

Outer Ear Infections in Iran: A Review

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Abstract

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BACKGROUND: Otitis externa is the fungal and bacterial infection of the outer ear.

AIM: We aimed to investigate the published papers about the outer ear infections in Iran and suggest standardised investigations and treatments.

METHODS: We used different electronic databases like PubMed, Scopus, Web of Science, Iranmedex, Google Scholar, and Magiran with specific keywords.

RESULTS: We obtained forty published full-text articles for review of data. Our results indicated the women were more infected than men. The ages of patients were < 1-81 years. As clinically symptoms, itching and Feel the ear fairy were the most common presenting complaints in most cases. Most infections were the pure bacterial and fungal origin, respectively. However, some of the studies were mixed fungal-bacterial infections — Pseudomonas spp. And Aspergillus niger were the most common bacteria and fungi isolates respectively in Iranian patents.

CONCLUSION: Fungal and bacterial specific cultures may be recommended, and anti-fungal drugs may be added, to treatment regimens in patients with otitis externa to reduce the clinical symptoms.

Introduction

Outer Ear Infection (Otitis Externa) refers to any infection of the auricle and ear canal, which is presented with no rupture and originated from microorganisms and accounts for about 5% to 20% of the total cases referring to the ear, nose, and throat clinics [1]. This type of infection is usually classified into two acute and chronic diseases [2]. Outer ear infection is one of the most common types of ear infections that physicians are faced with daily. The needs of information about the symptoms and causes of outer ear infections, this review study was performed for relevant clinical and laboratory investigations carried out in Iran. In the current study, all articles on humans' outer ear bacterial and fungal infections, bacterial-fungal infections, and drug

sensitivity tests, which were conducted in Iran and published in authentic Iranian and non-Iranian journals, were reviewed. All published articles were obtained in electronic databases like PubMed, Scopus, Web of Science, Iranmedex, Google Scholar, and Magiran. The search keywords included outer ear, ear infection, fungus, bacteria, bacterial-fungal infection, and Iran.

Exclusion Criteria

In each study, there are some factors causing the exclusion of the patients. In studies on the outer ear infections, some intervening factors including the use of antibiotics (antibacterial or antifungal, according to the type of examination or infection), eardrum rupture, negative result of direct tests, middle

ear lesions without outer ear infection and surgery history (except for the successful myringoplasty and tympanoplasty surgeries), as well as the patients' lack of willingness to participate in the study were considered as exclusion criteria, and those meeting these criteria were excluded from the outer ear infections studies [3], [4], [5].

Patients' Age

Surveys conducted in different regions of Iran in the field of outer ear infections have shown that such infections are observed in all ages and the age of participants in such studies ranged from 1-81 years. Children are among those being infected with ear infections. In a study, all age groups ranging from children below one to teenagers aged 18 years with a mean age of 2.4 ± 7.5 years old suffered from ear infections, most of whom were below the age of 6 years [3], [4], [5]. Meanwhile, the average age of the patients was 10.5 years old in another study [6]. In adults, bacterial infections are more common when they are 20-29 years [7], [8] and 30-40 years old [9]. A majority of the patients were within the fourth decade of their lives [4], [10], [11]. The lowest frequency was observed for the patients aged between 50 and 59 years [7].

Otomycosis has also been observed at different ages so that the individuals aged 7-81 fall into this category [5], [8], [12]. However, the oldest patients had different years of age in different studies. The most affected ages included 10-20 years [13], 20-29 years with the average age of 35.17 years [14], 30-34 years with the average age of 30.7 years [8], 35-44 years with an average age of 43.21 years [15], 30-50 years with an average age of 17-35 years [16] and 38-48 years [5].

Patients' Gender

There is a possibility of outer ear infections in both genders; however, various studies show different frequencies for both genders. In most studies, women were more likely than men to suffer from such infections: 54.31% [4] 67.3% [8], 74.2% [17] and 89.2% [7] (Table 1).

Of course, in an investigation on children with outer ear infections, it was revealed that a larger number of boys (60.7%) were affected than girls (39.3%) [3]. Fungal infections of outer ear were also observed in both genders; however, some studies showed that the infection was more common with a range of 50.29 to 82.9% among females than males [5], [8], [12], [14], [15], [16], [18], [19], [20], [21], [22], [23]. In some studies, males were more likely to be involved with fungal ear infections than females, so that the incidence rate in males varied from 53.96%-69.23% [12], [13], [24], [25], [26]. A review study, though, showed that the overall ratio of outer ear

fungal infections was 1/53 in males to females [27].

Table 1: The frequency of sex in otitis externa in Iran

Total	Gender		Ratio (m/F)	Reference
	Male (%)	Female (%)		
75	33 (44)	42 (56)	0.79	Akhi MT, 2001 [9]
70	12 (17.14)	58 (82.56)	0.21	Kochack Alavi SK, 2004 [7]
20	12 (60)	8 (40)	1.5	Afshari MA, 2005 [26]
15	4 (26.7)	11 (73.3)	0.36	Zareii Mahmoodabadi A, 2006 [19]
174	86 (49.4)	88 (50.6)	0.97	Balouchi M, 2006 [18]
70	12 (17.1)	58 (82.9)	0.21	Bineshian F, 2006 [14]
25	15 (60)	10 (40)	1.5	Pakshir K, 2008 [35]
52	36 (69.23)	16 (30.77)	2.25	Yegane Moghadam A, 2009 [24]
26	12 (46.7)	14 (53.3)	0.86	Zareii Mahmoodabadi A, 2010 [20]
120	36 (30)	84 (70)	0.43	Rajabnia R, 2010 [29]
246	157 (67.79)	89 (32.21)	1.76	Hajjertababar M 2010 [31]
118	61 (51.69)	57 (48.31)	1.07	Barati B, 2011 [12]
54	16 (29.63)	38 (70.37)	0.42	Berjis N, 2012 [21]
293	131 (44.7)	162 (55.3)	0.81	Saki N, 2013 [22]
114	67 (58.77)	47 (41.23)	1.43	Nowrozi H, 2014 [16]
100	38 (38)	62 (62)	0.61	Nemati S, 2014 [5]
49	34 (53.96)	15 (46.04)	2.27	Ebrahimzadeh A, 2014 [13]
6	25 (44.64)	31 (55.36)	0.81	Kiakojuji K, 2015 (JJM) [15]
129	76 (58.91)	53 (41.09)	1.43	Kazemi A, 2015 [25]
184	90 (48.91)	94 (51.09)	0.96	Kiakojuji K, 2015 [3]
1990	953 (47.89)	1037 (52.11)	0.92	--

Place of Residence

Although the place of residence can play an effective role in the infection rate due to the different economic and social conditions, surveys show that the frequency of villagers and urban residents' referral for the diagnosis and treatment of ear infections depends on various conditions, including attention to their illness, access to health care facilities, and the presence of specialists with private clinics. In some surveys, urban residents were more likely to refer to the clinics for the sake of ear infections, with a rate of 77.59%-86.3% in urban areas and 17.5%-22.41% in rural areas (3, 4, 24, 28, 29). Of course, the other studies indicated that the villagers (82.81%) were more affected by this disease than the urban population (17.19%) [11].

Patients' Occupation

The occupation of the affected is less likely to affect the ear infections; however, it was found that the housewives (37.7%) are more likely to suffer from the outer ear infections than those having other occupations. The most affected individuals are self-employed (18.83%) and clerks (18.1%) [4]. A survey on children also revealed that 50% of the affected were students and the rest were below school age [3]. In one study, all the infected were farmers [25].

Predisposing Factors

In Bacterial infection

In case of underlying illnesses and predisposing factors of outer ear bacterial infections, it has been noted that the use of ear cleaners (89.1%), ear manipulation (95.6%), swimming at sea (9.1%), and swimming in pools (5/5%) are the most important factors predisposing this disease [8]. Also, ear infection history can also play a role in this regard

[29].

Although the role of the seasons has been less concerned in these studies, a study has shown that the disease was more frequent in the autumn (57.3%) than in other seasons. Meanwhile, the lowest infection rate was observed in the spring (16%), though, no justification is reported in this case [9].

In Fungal infection

The factors influencing the fungal infection include the use of antibiotics and steroid (21.91%-88.5%), swimming (5.08-16%), a history of swimming at sea (10.3%) and bathing (66.6%) [5], [18]. Also, the use of ear cleaners (84.6%), ear manipulation (87.2%), and trauma can also be noted in this regard [8], [12], [30].

The season can also be introduced as a predisposing factor so that the heat, which is a factor affecting the growth of the fungi, can be a contributing factor in some cases. It has been suggested that the number of the affected is higher in summer than other seasons (30.4%-45.61%), even though, the rate of infection in the autumn was high (57.3%) as well. On the other hand, the lowest rates are observed in the spring and winter [9], [12], [16], [22].

Clinical Finding

Outer ear infections have different signs and symptoms depending on the severity of the disease and its causes. In bacterial infections, the most common symptoms are swelling (82-93.96%), discharge (64%-86.21%) and hearing loss (57.66% - 90.51%). Furthermore, itching, scaling, and a feeling of fullness in ears were also other symptoms of outer ear bacterial infections [3], [4], [11], [31]. Pain is one of the symptoms of outer ear bacterial infection, and it has been shown that 64.8% of ear pain is related to outer ear infection [32]. In general, pain is seen in patients with outer ear infections (74.3%-85.9%) [3], [23]. In these infections, the pus, and discharge, as well as cerumen (in chronic forms) are in bright colours (white, yellow) and dark colours (light brown-dark brown) and this can partly reflect the pathogens [11], [15], [20], [33].

Symptoms of outer ear fungal infection, although similar to bacterial infections, are low in severity and prevalent in different individuals with various symptoms [14]; however, the most common symptoms are swelling, discharge, itching, tinnitus, and hearing loss [16], [23].

The presence of lump (69.2%), itching (65%), and pain (55%), a feeling of fullness in ears (46%), pus (40%), and auditory impairment (33%) was among the reasons of referring to the clinics [12]. In the clinical examinations, the absence of fever (89.7%), ear sensitivity (71.8%), the presence of a

fungal lump in Otoscopy (69.2%) and epithelium scaling (59%) are also diagnosed by specialists [8]. A totally, the itching had the highest rate (Figure 1).

Sampling

To have a definite diagnosis of the disease, the samples of pus, lump, skin, or anything in the auditory canal should be extracted by ear, nose and throat specialists. This can be performed under a microscope using a sterile swab, speculum, suction or curette, depending on the available facilities, the type of lesion, and the physician's expertise [3], [4], [6], [12], [14], [15], [34], [35].

Direct examination and culture

The samples should be tested within the least possible time in the laboratory. The speed at which the samples are inoculated in a culture medium to grow bacteria or fungi according to a physician's request and its spread on the lam for direct testing would bring more accurate findings and more appropriate treatment. The direct result of direct culture and testing plays the most critical role regarding the bacterial or fungal pathogens, respectively.

In the samples spread on the lam using the hot-stained method, the presence of bacteria in various forms or true or false mycelium show the presence of Otitis Externa, which is also consistent with the culture results [3], [13], [15], [16], [19], [31]. The samples suspected to outer ear fungal infections are usually lightened by potassium hydroxide (10%) and examined microbiologically [8], [13], [16], [25].

Culture

Suitable culture media for initial isolation and identification of bacterial or fungal factors causing otitis are different and essential for the diagnosis of bacterial infection. Various environments have been used as the primary and specific media for isolating and identifying bacteria. Specific media for bacterial growth include the blood agar (Sheep Blood), EMB, Thioglycolate, Mac Conkey's Agar, Chocolate Agar (CHOC), and Eosin Methylene Blue Agar [5], [8], [12], [14], [30], [31].

Usually, the culture media are incubated for 18 to 24 h or a maximum of 48 h at 37°C for the bacterial growth [17], [29], [31]. In all cases, sterile conditions should be observed to prevent environmental contamination [35]. Considering that the diagnosis of the bacterial ear infection depends on the positive culture results [4]; therefore, in order to determine the identity of the bacteria observed on the plates, it is necessary to detect them in differential media such as TSI, Cimon Citrate agar, STM, MRVP, Urea agar or Lysine Decar Boxylase [4], [8].

Meanwhile, enzymatic methods and other methods including catalase test, mannitol fermentation, Optochin, oxidase, liquid citrate, and ONPG are also used for the final confirmation of bacteria [3], [8], [31].

Such media as Suburo Dextrose Agar (S), Chloramphenicol (Sc) or Cyclohexamide (Scc) have been used for the growth of fungal agents and initial isolation of these factors [4], [5], [8], [13], [14], [34]. Occasionally, penicillin and streptomycin antibiotics have been used instead of chloramphenicol [35]. These media are kept for 1 to 4 weeks at 25°C, 25°C-27°C, or 30°C, aiming the growth of fungal elements [4], [12], [34].

In addition, the fungi were prepared using different methods such as chopped samples, Lactophenol Cotton Blue staining for initial identification of fungi, sugar adsorption using API 20C AUX kit, chromosomal method for identification of yeasts [14], production of serum germinal tubes (stored at 37°C), generation of vesicles (Chlamydoconidia) using Corn Meal Agar along with Polysorbate 80 and chrome agar for the diagnosis of *Candida albicans* [14], [35], Malt Extract Agar, Yeast Malt Agar, and culturing on lam for string fungi [8], [12], [13], [16], [22], [29].

Microbial Pathogens

In most studies, bacteria are considered as the main cause of outer ear infection, and the fungus is the secondary reasons. In some studies, however, the involvement of both bacteria and fungus is also reported. The number of isolated organisms is different in different studies, and the number of species is reported to be up to 23 bacterial species [9] and 17 fungal species [29].

Bacterial etiological agents

Bacteria, which, after direct testing of pus and discharge, are reported in most studies as the main cause of outer ear infections, consist of many variations. In a majority of studies, *Pseudomonas aeruginosa* (25.8%-79.3%) and *Staphylococcus aureus* (12.4%-63.46%) were among the most common bacteria; however, other bacteria extracted from the outer ear infections include gram-negative bacilli (49.99%), coagulase-negative staphylococci (CoNS) (12.5%-37.96%), *Enterobacteriaceae* (24.08%), *Bacillus* species (18.9%-23.2%), Gram-positive cocci (20.45%), *diphtheriae* (17.24%), *Pseudomonas* (11.3%) and *streptococcus* (10.71%) species [4], [6], [7], [8], [9], [14], [17], [28], [31]. Aerobic bacteria play a significant role in outer ear infections, and they have also been identified as agents of outer ear infections over recent years. In a study of 75 patients with an outer ear infection, 9 species (10.23%) of obligatory anaerobic gram-negative bacilli, including 2 species of Bacteroides and 7 species of fusiform, and 54 species (61.36%) of optional anaerobic species were isolated [9]. In most studies showed *Pseudomonas* spp., *Bacillus* spp., CoNS and *S. aureus* were predominant etiological agents of bacteria in these studies (Table 2).

Mix Bacterial infection

Based on laboratory results, although the main cause of the disease is usually an organism (bacteria or fungus), more than one organism is isolated from the outer ear auditory canal in some studies, in which the decision to determine the major pathogen and the choice of appropriate treatment is to some extent difficult. In of Kiakjouri's et al., study in Babol, 35% of individuals with outer ear infection had several bacteria [28].

Table 2: The distribution of etiological agents of otitis externa in Iran

Number	Total (%)	Number of cases (%)	Number of Species	The most fungal agents N (%)			Number of Species	The most bacterial agents N (%)			Reference
1	52	52	ND	<i>Candida</i> spp. 26 (50)	<i>Aspergillus</i> spp. 10 (19.23)	<i>Penicillium</i> spp. 4 (7.69)	ND*	-	-	-	[33]
2	75	75	14	Yeast	Mycelia	-	16	<i>Pseudomonas</i> spp. 25 (31.65)	<i>Enterobacteriaceae</i> spp. 19 (24.08)	<i>S. aureus</i> 13 (16.45)	[9]
3	101	78	-	<i>A. niger</i> 10 (12.82)	<i>A. fumigatus</i> 5 (6.41)	-	6	<i>Pseudomonas</i> spp. 29 (35.89)	<i>Prodenia</i> spp. 5 (6.41)	<i>S. aureus</i> 4 (5.13)	[8]
4	70	73	15	-	-	-	8	<i>P. aeruginosa</i> 35 (47.9)	<i>Enterobacteriaceae</i> spp. 16 (21.4)	<i>S. aureus</i> 14 (19.2)	[7]
5	35	20	-	<i>A. niger</i> 14 (43.7)	<i>C. albicans</i> 5 (15.6)	<i>A. fumigatus</i> 4 (12.5)	-	-	-	-	[26]
6	174	120	7	<i>A. flavus</i> 48 (40)	<i>A. niger</i> 44 (36.7)	<i>C. albicans</i> 8 (6.6)	-	-	-	-	[18]
7	70	8	9	<i>C. parapsilosis</i> 5 (62.5)	<i>C. glabrata</i> 2 (25)	<i>C. krusei</i> 1 (12.5)	-	-	-	-	[14]
8	15	15	3	<i>A. niger</i> 8 (53.33)	<i>A. flavus</i> 2 (13.3)	<i>A. fumigatus</i> 1 (6.67)	-	-	-	-	[19]
9	92	92	7	-	-	-	3	Coagulase negative <i>S.</i> 42 (45.2)	<i>S. aureus</i> 9 (9.5)	<i>S. pneumoniae</i> 4 (4.7)	[37]
10	55	123	4	<i>A. niger</i> 48 (39)	<i>Candida</i> spp. 45 (36.6)	<i>A. flavus</i> 21 (17.1)	-	-	-	-	[23]
11	243	25	10	<i>Penicillium</i> spp. 8 (32)	<i>Candida</i> spp. 5 (20)	<i>Alternaria</i> spp. 2 (8)	-	-	-	-	[35]
12	120	17	5	<i>A. niger</i> 8 (47.1)	<i>A. flavus</i> 3 (17.6)	<i>Rhizopus</i> spp. 3 (5.8)	-	-	-	-	[34]
13	91	52	8	<i>A. niger</i> 32 (61.9)	<i>C. albicans</i> 7 (13.5)	<i>A. fumigatus</i> 3 (5.8)	-	-	-	-	[24]
14	120	116	-	-	-	-	3	<i>S. aureus</i> 24 (20.8)	<i>Bacillus</i> spp. 22 (18.19)	<i>Pseudomonas</i> spp. 13 (11.3)	[36]
15	179	-	-	-	-	-	-	-	-	-	[31]
16	120	154	17	<i>A. flavus</i> 19 (12.4)	<i>Cladosporium</i> 18 (11.7)	<i>Mycelia</i> sterile 18 (11.7)	-	-	-	-	[29]
17	57	26	8	<i>A. niger</i> 8 (30.8)	<i>A. flavus</i> 6 (23.1)	<i>C. albicans</i> 3 (11.5)	-	-	-	-	[20]
18	60	60	-	-	-	-	-	-	-	-	[28]
19	66	-	-	-	-	-	-	-	-	-	[6]
20	171	118	6	<i>A. flavus</i> 53 (44.52)	<i>A. niger</i> 45 (38.14)	<i>C. albicans</i> 9 (7.63)	-	-	-	-	[12]
21	54	54	7	<i>C. albicans</i> 13 (24.1)	<i>A. niger</i> 13 (24.1)	<i>A. flavus</i> 11 (20.4)	-	-	-	-	[21]
22	100	13	-	<i>A. niger</i> 8 (8)	<i>A. flavus</i> 3 (3)	<i>A. fumigatus</i> 2 (2)	-	-	-	-	[38]
23	124	88	ND	-	-	-	ND	<i>S. aureus</i> 25 (29)	<i>P. aeruginosa</i> 23 (25.8)	-	[17]
24	77	-	-	-	-	-	-	-	-	-	[32]
25	293	-	ND	<i>A. niger</i> 197 (67.2)	<i>A. flavus</i> 38 (13)	<i>C. albicans</i> 34 (11.6)	-	-	-	-	[22]
26	63	49	17	<i>Aspergillus</i> spp. 15 (30.61)	<i>T. mentagrophytes</i> 11 (24.5)	<i>Mucor</i> spp. 8 (16.33)	-	-	-	-	[13]
27	200	114	4	<i>A. niger</i> 102 (89.4)	<i>A. fumigatus</i> 6 (5.3)	<i>C. albicans</i> 5 (4.4)	-	-	-	-	[16]
28	100	43	4	<i>A. niger</i> 21 (49)	<i>C. albicans</i> 14 (23)	<i>A. fumigatus</i> 7 (16)	-	-	-	-	[5]
29	50	-	-	-	-	-	-	-	-	-	[40]
30	140	129	11	<i>A. niger</i> 73 (62.3)	<i>A. flavus</i> 24 (20.7)	<i>A. fumigatus</i> 11 (9.5)	-	-	-	-	[25]
31	56	33	4	<i>A. niger</i> 20 (35.71)	<i>A. flavus</i> 6 (10.71)	<i>C. albicans</i> 4 (7.14)	10	<i>Bacillus</i> spp. 13 (21.23)	<i>Streptococcus</i> spp. 6 (10.7)	<i>Pseudomonas</i> spp. 6 (10.71)	[3]
32	184	184	11	<i>A. niger</i> 39 (21.2)	<i>Penicillium</i> spp. 24 (13.04)	<i>Candida</i> spp. 19 (10.33)	7	<i>Bacillus</i> spp. 36 (19.58)	Coagulase negative <i>S.</i> 28 (15.22)	<i>Streptococcus</i> spp. 14 (7.6)	[10]
33	56	54	10	<i>A. niger</i> 31 (55.36)	<i>C. albicans</i> 8 (14.9)	<i>A. fumigatus</i> 3 (5.35)	-	-	-	-	[15]
34	116	101	-	-	-	-	8	<i>Bacillus</i> spp. 26 (22.4)	Coagulase negative <i>S.</i> 23 (19.43)	<i>Diphtheroid</i> spp. 20 (17.24)	[4]
Total	3280	2086	-	806 (38.64)	344 (16.49)	185 (8.87)	-	254 (12.18)	151 (7.24)	88 (4.21)	-

ND*: Not Determined.

This rate was 15.9% in another study, which contained anaerobic and aerobic bacteria as well as the fungi [9]. In other studies, the presence of two or more bacteria was found to be between 11.29%-14.74% [6], [17].

Non-pathogenic Bacteria

All organisms isolated from the ear were not pathogenic, and some of them were as normal flora. This is confirmed in some studies. In a study on the isolated bacteria from the outer ear canal, 60.4% and 93.1% of the outer ear infection in the ear samples of patients and healthy people were respectively non-pathogenic bacteria, and the rest were pathogenic ones [36].

Bacteria in the healthy individuals' ears

The healthy individuals' ears can also contain different microorganisms as a result of their direct exposure to the surroundings, manipulation of the ear, and proximity to their surrounding organs. Studies have shown that the coagulase-negative staphylococci with a frequency of 45.2%-66.5% are the most common bacterial agent in cancer patients and non-cancer individuals. Due to the high presence of *S.aureus* in cancer patients (11.9%-15.7%), it is inferred that cancer patients are at higher risk of outer ear bacterial infection [37].

On the other hand, the ear cerumen of the healthy individuals also consists of different bacteria, the most common of which are *S. epidermidis* (38.7%), *diphtheria* (22.4%), *Bacillus* (19.58%), coagulase-negative *Staphylococci* (15.22%) and *Streptococcus* (7.61%) [10], [36]. Further studies confirmed the presence of bacteria such as coagulase-negative *Staphylococci* and *diphtheria* [6].

Fungi etiological agents

Although the main resources on ear disease have noted that only 10% of the outer ear infections are caused by fungi [35], this ratio has undergone a major change over recent years so that some surveys have reported the range of this rate from 11.4% [14], 14.3% [3], 19.64% [15] and 33.25% [22] to 43% [5]. In a study of 171 patients, 69% had fungal organisms, and 25.15% had bacterial infection [12]. The number and species of fungi generating otomycosis have also changed over these two decades. The number of fungal species isolated from otomycosis has also reached 17 in various studies [29]. In a majority of studies, saprophytes are the main cause of otomycosis (57.33%) [13]; meanwhile, the *Aspergillus* is the main source (41.66%) of this disease [12], [13]. On most studies, *A. niger* has been the main cause of otomycosis, with a rate of above 50% (55.36%-

40.48%) [5], [16], [19], [22], [24], [26], [38] (Table 2).

In some other studies, the role of this species has been reported to be non-significant in otomycosis (9.9%-39%) [8], [10], [12], [15], [23]. Over recent years, other species of *Aspergillus*, including *A. flavus*, have been identified as important factors in otomycosis [3], [18]. These studies have implied that this species has caused 4%-23.1% of otomycosis cases and acts the same as *A. niger* [3], [12], [20], [22], [23], [29]. Of the other species of *Aspergillus*, the role of which has been highlighted in otomycosis, is *A. fumigatus*, varying from 5.3% to 20.5% in different studies [16], [22], [25]. In the past decades, the impact of other saprophytes has been low in otomycosis; however, with a decreased role of *A. niger* and increased role of other species of *Aspergillus* in recent years, other saprophytes, such as *Penicillium* spp (2-13%) [10], [22], *Cladosporium* spp (11.7%) [29] and *Alternaria* spp (11.11%) [13] play a role in otomycosis.

Fungi without a horizontal blade, such as *Mucor* spp and *Rhizopus* spp, have played a significant role in otomycosis, as documented in some studies [13], [34]. Yeasts are considered as the second group of fungi in otomycosis, whose role is reported to vary from 8.9% to 24.1% [8], [13]. They are even reported in some studies as the major agents of otomycosis [21]. Of the various species that play a critical role in otomycosis [29], the *Candida albicans* have had the central role in most studies. This species in various studies have been caused otomycosis in 7.14%-14.29% of the cases [3], [12], [16], [22]. Other species such as *C. tropicalis* (50%) [8], *C. glabrata*, and *C. parapsilosis* [14], and the like have been introduced as main factors causing otomycosis [15], [23]. The third category of fungi causing otomycosis is dermatophytes, which play a less vital role in this disease. In a study, its frequency was found to be 17.32%, with *Trichophyton mentagrophytes* and *Trichophyton violaceum*, as well as *Epidermophyton floccosum*, being the main drivers of this infection [13].

Mix fungal infection

Fewer studies have investigated the role of several fungi in otomycosis. Studies have shown that only one fungal agent is mostly involved in otomycosis [13], [29]; however, the presences of two fungi (14%) and more than 2 fungi (42.5%) have been reported in some cases [3], [13], [29].

Isolation of fungi from healthy individuals

Because of the ears' connection with their surroundings, the fungi have also been isolated from cultivating ear cerumen of healthy individuals (without infection). These fungi include *A. niger*, *Penicillium*, and *Candida* [10], *A. Niger*, *A. flavus* and *Rhizopus*

spp [34], Sterile mycelium, *Cladosporium* spp [29] (8%), *Penicillium* spp, *Cladosporium* spp and *Candida* spp [35], *Cladosporium* spp, *Alternaria* spp and *Penicillium* spp [28] and *Aspergillus* spp, *Mucor* spp and *Rhodoturula* spp [13].

Bacterial-fungal infections

In some cases, the ear infection may also be caused by both fungi and bacteria (regardless of the primary role of each in causing infection). This can be diagnosed based on the positive results of direct testing and culturing for fungi and the positive culture result for bacteria. Such infections are of importance, especially in the field of treatment, and cause problems of ear infections [39]. This rate varies from 7.24% [17] to 15.2% [8] in these studies.

Lack of growth

The outer ear canal samples do not always have a growing organism in the common media since clinical symptoms may indicate bacterial or fungal ear infection with no growing organisms in appropriate bacterial or fungal media. This, while demonstrating the value of the culture results for the initiation of the treatment, indicates that some of the outer ear canal lesions are caused by other infectious agents such as viruses and non-infectious agents. The study showed that the percentage of these infections (the positive result of direct testing and culture for the fungus and the positive culture results for bacteria) in the laboratory was 69% [12]. The percentage of the organism non-growth in different fungal or bacterial culture media varied from 3.537%-29.03% [3], [4], [5], [8], [10], [17], [28], [29] In some studies, the culture of infection-free cerumen also lacked growth, which varied from 16.25%-89.71% [29], [35].

The sensitivity of bacteria to medicine

The announcement of laboratory results of direct testing and culturing samples from outer ear infections are required to initiate the treatment of these patients; however, determining the sensitivity or resistance of these organisms to antibacterial antibiotics completes this cycle to help these patients more. Accordingly, a variety of methods are used to determine the sensitivity of the bacteria to drugs, the most common of which is gel diffusion using the Kirby-Bauer discs [6], [7], [17], [30], [37]. The bacteria isolated from the ear canal show different rates of sensitivity to antibiotics. In a study employing Hinton agar diffusion using paper plates, it was found that coagulase-negative *Staphylococci* isolated from the auditory canal of the hospitalised cancer patients are as much as 25% and 85% resistant to vancomycin and penicillin-G, respectively. In non-hospitalized cancer patients, the rates were 45% and 80%, respectively. On the other hand, all isolates of *S.*

aureus were resistant to vancomycin and penicillin-g. Instead, none of the isolates of *S. pneumonia* isolated from hospitalised cancer patients was resistant to tetracycline [37]. Another study suggested that most bacteria isolated from patients (94.52%) with outer ear infection were sensitive to ciprofloxacin and gentamicin (89%); however, the highest resistance was observed for amoxicillin (93.6%) and cloxacillin (78.8%). Sensitivity to ciprofloxacin was observed in 100% of *P. aeruginosa* and *S. aureus*. Furthermore, all isolates of *S.epidermidis* were sensitive to ciprofloxacin and gentamicin [7]. The highest sensitivity of *S. aureus* to medicine was observed for vancomycin (100%), gentamicin (92.3%), and trimethoprim (76.2%), even though, the highest observed resistance was observed for penicillin (100%), gluxacillin (84.6%) and sulfamethoxazole (76.2%) [30]. On the other hand, *S. aureus* was sensitive to vancomycin [6]. *Pseudomonas* spp was sensitive to vancomycin and ceftriaxone and resistant to cotrimoxazole [17].

Antifungal susceptibility testing

Given the difference in fungal sensitivity to antifungal drugs, it is advisable to begin the treatment of these patients by assessing the sensitivity or resistance of these organisms to antifungal drugs. Different methods are used to determine the sensitivity of fungi to medicine. The best method used in most studies is to determine the minimum inhibitory concentration (MIC) in a liquid medium (broth microdilution). Also, the Disk Gel Diffusion sensitivity identification method is also used in some other studies. In a sensitivity study, 15 fungal species from clinical specimens of otomycosis were tested against nystatin, clotrimazole, and miconazole in dilutions of 100 units per disc, 10 and 50 micrograms per disc, respectively. Also, the sensitivity of these fungi to different dilutions of sorbitan from 0.125-2 micrograms per disc was studied. The results showed that *Aspergillus* spp with the whole diameters between 21-32 mm were sensitive to the above drugs [40]. Also, it has been shown that the sensitivity of *A. niger* was greater to clotrimazole (95.4%) than fluconazole (90.47%); however, their difference was not significant [5].

Conclusion

The present study was a review of 9 studies investigating bacterial pathogens and 25 studies on fungal pathogens (eight of which had both bacterial and fungal pathogens). It was shown although outer ear infections are mainly caused by bacterial pathogens; the contribution of fungi to the growth of these infections is increasing, as it is evident in the

present review study. This is almost similar to the findings of other countries. On the other hand, the diversity of organisms (bacterial or fungal) is also changing, and new species are introduced as factors causing outer ear infections. Furthermore, some fungi that have played a minor role in otomycosis are isolated from these patients. Due to these changes, it seems that the methods of treatment for these patients should be modified and the use of antifungal drugs with the anti-bacterial antibiotics, as one method to improve or eliminate the problems of these patients, should be included in the treatment protocol. In addition to the improved recovery, this would lead to a reduced number of referrals and decreased costs.

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