

REVIEW

Otologic dysfunction in patients with COVID-19: A systematic review

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Abstract

Objective: To describe otologic dysfunction in patients with the novel SARS-CoV-2.

Review Methods: Search strategies acquired for each database included keywords. The keywords used were—Otologic OR Vestibular OR Audiologic and COVID-19 OR Coronavirus OR SARS-CoV-2. Resulting articles were imported into a systematic review software and screened for appropriateness.

To be eligible for inclusion in the analysis, the studies and case reports should have met the following criteria:

- i. Description of otologic dysfunction in COVID-19 patients
- ii. peer review

Studies were excluded if:

- i. the description of the specific dysfunction was inadequate
- ii. there were no original case descriptions

Data that met the inclusion criteria was extracted and analyzed.

Results: A total of 62 articles were identified and screened, seven articles met the inclusion criteria and were analyzed. The articles were mainly case reports (5) with 2 case series. There were 28 patients in total identified with the largest study comprising 20 patients. All patients presented with hearing loss, 27 of whom had audiometry. Three patients had associated vestibular symptoms (vertigo, otalgia, and tinnitus).

Conclusion: SARS-CoV-2 is a probable cause of middle ear infections and sensorineural hearing loss, secondary to spread of the novel virus into the middle ear and related neural structures.

KEYWORDS

audiologic, coronavirus, COVID-19, otologic, SARS-CoV-2, vestibular

1 | INTRODUCTION

Coronaviruses are large enveloped nonsegmented positive-sense RNA viruses.¹ These viruses usually cause mild respiratory illnesses in animals and humans but have been implicated in significant epidemics. Two outbreaks in recent memory that is, severe acute respiratory syndrome CoV (SARS-CoV) and Middle East respiratory syndrome CoV (MERS-CoV) highlighted their proclivity for worldwide spread and fatalities. There are no reports of any inner ear or vestibulocochlear nerve disorders specifically linked to these outbreaks, despite the neuroinvasive properties of the coronaviruses.^{2,3}

In December 2019, a report emerged from China of a case series of patients with pneumonia due to an unknown cause. The causative organism was later identified as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).⁴ The disease itself was termed novel coronavirus disease-2019 (COVID-19) and declared a global pandemic by the Director General of the World Health Organisation (WHO) on March 11, 2020.⁵

Viral upper respiratory tract infections have long been causally linked to new cases of otitis media.⁶ There is some controversy regarding the significance of individual viral species, but the human corona virus has been isolated from middle ear fluid and linked to otitis media in children.⁷ Recent reports have implicated SARS-CoV-2.⁸⁻¹¹ Most patients affected by SARS-CoV-2 are asymptomatic or experience mild symptoms.¹² The common symptoms including fever, cough, fatigue and gastrointestinal disorders have been well documented.¹³

Unusual presentations of the disease including tinnitus and hearing loss are emerging in the literature.¹⁴ Viral infections have been implicated in both congenital and acquired cases of hearing loss which may be unilateral or bilateral. The hearing loss associated with viral infections is typically, sensorineural, although conductive and mixed hearing losses have been documented. The pathogenesis of viral-induced hearing loss is varied and ranges from direct damage to the structures of the inner ear to immune-mediated damage.¹⁵

In this systemic review, we studied the otologic manifestations of SARS-CoV-2. A literature search using multiple medical search engines for the period up to July 31, 2020 was conducted. The keywords used were—Otologic OR Vestibular OR Audiologic and COVID-19 OR Coronavirus OR SARS-CoV-2.

2 | METHODS

2.1 | Search strategy and selection criteria

We did a systematic review in accordance with the PRISMA guidelines.¹⁶ We searched PubMed, Embase, Web of Science, Scopus, BMJ best practice, Google scholar and Cochrane Database of Systematic Reviews (July 2020) for relevant articles without date or language restrictions. The following PICOS (Participants, Interventions, Comparisons, Outcomes, and Study design) criteria were utilized:

2.2 | Definition of otologic dysfunction

For the purpose of this review, otologic dysfunction was defined as any subjective and objective impairment to the normal otologic, vestibular and audiologic function of the ear.

All the search terms were Medical Subject Heading terms.

The keywords use were—Otologic OR Vestibular OR Audiologic and COVID-19 OR Coronavirus OR SARS-CoV-2. The search strategy used in PubMed was modified to suit other databases. We also manually screened citations of relevant articles to identify additional studies.

To be eligible for inclusion in the analysis the following criteria were required:

- description of otologic dysfunction in COVID-19 patients
- peer review

Studies were excluded if:

- the description of the specific dysfunction was inadequate
- there were no original case descriptions

We began the study selection by screening titles and abstracts of articles retrieved from the search. For articles identified to be potentially relevant, the full text was then reviewed. The full text was also reviewed if a decision could not be made from reading the title and abstract alone. Two investigators (SM and MBA) independently screened the titles and abstracts of retrieved articles and disagreements

TABLE 1 Risk of bias table

Author, date, country	Bias due to deviations from intended intervention	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported results
Karimi-Galougahi et al 2020 ² (Turkey)	Low	Low	Low	Low
Fidan V 2020 ³ (Turkey)	Low	Low	Low	Low
Sriwijitalai W, Wiwanitkit V 2020 ⁹ Thailand	Low	Medium	Low	Medium
Ye W, Xianyang L. 2020 ¹¹ China	Low	Low	Low	Low
Degen et al 2020 ¹⁸ Germany	Medium	Low	Medium	Low
Mustafa 2020 ¹⁹ Egypt	Low	Medium	Low	Low
Kilic et al ²² (Turkey)	Low	Low	Low	Medium

TABLE 2 Summary of cases and otologic disorders

Author/s and country	Type of study	No. of patients	Age	Sex	Symptom/s	Otologic disorder
Karimi-Galougahi et al ² (Iran)	Case series	3	22	M	Hearing loss	SSNHL (L)
			40	F	Hearing loss	SSNHL (R)
			23	F	Hearing loss	SSNHL (L)
Fidan V ³ (Turkey)	Case report	1	35	F	Tinnitus	Otitis media
					Otalgia	Conductive hearing loss (R)
Sriwijitalai W, Wiwanitkit V ⁹ (Thailand)	Case report	1	Unknown	F	Hearing loss	SNHL
Ye W, Xianyang L. ¹¹ (China)	Case report	1	44	M	Otalgia	Otitis media (L)
Degen et al ¹⁸ (Germany)	Case report	1	60	M	Tinnitus	SNHL (L)
					Hearing loss	Complete deafness (R)
Mustafa ¹⁹ (Egypt)	Case series	20	20-50	U	Nil	Decreased high frequency pure tone thresholds
						Transient evoked otoacoustic emissions. amplitudes were significantly worse in the test group
Kilic et al ²² (Turkey)	Case report	1	29	M	Hearing loss	SNHL (R)

in the study selection were resolved by consensus. We quantified the inter-rater agreement for study selection using Cohen's κ coefficient.¹⁷

The selected studies were ranked using the ROBINS-1 tool for assessing risk of bias in non-randomized studies of interventions. Each reviewer then compiled a descriptive narrative of each study (Table 1).

Relevant studies were assessed based on the following categories; study type, aim, participant characteristics, definition of otologic dysfunction or synonymous terms used, sensitivity, specificity, positive and negative findings as well as the respective author comments and opinions. These findings were systematically tabulated (Table 2).

2.3 | Data analysis

Data extraction was done by two independent reviewers (SM and KRH) and compared, with disagreements resolved by discussion. We used a predefined and standardized data extraction form to collect information from all the eligible studies. All non-English-language studies were translated into English before data extraction with the use of Google Translate. From each eligible study, we extracted the year of publication; first author's name; type of study, number of patients, gender and clinical findings.

3 | RESULTS

A total of 62 (PubMed—26, Embase—3, Web of Science—1, Scopus—3, BMJ best practice—0, Google scholar—29 and Cochrane—0) articles were captured, articles were screened for both duplicates and content. Eight duplicate and 45 unrelated entries were removed. No additional articles were identified from the references found within the selected papers. The remaining nine articles had full text available and

were independently reviewed by the researchers. Seven articles met the inclusion criteria and were analyzed to compile the discussion.

3.1 | Study design of included studies

The studies were mainly mostly case reports. Follow-up was variable and ranged from 3 days to 10 months (Table 2).

3.2 | Study population of included studies

All of the studies had human participants.

3.3 | Age of patients

The patient population was adults with an equal number of males to female. The age at presentation varied between 20 and 60 years of age.

3.4 | Overall and study sample size

The total number of subjects across all studies was 28 patients. The largest study had 20 participants while the smallest included manuscript had 1 subject.

3.5 | Region of study origin

Amongst the seven studies, two were from Turkey and one study each from China, Egypt, Iran, Germany and Thailand.

3.6 | Clinical presentation

All patients presented with hearing loss (n=28).

Three patients presented with otalgia, vertigo and tinnitus.

3.7 | Investigations

5 patients had CT scans and 8 had MRI scans.

All patients tested Covid19 positive for RT PCR.

Twenty-seven patients had hearing tests done which ranged from audiograms to Oto-acoustic emissions. The patient featured in the case report by Ye W and Xianyang L did not have formal audiometry.¹²

3.8 | Treatment

There is no established treatment protocol for COVID19 otologic dysfunction based on the included studies.

4 | DISCUSSION

Currently there is no evidence supporting the presence of SARS-CoV-2 in the middle ear, but the findings documented above implicate the virus as a potential source of otologic disorders. The significance of confirming the presence of SARS-CoV-2 is important in fully elucidating the clinical presentations of COVID-19 and recognizing that viral particles can shed during examination and surgical procedures within this area creating potential infection risks.¹⁸

Otologic disorders may herald the onset of COVID-19. Fidan described a 35-year-old female who presented with acute otitis media (OM) and an associated unilateral hearing loss. The patient did not have symptoms suggestive of SARS-CoV-2 infection although her chest X-ray was abnormal. She was found to be PCR positive for SARS-CoV-2 and her OM was attributed to this. The presence of the virus was not confirmed in the exudate from the middle ear although one can presume a link between the OM and the virus found in the nasopharynx.⁹ Ye and Xianyang reported a 44-year-old male whose presentation to an ENT clinic with features suggestive of otitis media preceded his clinical presentation of pneumonia by 7 days. The patient tested positive for SARS-CoV-2. Unfortunately, the patient was not tested for SARS-CoV-2 initially, although he did test positive at the time of the pneumonia. The authors presumed that the otitis was the initial manifestation of COVID-19 in the patient.¹¹ Hearing loss has also been documented as a late complication of the disease. Degen et al described bilateral hearing loss in a patient hospitalized with severe pneumonia. Based on the patients' clinical findings (delirium) and MRI features (meningeal inflammation) the authors postulated that the hearing loss could be ascribed to Virus-triggered, immune-mediated inflammation.¹⁹

Hearing loss, both asymptomatic and symptomatic has been reported in patients with COVID-19. In a recent study, the audiograms of twenty COVID-19 positive patients were examined.¹⁹ These patients were asymptomatic for all known symptoms of SARS-CoV-2. The ages of the participants were kept between 20 and 50 years to avoid age related hearing deficits. Hearing thresholds for high frequency pure tones were found to be significantly decreased in comparison to healthy individuals. In addition, the transient-evoked otoacoustic emissions (TEOAE) of these patients had decreased amplitude when compared to their healthy counter parts. These findings are consistent with intracochlear damage, in particular it alludes to the involvement of cochlear hair cells secondary to viral damage. A single case of conductive hearing loss in a patient with confirmed COVID-19 has been documented. The presumed mechanism of hearing loss in this case was a middle ear effusion secondary to an ascending nasopharyngeal infection.⁹ There have been six case reports of sensorineural hearing loss (SNHL), four of which were documented to be sudden in onset (SSNHL) (Table 1).

Viruses, most notably herpes simplex have been implicated in cases of SSNHL.¹⁵ The pathogenesis of the hearing loss has not been definitively clarified but possible explanations have been expounded: inflammation of components of the auditory pathway and/ or cross-reaction between viral particles and antigens in the inner ear. The virus may indirectly be transmitted to structures of the inner ear from cerebrospinal fluid.²⁰ In patients with concomitant features of brainstem involvement a likely explanation is the attachment of the coronavirus to angiotensin-converting enzyme 2 surface receptors which can be found on both neurons and glial cells.²¹ Cure and Cure proposed that the hearing loss in patients with COVID-19 could be secondary to ischaemia of the hearing center secondary to thrombogenic phenomena related to SARS-CoV-2 infection.^{22,23}

4.1 | Strengths and limitations of review

One of the main strengths of this review is that it is the first review focusing on the novel coronavirus and otologic dysfunction of the search strategy. Our review has been able to identify a number of studies published since then. Our review includes 7 studies of a total of 28 patients.

The limitations include that there is still much research that needs to be done in this field with larger study populations.

5 | CONCLUSION

There is growing evidence suggesting that otologic disorders, specifically hearing loss can be part of the clinical spectrum of COVID-19 and may in some cases signal the onset of the disease. It is of utmost importance to appreciate the rare presentations of SARS-CoV-2 in ENT patients as these will not only facilitate the diagnosis, especially in early presentations of the disease but also help protect and decrease the exposure of the ENT surgeon to potential infection risks.

More research is needed in the otolaryngology field with regards to SARS-CoV-2 manifestations and prognosis thereof.

CONFLICT OF INTEREST

There is no conflict of interest.

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