No COVID-19 in Patients With Sudden Sensorineural Hearing Loss (SSNHL)

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Background: Various case reports have described sudden sensorineural hearing loss (SSNHL) in patients with the 2019 novel coronavirus disease (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Our aim was to determine the incidence of COVID-19 in patients with SSNHL.

Methods: All consecutive patients with audiometric confirmed SSNHL between November 2020 and March 2021 in a Dutch large inner city teaching hospital were included. All patients were tested for COVID-19 by polymerase-chain-reaction (PCR) and awaited the results in quarantine.

Results: Out of 25 patients, zero (0%) tested positive for COVID-19. Two patients had previously tested positive for COVID-19: at three and eight months prior to the onset of hearing loss.

Conclusions: This is the largest series to date investigating COVID-19 in SSNHL patients. In this series there is no apparent relationship between SSNHL and COVID-19.

Key Words: Corona—COVID-19—Deafness—Hearing—SARS-CoV-2—Sensorineural—Severe acute respiratory syndrome coronavirus 2—Virus.

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INTRODUCTION

Most patients with the 2019 novel coronavirus disease (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) suffer respiratory or gastrointestinal symptoms (1).

Apart from pulmonary involvement, it is well known that viral infections can cause hearing loss (2). Indeed, sensorineural hearing loss has also been attributed to COVID-19 (3). In several other countries some groups have described a rise in sudden sensorineural hearing loss (SSNHL) during the COVID-19 pandemic, whereas others did not confirm such an increase in incidence (4–6). Existing literature is mainly limited to case reports (7–14). As a consequence, it is currently unknown if COVID-19 has an association with SSNHL.

We, therefore, wanted to investigate any suspected relationship between SSNHL and COVID-19. All consecutive patients with SSNHL during a 5-month period at our department were tested for COVID-19. The aim was to determine the incidence of COVID-19 in patients with SSNHL.

METHODS

We adhered to the STROBE guidelines for reporting of prospective studies (15).

Study Design, Setting, and Participants

This is a prospective study performed in a large inner city teaching hospital (OLVG) in Amsterdam, the Netherlands.

All consecutive patients aged 18 years or older who presented to our department of Otorhinolaryngology between November 2020 and March 2021 with SSNHL were included. Patients with another plausible cause for the sudden hearing loss (e.g., Meniere's disease, trauma, infection), or a history of hearing loss (unless compliant with a patient's age or presbyacusis) were excluded.

Variables

All data were prospectively collected and entered into the patients' electronic medical records by the authors. Recorded baseline characteristics were age, sex, previous COVID-19 infection, average hearing loss as defined by the High Fletcher Index (HFI), other otologic complaints and otological history. Information on treatment, including the administration of oral corticosteroids (OCS) or intratympanal corticosteroids (ITC)

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was recorded. The primary outcome of this study was the prevalence of COVID-19 infection among the study population. Secondary outcomes of interest were (average) hearing improvement, and the results of serological investigations and MRI.

SSNHL was defined as sensorineural hearing loss of $\geq$30 decibels in hearing level (dB HL) at >2 consecutive frequencies which arose within 72 hours (16).

Measurements

All patients received standard audiological testing and were treated for SSNHL following standard care protocols as described in the Dutch guideline ''sensorineural hearing loss in adults'' (17). Pure-tone audiometry was performed conforming to ISO 8253 norms as described by the Dutch Society for Audiology (18). Pure-tone thresholds were determined with adequate masking in case of possible overhearing. In case of confirmed SSNHL, patients were treated as soon as possible with oral corticosteroids (OCS) unless there were contra-indications, or unless the patients objected to corticosteroids. In that case the patient received no treatment. OCS consisted of 1 mg/kg/day prednisolone once daily, with a maximum of 60 mg daily for 7 to 14 days. All patients were re-evaluated with new audiological testing which was scheduled 2 weeks after the first diagnosis.

Salvage therapy with ITC was offered to patients with SSNHL with no or incomplete hearing recovery after OCS. ITC therapy was started within 4 weeks after failure of OCS, and consisted of dexamethasone 10 mg/ml 0.4 to 0.8 ml with three or four sessions in total every 3 to 7 days. Serological investigations were performed in case of suspicion of Lyme disease (Borrelia Burgdorferi), Lues (Treponema Pallidum), Human Immunodeficiency Virus (HIV) or auto-immune disease. Magnetic Resonance Imaging (MRI) was performed to rule out cerebellopontine disease in case of nonrecovered hearing. According to the Dutch guideline, a MRI may be omitted in cases of recovered hearing.

COVID-19 testing consisted of polymerase-chain-reaction (PCR), and patients followed standard Dutch quarantine protocols until test results were complete. Patients were able to follow their test results online, or had a telephone appointment with the treating otolaryngologist after 1 day. All patients were informed about the impact of OCS on their immune response.

Bias

All data was collected prospectively and definitions were agreed upon prior to starting the study to avoid variations in the patient population. There was no missing data. Patients with SSNHL preferentially come to our hospital (despite the COVID-19 pandemic) versus being treated by general practitioners.

Study Size

A formal calculation of the sample size was not performed because we did not know the prevalence of COVID-19 associated SSNHL. Furthermore, due to the low incidence of SSNHL of approximately 5 to 20 cases per 100-thousand per year, a sufficiently powered study would require a long study period, which against the background of the current pandemic (including vaccine development and implementation) was not feasible (19).

Statistical Analysis

Data were analyzed using IBM SPSS statistics version 26 (IBM, Armonk, New York). Normally distributed continuous data were presented as mean with standard deviation (SD) and non-normally distributed continuous data were presented as median with interquartile range (IQR), unless specified otherwise. Categorical data were presented as frequency with percentage.

Ethics

Testing for COVID-19 in SSNHL patients was regarded as standard of care by our group during the five month period. Therefore we did not acquire Institutional Review Board (IRB) approval for this study nor written informed consent from patients. All included patients were, however, briefed on the reasons for testing for COVID-19 and all patients provided oral consent.

RESULTS

In total 25 patients with SSNHL were included. Thirteen (52%) patients were female and the median age was 66 (IQR: 24) years (see baseline characteristics in Table 1). All patients presented with unilateral SSNHL.

Average hearing loss at diagnosis was 73 (SD: 21) decibels in hearing level (dB HL). Hearing loss was the sole otological complaint in seven (28%) patients. Vertigo was present in six (24%) patients and 13 (52%) patients complained of tinnitus. Of note, none of the patients displayed other COVID-19 related symptoms.

None of the patients tested positive for COVID-19. Two (8%) patients had previously been tested positive for COVID-19. One patient tested positive three months prior to the onset of hearing loss, another patient eight months prior to the onset of hearing loss.

All but one (n = 24, 96%) patients were treated with OCS as one patient refused treatment with OCS. Hearing improved in 18 out of 25 (72%) patients, and in 7 (28%) out of 25 patients hearing improvement was complete, that is, comparable to the nonpathological ear. In the 18 patients with hearing improvement, hearing improved on average by 39 (SD: 20) dB HL. Hearing in the one patient not treated with OCS did not improve. ITC was administered in four patients; in none of these patients hearing improved beyond the initial improvement after administration of OCS. Serological investigation was performed and negative in four patients. MRI was

TABLE 1. *Baseline characteristics*

	Patients (n = 25)
Female sex	13 (52)
Age (years; median [IQR])	66 (26)
Average hearing loss (dB HL; average [SD])	73 (23)
Otological complaints	
– Hearing loss	25 (100)
– Otalgia	0 (0)
– Otorrhoea	0 (0)
– Vertigo	6 (24)
– Tinnitus	13 (52)

Data are expressed as n (%) unless otherwise specified.
dB HL, decibels in hearing level; IQR, interquartile range; SD, standard deviation.

performed in 12 patients, but did not reveal any relevant pathology.

DISCUSSION

This prospective observational study is the largest to date investigating COVID-19 in SSNHL to our knowledge. We, however, found no apparent relationship between SSNHL and the occurrence of COVID-19. The rate of COVID-19 in patients with SSNHL was zero. Two patients had tested positive for COVID-19 in the previous year. None of the patients had any other plausible cause for the hearing loss as determined by anamnestic or otoscopic investigation, serological testing, or MRI.

A recent study in asymptomatic patients with confirmed COVID-19 found increased high-frequency puretone thresholds and significantly reduced transient evoked otoacoustic emissions (TEOE's) compared to a control group, indicating possible cochlear damage (20). Almufarrij et al. reviewed all papers published on audiovestibular symptoms in patients with COVID-19 up to December 2020 (3). They found 56 papers in which COVID-19 had an association with various audiovestibular symptoms such as hearing loss, tinnitus and vertigo. However, these results are largely based on case-reports and retrospective questionnaires, which are prone to publication and recall bias.

One small series investigated COVID-19 in SSNHL, Kilic et al. performed a PCR-test on five patients with audiometric confirmed SSNHL and no other symptoms. One patient tested positive for COVID-19 (21). The authors concluded that SSNHL could be the only sign of otherwise asymptomatic COVID-19. However, this finding may be coincidental (22).

There is some discussion that hearing loss may be a component of ''long COVID'' rather than the acute infection. In this context there are two patients in the study who previously had COVID. This, however, could be coincidental.

It is well known that a viral infection such as measles, Rubella or cytomegalovirus can cause hearing loss (2). Intracellular entry of SARS-CoV-2 depends on binding to the surface receptor angiotensin-converting enzyme 2 (ACE2) (23). A recent animal study in mice found that ACE2 are present in middle ear spaces and cochlea, suggesting susceptibility to SARS-CoV-2 infection (24).

In this study, hearing improved in 72% of patients. This seems a little better than the 30 to 65% reported in literature (25).

Our study is limited by the fact that we included patients referred to our department for sudden hearing loss, audiometric confirmed SSNHL and no other COVID-19 related symptoms. We cannot rule out possible selection bias as we do not know if some patients with SSNHL were not, or did not want to be referred—particularly during the pandemic. This could include patients with COVID-19. Some patients with SSNHL and COVID-19 might be critically ill, and consequently these patients may not have been referred immediately as hearing loss was not a priority. This study also has strengths. Patients were included with audiological confirmed SSNHL, and we did not rely on subjective evaluation of patients' hearing.

Concluding, we found no apparent relationship between SSNHL and COVID-19.

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