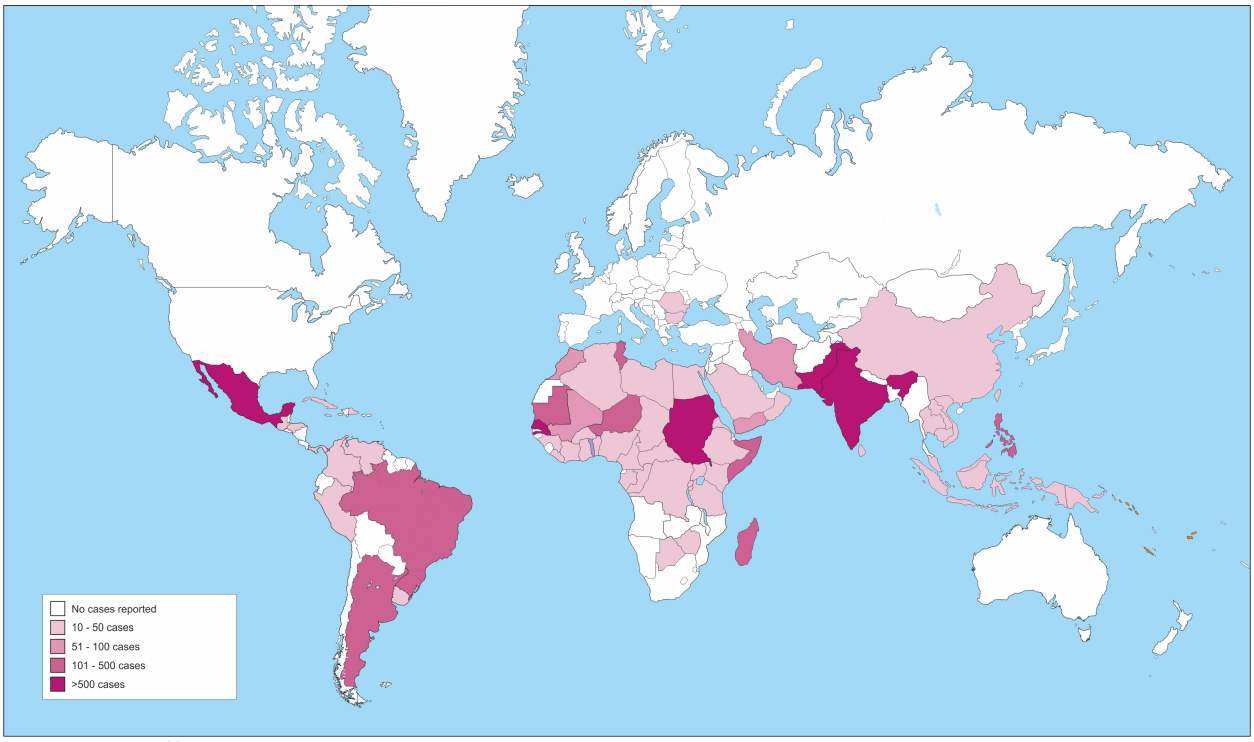


Figure 2: Mycetoma age distribution

based describing patients with late presentations. [5,25-32] The most common age of infection is young adulthood (70% of the cases are between ages 11 and 40), with some children and older people affected. In most countries men are affected more than women.

Figure 3: The 'Mycetoma Belt' depicted by case report numbers and reports to WHO [(27)]

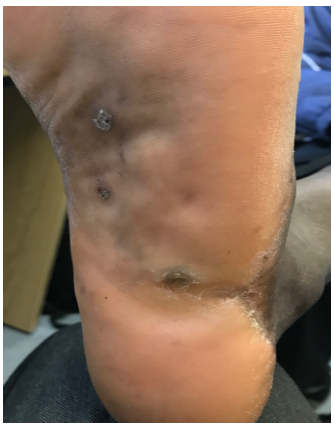


Mycetoma affect those doing outdoor activities and both genders are equally committed to these activities. [5,6,7,8] The majority of patients are farmers, workers, and students. Mycetoma frequently affects the poorest of the poor in remote endemic regions of low socioeconomic status, and the disease contributes further to their poverty and community economic loss. [1,2,3]

Clinical Presentation

Mycetoma patients tend to present late for medical treatment and the cause of that is multifactorial. [5,6,7] The disease is slowly progressive and initially painless. Other factors delaying medical help include the patients' low socio-economic status and health education level, financial constraints, long distances to secondary care facilities and the insecurity of many medical and health facilities in endemic villages. [34, 35]

The disease is characterised by the triad of a painless subcutaneous mass, multiple sinuses and purulent or seropurulent discharge that contains grains. [36] Grains are of various colours, sizes and consistent with the causative organism. Their colour can be black, white, yellow or red and that gives a clue to the causative agents. The subcutaneous mass usually spreads to involve the skin and the deep structures, resulting in destruction, deformity, and loss of function, and occasionally it can be fatal.



Mycetoma frequently affects the foot and hand and that is seen in more than 80% of patients. [37,38,39,40] Occasional cases of head and neck, chest, abdominal wall, perineum or gluteal region are recorded. [41,42,43,44]

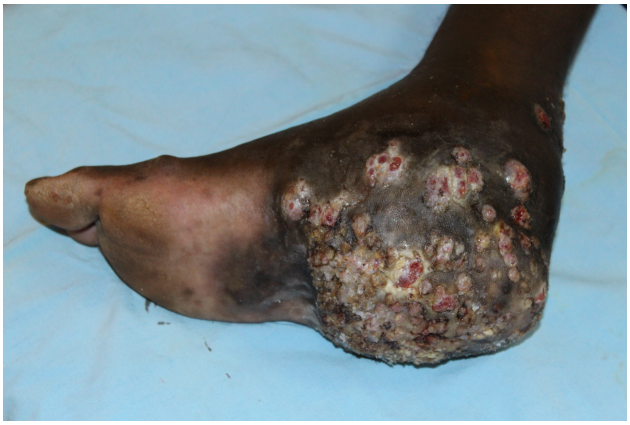


Figure 4: Eumycetoma of the foot

Rare mycetoma sites include the eye, sinuses, mastoid bone and scrotum. [45,46,47,48] Actinomycetoma lesions are more inflammatory, more destructive, and invade bone earlier. In contrast, eumycetoma has a slower presentation but ultimately can be just as destructive. [5,6,7]

Figure 5: Extensive heel and foot disease

The Differential Diagnosis

In endemic regions alternative diagnoses include thorn and foreign body granulomas and many benign soft tissue tumours such as fibroma and lipoma and infections such as chronic oesteomyetitis. [5,6,7]

Diagnosis

The identification of the mycetoma causative agent to the species level and the disease extent and spread along the tissue planes are both crucial and essential for appropriate treatment and management. [49] Individual grains, extracted from a sinus, have a distinctive appearance under direct microscopy, but their appearance is insufficient to determine the infection genus or species. Grains that are cultured may sometimes be positive. Surgical biopsy is important to obtain grains for culture and molecular identification and histopathological examination. [50-59]

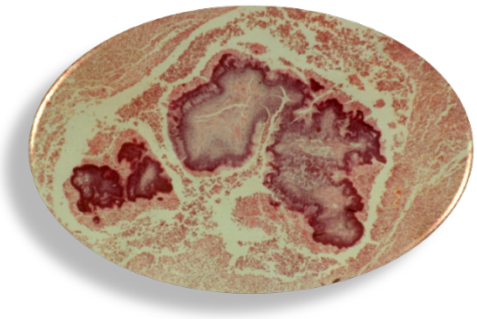


Figure 6: Microscopic appearance of *Actinomadura madurae*

Culture requires a range of media, including fungal, bacterial and mycobacteria plates and/or liquid culture. All of the bacteria and fungi causing mycetoma are tricky to identify, requiring years of experience and there are many variants and isolates that resemble others. Formal genetic identification using sequencing is most reliable. Susceptibility testing is not standardized and has not been well-correlated with treatment outcome.

Various imaging modalities are useful to define the extent of disease. Conventional X-ray, ultrasound to identify grains and MRI all have an essential place in determining the disease spread and to establish a plan of management. [60-63] Currently, the available diagnostic tests and

techniques are invasive, tedious, expensive and not field friendly. Most of them do not exist in endemic regions, and patients need to travel far to establish the diagnosis. [55]

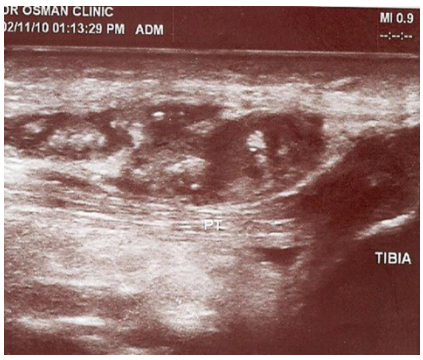


Figure 7: The ultrasound appearance

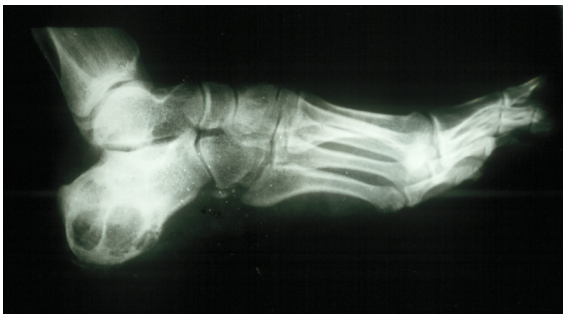


Figure 8: X-ray of a patient with eumycetoma foot of eumycetoma showing multiple big cavities

Treatment

Generally, actinomycetoma responds to a combination of chemotherapeutic agents. This combination is mandatory to avoid the development drug-resistant and for better disease eradication. [64,65,67,68] Current combinations recommended include co-trimoxazole (980 mg BD/day) and amoxicillin-clavulanic acid (1 gram/day). Second-line treatment is a combination of amikacin sulphate (15mg/kg/day) and co-trimoxazole (980 mg BD/day) given in a form of cycles - each cycle is 5 weeks. The treatment may last for more than one year, and the cure rate is 70-80%. [64,65,67,67]

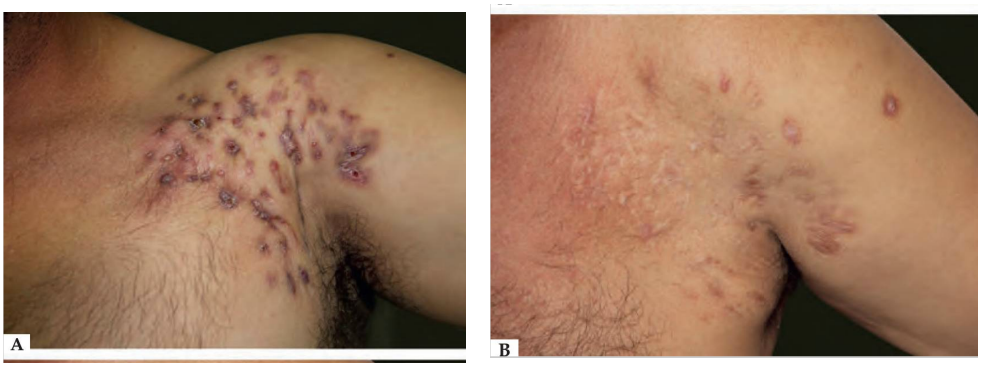


Figure 9: Actinomycetoma of the shoulder before and after antibiotic therapy [68]

The treatment of eumycetoma is prolonged with a low cure rate, high recurrence and dropout rates. It is a combination of antifungal treatment (currently itraconazole 400mg/day) and surgical excision. The excision ranges in extent from wide local excision, repetitive debridement to amputation. Surgery is indicated when the lesion is localised and for cases resistant to medical therapy, and it may be life-saving in advanced disease that is complicated by secondary bacterial infection, sepsis, massive bone involvement, and poor general condition. [69-71] Some data indicate that voriconazole may be a better choice for certain organisms, notably *Medicopsis* (*Pyrenochaeta*) *romeroi.*

Outcome

The majority of patients with actinomycetoma respond to therapy and are cured, unless the deep visceral invasion such as the brain or pelvic organs are affected. Some residual disability is seen, especially when joints are affected.

Eumycetoma patients usually respond poorly to medical therapy. Improvement is slow and hard to evaluate, even after months of therapy. Many patients eventually fail to complete education or lose their jobs and become a burden on families and the community. [5,6,7,8]

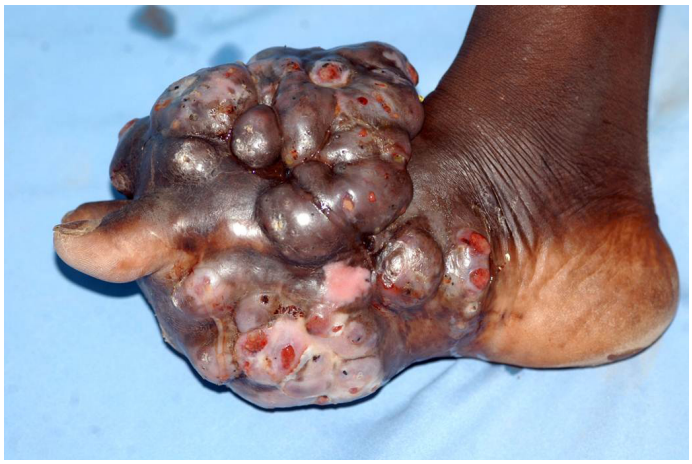


Figure 10: Late stage eumycetoma that is an all too common eventual outcome

Community management and prevention

Recently the Mycetoma Research Center (MRC), Sudan had reported on a new holistic approach to manage mycetoma patients locally at the village level. The MRC has established a regional mycetoma center in one of the endemic mycetoma villages in Sudan. The patients were treated locally in that center, the local medical and health personals were trained in early case detection and management, the local community was trained on mycetoma advocacy, and environmental conditions improvement. This comprehensive approach has also addressed the patients' socioeconomic constraints that deter timely presentation and treatment. This approach has also included active involvement of the local health authorities, community and civil society and donor contributions to deliver the optium management. [(3)]

Summary

To date and despite progress in mycetoma research, a huge knowledge gap remains in mycetoma pathogenesis and epidemiology resulting in the lack of objective and effective control programmes. Currently, the available disease control method is early case detection and proper management. However, the majority of patients present late with extensive disease and for many of them, heroic substantial deforming surgical excisions or amputation are the only prevailing treatment options. Likewise, there is no point-of-care diagnostic test for mycetoma. Urgent collaborative work is necessary to reduce patients suffering and to decrease the overall impact from this truly debilitating disease.

Public health needs:

- Global annual incidence and prevalence of mycetoma is not known, but it contributes to poverty exacerbation in many of the poorest countries. Improved burden statistics are required.
- Delays in diagnosis leads to more severe disease, which increases the need for major surgery, long-term disability and death. Campaigns to encourage affected patients to present early to medical centres for care will facilitate better outcomes.

- Widespread availability of trained microscopists, histopathologists and fungal culture technology (all WHO Essential Diagnostics), combined with imaging, are necessary to achieve definitive diagnosis and develop optimal treatment plans.
- Itraconazole, voriconazole and amikacin are required for therapy, combined with surgical expertise and monitoring capability.
- Public awareness of the disease and making mycetoma a notifiable disease will increase awareness and potentially decrease the rate of complications.
- Research to better understand environmental sources of the causative fungi, and the disease transmission are essential to deliver evidence-based advice to communities on prevention.

Hussein Suliman
Sahar Moubark Bakhiet
Ahmed Fahal
Mycetoma Research Centre, Khartoum, Sudam
September 2018

References:

1. Hay RJ, Fahal AH. Mycetoma: an old and still neglected tropical disease. Trans R Soc Trop Med Hyg. 2015; 109(3):169-70. doi:10.1093/trstmh/trv003.
2. Fahal AH. Mycetoma: A global medical and socio-economic dilemma. PLoS Negl Trop Dis 2017; 11(4): e0005509.
3. van de Sande W, Fahal A, Ahmed SA, Serrano JA, Bonifaz A, Zijlstra E; eumycetoma working group. Closing the mycetoma knowledge gap. Med Mycol. 2018 Apr 1; 56(suppl_1):153-164. doi: 10.1093/mmy/myx061.PMID:28992217
4. Zijlstra EE, van de Sande WW, Welsh O, Mahgoub ES, Goodfellow M, Fahal AH. Mycetoma. Lancet Infect Dis. 2016; 16(1):100-112. doi: 10.1016/S1473-3099(15)00359-X.
5. Fahal AH, EL Hassan AM, Mahgoub ES, Rahman ME, Mycetoma in the Sudan: The Mycetoma Research Centre Update. PLoS Negl Trop Dis. 2015 Mar 27; 9(3):e0003679. doi: 10.1371/journal.pntd.0003679. .
6. Fahal AH, Hassan MA. Br J Surg. 1992; 79(11): 1138-1141.
7. Fahal AH. Mycetoma. Review article, Khartoum Med J. 2011; 4(1): 514-523.
8. Fahal AH. Mycetoma thorn on the flesh Review article. Trans R Soc Trop Med Hyg. 2004; 98(1):3-11.
9. Fahal, AH Mycetoma in Richard, Guerrant, Walker, Peter, Tropical Infectious Diseases: Principles, Pathogens and Practice. Third edition, Elsevier Publisher, 2011, chapter 83, pp. 565-568
10. Fahal AH, Mycetoma in Mora-Montes HM, Leila M. Lopes-Bezerra L (Editors) Current Progress in Medical Mycology, Springer Nature 2017 pp 355-380. DOI 10.1007/978-3-319-64113-3
11. Nasr A, Abushouk A, Hamza A, Siddig E, Fahal AH. Th-1, Th-2 Cytokines Profile among Madurella mycetomatis Eumycetoma Patients. PLoS Negl Trop Dis. 2016 Jul 19; 10(7):e0004862. doi: 10.1371/journal.pntd.0004862. eCollection.
12. Al Dawi AF, Mustafa MI, Fahal AH, EL Hassan AM, Bakhiet SM, Mahgoub ES, Mergani A, Mukhtar MM. The Association of HLA-DRB1 & HLA-DQB1 and the occurrence of Eumycetoma. Khartoum Med J. 2013; 6(3): 923- 929
13. Ahmed AOA, Adelmann D, Fahal AH, Verbrugh HA, Van Belkum A, De Hoog S. Environmental occurrence of Madurella mycetomatis, major agent of human eumycetoma in Sudan. J Clin Microbiol. 2002 40(3): 1031-1036. PMID: 11880433.
14. Ahmed SA, van de Sande WJ, Stevens DA , Fahal AH, van Diepeningen A, Menken SBJ, and de Hoog GS. Revision of agents of black-grain eumycetoma in the order Pleosporales. Persoonia 2014; 33: 141–154.
15. de Hoog GS, van Diepeningen AD, Mahgoub el-S, van de Sande WW. New species of Madurella, causative agents of black-grain mycetoma. J Clin Microbiol. 2012; 50(3):988-94.

16. Mhmoud NA, Ahmed SA, Fahal AH, de Hoog GS, Gerrits van den Ende AH, van de Sande WW. Pleurostomophora ochracea, a novel agent of human eumycetoma with yellow grains. J Clin Microbiol. 2012; 50(9):2987-94
17. van de Sande WWJ, Fahal AH, de Hoog GS, Van Belkum A Madurella. In: Liu D, editor. Molecular detection of human fungal pathogens. Boca Raton: CRC Press, Taylor & Francis Group. 2011, pp. 117–128.
18. Ananthanarayan BA, Jayaram CK, Paniker MD. Textbook of Microbiology (8th ed.). Orient Longman Private Ltd. 2010, pp 618.
19. Aounallah A, Boussofara L, Ben Saïd Z, Ghariani N, Saidi W, et al. (2013) Analysis of 18 Tunisian cases of mycetoma at the Sousse hospital (1974–2010). Bull Soc Pathol Exot. 106(1): 5–8.
20. Cameron HM, Gatei D, Bremner AD. The deep mycoses in Kenya: a histopathological study. Mycetoma. East Afr Med J. 1973; 50 (8):382–95.
21. Develoux M, Ndiaye B, Dieng MT. Mycetomas in Africa. Sante. 1995; 5(4):211–7.
22. Agarwal SC, Mathur DR. Mycetoma in Northern Nigeria. Trop Geogr Med. 1985; 37(2):133–5.
23. Khatri ML, Al-Halali HM, Fouad Khalid M, Saif SA, Vyas MC. Mycetoma in Yemen
24. van de Sande WWJ, Maghoub ES, Fahal AH, Goodfellow M, Welsh O, Zijlstra E. The Mycetoma Knowledge Gap: Identification of Research Priorities. PLoS Negl Trop Dis 2014; 8(3): e2667. https://doi.org/10.1371/journal.pntd.0002667
25. Ahmed AO, van Leeuwen W, Fahal A, van de Sande W, Verbrugh H, van Belkum A. Mycetoma caused by Madurella mycetomatis: a neglected infectious burden. Lancet Infect Dis. 2004; 4(9):566-74.
26. Mahgoub ES, Murray IG. Mycetoma. London: Heinemann. 1973. p. 1–50.
27. van de Sande WW.Global burden of human mycetoma: a systematic review and meta-analysis. PLoS Negl Trop Dis. 2013 Nov 7;7(11):e2550. doi: 10.1371/journal.pntd.0002550. eCollection
28. Queiroz-Telles F, Fahal AH, Falci DR, Caceres DH, Chiller T, Pasqualotto AC. Neglected endemic mycoses. Lancet Infect Dis. 2017; 17(11):e367-e377. doi: 10.1016/S1473-3099(17)30306-7.
29. López-Martínez R, Méndez Tovar LJ, Lavalle P, Welsh O, Saúl A, (1992) Epidemiology of mycetoma in Mexico: study of 2105 cases. Gac Med Mex. 128(4):477–81.
30. López-Martínez R, Méndez-Tovar LJ, Bonifaz A, Arenas R, Mayorga J, et al. (2013) Update on the epidemiology of mycetoma in Mexico. A review of 3933 cases. Gac Med Mex. 149(5):586–92.
31. Lynch JB. (1964) Mycetoma in the Sudan. Ann R Coll Surg Engl. 35: 319–340.
32. Abbott PH. Mycetoma in the Sudan. Trans Roy Soc Trop Med Hyg. 1956; 50:11–24.
33. van de Sande WWJ, Maghoub ES, Fahal AH, Goodfellow M, Welsh O, Zijlstra E (2014) The Mycetoma Knowledge Gap: Identification of Research Priorities. PLoS Negl Trop Dis 2014, 8(3): e2667. https://doi.org/10.1371/journal.pntd.0002667
34. Bakhiet SM, Fahal AH, Musa AM, Mohamed ELSW, Omer RF, Ahmed ES, et al. (2018) A holistic approach to the mycetoma management. PLoS Negl Trop Dis 12(5):e0006391. https://doi.org/10.1371/journal.pntd.0006391
35. Van Belkum A, Fahal, AH, van de Sande WW. Mycetoma by Madurella mycetomatis: A completely neglected medico-social dilemma. In Hot Topics in Infection and Immunity in Children IX. Springer Science & Business Media New York 2012
36. Fahal AH, Suliman SH. Clinical presentation of mycetoma. Sudan Med J. 1994; 32: 46-66.
37. Omer RF, Seif EL Din N, Abdel Rahim FA, Fahal AH. Hand Mycetoma: The Mycetoma Research Centre Experience and Literature Review. PLoS Negl Trop Dis 2016;10(8): e0004886. doi:10.1371/journal.pntd.0004886
38. Fahal A, Mahgoub ES, EL Hassan AM, Jacoub AO, Hassan D. Head and Neck Mycetoma: The Mycetoma Research Centre Experience. PLoS Negl Trop Dis (2015) 9(3): e0003587. doi:10.1371/journal.pntd.0003587
39. Scolding PS, Abbas MAQ, Omer RF, Fahal AH. Madurella mycetomatis-Induced Massive Shoulder Joint Destruction: A Management Challenge. PLoS Negl Trop Dis 2016; 10(8): e0004849. doi:10.1371/journal.pntd.0004849

40. Mohamed ElSW, Seif El Din N, Fahal AH. Multiple Mycetoma Lung Secondaries from Knee Eumycetoma: An Unusual Complication. PLoS Negl Trop Dis. 2016 Jul 21; 10(7):e0004735. doi: 10.1371/journal.pntd.0004735. eCollection 2016.
41. Saad ESA, Fahal AH. Broncho-pleuro-cutaneous fistula and pneumothorax: Rare challenging complications of chest wall eumycetoma. PLoS Negl Trop Dis 2017; 11(9): e0005737. https://doi.org/10.1371/journal.pntd.0005737
42. Mohamed NA, Fahal AH. Mycetoma Pulmonary Secondaries from a Gluteal Eumycetoma: An Unusual Presentation. PLoS Negl. Trop Dis. 2016; 10(10): e0004945. doi:10.1371/journal. pntd.0004945.
43. Fahal AH, Arbab MAR, EL Hassan AM. Aggressive Clinical Presentation of Mycetoma due to Actinomadura Pelletierii. Khartoum Med J. 2012; 5(1): 699-702.
44. Mohamed, EW, Suleiman HS, Fadella, AI, Fahal, AH. Aggressive Perineal and Pelvic Eumycetoma: An unusual and challenging problem to treat. Khartoum Med J. 2012; (5)2:771-774.
45. Fahal AH, Suliman SH, Gadir AFA, EL Hag IA, EL Amin FI, Gumaa SA, Mahgoub ES. Abdominal wall mycetoma: an unusual presentation. Trans R Soc Trop Med Hyg. 1994; 88(1):78-80. PMID: 8154012.
46. Fahal AH, El Hassan AM, Abdelalla AO, Sheik HE, Cystic mycetoma: an unusual clinical presentation of Madurella mycetomatis. Trans R Soc Trop Med Hyg. 1998; 92:6-67.
47. Fahal AH, Sharfi AR, Sheikh HE, EL Hassan AM. Mycetoma: Uncommon complication. Trans R Soc Trop Med Hyg. 1996; 89: 550-552.
48. Fahal AH, Yagi HI, EL Hassan AM. Mycetoma induced palatal deficiency and pharyngeal plexus dysfunction. Trans R Soc Trop Med Hyg. 1996; 90: 676-677.
49. Ahmed AA, van de Sande W, Fahal AH. Mycetoma laboratory diagnosis: Review article. PLoS Negl Trop Dis. 2017; 11(8): e0005638. https://doi.org/10.1371/journal.pntd.0005638
50. Smit S, Derks MF, Bervoets S, Fahal A, van Leeuwen W, van Belkum A, van de Sande WW. Genome Sequence of Madurella mycetomatis mm55, Isolated from a Human Mycetoma Case in Sudan. Genome Announc. 2016 May 26;4(3). pii: e00418-16. doi: 10.1128/genomeA.00418-16
51. ELbadawi HS, Mahgoub E, Mahmoud N, Fahal AH. Use of immunoblotting in testing Madurella mycetomatis specific antigen. Trans R Soc Trop Med Hyg. 2016; 110(5):312-6.
52. Ahmed SA, van de Sande WW, Desnos-Ollivier M, Fahal AH, Mhmoud NA, de Hoog GS. Application of Isothermal Amplification Techniques for the Identification of Madurella mycetomatis, the Prevalent Agent of Human Mycetoma. J Clin Microbiol. 2015; 53(10):3280-5.
53. Paul A Hoskisson, Ralph Kirby, Vartul Sangal, Nicholas P Tucker, Jolanta Zakrzewska-Czerwinska, Katarzyna Wierzbicka, Paul R Herron, Chun-Jong Chu, Dr. govind chandra, Ahmed Fahal, Michael Goodfellow. The draft genome sequence of the human pathogen Streptomyces somaliensis, a significant cause of actinomycetoma. J Bacteriol. 2012; 194(13):3544-5.
54. Ibrahim AI, El Hassan AM, Fahal A, van de Sande WW. A histopathological exploration of the Madurella mycetomatis grain. PLoS One. 2013; 8(3): e57774. doi: 10.1371/journal.pone.0057774.
55. van de Sande WWJ, Fahal AH, Goodfellow M, Mahgoub ES, Welsh O, Zijlstra EE. Merits and Pitfalls of Currently Used Diagnostic Tools in Mycetoma. PLoS Negl Trop Dis 2014; 8(7): e2918. https://doi.org/10.1371/journal.pntd.0002918
56. Ahmed SA, van den Ende BHGG, Fahal AH, van de Sande WWJ, de Hoog GS. Rapid Identification of Black Grain Eumycetoma Causative Agents Using Rolling Circle Amplification. PLoS Negl Trop Dis 2014; 8(12): e3368. https://doi.org/10.1371/journal.pntd.0003368
57. Fahal AH, EL Toum EA, EL Hassan AM, Gumaa SA, Mahgoub ES. Host tissue reaction to Madurella mycetomatis: New classification. J Med Vet Mycol. 1995; 33: 15-17.
58. EL Hag IA, Fahal AH, Khalil EAG. Fine needle aspiration cytology of mycetoma. Acta Cytologica. 1996; 40(3): 461-46.

59. Fahal AH, Ahmed AO, Ismail A, Veress B. The immunopathology of actinomycetoma lesions caused by Streptomyces somaliensis. Trans R Soc Trop Med Hyg. 2001: 95(1); 89-92.
60. EL Shamy, ME, Fahal AH, Shakir MY, Homedia MMA. New MRI Grading System for the Diagnosis and Management of Mycetoma. Trans R Soc Trop Med Hyg. 2012; 106(12):738-42.
61. Fahal AH, Sheikh HE, EL Hassan AM. Pathological fracture in mycetoma. Trans R Soc Trop Med Hyg. 1996; 90: 675-676. PMID: 9015513.
62. Fahal AH, Sheikh HE, EL Lider MA, Homeida MA, EL Arabi YE, Mahgoub ES. Ultrasonic imaging in mycetoma. Br J Surg. 1997; 78: 765-766.
63. Abd El-Bagi MEB, Fahal AH. Mycetoma revisited. Incidence of various radiographic signs. Saudi Med J. 2009;30(4):529-33. PMID: 19370281.
64. Welsh O, Al-Abdely HM, Salinas-Carmona MC, Fahal AH. Mycetoma Medical Therapy. PLoS Negl Trop Dis 2014, 8(10): e3218. doi:10.1371/journal.pntd.0003218.
65. Fahal A, Mahgoub ES, EL Hassan AM, Abdel-Rahman ME, Alshambaty Y, Ed E Zijlstra A New Model for Management of Mycetoma in the Sudan. PLoS Negl Trop Dis 2014, 8(10): e3271. doi:10.1371/journal.pntd.0003271
66. Fahal, AH. Management of mycetoma. Expert Rev Dermatol. 2010; 5(1), 87–93.
67. Fahal AH, Elkhawad AO. Managing mycetoma: guidelines for best practice Expert Rev Dermatol 2013; 8(3): 301-307.
68. Reis CMS, Reis-Filho EG Mycetomas: an epidemiological, etiological, clinical, laboratory and therapeutic review* An Bras Dermatol. 2018 Jan-Feb; 93(1): 8–18.
69. Suleiman SH, Wadaella el S, Fahal AH. The Surgical Treatment of Mycetoma. PLoS Negl Trop Dis. 2016 Jun 23; 10(6):e0004690. doi: 10.1371/journal.pntd.0004690. eCollection 2016
70. Zein HAM, Fahal AH, Mahgoub, ES, EL Hassan T, Abdel Rahman, ME, The Predictors of Cure, Amputation & Follow-up dropout among Mycetoma Patients as seen at The Mycetoma Research Centre, University of Khartoum. Trans R Soc Trop Med Hyg. 2012; 106(11):639-44.
71. Wadal A, Elhassan TA, Zein HA, Abdel-Rahman ME, Fahal AH. Predictors of Post-operative Mycetoma Recurrence Using Machine-Learning Algorithms: The Mycetoma Research Center Experience. PLoS Negl Trop Dis. 2016; 10(10): e0005007. doi:10.1371/journal.pntd.0005007