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REVIEW

Turicella otitidis Extra-otic Infections in Humans – a Narrative Review

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ABSTRACT

Turicella otitidis *is a Gram-positive bacillus, commensal inhabitant of the external auditory canal. It is the causative agent of external otitis and otitis media. Extra-otic infections are rarely been identified especially in patients with comorbidities. A narrative review was performed based on a search of PubMed/Medline and Scopus databases to collect information on the epidemiologic, clinical and microbiologic data of extra-otic infections by* T. otitidis. *Studies published until December 2024 were screened and analyzed to extract data on pathogen characteristics, antibiotic resistance profiles, treatment and outcomes. A total of 13 studies reporting infections by T. otitidis other than otitis including an equal number of patients were eligible. The mean age of patients was 34.08 years (range, 3-75 years). A male predominance was observed (1.6:1). Four patients were immunocompromised and four underwent recent surgical procedures. The most common infection type was bacteremia (38.4%), followed by abscesses, mastoiditis, ocular infections and skin and soft tissues infections. In the majority of cases (63.6%) a single method of identification was applied, such as matrix-assisted laser desorption/ionization-time of flight mass spectrometry (MALDI-TOF MS), polymerase chain reaction (PCR), Vitek 2 automated system and analytical profile index (API) Coryne. Antimicrobial resistance to erythromycin was 80%, while all isolates were susceptible to vancomycin. Vancomycin (45.5%) and cephalosporins (45.5%) were the most commonly used antimicrobials. In all cases with available data, the outcome was favorable.* T. otitidis *is an emerging pathogen causing extra-otic infections in humans, especially in the presence of predisposing conditions. Future studies are warranted to elucidate the microorganism's pathogenicity and the factors and mechanisms underlying its virulence.*

Keywords: bacteremia, extra-otic infections, mastoiditis, ocular infections, *Turicella otitidis*.

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INTRODUCTION

Turicella spp. are Gram-positive, non-motile, non-spore-forming coryneform bacteria belonging to the family *Corynebacteriaceae*. It was first classified as a new genus by Funke *et al* in 1994, on the basis of the results of phylogenetic analysis, biochemical and chemotaxonomic features (1). *T. otitidis* is the only member of the genus. It has been identified as normal flora of the external auditory canal (EAC) (2) and is also involved in a variety of ear infections ranging from external otitis to acute and chronic otitis media (3, 4). Previous surgery, trauma or a tympanic membrane perforation can alter the micro-ecosystem, converting normal auricular flora into pathogens and providing access for *T. otitidis* to the middle ear (4). Its isolation frequency has been increased in recent years due to the incorporation of vaccines targeting the major otopathogens, such as *Streptococcus pneumoniae* and *Haemophilus influenza*, into national immunization programmes (4).

Extra-otic infections have rarely been reported in literature. For many years, *T. otitidis* was not distinguished from commensal coryneform bacteria and was considered contaminant uninvolved in the diseases (5). Recently, more cases of extra-otic infections by *T. otitidis* have been identified using advanced microbiological techniques.

The aim of this study was to provide a comprehensive literature review of the available information regarding extra-otic infections caused by *T. otitidis* and assess epidemiologic, clinical and microbiologic data, treatment and outcomes. ❑

MATERIALS AND METHODS

This review focused on identifying extra-otic cases of *T. otitidis* infec tions in humans, spanning from 1996 to 2024. The aim was to gather insights into clinical presentations, diagnostic challenges and treatment provided in previous documented infections. For this review, a comprehensive search in the PubMed/Medline and Scopus databases was conducted by two independent investigators. The search employed specific terms including "*Turicella otitidis*" AND "infections" OR "other than otitis" OR "extra-otic infections". The review encompassed case reports focusing on the patient's demographics, clinical presentations, diagnostic methods, antibiotic resistance profiles, treatment and clinical outcomes of *T. otitidis* extra-otic infections. Exclusion criteria included duplicate and irrelevant articles and those involving animals. Reviews and systematic reviews were also excluded.

The data extracted were cross-checked for accuracy and were compiled into a table that included the publication year, country of origin, patient's age and gender, infection site, underlying diseases, microbiological characteristics, the treatment used and the outcome, to allow for a detailed discussion. ❑

RESULTS

A total of 63 articles were identified from PubMed and Scopus databases. Finally, only 13 articles met the inclusion criteria and were forwarded for analysis (6-18). These studies presented data on 13 patients in total. The study selection process followed for the review is illustrated in Figure 1. Table 1 summarizes the patients' demographics (gender, age, country of origin) and clinical characteristics. Among the included cases, seven occurred in Europe (53.8%), four in North and South America (30.8 %), and

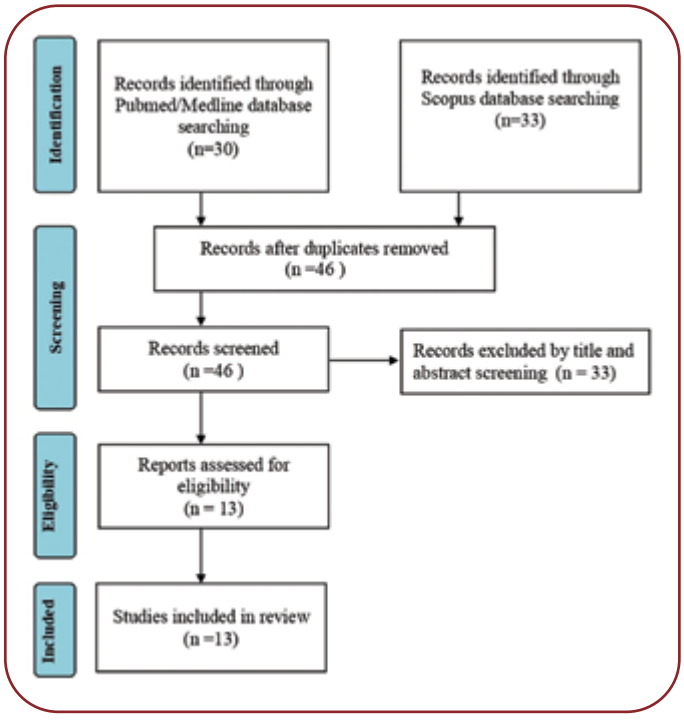

FIGURE 1. PRISMA flow diagram

TABLE 1. Characteristics of patients with extra-otic *Turicella otitidis* infections

Ref. no.	Year of isolation	Country of origin	Age (years)/ gender	Clinical manifestation	Underlying diseases/Risk factors	Method of identification	Treatment	Outcome
6	1999	Spain	7/M	Cervical abscess	NR	API Coryne	NR	NR
7	2001	USA	5/F	Mastoiditis	Otitis media	API Coryne, CAMP test	Cefotaxime i.v., ceftriaxone i.v.	Favorable
8	2001	Canada	3/F	Posterior auricular abscess	None	16S rRNA gene sequencing, CAMP test, HPLC	Surgical drainage of the abscess, cefuroxime i,v. x one day, cloxacillin i.v. x seven days, cephalexin per os x two weeks	Favorable
9	2002	France	10/M	Bacteremia	ALL, otitis externa	Morphotype, API Coryne, CAMP test	Amoxicillin (100 mg/kg) x seven days	Favorable
10	2009	France	3/F	Mastoiditis	Acute otitis media	NR	Cefotaxime (150 mg/kg/day) i.v. + vancomycin (40 mg/kg/day) i.v., amoxicillin-clavulanic acid per os x eight days	Favorable
11	2017	Romania	75/M	Bacteremia	Advanced age, diabetes mellitus, spastic paraplegia	Morphotype, API Coryne, CAMP test	Meropenem (3 g/day) + amikacin (1 g/day)	Favorable
12	2018	Poland	-/M	Bacteremia	Laminectomy, postoperative infection	NR	Rifampicin	Favorable
13	2020	China	69/F	Bacteremia	Diffuse large B-cell lymphoma	MALDI-TOF MS	Vancomycin	Favorable
14	2020	USA	71/M	Endophthalmitis	Intravitreal injections for neovascular age-related macular degeneration	PCR of the aqueous fluid	Intavitreal vancomycin +ceftazidime x four weeks	Favorable
15	2020	Greece	74/F	Palmoplantar eczema	NR	Vitek 2 system	Cefuroxime 500 mg twice daily x seven days	Favorable
16	2021	India	10/M	Keratitis	Multiple ocular surgeries, prolonged topical steroids	Vitek 2 system	Gatifloxacin 0.5% eye drops, cycloplegics	Favorable
17	2023	Italy	11/M	CVC-related bacteremia	ALL	MALDI-TOF MS	Rifampicin i.v., vancomycin CVC lock therapy, CVC removal	Favorable
18	2024	USA	71/M	Surgical site infection	Implantation of nerve stimulator device	MALDI-TOF MS	Vancomycin, amoxicillin-clavulanic acid, Device explantation, drainage of surgical sites	Favorable

F=female; M=male; NR=not reported; ALL=acute lymphoblastic leukemia; CVC=central venous catheter; API=analytical profile index; i.v.=intravenous; HPLC=high-performance liquid chromatography; CAMP=Christie-Atkins-Munch-Petersen; MALDI-TOF MS=matrix-assisted laser desorption/ionization time-of-flight mass spectrometry; PCR=polymerase chain reaction.

two in Asia (15.4%). All articles selected for the present review were case reports. Of the total studies, 76.9% were in English and 23.1% in languages other than English.

Based on the case presentation eight cases (61.5%) of *T. otitidis* infection were in males while five cases (38.5%) were in females. The mean age of the patients was 34.08 years ranging from three to 75 years. Of the total case reports, five cases (38.4%) were associated with bloodstream infections and two cases (15.4%) were attributed to abscesses. Moreover, mastoiditis was detected in two patients (15.4%) and ocular infections in two patients (15.4%), while another two patients (15.4%) developed a skin and soft tissue (SSTI) infections. Regarding patients' history, four (36.4%) were immunocompromised and an equal percentage of 36.4% underwent recent surgical procedures. Pathogen identification was accomplished with different methods. More precisely, in the majority of cases (63.6%) a single method of identification was applied, such as matrix-assisted laser desorption/ionization – time of flight mass spectrometry (MALDI-TOF MS), polymerase chain reaction (PCR), Vitek 2 automated system and analytical profile index (API) Coryne (the two latter are products of BioMérieux, Marcy L' Etoile, France). In 36.4% of cases, a combination of various techniques including API Coryne, biochemichal tests, 16S rRNA sequencing and high-performance liquid chromatography (HPLC) analysis were used to identify *T. otitidis*. In regard to antimicrobial susceptibilities, the minimal inhibitory concentrations of the antimicrobial agents were more frequently (57.1%) determined either by using broth microdilution or by E test. The susceptibility pattern noted among *T. otitidis* isolates was characterized by susceptibility to vancomycin (100%), linezolid (100%), aminiglycosides (100%), β-lactams (87.5%), fluoroquinolones (80%) and rifampicin (75%) and resistance to erythromycin (80%).

Based on the available data, 12 patients received antimicrobial treatment. Vancomycin and cephalosporins were the most frequently administered antimicrobial agents (in five patients each of them), followed by amoxicillin-clavulanic acid and rifampicin (in two patients each of them). Other antibiotics used included amoxicillin, cloxacillin and gatifloxacin. The antibiotics were administered either as monotherapy or as combination therapy. In two of the cases, topical treatment was used. Surgical treatment combined with antibiotics was applied to three out of 12 patients. In all cases with available data, the outcome was favorable. A death reported in one of the patients was not directly related to the *T. otitidis* infection. ❑

DISCUSSION

T. otitidis is an emerging pathogen also implicated in extra-otic infections due to its adaptability in various niches. *T. otitidis* genome contains genes for the synthesis of selenocysteine and its incorporation into selenoproteins, enhancing its adaptability to environmental conditions (19).

The present study summarizes the characteristics of the patients suffering from extra-otic infections by *T. otitidis* based on previously published studies and provides information regarding the epidemiology, microbiology, clinical characteristics, treatment and outcome.

The most common types of infection were bacteremia, ocular infections, mastoiditis, abscesses and SSTIs. Only a limited number of articles regarding *T. otitidis* extra-otic infections have been found in the current literature, rendering the establishment of accutate exact epidemiological data for these infections highly demanding. In this review, most patients were male, and the mean age was 34.08 years. Interestingly, most cases on *T. otitidis* extra-otic infections were reported in European countries (53.8%), 30.8% were reported in North and South American countries, while only 15.4% were identified in Asia.

A frequent condition in the medical histories of patients with extra-otic infection by *T. otitidis* was immunosuppression. More specifically, three patients had immunosuppression due to haematologic malignancies and one due to diabetes mellitus (9, 11, 13, 17). Patients with haematological malignancies are at increased risk of infections not only because of the malignancy itself but also because of neutropenia induced by intensive chemotherapeutic treatment. Bacteraemia is a relatively common serious complication occurring in around 15% of patients with haematological malignancies within the first years after diagnosis but the risk varies by type of malignancy (20). The role of *T. otitidis* in cases of bacteremia related to otitis is questioned. It is most probably considered as a result of sample contamination or transient bacteremia rather than an invasive infection (21). Other risk factors include otitis media complicated by mastoiditis, and surgical procedures (7, 10, 12, 14, 16, 18). Surgical site infections (SSIs) are among the most common healthcare infections occurring following 1%-3% of all surgical procedures (22).

Many *T. otitidis* infections were previously missed or underdiagnosed as it is was difficult to distinguish it from other corynebacteria in culture (5, 21). Accurate identification of isolates by use of modern advanced technology is important to define the spectrum of diseases caused by this species, to determine the epidemiology and to predict antimicrobial susceptibility, that is essential to guide treatment. MALDI-TOF MS has been recognized as a reliable method for rapid, cost-effective and accurate identification of *T. otitidis*. It is considered a powerful tool for identification of fastidious and slow growing bacteria (23, 24). Until 2017, conventional identification methods were used (6, 7, 9, 11), while in recent years in the majority of the studies included in the present review, pathogen identification was performed by MALDI-TOF MS (13, 17, 18). Molecular methods such as 16S rRNA sequencing, should be also employed for definitive identification of the microorganism.

There have been many reports concerning the organism's susceptibility to beta-lactams, such as penicillins and cephalosporins and β-lactam/β-lactamase inhibitors, vancomycin, linezolid and rifampicin and resistance to erythromycin, clindamycin and trimethoprin sulfamethoxazole (21). In the present review, resistance to erythromycin was observed in 80% of cases. Mutations in the 23S rRNA more frequently confer resistance in *T. otitidis* to macrolides and lincosamides (25). High-performance liquid chromatography analysis revealed that *Turicella otitidis* lacks of mycolic acid. This abscence affects cell wall permeability, thus confer-

ring resistance to antibiotics (26). Vancomycin and the cephalosporins were more frequently used to treat extra-otic infections by *T. otitidis*. Surgical procedures were applied in three cases, alongside antimicrobial treatment, and included surgical drainage of the abscess and surgical site, removal of a CVC and explantation of a nerve device stimulator (8, 17, 18). Although *T. otitidis* is susceptible to a wide range of antibiotics, its susceptibility to antibiotics should be monitored periodically for possible development of resistance. ❑

CONCLUSIONS

T. otitidis can cause extra-otic infections in humans, especially in the presence of predisposing conditions. Future studies are warranted to elucidate the pathogenicity of the microorganism and the factors and mechanisms underlying its virulence. ❑

Data availability: The data used in this study are available at Scopus and PubMed databases.

Conflicts of interest: none declared.

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