

Short- and Long-Term Self-Reported Audiovestibular Symptoms of SARS-CoV-2 Infection in Hospitalized and Nonhospitalized Patients

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Keywords

Coronavirus disease 2019 · Severe acute respiratory syndrome coronavirus 2 · Audiovestibular · Hearing loss · Tinnitus

Abstract

Background: Audiovestibular symptoms during the acute stage have been reported in patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), while very few studies investigated the long-term audiovestibular manifestations of SARS-CoV-2. **Objective:** The objective of this study was to examine the occurrence of short- and long-term audiovestibular symptoms associated with SARS-CoV-2 infection. **Method:** In this cross-sectional study, a questionnaire was distributed to severe hospitalized cases and nonhospitalized patients with mild disease, all with confirmed SARS-CoV-2 test results. Participants were inquired to report audiovestibular symptoms during the acute phase and at 6-month follow-up after contracting SARS-CoV-2. **Results:** A total of 301 participants completed the questionnaire. Auditory symptoms were reported by 21.9% and 1.99% of patients during the acute phase and 6 months post SARS-CoV-2 infection, respectively. During the acute phase of SARS-CoV-2 infection, aural fullness represents the most common symptoms (18.94%) followed by tinnitus (9.97%) and hearing loss (6.31%). Vestibular symptoms were reported by 34% during the acute phase; most commonly was dizziness (29.9%) fol-

lowed by vertigo (24.25%) and unsteadiness (8.31%). Long-term and persistent vestibular problems were reported by 3.99% patients. There were no statistically significant differences in self-reported audiovestibular symptoms between patients with severe SARS-CoV-2 disease compared to those with mild disease. **Conclusion:** The current study showed that audiovestibular symptoms are common among SARS-CoV-2 infected patients during the acute phase of the disease. However, these symptoms are mostly temporary and showed complete spontaneous recovery during the first 2 weeks postinfection.

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Introduction

In late December of 2019, a new strain of coronavirus first emerged in the Chinese city, Wuhan, Hubei province, caused by the strain severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and was subsequently referred to as COVID-19. On March 11, 2020, SARS-CoV-2 rapidly spread to several countries worldwide, and consequently, the World Health Organization declared COVID-19 as a pandemic of international concern. As of March 21, 2021, there were 120 million confirmed cases of COVID-19 and 2 million and 700 reported deaths worldwide and these figures continued to rise in most parts of the world. SARS-CoV-2 is highly conta-

gious and can spread through droplet transmission from cough and sneezing. The clinical manifestations of SARS-CoV-2 infection vary widely in terms of severity; ranging from asymptomatic infection (40–50%, [Oran and Topol, 2020]) to as severe as it develops into acute pneumonia and life-threatening conditions in some cases. The most common reported symptoms include fever, dry cough, headache, shortness of breath, and diarrhea. Of SARS-CoV-2 infected patients with severe clinical manifestations, approximately 20% require hospital admission [Wu and McGoogan, 2020] compared to infected patients with milder forms of SARS-CoV-2 infection who usually do not require hospitalization [Lavezzo et al., 2020]. Occasionally, some patients may experience neurological symptoms such as dizziness and altered consciousness [Baig, 2020] or ophthalmological symptoms such as dry eye, blurred vision, and conjunctivitis [Nasiri et al., 2021], and sensory dysfunction of smell and taste [Agyeman et al., 2020; Giacomelli et al., 2020]. These findings suggest that SARS-CoV-2 likely gains access to the central nervous system [Giacomelli et al., 2020; Meinhardt et al., 2021] and therefore potentially causing a variety of neurological manifestations including audiovestibular symptoms.

Some viral infectious diseases such as measles, mumps, zika virus, and cytomegalovirus are known to cause hearing loss, most commonly sensorineural hearing loss [Cohen et al., 2014]. The pathogenesis of these viral infections likely results from (1) direct invasion of the virus to structures of the inner ear and auditory nerve, (2) bystander dysfunction through compromising the host immune response to the virus, and (3) vascular pathologies [Cohen et al., 2014]. Some of these infectious diseases cause severe to profound congenital hearing loss while others are acquired and potentially manifest as progressive hearing loss or temporary alterations with spontaneous recovery in hearing sensitivity. Since the outbreak of COVID-19 pandemic, a growing body of research indicated an increased occurrence of audiovestibular disorders among infected individuals. According to an earlier systematic review, SARS-CoV-2 infection likely causes a wide range of audiovestibular symptoms among SARS-CoV-2 patients [Almufarrij et al., 2020]. Auditory symptoms in patients with SARS-CoV-2 has been reported in self-report questionnaire and few experimental studies including hearing loss [Karimi-Galougahi et al., 2020; Munro et al., 2020; Mustafa, 2020; Alves de Sousa et al., 2021] and tinnitus [Beukes et al., 2020; Viola et al., 2020]. There were also case reports of sudden sensorineural hearing loss (SSNHL) following contracting SARS-CoV-2 infection

[Degen et al., 2020; Kilic et al., 2020]. Dizziness and vertigo are now commonly being recognized as common SARS-CoV-2 symptoms during the acute phase [Lechien et al., 2020; Micarelli et al., 2020; Viola et al., 2020], and in particular, dizziness is identified as a persistent symptom post SARS-CoV-2 infection [Davis et al., 2020; Viola et al., 2020; Huang et al., 2021]. A systematic review conducted 1 year after the start of this pandemic revealed that the pooled estimate of prevalence of hearing loss, tinnitus, and vertigo due to SARS-CoV-2 infection was 7.6%, 14.8%, and 7.2%, respectively [Almufarrij and Munro, 2021]. Nevertheless, previous studies were largely based on findings at the acute phase of the infection or shortly after hospital discharge while others mostly involve non-hospitalized patients with very few studies [e.g., Munro et al., 2020] had systematically investigated the long-term impact of the infection (also known as long COVID) on the audiovestibular system.

Given the widespread and rapid transmission of SARS-CoV-2 infection, it is critical that the full-range of its clinical manifestations is readily recognized. The aim of the current study is to examine whether SARS-CoV-2 infection causes short- and long-term symptoms related to the auditory and vestibular systems using a structured questionnaire. The results of this study will form the basis for future experimental studies that will investigate the effects of SARS-CoV-2 infection on a larger scale using behavioral and electrophysiological audiological tests.

Materials and Methods

Participants

The objective of the study was to examine audiovestibular symptoms among hospitalized patients with severe SARS-CoV-2 disease and nonhospitalized patients with mild disease, with confirmed nasopharyngeal swab test results for SARS-CoV-2. Testing for SARS-CoV-2 was performed using polymerase chain reaction (PCR) test at the central laboratory of the National Center for Disease Prevention and Control in Riyadh, Saudi Arabia. The inclusion criteria required participants (1) to be ≥ 18 years of age; (2) to have had confirmed laboratory SARS-CoV-2 test results; (3) to sign a consent form to participate in the study. The online questionnaire also included a mandatory consent question before proceeding to the questionnaire. Patients with suspected SARS-CoV-2 but without laboratory positive test results were excluded. Hospitalized patients were recruited from the isolation unit at King Faisal General Hospital, a designated hospital for patients with COVID-19 in Al-Ahsa, Saudi Arabia. The second author distributed and collected questionnaires from hospitalized patients. Four patients refused to participate in the study. Nonhospitalized patients were recruited through advertisement in social media outlets via a direct online link and also through snowball sampling method. Data collection occurred between April 5 and November 8, 2020.

All participants completed the questionnaire at two time points: (1) during the acute phase of the disease; this period was identified as the first 14 days post positive PCR test results; (2) at 6-month follow-up post infection. Data at the 6-month follow-up time point were collected via telephone or completing an electronic version of the questionnaire. Participation in this study was voluntary with no compensation or incentives for participants.

Questionnaire Design and Distribution

The present study used a structured questionnaire which was developed in paper-based and electronic formats. The content of the questionnaire was initially developed in English and then translated to Arabic by the first author and then back translated to English by another person with a doctorate degree. The questionnaire consists of three sections and a total of 30 questions (online suppl. material 1; for all online suppl. material, see www.karger.com/doi/10.1159/000521963). Section 1 (questions 1 through 11) was designed to gather sociodemographic as well as questions pertaining to general health and clinical characteristics after contracting SARS-CoV-2 infection. Demographic data included age, gender, and occupation. For questions of general health, we asked participants to indicate the presence of pre-existing chronic diseases. For questions regarding clinical characteristics, participants were asked if they experienced any SARS-CoV-2-related symptoms including fever, cough, headache, chest pain, shortness of breath, loss of smell and taste, shortness of breath, diarrhea, and sore throat, and joint and back pain. We also asked participants if they were given antiviral drugs or any other medications for fever, cough, and pain relief. For hospitalized patients with severe SARS-CoV-2 disease who completed the questionnaire, we also reviewed medical charts for health and clinical characteristics. Section 2 was intended to evaluate auditory symptoms after confirmed diagnosis of SARS-CoV-2 infection. Participants were asked if they experienced hearing loss, tinnitus, aural fullness, speech understanding difficulties in quiet and noise background on a 4-point scale (no, mild, moderate, severe) as well as the duration of these symptoms. Participants were then asked if they had any long-standing auditory symptoms prior to contracting SARS-CoV-2 infection and if these symptoms became worse after contracting SARS-CoV-2 infection. Section 3 was intended to evaluate vestibular symptoms. Participants were asked if they experienced unsteadiness, dizziness, and vertigo on a 4-point scale (no, mild, moderate, severe). We provided participants with the clinical term of each vestibular symptom along with brief description that makes them easily understood in order to remove any overlap between the symptoms. Another question was used to specifically categorize severity, duration, frequency of dizziness and vertigo. Participants were then asked if SARS-CoV-2 causes their vestibular symptoms to become worse if they had long-standing dizziness or vertigo issues before the infection. We also asked participants to indicate the day/week onset of audiovestibular symptoms.

Although the questionnaire was not psychometrically validated, the questionnaire items were subjected to review by two clinical audiologists. The first author clearly drafted the questionnaires' items and sent it to the reviewers to ensure these items reflect on the aim and objectives of the study. The experts were asked to rate the relevance of each item on the questionnaire using a 4-point Likert scale (1 = not relevant, 2 = somewhat relevant, 3 = relevant, 4 = very relevant). The responses of the reviewers revealed that the questionnaire items were appropriate and relevant to the theme of

the study. To ensure that the content of the questionnaire is clear and understandable to participants, a pilot study using the questionnaire items was conducted on a sample of 4 SARS-CoV-2 infected, asymptomatic individuals. These individuals were asked to answer the questions and rate the clarity and understandability of the questions on Likert scale from 0 (not clear) to 5 (very clear). Ambiguous questions that were difficult to understand were examined and reworded accordingly. This review process revealed that all drafted items in the questionnaire are easily understandable and relevant to the purpose of the study.

Data Analysis

Statistical analyses were conducted using SPSS 23.0 for Windows (SPSS Inc., Chicago, IL, USA). Categorical variables were reported in percentages and continuous variables were reported as mean and standard deviation or as medians and interquartile ranges (IQRs), as appropriate. Chi-square (χ^2) test was used to examine any significant differences between qualitative variables and demographic and clinical characteristics between the hospitalized and nonhospitalized groups. For quantitative variables, we employed the Student's *t* test or Mann-Whitney test as appropriate. For each symptom category (auditory and vestibular), separate multiple linear regression analysis was conducted to examine the association between auditory and vestibular symptoms and demographic predictor variables (age, gender), comorbidities, SARS-CoV-2 symptoms, hospitalization, and antiviral drugs in addition to Dexamethasone. The strength of the association between presence of auditory and vestibular symptoms for each of these predictors was presented as β coefficient values, *p* value, and 95% confidence interval (CI). Ordinal logistic regression analyses (ordinal dependent variable measured on a 4-point Likert item, no, mild, moderate, and severe) were performed to test whether reporting each auditory and vestibular symptom in isolation is associated with demographic variables, clinical characteristics, and comorbidities, SARS-CoV-2 symptoms, and antiviral drugs use. Long-term auditory and vestibular symptoms were analyzed using binary logistic regression. *p* value less than or equal to 0.05 was considered statistically significant.

Results

Sociodemographic and Clinical Characteristics

A total of 301 patients with laboratory confirmed SARS-CoV-2 infection completed the questionnaire. The demographic and clinical characteristics of the study group are presented in Table 1. The study group comprised of 70.10% males and 29.9% females with a median age of 35 (IQR = 27–44). The median age of males and females was 36 years (IQR = 29–46) and 31 years (IQR = 23–40), respectively (online suppl. material 2 for all dataset).

Approximately, two-thirds (65.9%, *n* = 198) of participants did not require hospitalization, while 103 (34.22%) required medical care and admitted to hospital of which 4 patients (1.33%) were admitted to intensive care unit (Table 1). The mean age of the hospitalized and nonhospital-

Table 1. The demographic data and clinical characteristics of hospitalized and nonhospitalized SARS-CoV-2 infected patients (hospitalized, $n = 103$; nonhospitalized, $n = 198$)

Patient characteristics	Hospitalized, N (%)	Nonhospitalized, N (%)	<i>p</i> value	Total, N (%)
Age				
Mean	44.12	32.66	<0.001	36.58
SD	12.52	10.63		12.54
Sex				
Male	94 (91.26)	117 (59.09)	<0.001	211 (70.10)
Female	9 (8.74)	81 (40.91)	<0.001	90 (29.90)
Comorbidities				
No comorbidities	40 (38.83)	168 (84.84)	<0.001	208 (69.1)
Diabetes mellitus	31 (30.09)	8 (4.04)	<0.001	39 (12.96)
Hypertension	29 (28.16)	6 (3.03)	<0.001	35 (11.63)
Heart diseases	6 (5.83)	0	0.001	6 (1.99)
Chronic respiratory diseases	9 (8.74)	5 (2.53)	0.015	14 (4.65)
Anemia	8 (7.77)	7 (3.54)	0.109	15 (4.98)
Head trauma	0	2 (1.01)	0.306	2 (0.66)
Antiviral drugs				
Hydroxychloroquine	38 (36.89)	17 (8.59)	<0.001	55 (18.27)
Favipiravir	40 (38.83)	0	<0.001	40 (13.29)
Dexamethasone	10 (9.71)	0	<0.001	10 (3.32)
Remdesivir	1 (0.97)	2 (1.01)	0.511	3 (0.99)

Table 2. Frequency of general SARS-CoV-2 associated, self-reported symptoms (hospitalized, $n = 103$; nonhospitalized, $n = 198$)

SARS-CoV-2 symptoms	Hospitalized, N (%)	Nonhospitalized, N (%)	<i>p</i> value	Total, N (%)
Asymptomatic	2 (1.94)	33 (16.67)	<0.001	35 (11.63)
Symptomatic	101 (98.05)	165 (83.33)	<0.001	266 (88.37)
Cough	86 (83.49)	81 (40.91)	<0.001	167 (55.48)
Shortness of breath	72 (69.90)	39 (19.69)	<0.001	111 (36.88)
Fatigue	35 (33.98)	86 (43.43)	0.112	121 (40.19)
Fever	68 (66.02)	73 (36.86)	<0.001	141 (46.84)
Headache	26 (25.24)	81 (40.91)	0.007	107 (35.55)
Migraine	1 (0.97)	14 (7.07)	0.021	15 (4.98)
Loss of smell	12 (11.65)	92 (46.46)	<0.001	104 (34.55)
Loss of taste	20 (19.42)	70 (35.35)	0.004	90 (29.90)
Chest pain	24 (23.30)	20 (10.10)	0.002	44 (14.62)
Diarrhea	22 (21.36)	37 (18.69)	0.580	59 (19.60)
Back and joint pain	13 (12.62)	77 (38.89)	<0.001	90 (29.90)

ized groups was 44.12 (SD = 12.52) and 32.66 (SD = 10.63), respectively ($p < 0.001$). The mean duration for hospitalization was 6.33 ± 3.84 days, and the median was 5 (IQR = 4–8) days. Out of the 301 infected patients, 208 (69.10%) had one or more underlying comorbid conditions; the most common were diabetes mellitus (12.96%, $n = 39$), hypertension (11.63%, $n = 35$), anemia (4.98%, $n = 15$), chronic respiratory disease (4.65%, $n = 14$), and cardiovas-

cular disease (1.99%, $n = 6$) (Table 1). Univariate analysis showed a statistically significant differences between the hospitalized and nonhospitalized groups in relation to all underlying comorbid conditions ($p < 0.01$) except for anemia ($p = 0.109$) and head trauma ($p = 0.306$) (Table 1).

We then analyzed SARS-CoV-2-associated symptoms during the acute phase of SARS-CoV-2 infection (Table 2). Approximately, 11.63% ($n = 35$) were asymptomatic and

Table 3. Frequency of self-reported auditory symptoms among patients with SARS-CoV-2 infection (hospitalized, $n = 103$; nonhospitalized, $n = 198$)

	Hospitalized, $n = 103$	Nonhospitalized, $n = 198$	p value	Total, $n = 301$
Before SARS-CoV-2				
Hearing loss	5 (4.85)	18 (9.09)	0.143	23 (7.64)
Tinnitus	1 (0.97)	8 (4.04)	0.138	9 (2.99)
Acute phase of SARS-CoV-2				
Hearing loss				
Mild	3 (2.91)	11 (5.56)	0.302	14 (4.65)
Moderate	1 (0.97)	3 (1.52)	0.696	4 (1.33)
Severe	1 (0.97)	0	0.165	1 (0.33)
Total	5 (4.85)	14 (7.07)	0.373	19 (6.31)
Tinnitus				
Mild	8 (7.77)	15 (7.58)	0.953	23 (7.64)
Moderate	2 (1.94)	3 (1.52)	0.487	5 (1.66)
Severe	1 (0.97)	1 (0.51)	0.637	2 (0.66)
Total	11 (10.68)	19 (9.59)	0.959	30 (9.97)
Aural fullness				
Mild	10 (9.71)	34 (17.17)	0.047	44 (14.62)
Moderate	0	9 (4.55)	0.101	9 (2.99)
Severe	1 (0.97)	3 (1.51)	0.696	4 (1.33)
Total	11 (10.68)	46 (23.23)	0.059	57 (18.94)
SIQ				
Mild	2 (1.55)	3 (1.52)	0.784	5 (1.66)
Moderate	1 (0.97)	0	0.165	1 (0.33)
Severe	0	0	–	0
Total	3 (2.91)	3 (1.52)	0.366	6 (1.99)
SIN				
Mild	3 (2.91)	6 (3.3)	0.955	9 (2.99)
Moderate	0	1 (0.51)	0.470	1 (0.33)
Severe	0	0	–	0
Total	3 (2.91)	7 (3.54)	0.769	10 (3.32)
6 months after SARS-CoV-2				
Hearing loss	2 (1.94)	4 (2.02)	0.963	6 (1.99)
Tinnitus	1 (0.97)	4 (2.02)	0.146	5 (1.66)

SIQ, speech in quiet; SIN, speech in noise.

88.37% ($n = 266$) patients were symptomatic. Common findings of the SARS-CoV-2-associated symptoms included cough (55.48%), fever (46.84%), body weakness and fatigue (40.19), breathing difficulties (36.88%), headache (35.55%), loss of smell (34.55%), loss of taste (29.9%), pain in the back and joints (29%), diarrhea (19.60%), and chest pain (14.62%). SARS-CoV-2-associated symptoms among hospitalized severe cases and nonhospitalized mild cases were shown to be significantly different ($p < 0.01$) except for diarrhea ($p = 0.580$) and fatigue ($p = 0.118$).

Auditory Symptoms

Overall, 66 participants (21.93%) reported experiencing auditory symptoms during the acute phase following

positive SARS-CoV-2 PCR test results. Of these, 19 participants (6.31%) reported hearing loss, 30 participants reported tinnitus (9.97%), 57 participants reported aural fullness (18.94%), 6 participants reported speech understanding difficulties in quiet (1.99%), and 10 participants reported speech understanding difficulties in noise (3.32%) (Table 3). The mean age of participants who experienced auditory symptoms was 37.36 years ($SD = 13.54$), and most participants were predominately males (44 [14.6%] males vs. 26 [8.6%] females). Compared to hospitalized severe SARS-CoV-2 cases, nonhospitalized participants with mild forms of the disease reported more hearing loss (4.56% vs. 1.66%), tinnitus (6.31% vs. 3.65%), aural fullness (15.28% vs. 3.65%), and speech understand-

Table 4. Univariable and multivariable linear regression results for auditory symptoms

	Univariable linear regression		Multivariable linear regression	
	β (95% CI)	<i>p</i> value	β (95% CI)	<i>p</i> value
Gender	0.47 (−0.46 to 0.65)	0.023	0.26 (−0.14 to 0.66)	0.202
Age	0.01 (−0.1 to 0.02)	0.223	–	–
Diabetes	0.16 (−0.72 to 0.39)	0.567	–	–
Hypertension	0.24 (−0.34 to 0.82)	0.421	–	–
Cardiovascular	−0.38 (−1.71 to 0.95)	0.576	–	–
Respiratory	0.61 (−0.27 to 1.49)	0.174	–	–
Anemia	0.52 (−0.31 to 1.38)	0.230	–	–
Cough	0.07 (−0.30 to 0.45)	0.704	–	–
SOB	0.18 (−0.20 to 0.57)	0.351	–	–
Fatigue	0.702 (0.33–1.07)	<0.001	0.30 (−0.12 to 0.72)	0.156
Fever	0.28 (−0.09 to 0.65)	0.145	–	–
Headache	0.59 (0.21–0.97)	0.003	0.14 (−0.28 to 0.57)	0.502
Migraine	0.59 (−0.26 to 1.44)	0.173	–	–
Loss of smell	0.89 (0.52–1.27)	<0.001	0.68 (0.20–1.15)	0.006
Loss of taste	0.45 (0.05–0.86)	0.028	−0.17 (−0.64 to 0.31)	0.495
Chest pain	0.64 (0.12–1.16)	0.017	0.47 (−0.06 to 1)	0.081
Diarrhea	0.31 (−0.16 to 0.77)	0.201	–	–
Back and joint pain	0.87 (0.47–1.26)	<0.001	0.52 (0.09–0.95)	0.018
Symptoms, <i>n</i>	0.51 (0.25–0.78)	<0.001	−0.01 (−0.38 to 0.36)	0.597
Hospitalization	−0.23 (−0.62 to 0.16)	0.250	–	–
Antiviral drugs	−0.08 (−0.28 to 0.12)	0.423	–	–

ing difficulties in quiet (0.99% vs. 0.99%) and in noise (2.33% vs. 0.99%). With regards to severity, the majority of participants reported auditory symptoms predominantly in the scale of mild degree. Thirty-four (11.29%) participants reported having long-standing auditory symptoms prior to SARS-CoV-2 infection (Table 3) of which 5 (11.63%) participants reported their auditory symptoms had become worse following SARS-CoV-2 infection. The average duration of auditory symptoms following positive SARS-CoV-2 test results was 7.8 ± 16.5 days. With regard to distribution of auditory symptoms, 23 participants reported at least one symptom, while 21 and 11 participants reported experiencing a combination of two and three auditory symptoms, respectively.

A linear regression analysis was conducted to compare the total score of the five auditory symptoms (hearing loss, tinnitus, aural fullness, and hearing difficulties in quiet and noise backgrounds) with demographic variables, comorbid conditions, SARS-CoV-2 symptoms, hospitalization, and antiviral drug (Table 4). Univariable linear regression revealed that gender and various SARS-CoV-2 symptoms including body weakness and fatigue, headache, loss of smell, loss of taste, chest pain, back and joint pain, and number of symptoms were associated with experiencing auditory symptoms. In multivariable linear regression analysis, loss of smell ($\beta = 0.68$; 95% CI: 0.20–

1.16, $p = 0.005$) and pain in back and joints ($\beta = 0.53$; 95% CI: 0.09–0.96, $p = 0.017$) were the only variables significantly associated with experiencing auditory symptoms during the acute phase of SARS-CoV-2 infection (Table 4). These findings indicate that for a one-unit increase in report of loss of smell and pain in back and joints symptoms, the likelihood of experiencing auditory symptoms is increased by 0.68 and 0.53, respectively, given that all the other predictors in the model are held constant. To further examine the impact of demographic data, clinical characteristics, and SARS-CoV-2 symptoms on the likelihood that participants would experience each auditory symptom in isolation, we conducted separate ordinal logistic regression analyses considering the categorical severity degree of each symptom as the dependent variable. Statistical analysis results are presented in online supplementary material 3. The results of the ordinal logistic regression models showed that experiencing hearing loss is associated with the following predictors (chronic respiratory disease [OR = 8.6, 95% CI: 1.20–66.16, $p = 0.039$], headache [OR = 3.84, 95% CI: 1.14–12.96, $p = 0.030$], and loss of smell [OR = 5.18, 95% CI: 1.18–22.79, $p = 0.030$]) (online suppl. material 3). The odds of experiencing tinnitus increased with age (OR = 1.05, 95% CI: 1.01–1.1, $p = 0.024$), loss of smell (OR = 5.82, 95% CI: 1.66–20.41, $p = 0.006$), loss of taste (OR = 0.25, 95% CI: 0.08–0.79,

Table 5. Frequency of self-reported vestibular symptoms among patients with SARS-CoV-2 infection

	Hospitalized, <i>n</i> = 103	Nonhospitalized, <i>n</i> = 198	<i>p</i> value	Total, <i>n</i> = 301
Before SARS-CoV-2				
Unsteadiness	2 (1.94)	8 (4.04)	0.335	10 (3.32)
Dizziness	5 (4.85)	14 (7.07)	0.453	19 (6.31)
Vertigo	3 (2.91)	8 (4.04)	0.621	11 (3.65)
Acute phase of SARS-CoV-2				
Unsteadiness				
Mild	5 (4.85)	13 (6.57)	0.552	18 (5.98)
Moderate	4 (3.88)	1 (0.51)	0.03	5 (1.66)
Severe	2 (1.94)	0	0.049	2 (0.66)
Total	11 (10.68)	14 (7.07)	0.03	25 (8.31)
Dizziness				
Mild	23 (22.33)	34 (17.17)	0.278	57 (18.94)
Moderate	4 (3.88)	20 (10.10)	0.059	24 (7.97)
Severe	3 (2.19)	6 (3.03)	0.955	9 (2.99)
Total	30 (29.13)	60 (30.30)	0.235	90 (29.90)
Vertigo				
Mild	11 (10.68)	36 (18.18)	0.089	47 (15.61)
Moderate	5 (4.85)	12 (6.06)	0.667	17 (5.65)
Severe	3 (2.91)	6 (3.03)	0.955	9 (2.99)
Total	19 (18.45)	54 (27.27)	0.345	73 (24.25)
6 months after SARS-CoV-2				
Vestibular problems	3 (2.91)	9 (4.55)	0.101	12 (3.99)

$p = 0.019$), back and joint pain (OR = 4.86, 95% CI: 1.52–15.53, $p = 0.008$), diabetes mellitus (OR = 3.84, 95% CI: 1.14–12.96, $p = 0.006$), and hypertension (OR = 4.11, 95% CI: 1.01–16.808, $p = 0.049$) (online suppl. material 3). Aural fullness was associated with age (OR = 1.04, 95% CI: 1.002–1.08, $p = 0.038$), chronic respiratory diseases (OR = 4.74, 95% CI: 1.03–21.88, $p = 0.046$), loss of smell (OR = 2.84, 95% CI: 1.09–7.34, $p = 0.038$), and back and joint pain (OR = 2.87, 95% CI: 1.27–6.48, $p = 0.011$) (online suppl. material 3). Overall, the regression analyses (linear and ordinal) consistently revealed that the odds of experiencing auditory symptoms were significantly higher among participants who experienced loss of smell during the acute phase of SARS-CoV-2 infection.

At 6-month follow-up after symptoms onset, a total of 11 (3.65%) participants reported experiencing prolonged and persistent auditory symptoms, specifically mild hearing loss (1.99%, $n = 6$) and tinnitus (1.33%, $n = 4$). The proportion of experiencing long-term auditory symptoms was higher among nonhospitalized mild cases compared to hospitalized severe cases (8 [2.66%] vs. 2 [0.66%]) (Table 3). A binary logistic regression analysis revealed that none of the demographic, clinical characteristics, comorbid conditions, and SARS-CoV-2 symptoms are statistically significant predictors of long-term auditory

symptoms (online suppl. material 3). Nonetheless, headache as well as body weakness and fatigue represent strong predictors (although not statistically significant) with the odds of experiencing long-term auditory issues being higher among participants with headaches (OR = 22, $p = 0.051$) and fatigue (OR = 27.9, $p = 0.071$) during the acute phase of the infection (online suppl. material 3).

Vestibular Symptoms

Overall, 105 participants (34.88%) reported experiencing vestibular symptoms during the first 1–2 weeks following positive SARS-CoV-2 PCR test results. Of these, 25 participants reported unsteadiness (8.31%), 90 participants reported dizziness (29.90%), and 73 participants reported vertigo attacks (24.25%) (Table 5). Participants who reported experiencing vestibular symptoms were younger (33.35 ± 10.98 years) and more likely to be males (65 [61.9%] males vs. 40 [38.09%] females). Participants' responses with regard to severity of vestibular symptoms indicated that the majority reported greater frequency of mild to moderate vestibular symptoms in both severe hospitalized and mild nonhospitalized cases. With regard to the distribution of vestibular symptoms, 42 participants reported experiencing only one vestibular symptom, while 43 and 20 participants reported experiencing

Table 6. Univariable and multivariable linear regression results for vestibular symptoms

	Univariable linear regression		Multivariable linear regression	
	β (95% CI)	<i>p</i> value	β (95% CI)	<i>p</i> value
Gender	0.51 (0.11–0.91)	0.013*	0.38 (–0.01 to 0.77)	0.059
Age	–0.004 (–0.02 to 0.01)	0.609	–	–
Diabetes	–0.46 (–1.0 to 0.9)	0.104	–	–
Hypertension	–0.16 (–0.74 to 0.42)	0.594	–	–
Cardiovascular	0.43 (–0.89 to 1.76)	0.523	–	–
Respiratory	–0.51 (–1.38 to 0.38)	0.260	–	–
Anemia	1.15 (0.30–1.99)	0.008*	0.78 (–0.06 to 1.6)	0.07
Cough	0.23 (–0.15 to 0.60)	0.229	–	–
Shortness of breath	0.24 (–0.14 to 0.63)	0.216	–	–
Body weakness and fatigue	0.80 (0.43–1.17)	<0.001*	0.51 (0.10–0.91)	0.014
Fever	0.21 (–0.16 to 0.58)	0.270	–	–
Headache	0.49 (0.10–0.87)	0.013*	0.1 (–0.3 to 0.50)	0.62
Migraine	0.59 (–0.27 to 1.43)	0.177	–	–
Loss of smell	0.50 (0.12–0.89)	0.011*	0.08 (–0.39 to 0.56)	0.723
Loss of taste	0.49 (0.09–0.89)	0.017*	0.19 (–0.29 to 0.66)	0.441
Chest pain	0.79 (0.28–1.31)	0.003*	0.53 (0.02–1.04)	0.043
Diarrhea	0.43 (–0.04 to 0.89)	0.072	–	–
Back and joint pain	0.71 (0.32–1.11)	<0.001*	0.33 (–0.09 to 0.75)	0.13
Number of symptoms	0.59 (0.22–0.75)	0.218	–	–
Hospitalization	–0.07 (–0.46 to 0.32)	0.724	–	–
Antiviral drugs	–0.06 (–0.26 to 0.14)	0.579	–	–

a combination of two and three vestibular symptoms, respectively. The average duration of SARS-CoV-2-associated vestibular symptoms was 4.6 ± 8.8 days. Thirty-nine (12.95%) participants reported having long-standing vestibular issues prior to SARS-CoV-2 infection (Table 5), of which 10 (25.64%) participants reported that their vestibular problems became worse following contracting SARS-CoV-2 infection.

A linear regression was conducted to compare the total score for the 3 vestibular symptoms (i.e., unsteadiness, dizziness, and vertigo) with demographic variables, comorbid conditions, SARS-CoV-2 symptoms, antiviral drugs, and hospitalization (Table 6). Vestibular symptoms were only strongly associated with body weakness and fatigue ($\beta = 0.55$; 95% CI: 0.13–0.96, $p = 0.010$) and gender ($\beta = 0.47$; 95% CI: 0.04–0.90, $p = 0.032$). We further conducted ordinal logistic regression analyses to assess the impact of demographic data, clinical characteristics, and SARS-CoV-2 symptoms on the likelihood that participants would experience each vestibular symptom in isolation considering the severity degree of each symptom as the dependent variable (online suppl. material 3). The analyses revealed that unsteadiness is significantly associated with diabetes mellitus (OR = 0.08, 95% CI: 0.01–0.79, $p = 0.031$), dizziness is significantly associated

with report of body weakness and fatigue (OR = 3.04, 95% CI: 1.69–5.45, $p = 0.031$), gender (OR = 0.47, 95% CI: 0.25–0.88, $p = 0.017$), and report of back and joints pain (OR = 1.93, 95% CI: 1.02–3.65, $p = 0.042$), and vertigo was found to be significantly associated with report of body weakness and fatigue (OR = 1.96, 95% CI: 1.05–3.67, $p = 0.035$) and chest pain (OR = 2.27, 95% CI: 1.08–4.78, $p = 0.031$). Overall, these analyses revealed a significant contribution of body weakness and fatigue to the manifestation of vestibular symptoms during the acute phase of SARS-CoV-2 infection.

At 6-month follow-up after symptoms onset, a total of 12 (3.99%) participants reported experiencing prolonged and persistent vestibular issues. The proportion of experiencing long-term auditory symptoms was higher among mild nonhospitalized cases compared to severe hospitalized cases (9 [4.55%] vs. 3 [2.91%]) (Table 5). A binary logistic regression analysis revealed that the none of the demographic, clinical characteristics, comorbid conditions, and SARS-CoV-2 symptoms are statistically significant predictors of long-term vestibular issues (online suppl. material 3). Nonetheless, consistent with previous regression analyses body weakness and fatigue represents a strong predictor (although not statistically significant) with the odds of experiencing long-term vestibular issues

being higher among participants with body weakness and fatigue (OR = 4.23, $p = 0.131$) during the acute phase of the infection (online suppl. material 3).

When considering both auditory and vestibular symptoms, 38 participants reported experiencing both auditory and vestibular symptoms. Notably, in all regression analyses, including both auditory and vestibular symptoms, there was no impact on short- and long-term self-report of audiovestibular symptoms for patients treated with antiviral drugs and/or dexamethasone compared to patients not receiving these treatments.

Discussion

SARS-CoV-2 infection typically causes mild or subclinical characteristics. In symptomatic patients, SARS-CoV-2 causes a wide spectrum of clinical manifestations including dry cough, fever, shortness of breath, and diarrhea. Nevertheless, the spectrum of the SARS-CoV-2 infection clinical manifestations is increasing as the pandemic was spreading to include neurological manifestations such as headache, loss of smell and taste, encephalitis, impaired consciousness, skeletal muscle injury, and reports of isolated cases of Guillain-Barre syndrome [Ellul et al., 2020; Mao et al., 2020; Whittaker et al., 2020] suggesting the SARS-CoV-2 likely gains access to the nervous system. Audiovestibular symptoms in patients with SARS-CoV-2 has also been reported in the literature (see review in [Almufarrij and Munro, 2021]) including tinnitus [Beukes et al., 2020; Viola et al., 2020], hearing loss [Karimi-Galougahi et al., 2020; Munro et al., 2020; Mustafa, 2020], dizziness [Viola et al., 2020], and vertigo [Lechien et al., 2020; Viola et al., 2020]. Similar audiovestibular manifestations have also been noted in other well-known viral infections, including cytomegalovirus, measles, mumps, and meningitis [Cohen et al., 2014]. Our study used a questionnaire to determine the short- and long-term manifestations of audiovestibular symptoms among severe hospitalized cases and nonhospitalized cases with mild forms of SARS-CoV-2 disease cases with confirmed test results for SARS-CoV-2 and to determine demographic and clinical characteristics associated with the manifestations of audiovestibular symptoms. The overall findings of the current study showed that audiovestibular involvement is common in the acute phase of SARS-CoV-2 and spontaneously resolved when evaluated after 6 months postinfection in most patients. Aural fullness was the most commonly reported auditory symptom during the acute phase of the infection, which

was completely resolved during the first 2 weeks. Hearing loss and tinnitus during the acute phase were reported by 6.31% and 9.97%, respectively and about 3% reported persistent hearing loss or tinnitus after 6 months. Vestibular symptoms during the acute phase were reported in the range from 25 to 29% of the total sample while persistent vestibular symptoms were only reported by about 3.9% of total cases.

Auditory Symptoms

Newly acquired hearing loss of varying degrees in the acute phase of SARS-CoV-2 infection was reported by 19 patients with an estimated prevalence of 6.3% of which 14 (7.07%) were nonhospitalized with mild disease and 5 (4.85%) were hospitalized with severe disease; most reported experiencing mild degree of hearing loss. Our estimate (6.3%) is roughly consistent with estimated prevalence of 7.6% reported in a systematic review that included questionnaire-based epidemiological surveys and studies using a battery of audiological tests [Almufarrij and Munro, 2021]. To investigate the manifestations of auditory symptoms in SARS-CoV-2 patients, a few previous studies used a battery of auditory tests and these studies yielded inconsistent results. Two studies showed increased high-frequency audiometric thresholds among SARS-CoV-2 patients with moderate-to-severe disease [Alves de Sousa et al., 2021], mild disease [Ricciardiello et al., 2021], and those with asymptomatic disease [Mustafa, 2020]. In conjunction with the elevated audiometric thresholds, Mustafa [2020] showed that asymptomatic individuals had lower amplitudes of transient otoacoustic emissions (TEOAEs) compared to uninfected controls. In contrast, Daikhes et al. [2020] did not find statistically significant differences in terms of audiometric thresholds among asymptomatic and those with moderate SARS-CoV-2 disease although they exhibited lower amplitude and signal-to-noise ratio of TEOAE suggesting possible subclinical auditory dysfunction post SARS-CoV-2 infection. In the contrary, Dror et al. [2020] did not find significant differences between recovered asymptomatic SARS-CoV-2 patients and controls in TEOAE, distortion product otoacoustic emissions, or auditory brainstem responses. Future well-designed studies are needed to reconcile these inconsistencies and to establish the role of SARS-CoV-2 infection on cochlear and retrocochlear function as well as at threshold and suprathreshold levels.

Regression analysis revealed that experiencing neurological symptoms such loss of smell and headache as well as having pre-existing chronic respiratory disease were associated with experiencing self-reported hearing loss

during the acute phase of SARS-CoV-2 infection. Interestingly, a large study of 4,182 incident SARS-CoV-2 cases found that asthma was the only pre-existing condition significantly associated with experiencing SARS-CoV-2 symptoms lasting ≥ 28 days [Sudre et al., 2021].

With regard to long-term manifestations of self-report hearing difficulty, almost 98% of the cases in the current study reported complete spontaneous hearing recovery during the 2 weeks period post SARS-CoV-2 infection. Long-term and persistent auditory symptoms (6 months post SARS-CoV-2 infection) were reported by 11 patients; 6 (1.99%) participants reported hearing loss and 5 (1.66%) patients reported tinnitus. Of which, 8 (2.65%) participants were nonhospitalized with mild disease, and more likely to be males. Three patients with long-term, persistent hearing loss were on antiviral drugs during the acute phase of the infection (2 patients were on hydroxychloroquine and 1 patient was on favipiravir). It is still unknown whether these long-term hearing loss manifestations are irreversible. There are case reports of irreversible SSNHL post SARS-CoV-2 infection [Koumpa et al., 2020; Lamounier et al., 2020; Lang et al., 2020]. Although SSNHL is idiopathic in most cases, viral etiologies are considered one of the most likely etiologies of SSNHL in addition to vascular pathologies and immune-mediated mechanisms [Chen et al., 2019]. Our self-reported data reinforce previous findings on the manifestation of hearing loss among SARS-CoV-2 patients; however, attempts should be considered to elucidate the nature of hearing loss over a longer period of time using a set of basic audiometric tests.

Tinnitus as a newly acquired symptom was reported in 30 patients (9.97%) of which 10.68% were hospitalized and 9.59% were nonhospitalized patients; with the majority (7.64%) reported mild tinnitus. Our figure falls within previously reported estimates ranging from 0.35% to as high as 35% [Beukes et al., 2020; Davis et al., 2020; Lechien et al., 2020; Micarelli et al., 2020; Viola et al., 2020]. Furthermore, tinnitus was rated as more bothersome during SARS-CoV-2 pandemic among noninfected young individuals with pre-existing chronic tinnitus [Beukes et al., 2020]. Psychological factors such as anxiety, stress, and depression are strongly associated with tinnitus [Zoger et al., 2006; Krog et al., 2010; Falkenberg and Wie, 2012]; all of which are prevalent among individuals during SARS-CoV-2 pandemic [Passos et al., 2020; Salari et al., 2020]. This suggests that these psychological and emotional factors could lead to the manifestation of newly acquired tinnitus and exacerbation of pre-existing tinnitus [Beukes et al., 2020]. Regression analysis revealed that experiencing tinnitus during the acute phase of SARS-CoV-2 infection

was associated with other neurological symptoms such as loss of smell and taste; as it was also a predictor for experiencing hearing difficulties during the acute phase. Loss of smell and taste are very common neurological symptoms of SARS-CoV-2 and represent early predictors of SARS-CoV-2 infection. A possible explanation includes the viral pathophysiology mediated by the overexpression of angiotensin-converting enzyme 2 (ACE-2) receptors, the cellular receptor for the SARS-CoV-2. This receptor is commonly found in oral and nasal mucosa epithelium cells [Xu et al., 2020] and possibly overexpressed in regions along the auditory pathway.

Aural fullness was the most commonly reported auditory symptom in which various severity degrees were reported by 57 patients with an estimated prevalence of 18.94%. Aural fullness is a recognized classical symptom of transient eustachian tube dysfunction [Iwano et al., 1991; Park et al., 2012] which may be triggered by many causes, the most common being upper respiratory viral infections. Anatomically, the eustachian tube connects the middle ear cavity with the nasopharynx; the primary site of infection and virus isolation of SARS-CoV-2; thus, it was postulated that SARS-CoV-2 likely gains access to the middle ear cavity [Frazier et al., 2020]. Dysfunction of the eustachian tube results in development of negative pressure within the middle ear space, leading to the release of pro-inflammatory cytokines causing swelling of the eustachian tube lining. This mucosal edema results in inability of the eustachian tube to open which subsequently results in disturbance of gasses equilibrium between the middle ear and nasopharynx, leading to a feeling of aural fullness. Indeed, the cellular receptor for the SARS-CoV-2, the ACE-2 was detected in eustachian tube and middle ear of mice and middle ear tissues [Uranaka et al., 2020] and in autopsy of the middle ear tissues of SARS-CoV-2 positive decedents [Frazier et al., 2020] indicating that these structures are likely susceptible to SARS-CoV-2 infections. Overall, our findings indicate that transient and reversible auditory symptoms are common manifestations of SARS-CoV-2 infection. Future behavioral and electrophysiological studies are necessary to demonstrate possible causal relationship and elucidate the mechanisms leading to audiovestibular dysfunction after contracting SARS-CoV-2 infection.

Vestibular Symptoms

Vestibular problems represent one of the most common complaints in clinical practice. Epidemiological studies indicated that 15–30% of the general population are affected by vestibular problems [Neuhauser et al., 2005;

Neuhauser, 2016]. Vestibular problems are increasingly being recognized as common SARS-CoV-2 symptoms during the acute phase [Lechien et al., 2020; Micarelli et al., 2020] and also a long persistent symptom post SARS-CoV-2 infection [Davis et al., 2020; Viola et al., 2020; Huang et al., 2021]. The results of the current study showed that 18% of the total sample with confirmed SARS-CoV-2 infection reported vestibular symptoms; 8.31% reported unsteadiness, 29.90% reported dizziness, and 24.25% reported rotatory vertigo attacks. Our findings are consistent with previous studies reporting dizziness as the most common vestibular symptoms among SARS-CoV-2 patients [Viola et al., 2020; Saniasiaya and Kulasegarah, 2021] in addition to dizziness being a predictor for severe SARS-CoV-2 (OR = 1.83; 95% CI: 1.00, 3.34) [Mudatsir et al., 2020]. Furthermore, 25.64% of participants in the current study with long-standing vestibular issues reported that their vestibular problems became worse following contracting SARS-CoV-2 infection. Regression analyses revealed a significant contribution of body weakness and fatigue to the manifestation of vestibular symptoms during the acute phase of SARS-CoV-2 infection. At 6-month follow-up after symptoms onset, 3.99% of participants reported experiencing prolonged and persistent vestibular issues. Previous cohort studies, for example, found that dizziness as a long-term SARS-CoV-2 symptom (6-month follow-up) was reported by 6% among 1,733 discharged SARS-CoV-2 patients [Huang et al., 2021]. Regression analyses did not show any significant predictors for long-term vestibular problems although body weakness and fatigue represented a strong predictor (albeit not statistically significant) with the odds of experiencing long-term vestibular issues. Fatigue represents one of the most common symptoms during the acute phase [Hu et al., 2021] and also to it being the most common long-term symptom among SARS-CoV-2 patients [Davis et al., 2020; Sudre et al., 2021]. Additionally, it is well known that psychological factors such as anxiety, stress, and depression are associated with vestibular problems in a vicious cycle [Monzani et al., 2001; Eckhardt-Henn et al., 2008; Yuan et al., 2015], and all of which are prevalent among individuals during SARS-CoV-2 pandemic [Passos et al., 2020; Salari et al., 2020]. This suggests that these psychological factors could lead to the manifestation of new vestibular symptoms and exacerbation of pre-existing vestibular disorders.

Sociodemographic and Clinical Characteristics Predictors of Audiovestibular Symptoms

The age factor has been clearly noted in this SARS-CoV-2 pandemic. Previous reports showed that infected

older individuals are associated with more severe clinical symptoms and outcomes, and the association between age and symptoms/outcome was often attributed to increased coexisting conditions in the elderly. Nonetheless, we did not find statistically significant increase in the overall reports of audiovestibular symptoms among older compared to younger participants in our study. When considering each auditory symptoms in isolation in the ordinal regression analyses, older age was only associated with reports of experiencing tinnitus and aural fullness. It is noteworthy to mention that diabetes mellitus and hypertension could potentially represent confounding factors to the manifestations of audiovestibular symptoms. In the current study, diabetes mellitus and hypertension are the most common comorbid conditions, and diabetes mellitus was significantly associated with experiencing tinnitus and unsteadiness during the acute phase of SARS-CoV-2 infection. Evidence suggests that diabetes mellitus is a major risk factor for hearing loss and vestibular dysfunction [Agrawal et al., 2010; Horikawa et al., 2013].

Research literature reports cases of potential ototoxic effects of hydroxychloroquine, causing both reversible and irreversible sensorineural hearing loss and tinnitus [Prayuenyong et al., 2020]. In our study, no significant negative effect of hydroxychloroquine treatment was observed in audiovestibular manifestations; consistent with some previous studies [Alves de Sousa et al., 2021]. Although regression analysis did not predict increased odds of experiencing audiovestibular symptoms among participants taking antiviral drugs, 3 out of the 6 patients with persistent hearing loss were on hydroxychloroquine and favipiravir during the acute phase of the infection. A mini review of case reports revealed that the onset of hearing loss post hydroxychloroquine treatment varied from 1 month to several years [Prayuenyong et al., 2020]. These findings suggest close long-term audiological monitoring for patients with reports of hearing loss and tinnitus post SARS-CoV-2 infection treated with hydroxychloroquine using audiological testing sensitive for early identification of possible auditory dysfunction such as OAEs technologies and extended high-frequency audiometry or other testing sensitive for subclinical hearing loss. We also aimed in the current study to compare the manifestations of audiovestibular symptoms across the clinical spectrum of the disease by including patients with mild and severe SARS-CoV-2 disease. Overall, there were no statistically significant differences in reporting audiovestibular symptoms between patients with severe disease compared to nonhospitalized patients with mild disease;

however, patients with mild SARS-CoV-2 disease tend to report generally higher proportion of audiovestibular symptoms compared to hospitalized patients with severe symptoms of the disease perhaps in part due to more intensive medical intervention once being diagnosed with SARS-CoV-2 infection. This finding is consistent with the findings of a meta-analysis by Fernandez-de-Las-Penas et al. [2021] that revealed nonhospitalized patients experienced vertigo significantly more frequently than hospitalized SARS-CoV-2 infected patients at onset or at hospital admission (31.9% vs. 5.74%) and at more than 3 months after hospitalization (12.7% vs. 4.2%).

Proposed Mechanisms of Audiovestibular Manifestations among SARS-CoV-2 Patients

Although it is beyond the scope of the current study to determine the underlying mechanisms behind audiovestibular symptoms, a number of hypotheses are currently discussed as our knowledge of the disease progresses and based on our understanding of ear-related manifestations from other infectious diseases. The inner ear is particularly vulnerable to insults of viral origins with the most common symptoms include sensorineural hearing loss, vertigo, tinnitus, and aural fullness. The mechanisms of audiovestibular manifestations associated with acute viral infections involve direct damage of the structures of the inner ear or cochleovestibular nerve via a direct viral effect or an autoimmune-mediated process ([Cohen et al., 2014], for a brief review, see [Almufarrij and Munro, 2021]). Although SARS-CoV-2 is a primarily a respiratory tract disease, there is evidence that suggests it also invades the central nervous system which could be associated with the presentation of a broad range of neurological diseases and manifestations including headache, impaired consciousness, encephalitis, and ischemic stroke [Whittaker et al., 2020]. In particular, neuroinvasion of SARS-CoV-2 to the nervous system is still poorly understood. It has been suggested that access and spread of SARS-CoV-2 to the central nervous system might occur through the olfactory pathway [Giacomelli et al., 2020; Meinhardt et al., 2021] which may in part explain the predominant manifestation of olfactory dysfunction among infected patients; a symptom significantly associated with experiencing auditory symptoms during the acute phase of the infection observed in our study (see Table 4).

Nevertheless, it is still unclear whether such audiovestibular symptoms are caused by direct damage of the SARS-CoV-2 virus to the audiovestibular system or by secondary immune-induced processes. There is some evidence that suggests SARS-CoV-2 may potentially cause

some auditory symptoms, particularly after ACE-2, cellular receptor for the SARS-CoV-2, was detected in multiple regions of the middle and inner ears including middle ear tissues, eustachian tube, nuclei of the hair cells in the organ of Corti, in the stria vascularis, and the spiral ganglion cells of mice tissues [Uranaka et al., 2020]. Furthermore, the presence of SARS-CoV-2 viral particles was also confirmed in the mastoid and the middle ear of two of three decedents with confirmed SARS-CoV-2 infection [Frazier et al., 2020]. Possible involvement of SARS-CoV-2 to areas of the brainstem, a region that receives the primary afferents of the majority of the cranial nerves including cochleovestibular nerve, has also been suggested taking in consideration the findings from previous studies on other coronaviruses [Li et al., 2020] and recent observations from SARS-CoV-2 [Meinhardt et al., 2021]. Furthermore, an autoimmune-mediated mechanism was also proposed as a potential mechanism. In severe cases of SARS-CoV-2 infection, an autoimmune-mediated process causes an uncontrolled viral replication and an exaggerated systemic response leading to increased production of pro-inflammatory cytokine levels (i.e., cytokine storm); constituting a potential source of damage for many body organs including the inner ear [Degen et al., 2020; Koumpa et al., 2020; Alves de Sousa et al., 2021]. Vascular pathologies were also proposed as a potential mechanism for SARS-CoV-2 mediated audiovestibular manifestations given the evidence that a significant proportion of SARS-CoV-2 patients develop coagulation abnormalities [Connors and Levy, 2020; Levi et al., 2020; Mao et al., 2020]. The inner ear is an end organ with no collateral circulation with respect to its blood supply. The vasculature of the cochlea is highly sensitive and thus susceptible to even minor insults that compromise circulation to the cochlea and vestibular end organs [Trune and Nguyen-Huynh, 2012]. This compromised circulation increases susceptibility of inner ear structures to develop thrombosis or hypoxia and hence contributes to the manifestations of audiovestibular disorders, particularly SSNHL [Trune and Nguyen-Huynh, 2012].

Limitations

This study has a few important limitations that need to be considered. First, a major limitation of the current study is the self-report nature of the data included, which cannot replace behavioral and electrophysiological assessments of auditory and vestibular function. Second, our recruitment process with advertisement via social media platforms may have introduced sampling bias. Potential nonhospitalized participants with more severe fa-

tigue or older individuals are less likely to respond to our study advertisement or possibly unable to complete the online questionnaire. Nevertheless, we also used snowball sampling technique to reach a wider range of nonhospitalized patients with mild forms of SARS-CoV-2 disease. Third, our study is a single-center study with a relatively small sample size; further multicenter studies with larger samples size are required. A key strength of our study is the prospective longitudinal design, while we were able to recruit participants during the acute phase of SARS-CoV-2 infection and then follow-up after 6 months. Second, our sample was representative of both hospitalized and nonhospitalized patients and covered the COVID-19 clinical spectrum from asymptomatic disease to mild upper respiratory tract disease to severe disease.

Conclusion

Self-reported auditory symptoms were reported by 21.9% of patients during the acute phase and 1.9% of patients 6 months post SARS-CoV-2 infection. During the acute phase of the infection, aural fullness represents the most common symptoms (18.94%) followed by tinnitus (9.97%) and hearing loss (6.31%). Vestibular symptoms were reported by 34% during the acute phase of SARS-CoV-2 infection, most commonly was dizziness (29.9%) followed by vertigo (24.25%) and unsteadiness (8.31%). However, these symptoms are mostly temporary and showed complete spontaneous recovery when evaluated 6 months postinfection among the majority of this cohort of patients. Few patients (around 3–4%) reported experiencing auditory and vestibular symptoms at 6-month follow-up period. These data must be interpreted with caution since auditory and vestibular function tests were not

performed. These findings highlight a need to perform further behavioral and electrophysiological examination of the possible role of auditory and vestibular dysfunction in patients with SARS-CoV-2 infection.

Statement of Ethics

This study was reviewed and approved by the institutional review boards of the University of Hail (Protocol number: H-2020-001) and the Directorate of Health Affairs in Al-Ahsa region (Protocol number: 32-30-2020). Written informed consent was obtained from all participants.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Conceptualization: Ali A. Almishaal. Formal analysis: Ali A. Almishaal. Data collection: Ali A. Almishaal, Ali A. Alrushaidan. Methodology: Ali A. Almishaal, Ali A. Alrushaidan. Project administration: Ali A. Almishaal. Writing – original draft: Ali A. Almishaal. All authors read and approved the final manuscript.

Data Availability Statement

The data that support the findings of this study are included in this article and its online supplementary materials available in figure share.

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