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Otomycosis, Review

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Abstract **Review Article**

The word "otomycosis" refers to a specific type of fungal infection affecting the external auditory canal. It appears to be a highly prevalent clinical condition seen in otorhinolaryngology outpatient departments worldwide. Most *Aspergillus* and *Candida* species are the etiological microorganisms that form biofilm inside the ear canal. The development of otomycosis can be caused by improper self-cleaning, self-medication, and the insertion of needless instruments into the ear canal. Ear pain, discharge from the ears, and hearing loss are the main signs of otomycosis. Therefore, in order to take a percussive action during the primary stage of infection, the correct diagnosis is imperative. However, special medical attention is required, particularly in patients with low immunity, when infection spreads to a mastoid area with a suppurative condition. The purpose of this thorough review is to raise awareness of the importance of good health education and self-hygiene in order to maintain a healthy lifestyle. The majority of cases of otomycosis affect one ear, and immunocompromised patients are more likely to experience bilateral involvement. The most often mentioned risk factors include swimming, applying mustard oil to ears, overusing antibiotic ear drops, using Q-tips, wooden sticks, metal pickers, and self-cleaning of ears with these items. *Staphylococcus aureus* is the most frequently implicated bacterium in cases of concurrent otomycosis. In order to lower the incidence of otomycosis, this literature review emphasizes the necessity of education in order to eliminate the previously mentioned predisposing risk factors.

Keywords: External ear, ear canal, Aspergillus, Otitis, Candida.

I. INTRODUCTION

Otomycosis, also referred to as ear infectious disease, affects the external ear canal and is more common in warm, humid, and dusty environments [1]. It causes inflammation. *Aspergillus* and *Candida* are common fungal species that are used as causative agents or microorganisms. *Candida albicans* causes white, fluffy otorrhoea, while *Aspergillus niger* and Aspergillus fumigates give off a black pepper-like appearance [2]. Otomycosis can be caused by a swimming habit (not drying the ear after swimming), persistent and recurrent infections in the ear, using ear drops without a doctor's advice, using steroid-containing medications and oil, excessive ear wax buildup, not cleaning the ear [3] Opportunistic fungal infections have become more significant in medicine in recent years due to weakened immune systems. But these kinds of fungi are extremely widespread across all demographic groups, and they primarily infect immunocompetent hosts [4]. It is important to take extra precautions to avoid hearing loss. Treatment ought to be started as soon as possible, particularly for inpatients with weakened immune systems [5].

Recent molecular techniques and analyses have revealed that the *Aspergillus niger* complex comprises 28 different species of black molds, with *A. tubingensis* and *A. niger* being the most common causes of otomycosis. Despite their rarity, *A. welwitschiae*, *A. awamori*, and *A. foetidus* have also been reported to be the species responsible for this infection [6]. The precise molecular identification of these black fungi is essential for the development of rapid diagnostic tests for *Aspergillus* otomycosis and the selection of the best course of treatment for the different species in this complex. Although species of the *A. flavus* complex are also frequently isolated, *A. terreus*, *A. fumigatus*, *A. versicolor*, and *A. luchuensis* are less frequently the cause of infections than the previously mentioned molds [7]. Over the course of the preceding year, *A. sydowii* was identified as a potential human pathogen in immunocompromised patients. In two cases, the fungi were identified through molecular analysis using external auditory canal material extracted during tympanomastoidectomy procedures [8].

A frequent cause of otomycosis, aside from *Candida albicans*, has also been identified as *C.*

parapsilosis, especially in Europe where it is highly prevalent. Other *Candida* species, such as *Candida lustaniae*, *Candida guilliermondii*, *Candida famata*, *Candida tropicalis*, *Candida krusei*, and *Candida glabrata*, have also been isolated and identified as the etiological agents of the external auditory canal infection, despite their relatively low incidence [9]. Also found to colonize external auditory canal skin and possibly be the source of the infection is *C. auris*, a highly pathogenic fungal pathogen that is still in its infancy.This has the potential to spread and is highly concerning because of its multi-drug resistance [10].

A recurrence of otomycosis is possible if treatment is not administered appropriately. One of the reasons for recurrence is also the rising number of antifungal resistance cases. So proper care and monitoring are necessary to stop the spread of fungal infection [11]. Educating people about otomycosis and its treatment is the goal of this thorough review.

II. LITERATURE REVIEW

A. Epidemiology

The intricate structure of the ear aids in both hearing and maintaining balance. various types of ear problems in patients of various ages. Otitis externa, an inflammatory condition that can be acute or chronic, affects 4 out of every 100 people. Acute cases account for 3-5% of cases, while chronic cases affect 3-5% of the population [12]. In Iraq of Hilla city, According to one study (51.6% males, 48.4% females), males were more affected than female patients with otomycosis [13]. 101 patients (74.8%) with otomycosis were diagnosed out of 135 patients who were suspected of having the disease; 44 patients (43.6%) were male and 57 patients (56.4%) were female. Eighty-three cases, or 82.8% of the patients under study, had unilateral disease in Basrah, Iraq [14]. On the other hand, Mosal City, Iraq demonstrated a higher prevalence of females in 26 specimens (43.3%). The most common condition in the aged group of 15–40 years specimens (31.3%) was otomycosis [15, 16]. Some of the studies 17 and 18 reported otomycosis in Iraq.

According to a study conducted in Saudi Arabia, approximately 49.3% of participants had ear problems, 37% of elderly patients had hearing impairment, and 9.4%–2.9% of participants had otitis media [19]. A study found that whereas children under 4 had acute ear infections, patients in the 15–44 age range experienced chronic infections [20]. A few research studies otomycosis was reported to have a high incidence in tropical countries in [21-25]. It has been observed that otomycosis infections tend to start more frequently in July and August, and young patients in the managed group had higher rates of ear infections [26-28], While the prevalence of otomycosis in female patients is lower, some studies [29-33] reported female otomycosis in female patients. In 2015, reported a high incidence of otomycosis in the 21–30 year old age group [34].

In particular, many species of mold and yeast have been found in Africa [35], Central America [36], South America [37], Asia [38-40], and Central America [41]. Seasonality has not been observed in surveys carried out in Europe [7].

B. Pathogenesis

The outer surface of the ear has a higher potential for fungal colonization because it is a humid area with a pH that is favorable for microbes [42]. The precise microbiological test and clinical observation organism responsible for the infection must be identified. Before, it was believed that otomycosis was exclusively caused by fungi, but additional research revealed that bacteria can also cause this infection [43].

The correlation between *Staphylococcus aureus and pseudomonas aeruginosa* with the otomycosis has been documented. In 2011, reported that 10% of fungi were associated with principal requirement [44]. Additionally, it has been noted through otoscopic examination that a black fuzzy growth on the cerebrumen may obstruct the external auditory canal, resulting in mild hearing loss. Furthermore, candida albicans is observed to have a stronger correlation with otomycosis than any other species. Compared to A. niger, A. fumigatus is more common to cause invasive otomycosis [45]. These saprophytic microbes can become pathogenic if the balance between fungal and bacterial growth is disturbed, especially if non-specific and specific body defense mechanisms are compromised [44, 46]. Otomycosis is caused by two different kinds of factors: environmental and host-derived. It should come as no surprise that tropical and subtropical areas have the highest prevalence of otomycosis since these areas have the warm, humid climate that is the main external risk factor for the disease [47, 48]. The unique anatomy of the external auditory canal, excessive cerumen secretion, localized ear canal trauma, wearing hearing aids with an occlusive mold, and immunocompromised health status are examples of host-derived risk factors. Otomycosis may also develop as a result of an earlier external auditory canal bacterial infection that was managed with topical antibiotics. In patients with untreated dermatomycosis, the illness may also arise from autoinfection of the canal [49, 50].

C. Diagnostic protocols

The primary methods for diagnosing otomycosis are the history, clinical manifestation, and otoscopic examination of the eardrum and canal. However, additional testing such as microbiological analysis or histological examinations may be necessary in severe or protracted cases of otomycosis in order to confirm the diagnosis and identify the causative organism. Rarely, imaging tests may also be utilized to assess the infection's severity or rule out other potential explanations for the symptoms [51, 52]. Differentiating between otomycosis and other infections can be challenging, particularly when diffuse external otitis is

present. Diagnosis is made more challenging when the sampled material contains bacteria or fungi, such as *Klebsiella* spp., *Pseudomonas* spp.,*S. aureus*, coagulase-negative *Staphylococci* [53].

Conventional methods for obtaining laboratory-based evidence for the diagnosis of otomycosis are employed. Microscopical analysis is an indispensable, quick, inexpensive, and simple technique for identifying fungi in patient material. Wet mount (native or containing chloralactophenol or KOH) is still a useful technique for screening and direct microscopy examination since it enables the prompt identification of fungal blastoconidia-yeast and pseudohyphal-hyphal forms in patient material. These methods do, however, have limitations, such as decreased sensitivity, an inability to identify the species of causal agents, and difficulties distinguishing infectious agents from contaminants [54].

The process of growing, isolating, and identifying the fungus from the sampled material remains the most dependable way of diagnosis [55]. It is crucial to stress the necessity of multiple mycological examinations, up to three in number, in order to correctly interpret cultivation-based mycological results and differentiate fungal causative agents from fungal microbiota, or transitory fungal flora. These are excellent but labor-intensive methods that allow antimicrobial susceptibility testing, etiological agent identification, and genetic and biochemical characteristic determination [7]. Both bacteriological and mycological analyses are necessary for microbiological examination. Selective media are used in the cultivation of infectious agents to isolate molds, yeasts, and bacteria. Sabouraud agar is mixed with dextrose or maltose (SDA), antibacterial drugs to inhibit bacterial growth, and cycloheximide to inhibit mold growth in order to isolate yeast in vitro. It is recommended to cultivate yeast in an aerobic environment at 37℃ for 48–72 hours. It has been recommended to use Candida-chromogenic media, which allows the differentiation of *Candida* species even in the primary isolate based on the discoloration of the colonies, since *Candida* spp. is the primary cause of otomycosis. Chromatogenic selective media can be used to facilitate the differentiation of three species of *Candida* during primo-isolation: *Candida albicans* forms green colonies, *Candida tropicalis* forms blue colonies, and *Candida krusei* forms pink colonies with a rough appearance [57]. These media are extremely important because they make it possible to diagnose mixed infections resulting from various species of Candida, something that cannot be done with other media. It's crucial to provide molds the ideal conditions during mycological analyses. This includes media with increased carbohydrate content and inactive antibacterial medications. Furthermore, it is recommended that molds be cultivated for (7–14) days at (26–28) ℃ in an aerobic environment (note that certain mold species require this temperature for growth) [58]. If the protocols for culturing fungi, especially molds, are not followed, the microbiological examination may result in a false positive in a specific percentage of patients. Assimilation, other biochemical tests, or even automated systems (VITEK) in more advanced labs can be used to distinguish between different species of yeast. These tests are used to identify the unique phenotypic traits of various species.

Researchers and scientists are working to develop non-culture techniques that can reduce the delay between sample and results to circumvent the limitations and drawbacks of traditional techniques. Through molecular analysis of black *Aspergilli* isolates from patients with otomycosis, a high species diversity was discovered within the *Aspergillus niger* complex in one study. This method may make it possible to create quick molecular testing for otomycosis by identifying targets for identification at the molecular level [59]. *Aspergillus* molds' partial-tubulin gene sequences were analyzed, and it was discovered that *A. niger* and *A. tubingensis* were less sensitive to antifungal drugs than other species. Identification of the infectious agents as soon as possible and with precision can help choose the best antimycotics in a timely manner [60].

D. Treatment

Experts disagree on the best course of action for treating fungal infections due to the absence of official therapeutic guidelines and protocols. Furthermore, there is no indication of how long the treatment will last. Determining the best course of action therefore requires careful evaluation of the available data, patient characteristics, and clinical judgment [61].

Many authors feel that in order to select the most effective antimycotic, Using the previously established specific sensitivity and determining the causative agent are essential. Nevertheless, some authors contend that, independent of the type of infection, it is wise to choose a suitable course of action based on the medication's general efficacy and qualities. A combination of oxytetracycline, polymyxin B, and dexamethasone is usually administered for a maximum of 15 days to treat otomycosis locally, with nystatin being the first-choice medication in France. This polyene is highly active against molds and yeasts, but its efficacy against Aspergillus spp., one of the main causes of otomycosis, has been the subject of conflicting opinions in the literature [62]. However, clotrimazole, a topical imidazole, is acknowledged as the preferred medication in the USA for the management of simple otomycosis [63]. As a result, new research from India indicates that topically applied 1% clotrimazole cream may be an effective treatment for otomycosis. However, because of its lower efficacy against Aspergillus otomycosis, clotrimazole is not considered a first-choice medication in some smaller sample size studies [64].

Otomycosis may also be treated with other antifungal medications, including ciclopiroxolamine, isoconazole, bifonazole, and miconazole [65]. Nonetheless, research conducted in vitro and through treatment monitoring has demonstrated that these antifungals act differently on molds and yeasts, with miconazole having less of an impact on different species of the genus Candida [66]. Research has also indicated that efinaconazole, lanoconazole, and luliconazole exhibit good in vitro effectiveness against Aspergillus species. The most frequent agents causing otomycosis, A. niger and A. tubingensis were found to be less susceptible to ravuconazole [67]. Sertaconazole treated otomycoses well in a study conducted last year that compared its clinical efficacy with other imidazoles; however, when compared to treatment with miconazole and clotrimazole, no significant difference was observed [68].

A recent study involving more than 300 patients with fungal ear infections in Russia suggested that in order to evaluate the efficacy of treatment, mycological control be required in addition to clinical examination [69]. The results of the study indicated that the most effective treatments for *Candida* otomycosis were clotrimazole or allylamines (terbinafine and naftifine), while the most effective local treatments for mold-induced otomycosis were terbinafine, naftifine, and chlornitrophenol. It was observed that at least three to four weeks of continuous laboratory monitoring should be spent applying local antifungal treatments. Comparable results were observed in a Serbian study using an analogous design, which demonstrated that naftifine and nystatin were more effective than clotrimazole in treating patients with Aspergillus otomycosis [40].

These results support the potential effectiveness of allylamines, such as terbinafine and naftifine, in the treatment of otomycosis caused by yeasts or molds, as also indicated by a recent study [64], which demonstrated that terbinafine was nonon-toxic to the inner ear end organs at a dosage of 0.4 mg.

As per Khrystyna Herasym's (2016) findings, otomycosis has been studied for treatment with various antiseptics, acidifying agents, and medications containing antiinfective agents with corticosteroids; however, there is insufficient evidence to suggest that these treatments are more effective than antimycotic ones. Topical antifungal drugs should also be applied following thorough ear canal debridement for patients with noninvasive infections [65].

Another significant point is that antifungal ointments have clear advantages over liquid formulations. Creams with a higher viscosity are believed to be safer to use in patients with perforated eardrums because they remain on the skin's surface longer, reducing the possibility that the medication will enter the middle ear [45].

One recommended use practice is to soak cotton wool or gauze pads in liquid antimycotic formulations and place them into the ear canal for five to ten minutes, twice a day [60]. Along with all of the previously mentioned treatment options, it's critical to return the ear canal to its physiological state by limiting topical medication use and shielding the canal from additional harm that could upset the balance of the environment [70].

Triazole antifungal drugs (fluconazole, itraconazole, voriconazole, posaconazole) are examples of systemic antimycotics that may be used in cases of severe otomycosis or when previous local therapy has not worked [58]. These medications work well against infections brought on by *Aspergillus* and *Candida* fungi, and they are crucial for treating more complicated forms of the illness, particularly when meningitis and mastoiditis are present [71].

Examining the antifungal susceptibility in vitro, however, revealed that the otomycosis-causing agents, fluconazole (MIC = 32 mg/mL), may have varying effects on non-albicans Candida species. It was further demonstrated that *C. krusei* was less sensitive to itraconazole (MIC = 0.5 mg/mL) in addition to fluconazole. This emphasizes how crucial it is to pinpoint particular causative agents and carry out susceptibility testing in order to help determine which systemic antifungal therapy is best for treating severe cases of otomycosis [7].

III. CONCLUSION

Otomycosis is usually a benign condition that poses no threat to life, much like other superficial fungal infections. However, the high frequency of these infections, the frequent occurrence of chronicity, the decline in the quality of life of those afflicted, and uncommon side effects that call for a different approach to diagnosis and treatment (such as perforation of the tympanic membrane or widespread infection affecting the central nervous system, bones, and nerves).

In cases of persistent inflammation of the external auditory canal, laboratory analyses are recommended. Microbiological examination should include not only bacteriological analysis but also mycological analysis, which includes methods for isolating mushrooms.

Molds and yeasts alike. It might be necessary to conduct up to three serial cultures in order to accurately interpret the results and distinguish between saprophytic and pathogenic fungi.

Specific fungal causative agents should be taken into consideration when choosing a treatment plan,

including the antimycotics to use and the application technique. Systemic antifungal medications, however, need only be taken into consideration in situations involving immunodeficiency. Following established procedures and guidelines for diagnosis and treatment can be very helpful in selecting the appropriate medication and duration of care.

Conflict of Interest: Authors declare that they have no conflict of interest.

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