

A study of clinico-mycological profile and treatment of primary otomycosis



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ABSTRACT

Background: Otomycosis is a superficial mycotic infection of the external auditory canal. Clinical presentation, along with otoscopic findings, is sufficient to make the diagnosis in most of the cases. Treatment includes aural cleaning followed by the instillation of anti-fungal ear drops. In the recent years, there has been an increasing trend of antifungal resistance for the commonly used antifungals such as fluconazole and clotrimazole. Drug sensitivity patterns have also shown variability from one region to another. **Aims and Objectives:** To evaluate the clinico-mycological profile along with antifungal susceptibility pattern and treatment outcome of primary otomycosis. **Materials and Methods:** A total of 230 clinically diagnosed patients of primary otomycosis were included in this prospective study. Microbiological causes were evaluated by KOH wet mount and culture of samples collected from external auditory meatus using sterile swabs. Fungal culture was done on Sabouraud dextrose agar with chloramphenicol at 25°C and 37°C. Anti-fungal susceptibility test was done by disk diffusion method using medium Muller-Hilton agar with glucose and methylene blue. All the patients were treated with the removal of fungal debris with topical clotrimazole instillation and were followed up after 7 days. Non-responders were treated with topical itraconazole. **Results:** Male-to-female ratio in study participants was 1:1.3. The most frequently observed risk factor was the instillation of oil in the ear (20%). Ear itching was the commonest symptom (70.9%). Positive fungal growth was seen in 203 (88.3%) cases. *Aspergillus* was present in 185 (91.1%) cases, followed by *Candida* in 18 (8.9%) cases. Voriconazole had the highest sensitivity followed by itraconazole. 167 (83.3%) patients responded to primary treatment (topical Clotrimazole), 36 (16.7%) patients were non-responders. **Conclusion:** All the clinically suspected patients should be evaluated for fungal positivity, which may further guide in the selection of appropriate anti-fungal agents. Awareness regarding the predisposing factors for otomycosis in the general population may result in a significant drop in the incidence of otomycosis.

Key words: Otomycosis; *Aspergillus*; *Candida*; Clotrimazole; Itraconazole

INTRODUCTION

Otomycosis is a superficial fungal infection of the external auditory canal. Prevalence of otomycosis range from 9% to 27% among patients who present with signs and symptoms of otitis externa and up to 30% in patients with discharging ears.^{1,2} Presenting complaints include itching and pain in the ear, ear discharge, hearing difficulty, ringing sensation, and heaviness in the ear. Otoscopy may demonstrate black,

grey, yellow, or white discharge with debris, occasionally with visible fungal hyphae.

Otomycosis can be primary or secondary. It is termed primary when fungi are the primary pathogens and is defined as "Otomycosis in an immuno-competent individual, with the absence of any other external or middle ear pathology." Term secondary otomycosis is defined as "Otomycosis in patient with existing bacterial otitis externa/

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media or postoperative ears or history of an existing fungal infection in other parts of the body or serious debilitating disease or in an immunocompromised patient.³

Risk factors for otomycosis include humid climate, ear instrumentation, ear oil instillation, immunocompromised status, and increased frequency of topical antibiotic/steroid use.^{2,3} Though a mild condition, it may result in severe infection among immunocompromised patients. In patients with perforated tympanic membrane, involvement of the middle ear may result in a prolonged burden of disease requiring extensive treatment and follow-up. *Aspergillus* species (spp.) are the most common fungal pathogen, with as high as 80% of the total cases attributable to it. *Candida* spp., *Penicillium* spp., and *Rhizopus* spp. are the other common fungal pathogen.^{3,4} Treatment includes aural cleaning followed by the instillation of topical anti-fungal ear drops and control of predisposing factors.

In recent years, there has been an increasing trend of antifungal resistance for the commonly used antifungals such as fluconazole and clotrimazole.^{5,6} Drug sensitivity patterns have also shown variability from one region to another. Proper management of otomycosis requires correct identification of the underlying fungal species as well as the drug sensitivity pattern specific to a particular location.

Aims and objectives

To evaluate the clinico-mycological profile along with antifungal susceptibility pattern and treatment outcome of primary otomycosis at a tertiary care center in North India.

MATERIALS AND METHODS

A prospective study was conducted for 2 years in departments of Otorhinolaryngology and Microbiology at a tertiary care center in North India. Ethical clearance was obtained from the institutional ethical committee. A predesigned pro forma was used to evaluate and analyze demographic profile, predisposing factors, clinical features, mycological profile, and treatment response.

Inclusion criteria

A total of 230 patients, aged above 10 years, presenting with symptoms and signs of primary otomycosis in the outpatient department of Otorhinolaryngology were included in the study. Clinical features used for the diagnosis of otomycosis was the presence of symptoms like itching, otalgia, ringing sensation in the ear, the feeling of ear blockage, reduced hearing sensitivity, and otoscopic findings like masses of spore/hyphae or curd-like gray-white or blackish discharge.

Exclusion criteria

Otomycosis with the following conditions was classified as secondary otomycosis and was excluded from the study.

1. Bacterial otitis externa, chronic otitis media, ear surgery
2. Serious debilitating diseases like malignancies, diabetes, tuberculosis, and other chronic granulomatous disease
3. Immunocompromised condition and history suggestive of fungal disease elsewhere in the body.

History of instillation of mustard/coconut oil in the ear, use of ear drops, wooden sticks or metal wax picks for self-cleaning of ears, swimming, and immuno-compromised state were noted. History indicative of fungal infection elsewhere in the body was elicited to rule out secondary otomycosis. Complete ear, nose, and throat examination was done in all patients. Routine blood and urine analysis, ELISA for HIV, and random blood sugar was done.

From the included cases, two samples from external auditory meatus debris/secretion were collected with sterile swabs. Samples were transported to the microbiology department, within 60 min, for mycological investigations. Of the two samples, one was for KOH wet mount, which was examined under $\times 10$ and $\times 40$ light microscopy for direct visualization of fungal elements. The other sample was for fungal culture on 2 Sabourauds dextrose agar with chloramphenicol at 25°C and 37°C. If growth was seen, the morphology of fungal isolates was further demonstrated by Lacto phenol cotton blue staining. The identification of *Candida* was made by using the Germ tube test. Anti-fungal susceptibility test was done by disk diffusion method using medium Muller–Hilton agar with glucose and methylene blue.

All the patients were treated by removal of fungal debris by aural toileting, followed by topical Clotrimazole 4 drops, 3 times a day for 7 days with avoidance of oil and water entry in the ear. Patients were followed up after 7 days and a repeat ENT examination was done. Repeat ear swabs were sent for KOH wet mount and sabouraud dextrose agar culture. For symptomatic patients and positive KOH wet mount after 7 days, treatment was changed according to anti-fungal susceptibility test.

RESULTS

230 patients fulfilling the eligibility criteria were enrolled in the study. There were 98 (42.6%) males and 132 (57.4%) females. In 211 (91.7%) patients, only unilateral ear involvement was observed, 110 (47.8%) had right ear involvement, and 101 (43.9%) had left ear involvement, while bilateral otomycosis was seen in 19 (8.3%) patients (Figure 1). The common predisposing factors were

instillation of mustard/coconut oil (20%), antibiotic ear drop use (12.6%), self-cleaning (10.4%), and swimming/water instillations (4.9%).

Itching (70.9%) was the most common presenting complaint, followed by the sensation of the blocked ear (39.6%), ear discharge (37.4%), pain in the ear (30.9%), hearing difficulty (9.6%) and ringing sensation in ear (7.8%). 189 (82.2%) patients were KOH wet mount positive. Fungal culture positivity was seen in 203 (88.3%) cases (Table 1). *Aspergillus* genus was the dominant pathogen (91.1%). There were only 18 (8.9%) cases where *Candida* was identified. Within the *Aspergillus* genus, *Aspergillus niger* (50.2%) was the most common pathogen, followed by *Aspergillus flavus* (30.0%) and *Aspergillus fumigatus* (10.8%) (Table 2 and Figure 2).

Among different antifungals used, Voriconazole had the highest sensitivity (94.1%), followed by itraconazole (92.6%) and clotrimazole (81.3%). Caspofungin (12.3%) and fluconazole (7.9%) were the least sensitive antifungals (Table 3 and Figure 3).

Table 1: Distribution of cases according to specific investigation finding

S. No.	Finding	No. of cases	Percentage
1.	KOH wet mount positive	189	82.2
2.	Fungal culture positive	203	88.3

Table 2: Microbiological profile of culture positive specimen (n=203)

S.No.	Fungal species isolated	No. of cases	Percentage
1.	<i>Aspergillus</i>	185	91.1
	<i>Aspergillus niger</i>	102	50.2
	<i>Aspergillus flavus</i>	61	30.0
	<i>Aspergillus fumigatus</i>	22	10.8
2.	<i>Candida</i>	18	8.9

167 (83.3%) patients responded to primary treatment (topical clotrimazole), 36 (16.7%) patients were non-responders. All the non-responders were given topical Itraconazole ear drops, and all responded effectively on subsequent follow-up.

DISCUSSION

Otomycosis is a superficial mycotic infection of the external auditory canal, frequently encountered in the outpatient department by otolaryngologists. Fungi are found abundantly on decaying plant matter and can get blown by the wind with soil particles or can be carried away by water vapors during the rainy season. This correlates well with a higher rate of fungal infections during the rainy season. The relative humidity is high during the rainy season, approx 75–100%, these conditions are very conducive for fungal growth,² and additionally, the moisture, warmth, and acidic pH of the external auditory canal provide an ideal growth environment for the fungi.



Figure 2: Sabouraud dextrose agar with chloramphenicol medium showing growth of *Aspergillus flavus*



Figure 1: Otoscopic image of left ear showing fungal spores and debris suggestive of left otomycosis



Figure 3: Antifungal susceptibility testing of *Aspergillus fumigatus*

Table 3: Antifungal Susceptibility profile (n=201)

S. No.	Antifungal	<i>Aspergillus flavus</i> (n=61)			<i>Aspergillus fumigatus</i> (n=22)			<i>Aspergillus niger</i> (n=102)			<i>Candida</i> (n=18)		
		S	R	Sens	S	R	Sens	S	R	Sens	S	R	Sens
1.	Clotrimazole	45	16	73.8	16	6	72.7	87	15	85.3	17	1	94.4
Overall sensitivity=81.3%; $\chi^2=5.251$; P=0.154													
2.	Voriconazole	53	8	86.9	21	1	95.5	99	3	97.1	18	0	100.0
Overall sensitivity=94.1%; $\chi^2=5.211$; P=0.157													
3.	Itraconazole	53	8	86.9	22	0	100.0	97	5	95.1	18	0	100.0
Overall sensitivity=92.6%; $\chi^2=4.896$; P=0.180													
4.	Fluconazole	8	53	13.1	3	19	13.6	5	97	4.9	0	18	0.0
Overall sensitivity=7.9%; $\chi^2=6.351$; P=0.096													
5.	Caspofungin	16	45	26.2	5	17	22.7	2	100	2.0	2	16	11.1
Overall sensitivity=12.3%; $\chi^2=24.124$; P<0.001													

Obsessive manipulation of the external ear with any hard objects, such as wooden sticks or metal wax picks to clean the ear, and vigorous rubbing of the ears for relief from itching is also a common practice. These practices may cause unnoticed minor trauma to the skin of the external auditory canal and deposition of fungal conidia in the wound, thus creating, thereby leading to fungal infection.⁷

While some studies have reported otomycosis as more common among young men⁸⁻¹¹ as in our study, many others have reported it to be so among young females^{2,12-14} between 12 and 30 years. The predisposing factors observed in the study population were mustard/coconut oil use (20%), antibiotic ear drop use (12.6%), self-cleaning (10.4%), and swimming/water instillation (4.9%). However, in a study by Ahmed et al.,¹⁵ the most commonly identified predisposing factor was self-inflicted trauma to the auditory canal (36%) followed by swimming (27%), associated chronic disease (21%), and prolonged use of antibiotics/immunosuppressives (16%). Mustard oil instillation is a commonly used agent to relieve itching in the ear and has a significant association with otomycosis.¹⁰ Presenting symptoms were itching (70.9%), the sensation of a blocked ear (39.6%), ear discharge (37.4%), pain in the ear (30.9%), hearing difficulty (9.6%) and ringing sensation in the ear (7.8%). Other studies^{2,7,8,14} have also shown similar symptoms, with itching being the most common. Otomycosis can be classified into primary or secondary type.³ Fungal otitis externa in an immuno-competent individual with no other external or middle ear pathology is termed as primary otomycosis. Fungal otitis externa in the following patients is termed as secondary otomycosis (a) existing bacterial otitis externa/media (b) postoperative ears (c) history of an existing fungal infection in other parts of the body (d) serious debilitating disease (e) an immunocompromised patient.

Out of total of 230 samples, fungi were isolated in 203 samples, with a high isolation rate of 88.3%. *Aspergillus* was observed in (91.1%) of the total fungal isolates

and there were only 18 (8.9%) cases where *Candida* was identified as the pathogen. *Aspergillus* has also been reported as the most common constituent in other studies.^{10,16-19} Within *Aspergillus* genus, *A. niger* (50.2%) was the most common species, followed by *A. flavus* (30.0%) and *A. fumigatus* (10.8%). In some studies, however, other species of *Aspergillus*, such as *fumigatus* and *flavus* were found to be the most commonly implicated fungi.⁹ In some other studies, *Candida* was reported to be the most common fungi isolated in cases of otomycosis.^{12,20,21}

Antifungal susceptibility testing is performed by microbiology laboratories as a tool to aid in the selection of the optimal antifungal agent. It provides an *in vitro* measure of susceptibility and resistance by determining the concentration of drug required to inhibit an organism to a specified degree. As more therapeutic choices became available, the value of detecting antifungal resistance and the need for optimization of the antifungal choice increased. Antifungal susceptibility testing may be used to determine susceptibility profiles and empirical therapy for local fungal pathogens.²² Among different antifungals used voriconazole had the highest sensitivity (94.1%), followed by itraconazole (92.6%) and clotrimazole (81.3%). Caspofungin (12.3%) and fluconazole (7.9%) were the least sensitive antifungals.

Gharaghani et al.,²³ too in their study found caspofungin to be resistant in a high proportion of *Candida* specimens (77.8%). They also observed a low sensitivity of fluconazole against *Aspergillus* species, and terbinafine was found to be the most effective antifungal agent against both *Aspergillus* as well as *Candida* species. Sarwestani et al.,¹⁶ demonstrated a wide variability in the sensitivity of clotrimazole against different *Aspergillus* species. However, the study at hand did not find any significant difference with respect to the sensitivity pattern of clotrimazole against different *Aspergillus* species as well as *Candida*.

A total of 167 (83.3%) patients responded to primary treatment and 36 (16.7%) were non-responders. All

the non-responders to primary treatment were given itraconazole and all of them were symptom free on next follow-up after 7 days. Response to primary treatment (Clotrimazole) was seen in 82.1% while all the non-responders to primary treatment responded positively to secondary treatment (Itraconazole). Other studies have also shown similar responses to clotrimazole and itraconazole in otomycosis.^{24,25} Itraconazole is an effective alternative to a traditional method of treatment for otomycosis.²⁵ Compared to the study under discussion, different response to primary treatment was noted in several other studies. For instance, Prasad et al.,³ reported that only 23% of the otomycotic patients were treated with clotrimazole alone and were cured completely. They required combined use of antifungals and antibiotics in the remaining 77% of patients and reported complete remission in all of them too. Additional use of antibiotics in their study could be owing to the concomitant presence of bacterial pathogens in a sizeable proportion of their cases (63%).

Limitations of the study

We have used the conventional methods to isolate and characterize the fungal agents. In future studies, the use of culture independent diagnostics and molecular detection of resistance may be rapid and efficacious.

CONCLUSION

Otomycosis is a highly prevalent disease in Indian population with a significant discomfort to the patients. This study revealed *Aspergillus* spp. to be the main contributory pathogen for primary otomycosis. While resistance against fluconazole and caspofungin was the characteristic finding, voriconazole and itraconazole were found to be highly sensitive. In view of high culture positivity rate, it is prudent that all the clinically suspected patients should be evaluated for fungal positivity, which may further guide in selection of appropriate anti-fungal agent. Awareness regarding the predisposing factors for otomycosis in the general population may result in a significant drop in the incidence of otomycosis.

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IA- Implementation of study protocol and prepared first draft of manuscript; **RKG-** Implementation of study protocol and manuscript preparation; **AB-** Concept and design of the study; **FSM-** Manuscript revision; **SS-** Literature survey, statistical analysis and interpretation; **FH-** Implementation of study protocol; **AS-** Data analysis; **HS-** Data collection.

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