



# Asian Journal of Epidemiology

ISSN 1992-1462

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### Mycetoma in Iran: Study of 62 Cases

<sup>1</sup>S.J. Hashemi, <sup>2</sup>A. Nasrollahi, <sup>1</sup>M. Guerami, <sup>1</sup>R. Daei, <sup>3</sup>K. Pakshir and <sup>1</sup>A. Zibafar

<sup>1</sup>Department of Medical Mycology, Tehran University of Medical Sciences, Iran

<sup>2</sup>Islamic Azad University, Tonekabon Branch, Iran

<sup>3</sup>Department of Medical Mycology, Shiraz University of Medical Sciences, Iran

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**Abstract:** This research presents a retrospective study of 62 cases of mycetoma in Iran that were diagnosed clinically and microbiologically from 1972 to 2005. In 1972 mycetoma has been first report in Iran by medical mycology department of Tehran University. We retrospectively compared the overall prevalence of mycetoma and the prevalence of infective agent in Iran during 33 years. In this study age, sex, job, infective agent and anatomical site of infection have been considered. Retrospective analysis of the records revealed that the ratio of actinomycetoma and eumycetoma was 42:20 that differed significantly ( $p < 0.01$ ). *Actinomadura madurae* ( $n = 11$ ) in actinomycetoma and *Pseudallescheria boydii* ( $n = 9$ ) in eumycetoma were predominant agents. The male to female ratio was 41:21 and the peak age for infection was between 40-50 years old but there is no a significant differences between age groups ( $p > 0.05$ ) and the earliest age of onset was 18 and the latest 65. The single most common site of infection is foot but generally hand and other limbs can infected and 54.4% of infected area was in palm and disease can infected other area with less frequency. A total of 49 cases were pedal mycetoma and 13 cases were in extra pedal areas. The results show that farmers with 45.2% are at greater occupation risk of mycetoma ( $p < 0.01$ ).

**Key words:** Mycetoma, *Pseudallescheria boydii*, *Actinomadura madurae*

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### INTRODUCTION

Mycetoma is a chronic granulomatous disease of the cutaneous and subcutaneous tissue, which sometimes involves bones, muscle and neighboring organs. The infection caused by actinomycetes or by true fungi. Clinically the disease is characterized by indolent, deforming, swollen lesions and sinuses involving cutaneous and subcutaneous tissue, fascia and bones that usually occurring on foot or hand. For the first time Gill described the disease in the Madura distinct of India in 1842. On the other hand in 1813, Pinoy described the mycetoma produced by aerobic bacteria that belong to the actinomycete group (Saag *et al.*, 2000).

Generally this agent present in soil or on vegetable as saprophytes. The disease usually occurs in journey prone part of body months or years after the relevant trauma (Hay, 1996; Fahal and Hassan, 1992). At least 10 geophilic actinomycetes are reported to cause actinomycetoma but many more similar organisms are known without pathogenic significance (Ahmad *et al.*, 2003; Fletcher *et al.*, 2001).

The single most common site of infection is foot and the symptoms generally appear after a long incubation period (Maiti and Halder, 1998). The disease advances slowly per months or years, typically with minimal pain. When pain is experienced, it is usually due to secondary infections or bones involvement. Although it is rarely fatal, mycetoma causes deformities and potential disability at the advance stage (Saag *et al.*, 2000; Hay, 1996).

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**Corresponding Author:** S.J. Hashemi, Department of Medical Mycology, Tehran University of Medical Sciences, P.O. Box 14155-6446, Tehran, Iran Tel: +98-21 88951583 Fax: +98-21 66462267

Generally in the regions where the disease is endemic, thorny trees such as acacia are abundant. The wounds caused by the thorns may facilitate the entry of the soil-borne organisms, or the causative agents may grow saprophytically on the thorns and enter the body as the thorn penetrates the tissue. Mycetoma has been divided to two groups Eumycetoma and Actinomycetoma. Eumycetoma can be produced by a variety of fungi such as, *Acremonium* sp., *Fusarium* sp., *Pseudoallescheria boydii*, *Exophiala jeanselmei*, *Madurella grisea*, *Madurella mycetomatis*, however actinomycetoma are mainly produced by bacteria of 4 genera *Nocardia*, *Actinoadura*, *Streptomyces* and *Actinomycete* (Hay, 1996; Gumaa, 1994).

It should be mentioned that the geographic distribution of the pathogenic agents determined by the annual rainfall, for example in North of Iran with rainy and humid status, the prevalent agent is Actinomycetes and *Nocardia* which leads to actinomycetoma, so in a retrospective study we decided to determine the prevalence of mycetoma and its causative agents in different parts of Iran (Zaini *et al.*, 1999).

## MATERIALS AND METHODS

The 62 cases of mycetoma which were clinically and microbiologically confirmed mostly in the Medical Mycology Department, School of Public Health, Tehran University between 1972 that the first case of mycetoma has been reported and 2005 were studied. The records included general information such as date of diagnosis, age, sex, occupation, resident, initial site of lesion and duration of the disease.

The diagnosis of all cases was established by microscopic findings and culturing of the specimens included visible granules and discharge collections that were processed in multiple sets in Sabouraud's dextrose agar media with and without chloramphenicol and Brain Heart Infusion agar at 37°C incubation. At last isolates were identified by studying colony morphology, fungal morphology and their conidiogenesis and *Actinomycetes* were diagnosed by use of casein, xanthine tyrosine and urea tests.

The initial sites of lesions were classified into two parts; pedal parts included sole, ankle, leg, knee and toe and the extra pedal areas included arm, fore arm, elbow, palm, finger, wrist and buttock. According to nature of job cases were divided to farmer, other manual and sedentary workers.

The injuries were classified in five categories that pointed injuries such as pricking that had special importance in the epidemiology of mycetoma and the other included cuts, operated injuries, scratch and war injuries.

## RESULTS

According to this study among 62 cases of mycetoma 20 cases (30.65%) were Eumycetoma and 42 cases (69.35%) were Actinomycetoma. The distribution of causal agents was as follows: *Pseudoallescheria boydii*, (n = 8), *Madurella mycetomatis* (n = 2), *Aspergillus flavus* (n = 1), *Aspergillus fumigatus* (n = 1), *Exophiala jeanselmei* (n = 1), *Fusarium spp.* (n = 1), *Pcilomyces spp.* (n = 1) and unidentified eumycetoma agents (n = 5).

*Actinoadura madurae* (n = 11), *Nocardia asteroides* (n = 9), *N. caviae* (*N. otitidiscaviarum*) (n = 6), *N. brasiliensis* (n = 1), *Nocardia spp.* (n = 5), *Actionmyces Israeli* (n = 1), *Streptomyces somaliensis* (n = 1), *S. spp.* (n = 1) and unidentified actinomycetoma agents (n = 7).

In this survey the earliest age of onset was 18 and the latest 65. The most prevalence of disease was seen in 41-50 age groups with 15(24.2%) frequency. It should be mentioned that among the cases, 41(64.5%) were male and 21(35.5%) were female with a risk about 2:1. Involvement of men is more common because of their job and outdoor activity, but there wasn't a significant difference between sex groups ( $p > 0.05$ ). More information about distribution of mycetoma based on age was shown in Table 1.

Table 1: Incidence of mycetoma in relation to age and sex

Sex	Age group (years)					
	<21	21-30	31-40	41-50	51-60	>60
Male (n = 41) 65.5%	2	8	10	11	6	2
Female (n = 21) 35.5%	1	5	6	6	2	0
Total (n = 62)	3	13	16	17	8	2

Table 2: Risk factor-related differences of mycetoma incidences in pedal and extra pedal parts of the body

Part of body	Sex		Type of mycetoma		Occupation	
	Male	Female	Actinomycotic	Eumycotic	Farmer	Others
Pedal (n = 49)	29	20	32	17	18	30
Extra pedal (n = 13)	12	1	10	3	10	4
Total	41	21	42	20	28	34
p-value	>0.05		<0.01		<0.01	

Localization of the infection based on site of lesion were; pedal (n=49) included sole (n = 34), ankle (n = 5), leg (n = 5), knee (n = 3) and toe (n = 2). Extra pedal (n = 13) included palm (n = 3), wrist (n = 3), buttock (n = 2), arm (n = 2), fore arm (n = 1), elbow (n = 1) and finger (n = 1).

The single most common site of infection is foot but generally hand and other limbs can be infected. In our study the most infected limb is foot specially palm with 54.4% of infected areas and other areas with less frequency such as fore arm, elbow and finger. The incidence of mycetoma in pedal was almost four times higher than that of extra pedal areas (p = 0.01). This might be the result of high occupational risk of trauma and soil contact especially in agricultural workers.

The result shows that farmers with 28 (45.2%) are at greater occupational risk of mycetoma. The difference (p<0.01) between farmers with other occupations might be the result of their occupational risk in farm that they have a high risk for pricking injuries by thorns and plants. The more information was shown in Table 2 include etiology agent, job and anatomical site of lesion.

A history of previous injury was noticed in more than 50% (n = 35) of them, in some barefoot walking in soil and farm was frequent and in some others there was no history of proven trauma. Pricking injuries (n = 29) comprised of puncture with a thorn, wooden spicule, plant fiber or needle. The incidence of mycetoma associated with pricking was significantly higher (p<0.01). Other injuries included war injuries (n = 2), cut (n = 1), operated injury (n = 1) and scratch (n = 1). Granules were detected in 53 cases and most of them were white in color and soft. In 12 cases direct examination has been negative but the agents were isolated in culture. In two cases partially acid-fast branching filaments were seen in stain and branching filaments in the KOH preparations, but results of culture were negative and suspected to be due to *Nocardia* species. In one case any granule was not seen neither macroscopically nor in histological sections, but Gram positive, acid-fast branching filament was observed in pus smear, nor in culture *Nocardia asteroides* was isolated.

## DISCUSSION

We retrospectively compared the overall prevalence of mycetoma and its infective agent in Iran during 33 past years. In our study we have considered not only the age, sex and job but also the site of infection.

We studied 62 cases of mycetoma retrospectively since 1972 to 2005 in Iran. Among 62 cases 42 (30.65%) was actinomycotic mycetoma and 20 (69.35%) were related to eumycotic mycetoma, therefore according to our findings actinomycetoma is significantly more prevalent in Iran (p<0.05) which is also detected in the most reports and the ratio of actinomycetoma to eumycetoma is 3:1 (Dieng *et al.*, 2005; Daoud *et al.*, 2005).

Most of present cases have belonged to rainy and humid status in north of Iran. Dieng *et al.* (2003) reported 130 cases of mycetoma in Senegal from 1983 to 2000. Among their study they found that the geographical distribution of pathogenic agents was determined by the annual rainfall. Mycetoma is endemic around the tropic of cancer, 15° Souths and 30° North of the equator, in tropical, subtropical and temperate regions. Mexico, Venezuela, India, Pakistan, Senegal and Somalia have the highest incidence of disease wide. The United States, Asia and other Latin American countries have reported cases less frequently (Saag *et al.*, 2000; Hay, 1996). Generally environmental condition such as the temperature and humidity of the area must be suitable for the growth of the pathogenic organisms in the soil (Saag *et al.*, 2000). Agents which caused mycetoma are present in soil or on vegetable as saprophytes (Saag *et al.*, 2000; Hay, 1996).

In present study the most prevalent infective agent is *Actinomadura madurae* (n = 11) that is like as the reports from Tunisia, Algeria and Morocco (Daoud *et al.*, 2005). Some investigators determined the etiologic agents of mycetoma in Iran (Zaini *et al.*, 1999; Hashemi and Gramishoar, 2001). The results of their survey provided information for the first time on the prevalence of etiologic agents of mycetoma in the soil and plants of Iran. They found that especially north of Iran based on rainy and humid condition actinomycetoma is more common.

In this disease age has been considered as an important factor but in our study there wasn't significant differences between age groups ( $p>0.05$ ) and the peak age for infection was between 40 and 50 years old. This matches with data from medical literature setting the age of onset as being the active period of life about 40 years old (Daoud *et al.*, 2005; Dieng *et al.*, 2005, 2003; Khatri *et al.*, 2002).

It should be mentioned that among the 62 cases which reported 41 cases (64.5%) were male and 21 cases (33.9%) were female. Involvement of men is more common and it is related to their job and their activity which is out door, but there wasn't a significant difference between sex groups. We have tested our data and found that there is no correlation (Spearman correlation) between sex groups ( $p>0.05$ ) that is similar to Daoud *et al.* (2005). Maiti *et al.* (2002) investigations about mycetoma in exposed and no exposed parts of body show that the (male/female) cases ratios of two parts of body is also different (Maiti and Haldar, 1998).

We have considered that occupational risk in our groups and our results show that farmers are at greater occupation risk of mycetoma. Among the cases 45.2% was farmers we can interpret these data because they have a high risk of injuries that permit infection with saprophytic agents. It should be considered that the trauma is not the only factor for the outcome of the disease but also the viability of the organism and local wound conditions can also modify the outcome (Maiti and Haldar, 1998).

Epidemiological information generated from retrospective analysis of 212 mycetoma cases attending Calcutta school of tropical medicine during 1986 to 1997 revealed that mycetoma which occurred on covered parts of body significantly differed from mycetoma occurring on exposed parts (Maiti and Haldar, 1998; Maiti *et al.*, 2002).

In present study the most common area for infection was pedal mycetoma because it has the most contact with thorns and plants in out door due to some habits such as barefoot walking or agricultural activity. Fungal and bacterial agents are saprophytes in soil or plants and the inoculation of the agent is generally was done by soiled tools (Hashemi and Gramishoar, 2001; Akhtar and Latief, 1999).

Finally it should be mentioned that mycetoma are rare in Iran and only appear sporadically. Since the first Iranian case reported in 1972, only 62 cases were reported up to 2005 almost 2 cases per year.

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