



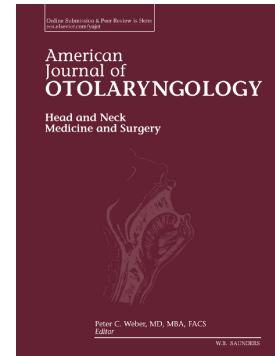
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## Journal Pre-proof

Audiological and vestibular symptoms following SARS-CoV-2 infection and COVID-19 vaccination in children aged 5–11 years

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**Title of the Article**

**Audiological and vestibular symptoms following SARS-CoV-2 infection and COVID-19 vaccination in children aged 5-11 years**

**Running title**

Audio-vestibular symptoms after COVID-19 vaccination in children

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## Abstract

### Purpose

The present study assessed the prevalence of audio-vestibular symptoms following SARS-CoV-2 infection or COVID-19 vaccination among children, comparing the two groups. A further aim was to evaluate whether children with pre-existing unilateral hearing loss were more prone to adverse events.

### Materials and Methods

This retrospective study included children aged 5-11 years with normal hearing or a proven history of unilateral hearing loss who contracted SARS-CoV-2 or received two doses of COVID-19 vaccine. Tinnitus, hyperacusis, aural fullness, otalgia, otorrhea, new-onset hearing loss, vertigo and dizziness were investigated as possible complications of SARS-CoV-2 infection or the COVID-19 vaccine.

### Results

This study included 272 children (143 boys, 129 girls), with a mean age of  $7.8 \pm 2.3$  years. Among these, 120 were affected by pre-existing unilateral hearing loss.

The most common audio-vestibular symptoms reported by children following SARS-CoV-2 infection and COVID-19 vaccination were aural fullness (33/132, 25%) and dizziness (5/140, 3.6%), respectively. All symptoms following COVID-19 vaccination resolved within 24 hours.

Compared to children who received the COVID-19 vaccine, those infected with SARS-CoV-2 had a higher prevalence of tinnitus ( $p=0.009$ ), hyperacusis ( $p=0.003$ ), aural fullness ( $p<0.001$ ), otalgia ( $p<0.001$ ), otorrhea ( $p<0.001$ ), and vertigo ( $p=0.006$ ). Two girls also experienced new-onset unilateral sensorineural hearing loss following SARS-CoV-2 infection.

Children with a known history of unilateral hearing loss did not have a higher prevalence of audio-vestibular symptoms than children with normal hearing.

### Conclusions

Our results suggest that the COVID-19 vaccine is safe and can be recommended for children with unilateral hearing loss without fear of possible audio-vestibular sequelae.

### Keywords:

SARS-CoV-2 infection; COVID-19 vaccination; unilateral hearing loss; balance disorders; children

**Author Declarations****Author agreement:**

All authors have approved the manuscript and agree with its submission.

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The authors declare that they have no conflicts of interest/competing interests.

**Ethics approval:**

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Written informed consent was obtained by the children's parents.

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**MA:** substantial contributions to the conception, design, acquisition, interpretation, analysis of data for the work; drafting the work; final approval of the version to be published; agreement to be accountable for all aspects of the work.

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**GC:** substantial contributions to the conception, design, and interpretation, analysis of data; revising the work critically for important intellectual content; giving final approval of the version to be published; agreement to be accountable for all aspects of the work.

## INTRODUCTION

People of all ages are susceptible to SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) infection, with children and adolescents under 20 years of age accounting for 21% of reported COVID-19 (coronavirus disease 19) cases and 0.4% of all COVID-19 deaths [1]. Some systematic reviews have shown that COVID-19 appears to be less severe and has a better prognosis in children than adults [2,3] for various reasons, including different immune responses and expression patterns of the angiotensin converting enzyme (ACE) 2 receptor, viral interferences, pre-existing cross-reactive antibodies, healthier blood vessels, and age-related differences in the nasopharyngeal microbiota [4,5].

However, although SARS-CoV-2 infection is often asymptomatic or paucisymptomatic in pediatric patients, some serious complications, such as *multisystem inflammatory syndrome in children* (MIS-C) and *long COVID*, can develop [6]. According to the *Centers for Disease Control and Prevention* (CDC), approximately 1 in 3 children younger than 18 years old hospitalized with COVID-19 have no underlying medical conditions, and almost half of all reported cases of MIS-C occur in children aged between 5 and 11 years [7].

In Italy, since the beginning of the pandemic, more than 10,000 children aged 11 years or under have been hospitalized due to COVID-19 [8]. Therefore, in this context, COVID-19 vaccination represents an important tool to protect not only frail pediatric patients but also children without comorbidities from severe disease, hospitalization, or death due to SARS-CoV-2 infection [7]. Additional reasons for vaccinating children include reducing community transmission and avoiding quarantine, school closures and other restrictions on social activities, resulting in psychological and physical benefits for the pediatric population [8,9].

In Italy, on December 1, 2021, the Scientific-Technical Committee of AIFA (Italian Medicines Agency) approved the use of the Pfizer-BioNTech (BNT162b2) vaccine for children aged 5 to 11 years, with two doses administered three weeks apart [10]. Each dose of antigen in the vaccine is 10 µg, one-third of that administered starting at 12 years of age (30 µg) [8,10]. Since then, our Pediatric Outpatient Audiology Clinic has been contacted by phone, email or in-person visits by several parents of children affected by pre-existing unilateral hearing loss to inquire about the possibility that COVID-19 vaccination could negatively impact the audio-vestibular system and worsen the hearing threshold of the child's healthy ear. However, despite an extensive search, we failed to identify any report that specifically investigated this important issue.

Therefore, we decided to conduct a retrospective study aimed at assessing the prevalence of audiological and vestibular symptoms following SARS-COV-2 infection or COVID-19 vaccination among children aged 5-11 years, specifically investigating whether children with pre-existing unilateral hearing loss are more prone to adverse events.

## MATERIALS AND METHODS

This retrospective study was conducted at the Pediatric Audiology Outpatient Clinic of the "Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico" (third-level referral audiological center) in Milan (Italy) between January 1, 2022, and July 31, 2022.

The study inclusion criteria were as follows:

- 1) Children 5 through 11 years of age with a recent history of SARS-CoV-2 infection, confirmed by nasopharyngeal swabs processed by reverse transcription polymerase chain reaction (RT-PCR), or children who received two doses of Pfizer-BioNTech (BNT162b2) COVID-19 vaccine;
- 3) A proven history of normal hearing (confirmed by pure tone audiometry performed no more than 6 months earlier) or a history of unilateral sensorineural hearing loss (diagnosed at least 6 months earlier) of unknown etiology;
- 4) Audiological assessments (otomicroscopy, tympanometry, and pure tone audiometry) performed 3-6 weeks after the diagnosis of SARS-CoV-2 infection or 1-2 weeks after the second dose of COVID-19 vaccine.

This study excluded children with the following conditions:

- a recent history (< 6 months) of audiological and/or vestibular symptoms prior to the diagnosis of SARS-CoV-2 infection or the administration of COVID-19 vaccine.
- a family history of hearing loss
- congenital malformations or pathologies of the outer, middle and inner ear and/or acoustic nerve
- congenital cytomegalovirus infection
- genetic syndromes associated with hearing loss
- mutations in genes associated with hearing loss, identified by "next-generation sequencing"
- otomicroscopic evidence of middle ear effusion and type B (flat) tympanogram
- recent head trauma, exposure to ototoxic drugs, exposure to loud noises or systemic infections.

Children with normal hearing were referred to our Pediatric Audiology Outpatient Clinic for ear wax removal or according to the audiological surveillance program, while children with unilateral hearing loss had a scheduled follow-up visit.



A detailed medical history was collected for each child through targeted questions posed by experienced physicians. The audio-vestibular symptoms investigated during the visit and analyzed in the present study were tinnitus, hyperacusis, aural fullness, otalgia, otorrhea, vertigo and dizziness. The patients' parents helped to accurately define the onset and duration of symptoms following SARS-CoV-2 infection or single doses of COVID-19 vaccine.

This retrospective study was conducted according to the World Medical Association's Declaration of Helsinki and approved by the local ethics committee. Informed consent was obtained from the children's parents.

#### *Statistical analysis*

We used the chi-squared test or Fisher's exact test to analyze categorical variables. Statistical analyses were performed with Stata 16 software (StataCorp. 2019). A P value of  $< 0.05$  was accepted as statistically significant.

## **RESULTS**

A total of 272 children (143 boys, 129 girls) met the inclusion criteria, and they had a mean age of 7.8 ( $\pm 2.3$ ) years (range 5-11). Of these, 120 were affected by pre-existing unilateral sensorineural hearing loss (ranging from mild to profound). Overall, 132 children had been affected by SARS-CoV-2 infection, while 140 had received two doses of COVID-19 vaccine. The characteristics of the study population are summarized in **Table 1**.

The most common audio-vestibular symptoms reported by the children following SARS-CoV-2 infection and COVID-19 vaccination were aural fullness (33/132, 25%) and dizziness (5/140, 3.6%), respectively (**Table 2**). Compared to children who received the COVID-19 vaccine, those infected with SARS-CoV-2 had a higher prevalence of tinnitus ( $p=0.009$ ), hyperacusis ( $p=0.003$ ), aural fullness ( $p<0.001$ ), otalgia ( $p<0.001$ ), otorrhea ( $p<0.001$ ), and vertigo ( $p=0.006$ ) (**Table 2**).

Among patients with SARS-CoV-2 infection, any audio-vestibular symptoms, except vertigo, started most frequently within 2 weeks of a virologically confirmed diagnosis (**Table 3**). All audio-vestibular symptoms following COVID-19 vaccination (14/14, 100%) resolved spontaneously within 24 hours, while most audio-vestibular symptoms following SARS-CoV-2 infection (83/109, 76.1%) persisted for a minimum of 5 days. Among children with vertigo, 3 (42.9%) cases received a confirmed diagnosis of vestibular neuritis and 1 (14.3%) of labyrinthitis; in the remaining 3 cases (42.9%), there was no clinical evidence of vestibular or central impairment.

New-onset sensorineural hearing loss was found in two girls following SARS-CoV-2 infection: a 10-year-old girl experienced a unilateral hearing loss of mild grade, while an 11-year-old girl experienced a unilateral hearing loss of moderate grade. No cases of hearing loss were observed following COVID-19 vaccination.

Children with pre-existing unilateral hearing loss did not have a higher prevalence of audio-vestibular symptoms than children with normal hearing, either after SARS-CoV-2 infection (**Table 4**) or after COVID-19 vaccination (**Table 5**).

## DISCUSSION

The present study assessed the prevalence of audiological and vestibular symptoms following SARS-COV-2 infection or COVID-19 vaccination among children aged 5-11 years who attended a third level referral audiological center.

While several studies have described audio-vestibular disorders, such as sudden sensorineural hearing loss, tinnitus, and vertigo, as possible manifestations following SARS-CoV-2 infection [11-12] and COVID-19 vaccines in adults [13-15], there are very few reports concerning the pediatric population [16-19].

*Hijazi et al.* found that the only otologic symptoms in 650 pediatric patients with COVID-19 were otalgia and ear fullness, reported in 1.8% and 0.5% of cases, respectively [16]. A recent systematic review and meta-analysis of otorhinolaryngological manifestations of COVID-19 in pediatric patients confirmed that hearing loss and vertigo were rarely reported [17]. A study by *Tufatulin et al.* that evaluated 87 children in three cities in Russia found no cases of hearing loss or central auditory processing disorders after SARS-CoV-2 infection [18]. Conversely, *Swain et al.* reported that among 192 children with COVID-19, 20 (10.4%) presented with tinnitus, 16 (8.3%) with hearing loss, and 8 with both hearing loss and tinnitus (4.2%) [19].

In the present study, the main audiological/otologic symptoms reported by children after SARS-CoV-2 infection were aural fullness (25%) and otalgia (17.4%), followed by hyperacusis (11.4%), tinnitus (8.3%) and otorrhea (8.3%), and they were probably due to inflammation of the nasopharynx leading to eustachian tube dysfunction [20]. Moreover, among patients with SARS-CoV-2 infection, dizziness and vertigo were reported in 6.8% and 5.3% of cases, respectively. Interestingly, while most cases of dizziness started within the first two weeks, the onset of vertigo in 6 out of 7 cases was between 2 and 4 weeks after the virologic diagnosis. This could be explained by a different etiopathogenic basis; indeed, dizziness is often due to psychological and metabolic causes exacerbated by stress during acute infection and mandatory quarantine, while vertigo may be the consequence of acute peripheral vestibulopathy caused by SARS-CoV-2 infection through direct damage, interaction with ACE-2 receptors, ischemia of the vasa nervorum, inflammatory demyelination or reactivation of herpes simplex virus 1 in the vestibular ganglia [12].

*Gürkaş et al.* found that only one of 312 children complained of vertigo [21]. *Giannantonio et al.* described the case of a child with COVID-19-induced vestibular neuritis who recovered spontaneously after one month [22]. In a study by *Dilber et al.*, dizziness was observed in 55 of 382 (14.4%) pediatric patients, and 3 (0.8%) children were hospitalized due to dizziness [23]. Furthermore, dizziness was considered one of the most common symptoms of *long COVID* in children [24].

Almost all adverse audio-vestibular effects of COVID-19 vaccines have been described in adult patients [13-15]. In the United States, approximately 8.7 million doses of Pfizer-BioNTech COVID-19 (BNT162b2) vaccine were administered to children aged 5–11 years between November 3, 2021, and December 19, 2021, with 4,249 reports of adverse events after vaccination; most cases (97.6%) were not serious. Dizziness was reported by 244 children, accounting for 5.9% of all adverse effects [25]. Overall, several clinical trials and surveillance studies based on real-life data have widely demonstrated that two doses of the BNT162b2 vaccine are safe, immunogenic, and effective at preventing symptomatic COVID-19 in children aged 5–11 years [8, 25-28].

In this study, we observed 14 transient audio-vestibular symptoms following administration of the COVID-19 vaccine. These symptoms occurred within 1 week of the first dose (n=5), within one week of the second dose (n=3), or within one week of both doses (n=6) and resolved spontaneously within 24 hours. The most common audio-vestibular symptoms reported by children after COVID-19 vaccination were dizziness (3.6%) and aural fullness (2.9%), followed by hyperacusis (2.1%) and tinnitus (1.4%). The pathophysiological mechanisms underlying these symptoms are unclear, but abnormal autoimmune responses and anxiety-related adverse events following immunization may be hypothesized [13-15].

Children with pre-existing unilateral hearing loss did not have an increased risk of developing audio-vestibular symptoms following COVID-19 vaccination, highlighting that authorized COVID-19 vaccination is not a risk factor for hearing impairment in this clinical population.

The present study has several limitations. First, it is retrospective and not population based. Moreover, a relatively small number of pediatric patients were assessed in a single audiologic center. Another important limitation is the short evaluation period with no subsequent follow-up. Future developments of this research could involve evaluating the possible long-term consequences of SARS-CoV-2 infection and COVID-19 vaccination on the auditory and vestibular systems in children.

Further population-based multicenter studies are needed to confirm our findings.

## CONCLUSIONS

To the best of our knowledge, this is the first study to specifically evaluate audio-vestibular symptoms in children aged 5-11 years following SARS-CoV-2 infection or COVID-19 vaccination and to determine whether children with pre-existing unilateral hearing loss are more prone to adverse events.

Children who received two doses of the COVID-19 vaccine had a significantly lower prevalence of tinnitus, hyperacusis, aural fullness, otalgia, otorrhea and vertigo than children infected with SARS-CoV-2. Moreover, all audio-vestibular symptoms following COVID-19 vaccination were transient and resolved within one day, and children affected by pre-existing unilateral hearing loss did not show an increased risk of adverse events.

In conclusion, the present study confirms the safety of the COVID-19 vaccine with regard to the audio-vestibular system. Conversely, it also demonstrates that SARS-CoV-2 infection can cause audio-vestibular symptoms in a high percentage of the pediatric population.

Furthermore, the results of this study suggest that COVID-19 vaccination can be safely recommended for children with pre-existing unilateral hearing loss, as no risk of cochlear or vestibular damage emerged in the studied population.

**Author Declarations****Author agreement:**

All authors have approved the manuscript and agree with its submission

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## References

1. UNICEF. COVID-19 confirmed cases and deaths. 2022. Available from: <https://data.unicef.org/resources/covid-19-confirmed-cases-and-deaths-dashboard/> Accessed 9 Aug 2022
2. Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. *Acta Paediatr* 2020;109(6):1088-1095. <https://doi.org/10.1111/apa.15270>
3. Hoang A, Chorath K, Moreira A, Evans M, Burmeister-Morton F, Burmeister F, et al. COVID-19 in 7780 pediatric patients: A systematic review. *EClinicalMedicine* 2020;24:100433. <https://doi.org/10.1016/j.eclinm.2020.100433>
4. Brodin P. Why is COVID-19 so mild in children?. *Acta Paediatr* 2020;109(6):1082-1083. <https://doi.org/10.1111/apa.15271>
5. Zimmermann P, Curtis N. Why is COVID-19 less severe in children? A review of the proposed mechanisms underlying the age-related difference in severity of SARS-CoV-2 infections. *Arch Dis Child* (2020);archdischild-2020-320338. <https://doi.org/10.1136/archdischild-2020-320338>
6. Esposito S, Principi N, Azzari C, Cardinale F, Di Mauro G, Galli L, et al. Italian intersociety consensus on management of long covid in children. *Ital J Pediatr* 2022;48(1):42. <https://doi.org/10.1186/s13052-022-01233-6>
7. Centers for Disease Control and Prevention. Why Children and Teens Should Get Vaccinated Against COVID-19. Updated July 21, 2022. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/why-vaccinate-children-teens.html> Accessed 9 Aug 2022
8. Sacco C, Del Manso M, Matec-Urquiles A, Rota MC, Petrone D, Riccardo F, et al. Effectiveness of BNT162b2 vaccine against SARS-CoV-2 infection and severe COVID-19 in children aged 5-11 years in Italy: a retrospective analysis of January-April, 2022. *Lancet* 2022;400(10346):97-103. [https://doi.org/10.1016/S0140-6736\(22\)01185-0](https://doi.org/10.1016/S0140-6736(22)01185-0)
9. Zimmermann P, Pittet LF, Finn A, Pollard AJ, Curtis N. Should children be vaccinated against COVID-19?. *Arch Dis Child* 2022;107(3):e1. <https://doi.org/10.1136/archdischild-2021-323040>
10. AIFA. AIFA approves Comirnaty vaccine for ages 5 to 11. 2021. Available at: <https://www.aifa.gov.it/en/-/aifa-approva-il-vaccino-comirnaty-per-la-fascia-di-et%C3%A0-5-11-anni> Accessed 9 Aug 2022
11. Jafari Z, Kolb BE, Mohajerani MH. Hearing Loss, Tinnitus, and Dizziness in COVID-19: A Systematic Review and Meta-Analysis. *Can J Neurol Sci* 2022;49(2):184-195. <https://doi.org/10.1017/cjn.2021.63>

12. Aldè M, Barozzi S, Di Bernardino F, Zuccotti G, Consonni D, Ambrosetti U, et al. Prevalence of symptoms in 1512 COVID-19 patients: have dizziness and vertigo been underestimated thus far? [published online ahead of print, 2022 Jan 30]. *Intern Emerg Med* 2022;1-11. <https://doi.org/10.1007/s11739-022-02930-0>
13. Wichova H, Miller ME, Derebery MJ. Otolgic Manifestations After COVID-19 Vaccination: The House Ear Clinic Experience. *Otol Neurotol* 2021;42(9):e1213-e1218. <https://doi.org/10.1097/MAO.0000000000003275>
14. Pisani D, Gioacchini FM, Viola P, et al. Audiovestibular Disorders after COVID-19 Vaccine: Is There an Association?. *Audiol Res* 2022;12(3):212-223. Published 2022 Apr 21. <https://doi.org/10.3390/audiolres12030024>
15. Colizza A, Ralli M, Turchetta R, Minni A, Greco A, de Vincentiis M. Otolaryngology adverse events following COVID-19 vaccines. *Eur Rev Med Pharmacol Sci* 2022;26(11):4113-4116. [https://doi.org/10.26355/eurrev\\_202206\\_28981](https://doi.org/10.26355/eurrev_202206_28981)
16. Hijazi LO, Alaraifi AK, Alsaab F. Otolaryngology manifestations of COVID-19 in pediatric patients. *Int J Pediatr Otorhinolaryngol* 2021;144:110701. <https://doi.org/10.1016/j.ijporl.2021.110701>
17. Yadav M, Singh A, Meena J, Sankar JM. A systematic review and meta-analysis of otorhinolaryngological manifestations of coronavirus disease 2019 in paediatric patients. *J Laryngol Otol* 2022;136(7):588-603. <https://doi.org/10.1017/S0022215122000536>
18. Tufatulin GS, Boboshko MY, Garbaruk EE, Anyushkin SA, Alieva DI, Kreisman MV, et al. Sostoyanie slukha u detei, perenesshikh novuyu koronavirusnuyu infektsiyu (COVID-19) [Hearing function in children after new coronavirus infection (COVID-19)]. *Vestn Otorinolaringol* 2021;86(5):28-34. <https://doi.org/10.17116/otorinol20218605128>
19. Swain SK, Panda S, Jena PP. Hearing loss and tinnitus among pediatric patients with COVID-19 infection: our experience. *MGM J Med Sci* 2022;9:66-71
20. Bhatta S, Sharma S, Sharma D, Maharjan L, Bhattachan S, Sah MK, et al. Study of Hearing Status in COVID-19 Patients: A Multicentered Review. *Indian J Otolaryngol Head Neck Surg* (2021); <https://doi.org/10.1007/s12070-021-02710-w>
21. Gürkaş E, Dünya B, Köken ÖY, Demirdağ TB, Yılmaz D, Özyürek H, et al. Neurologic Manifestations of COVID 19 in Children: Prospective Study in a Single Center. *Ann Indian Acad Neurol* 2021;24(6):891-895. [https://doi.org/10.4103/aian.AIAN\\_225\\_21](https://doi.org/10.4103/aian.AIAN_225_21)



22. Giannantonio S, Scorpecci A, Montemurri B, Marsella P. Case of COVID-19-induced vestibular neuritis in a child. *BMJ Case Rep* 2021;14(6):e242978. Published 2021 Jun 1. <https://doi.org/10.1136/bcr-2021-242978>
23. Dilber B, Aydın ZGG, Yeşilbaş O, Sağ E, Aksoy NK, Gündoğmuş F, et al. Neurological Manifestations of Pediatric Acute COVID Infections: A Single Center Experience. *J Trop Pediatr* 2021;67(3):fmab062. <https://doi.org/10.1093/tropej/fmab062>
24. Borch L, Holm M, Knudsen M, Ellermann-Eriksen S, Hagstroem S. Long COVID symptoms and duration in SARS-CoV-2 positive children - a nationwide cohort study. *Eur J Pediatr* 2022;181(4):1597-1607. <https://doi.org/10.1007/s00431-021-04345-z>
25. Hause AM, Baggs J, Marquez P, Myers TR, Gee J, Su JR, et al. COVID-19 Vaccine Safety in Children Aged 5-11 Years - United States, November 3-December 19, 2021. *MMWR Morb Mortal Wkly Rep* 2021;70(5152):1755-1760. <https://doi.org/10.15585/mmwr.mm705152a1>
26. Walter EB, Talaat KR, Sabharwal C, Gurtman A, Lockhart S, Paulsen GC, et al. Evaluation of the BNT162b2 Covid-19 Vaccine in Children 5 to 11 Years of Age. *N Engl J Med* 2022;386(1):35-46. <https://doi.org/10.1056/NEJMoa2116298>
27. Fowlkes AL, Yoon SK, Lutrick K, Gwynn L, Burns J, Grant L, et al. Effectiveness of 2-Dose BNT162b2 (Pfizer BioNTech) mRNA Vaccine in Preventing SARS-CoV-2 Infection Among Children Aged 5-11 Years and Adolescents Aged 12-15 Years - PROTECT Cohort, July 2021-February 2022. *MMWR Morb Mortal Wkly Rep* 2022;71(11):422-428. <https://doi.org/10.15585/mmwr.mm7111e1>
28. Capponi M, Pulvirenti F, Cimola JL, Brindisi G, Conti MG, Colaiocco G, de Castro G, Guido CA, Duse M, Midulla F, Zicari AM, Spalice A. Short-Term Side Effects and SARS-CoV-2 Infection after COVID-19 Pfizer-BioNTech Vaccine in Children Aged 5-11 Years: An Italian Real-World Study. *Vaccines* 2022; 10(7):1056. <https://doi.org/10.3390/vaccines10071056>

**Table 1. Characteristics of the study population.**

	<b>SARS-CoV-2 infection</b>	<b>COVID-19 vaccine</b>	<b>P-Value</b>
	<b>N</b>	<b>N</b>	
<b>Sex</b>			
Male	69	74	0.92
Female	63	66	
<b>Age</b>			
5 to < 8 years	69	65	0.34
8 to < 12 years	63	75	
<b>Hearing</b>			
Normal	76	76	0.58
Unilateral hearing loss	56	64	
<b>Total</b>	132	140	

Table 2. Audio-vestibular symptoms following SARS-CoV-2 infection and COVID-19 vaccination.

	N	Tinnitus N (%)	P- Value	Hyperacusis N (%)	P- Value	Aural fullness N (%)	P- Value	Otalgia N (%)	P- Value	Otorrhea N (%)	P- Value	Vertigo N (%)	P- Value	Dizziness N (%)	P- Value
<b>SARS-CoV-2</b>	132	11 (8.3%)	<b>0.009</b>	15 (11.4%)	<b>0.003</b>	33(25%)	<b>&lt;0.001</b>	23(17.4%)	<b>&lt;0.001</b>	11(8.7%)	<b>&lt;0.001</b>	7(5.3%)	<b>0.006</b>	9(6.8%)	0.28
<b>COVID-19 vaccine</b>	140	2 (1.4%)		3 (2.1%)		4(2.9%)		0(0.0%)		0(0%)		0(0%)		5(3.6%)	

Table 3. Onset of audio-vestibular symptoms following SARS-CoV-2 infection and COVID-19 vaccination.

	SARS-CoV-2 infection			COVID-19 vaccine			
	Onset within 2 weeks N (%)	Onset between 2 and 4 weeks N (%)	N (total)	Onset within a week of the 1st dose N (%)	Onset within a week of the 2nd dose N (%)	Onset within a week of the 1st and 2nd dose N (%)	N (total)
<b>Tinnitus</b>	9 (81.8%)	2 (18.2%)	11	1 (50%)	0 (0%)	1 (50%)	2
<b>Hyperacusis</b>	14 (93.3%)	1 (6.7%)	15	2 (66.7%)	1 (33.3%)	0 (0%)	3
<b>Aural fullness</b>	31 (93.9%)	2 (6.1%)	33	1 (25%)	1 (25%)	2 (50%)	4
<b>Otalgia</b>	21 (91.3%)	2 (8.7%)	23	0 (0%)	0 (0%)	0 (0%)	0
<b>Otorrhea</b>	11 (100%)	0 (0%)	11	0 (0%)	0 (0%)	0 (0%)	0
<b>Vertigo</b>	1 (14.3%)	6 (85.7%)	7	0 (0%)	0 (0%)	0 (0%)	0
<b>Dizziness</b>	7 (77.8%)	2 (22.2%)	9	1 (20%)	1 (20%)	3 (60%)	5

Table 4. Audio-vestibular symptoms following SARS-CoV-2 infection according to children's pre-existing hearing status.

	N	Tinnitus N (%)	P- Value	Hyperacusis N (%)	P- Value	Aural fullness N (%)	P- Value	Otalgia N (%)	P- Value	Otorrhea N (%)	P- Value	Vertigo N (%)	P- Value	Dizziness N (%)	P- Value
<b>Hearing</b>															
Normal	76	7 (9.2%)	0.76	7 (9.2%)	0.41	20 (26.3%)	0.84	16 (21.1%)	0.25	7 (9.2%)	0.76	7 (9.2%)	<b>0.02</b>	4 (5.3%)	0.49
Unilateral hearing loss	56	4 (7.1%)		8 (14.3%)		13 (23.2%)		7 (12.5%)		4 (7.1%)		0 (0%)		5 (8.9%)	

Table 5. Audio-vestibular symptoms following COVID-19 vaccination according to children's pre-existing hearing status.

	N	Tinnitus N (%)	P- Value	Hyperacusis N (%)	P- Value	Aural fullness N (%)	P- Value	Otalgia N (%)	P- Value	Otorrhea N (%)	P- Value	Vertigo N (%)	P- Value	Dizziness N (%)	P- Value
<b>Hearing</b>															
Normal	76	1 (1.3%)	0.99	2 (2.6%)	0.99	3 (3.9%)	0.63	0 (0%)	1	0 (0%)	1	0 (0%)	1	4 (5.3%)	0.38
Unilateral hearing loss	64	1 (1.6%)		1 (1.6%)		1 (1.6%)		0 (0%)		0 (0%)		0 (0%)		1 (1.6%)	

## Highlights

- SARS-CoV-2 infection can cause audio-vestibular symptoms in children.
- Audio-vestibular symptoms following COVID-19 vaccination are rare and transient.
- COVID-19 vaccination is safe for children with unilateral hearing loss.

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