Newborn Hearing Screening Results of Infants Born To Mothers Who Had COVID-19 Disease During Pregnancy: A Retrospective Cohort Study

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Objective: Viral infections are known to be a risk factor for neonatal hearing loss. COVID-19 infection has been reported to affect hearing test results in one small sample sized study. We aimed to investigate the incidence the risk of neonatal hearing loss in infants of mothers who had COVID-19 infection during pregnancy, regarding their trimesters, by evaluating the neonatal hearing screening results.

Design: In this retrospective case-control study, neonatal hearing test results of 458 women with a history of COVID-19 infection in pregnancy were compared with 339 women who gave birth before the pandemic. Data of pregnant women who attended the COVID-19 outpatient clinic of the emergency service of a tertiary pandemic hospital and who had confirmed infection with a reverse transcriptase–polymerase chain reaction (RT-PCR) test were determined from the hospital's records and their neonatal hearing screening results were analyzed from the national database. Neonates born before <34 weeks, and with reported risk factors in the database such as congenital anomaly or known TORCH infection during pregnancy were excluded. The screening tests, Automated Auditory Brainstem Response or Transient Evoked Otoacoustic Emission (TEOAE), were used for screening, and patients who failed the first screening were reevaluated at least 2 weeks apart with a second screening.

Results: The incidence of failed second screening was 1.3% in the COVID-19 group and 2.9% in controls, and no significant difference was observed between the two groups according to the final screening results on the second test. Among the 458 mothers, 8 were infected in first trimester, 126 in second trimester, 127 in third trimester but did not deliver within 15 days after infection and 197 were positive at birth. Six neonates in the infected group failed the second screening (3 [2.4%] in the second trimester, 1 [0.8%] third trimester, and 2 [1.0%] positive at birth).

Conclusions: COVID-19 infection during pregnancy was not found to be a risk factor for hearing loss, according to the newborn hearing screening results.

Keywords: Audiometry, COVID-19 infection, Newborn hearing screening, Placental transmission, Pregnancy.

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INTRODUCTION

The novel coronavirus infection (SARS-CoV-2) first broke out in China, and within a few months, in March 2020, the World Health Organization declared COVID-19 to be a pandemic. As a novel disease with many unknowns relating to diagnosis, management, and prognosis, the COVID-19 disease was a challenge for physicians: it was more than a respiratory viral infection, with effects being observed in many other organs and systems (Singh et al. 2021). The disease was of particular concern in vulnerable populations, such as patients with chronic or malignant diseases, elderly patients, pregnant women, and their newborns. The early outcomes of the disease for the population that included children, adults, and the elderly, were more easily interpreted, but apart from a prognosis for pregnant women and their fetuses, the consequences of intrauterine exposure to COVID-19 could only be understood through future cohort studies.

It is known that some viral infections during pregnancy can affect the developing fetus and cause anomalies. Sensorineural defects are one of the more serious complications of intrauterine exposure to certain viruses, such as the cytomegalovirus (CMV), rubella virus, and varicella-zoster virus, and to certain parasites, such as the toxoplasma gondii (Beswick et al. 2012; Gurlek & Colak 2019; Satterfield-Nash et al. 2020; Buca et al. 2021). The timing of the viral infection is also a significant factor as the placental transmission of some infections is more likely in particular trimesters, and the trimester when exposure occurs will alter the risk for developing an anomaly.

The placenta expresses the angiotensin-converting enzyme-2 (ACE-2) receptor, which the SARS-CoV-2 penetrates. Although uncommon, vertical transmission of SARS-CoV-2 virus has been demonstrated with the reverse transcriptase–polymerase chain reaction (RT-PCR) technique, and the virus has been detected in the placenta, amnion, and blood of newborns born to mothers infected with the SARS-CoV-2 virus. This vertical transmission was also confirmed with newborns who were positive for the IgM antibodies, which do not cross the placenta (Badr et al. 2020; Konstantinidou et al. 2021).

Recently, limited studies on the COVID-19 disease have been published, showing that it affects the audiological profile of COVID-19 cases, both in adults and in the newborns of women who had confirmed COVID-19 disease while pregnant (Mustafa 2020; Celik et al. 2021). A study of 20 adults analyzed the cochlear functions of patients with COVID-19 infection and reported that transient evoked otoacoustic emission (TEOAE) amplitudes were significantly worse in these patients compared with controls, suggesting that, even if the patients were asymptomatic, cochlear hair cell functions could be affected (Mustafa 2020). Further, insufficiency in the medial olivocochlear efferent system was detected in infants born to

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mothers who had COVID-19 during pregnancy (Celik et al. 2021). Hypothesizing that the possible placental transmission of SARS-CoV-2 may carry a risk of intrauterine infection, and knowing that hearing loss is an important consequence of some viral infections, we aimed to evaluate the hearing screening results of newborns born to mothers who had the COVID-19 infection during pregnancy or who had active COVID-19 infection when they gave birth.

MATERIALS AND METHODS

This retrospective cohort study was conducted in a tertiary hospital that was also a reference center for pregnant COVID-19 patients in the city. The study was approved by the Turkish Ministry of Health, with number 2020-07-08T14_01_10, and by the institutional ethics committee on 19/08/2020 (#E1-20-1075). The study was conducted according to the principles of the Declaration of Helsinki (JAMA 2013).

The data for pregnant women who were confirmed positive for COVID-19 infection by an RT-PCR test between March 2020 and October 2020 were obtained from the records of the emergency service of the Women and Birth Hospital of Ankara City Hospital. Women who gave birth in this hospital before January 2020 were selected for the control group to eliminate the possibility of asymptomatic COVID-19 infection. Pregnant women who tested negative for COVID-19 during the pandemic period were also excluded to eliminate any false negatives. The data for newborns >34th week of gestation were listed according to the timing of the mother's COVID-19 infection during pregnancy. We excluded infants with risk factors such as a preterm delivery, or a TORCH infection during pregnancy, and those with any diagnosed intrauterine anomaly or syndrome. The patients were grouped as pregnant women who had confirmed coronavirus infection during their first trimester (<13 weeks), during the second trimester (13–28 weeks), during the third trimester (>28 weeks), those who were infected at the time of delivery (a positive PCR result within 15 days before delivery), and the control group (who gave birth before December 2019).

The hearing screening test is performed on every newborn as part of the national health system, and the data are collected in an online database that also includes maternal, neonatal, and birth data, and which can be reached with the personal identity number. Therefore, even if the patients gave birth in other hospitals, the hearing screening results were accessible through the system, provided the patient attended the screening. The newborns were tested with either the Auditory Brainstem Response or the Transitory Evoked Otoacoustic Emission (TEOAE) test. If the neonates failed the first test, reevaluation was performed at least 15 days later. The neonates who also failed the second test were referred to a tertiary center; however, further details are not reported in the database.

Statistical Analysis

Statistical analysis was performed using the SPSS (Statistical Package for the Social Sciences) 23.0 (SPSS Inc., Chicago, IL). The descriptive statistics were reported with numbers and frequencies. Distributions of parameters were analyzed by the Kolmogorov-Smirnov test and the Shapiro-Wilks test. Mean and standard deviation were used to describe continuous variables with a normal distribution, and median (minimum-maximum) levels were used for variables without a normal distribution. Pearson's Chi-Square Test and Fisher's Exact Test were performed for the analysis of categorical variables where appropriate. $p < 0.05$ were considered significant.

RESULTS

A total of 797 patients were included: 458 women who had a confirmed COVID-19 infection during pregnancy or at the birth formed the study group, while 339 healthy women were included in the control group. For the hearing screening, Auditory Brainstem Response was used for 735 neonates, and TEOAE was used for 62 neonates.

Table 1 summarizes the demographic characteristics of the pregnant women with a history of COVID-19 infection and those of the healthy control group. It also shows the hearing screening results for their infants. There were no significant differences between the groups in terms of maternal age, week of birth, birth weight, and babies' gender. The cesarean section (C/S) rate was higher in the group with a COVID-19 history. Of the infants, 12.4% in the COVID-19 group failed their first screening test, while the rate was 9.4% in the control group ($p = 0.211$). The second screening showed that 1.3% of the COVID-19 group and 2.9% of the control group were at risk for hearing loss and they were referred for further evaluation; however, no statistically significant difference was found between the groups ($p = 0.103$).

The patients were also grouped according to the trimester when they had the COVID-19 infection as being in either the first trimester, second trimester, third trimester, or positive at birth (a positive PCR result within 15 days before delivery). These groups were compared with the control group regarding the hearing screening results, as reported in Table 2. The neonates of mothers who had COVID-19 infection during their second and third trimesters had higher rates of failure for the first screening test, which was significantly different from the other groups ($p = 0.031$). Nevertheless, when the final hearing screening test results for all five groups were compared (control group, COVID-19 groups for first, second, third trimester, and mothers who were positive at birth), there were no significant differences relating to the timing of the COVID-19 infection.

TABLE 1. Comparison of the demographic characteristics and hearing screening results of pregnant women with a history of COVID-19 infection and healthy control group

	COVID (n = 458)	Control (n = 339)	*p*
Age	28 (16–45)	28 (20–40)	0.213*
Birthweight	3240 (2100–3240)	3190 (2300–4545)	0.552*
Birth week	39 (34–42)	38 (34–41)	0.893*
Gender			
Female	225 (49.1%)	171 (50.4%)	0.721†
Male	233 (50.9%)	168 (49.6%)	
Delivery method			
Vaginal	196 (43.8%)	232 (67.4%)	<0.001‡
C/S	251 (56.2%)	107 (32.6%)	
First screening			
Normal	401 (87.6 %)	307 (90.6 %)	0.211†
Failed	57 (12.4 %)	32 (9.4%)	
Second screening			
No	452 (98.7%)	329 (97.1%)	0.103‡
Yes	6 (1.3%)	10 (2.9%)	

*Mann-Whitney U test.
†Fishers Exact test.
‡Pearson's Chi-Square test.
p < 0.05 considered significant.

TABLE 2. Hearing screening outcomes of the neonates of women regarding the timing of COVID-19 infection

	Negative (n = 339)	First trimester (n = 8)	Second trimester (n = 126)	Third trimester (n = 127)	Positive at birth (n = 197)	*p*
First screening						
Passed	307 (90.6%)	8 (100%)	104 (82.5%)	108 (85.0%)	181 (91.9%)	0.031
Failed	32 (9.4%)	0	22 (17.5%)	19 (15.0%)	16 (8.1%)	
Second screening						
Passes	329 (97.1%)	8 (100%)	123 (97.6%)	126 (99.2%)	195 (99.0%)	0.444
Failed	10 (2.9%)	0	3 (2.4%)	1 (0.8%)	2 (1.0%)	

Pearson's Chi-Square test.
$p < 0.05$ considered significant.

DISCUSSION

In the current report, we evaluated the hearing screening results of 458 neonates whose mothers had a history of COVID-19 infection during their pregnancy, taking their trimester into consideration, and we compared these results with those of 339 neonates whose mothers had no history of COVID-19 infection. According to the results obtained, the risk of congenital hearing loss was 1.3% in the neonates with maternal COVID-19, and a history of COVID-19 infection during pregnancy was therefore not a risk factor for neonatal hearing loss. To the best of the author's knowledge, this is the first report on neonatal hearing outcomes following COVID-19 infection during pregnancy.

COVID-19 infection was first detected in December 2019 with many unknowns, and apart from its being a respiratory tract infection, the novel coronavirus was found to have many effects on other systems (Dey et al. 2021). Neurological manifestations of the disease were reported as the cases emerged (Aasfara et al. 2021; Fidan et al. 2021; Narozny et al. 2021). The findings suggested a relationship between COVID-19 infection and audiocochlear symptoms such as vertigo, tinnitus, and hearing loss (Almufarrij & Munro 2021).

Only two studies in the literature evaluate audiological functions in cases of COVID-19, one of which evaluates adults, while the other evaluates the neonates of pregnant mothers with COVID-19 infection. However, these preliminary studies included only a limited number of cases. Mustafa et al. (2020) compared the TEOAE results for 20 patients with COVID-19 infection with those of healthy controls and reported a significant reduction in the TEOAE amplitude and worse results in the high-frequency pure tone thresholds of the COVID-19 patients, although the hearing sensitivity was normal in all participants. The only study on neonatal hearing results following maternal COVID-19 infection was reported by Celik et al. for 37 cases. They reported a significant difference in TEOAE results and an impairment in the medial olivocochlear efferent system.

The C/S rate for the COVID-19 positive group was higher than that for the controls in our study. There are no recommendations that COVID-19 positive mothers should deliver via C/S; however, the increased C/S rate can be interpreted as reflecting the lack of knowledge regarding the best birth method at the beginning of the pandemic (our study included mothers who were the earliest cases), and the physical condition of the infected mothers may have prompted the doctors to deliver the babies by C/S.

Considering the limitations of our study, the limited number of pregnant women who had COVID-19 infection during their first trimester restrains us from making any specific comment regarding early pregnancy. The reason for the limited number of patients in their first trimester is that, despite the long period covered, only a limited number of cases had COVID-19 infection during their first trimester. With the steadily increasing number of cases since that time, future researchers should be able to provide more information on the effect of COVID-19 infection during the first trimester. Another limitation of our study is that the pregnant women with COVID-19 infection were referred to our hospital and delivered in other centers after their infection was healed. Not all the women who had COVID-19 infection during pregnancy delivered in the same hospital, with the exception of those who were COVID-19 positive arrived already in active labor. This means that delivery outcomes and hearing test results had to be obtained retrospectively from the national hearing screening database. The TORCH screening results for the mothers were unknown, as laboratory data of mothers were not recorded in the database of hearing screening. However, since any reported history of infection, or signs that suspects TORCH infection such as fever, rash, hepatomegaly, seizures, ventriculomegaly, or heart defects were reported as presence of risk factors in the database, we assumed that the newborns were free of infection even if we did not see the TORCH laboratory results. Furthermore, since the final data were collected from the national database, two tests, AABR and TEOAE, were used for the hearing screening. The study evaluated the hearing screening results for newborns only, and as subsequent diagnostic test results are not reported in the database, the final incidence of neonatal hearing loss could not be identified. In future, a more detailed examination could be made by considering the severity of the mother's infection or by specifically evaluating the newborns for placental transmission. The strength of our study lies in the large number in our study group, and despite the limitations mentioned, the aim of the study, namely, to evaluate whether COVID-19 infection is a risk factor for hearing loss, was achieved, and the final results of the screening test allow us to conclude that it is not a risk factor.

CONCLUSIONS

The newborn hearing screening results indicate that COVID-19 infection during pregnancy is not a risk factor for hearing loss. Large-scale, multicenter studies of pregnant women are needed to support our results and to make a definite judgment regarding neonatal outcomes.

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The study was reviewed and approved by the ethics committee of University of Health Sciences, Ankara City Hospital (Ethics approval reference

number: #E1-20-1075 date 19/08/2020). All procedures were performed according to the Declaration of Helsinki.

The data supporting this study is available through the corresponding author upon reasonable request.

Z.A.O.K. raised the presented idea. Z.A.O.K., A.S.O.E., and B.D. designed the study. A.S.O.E. and G.N.B. conducted the analyses. Z.A.O.K., A.S.O.E., D.S., and C.T. developed the first draft of the article. G.N.B. and B.D. participated in data analysis, interpretation, and draft revision. U.Y.S. and C.A.A. participated in data collection and result interpretation. A.S.O.E. and O.M.T. designed the study and critically revised the article. All authors contributed to the writing of the article, and have read and approved the final article.

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