The Effect of Covid-19 Disease During Pregnancy on Newborn Screening ABR Results

Sedat Alagoz [1], Sefa Arlier [2], Vedat Delibas [1], Kubra Irday Demir [3], Tugce Kucukoglu Cicek [4], Sadik Kukrer [2], Talih Ozdas [1]

1 Health Sciences University Adana City Training and Research Hospital, ENT Clinic, Adana, Türkiye
2 Health Sciences University Adana City Training and Research Hospital, Department of Obstetrics and Gynecology, Adana, Türkiye
3 Health Sciences University Adana City Training and Research Hospital, Department of Pediatrics, Adana, Türkiye
4 Ceyhan State Hospital, ENT Clinic, Adana, Türkiye

Abstract

Aim: In our study, it was aimed to compare the newborn screening ABR (Auditory Brainstem Responses, AABR) results of babies of mothers who had Covid-19 (Coronavirus disease-2019) during pregnancy and babies of mothers who did not have Covid-19.

Methods: Newborns who underwent hearing screening tests in Adana Hospital Audiology Unit between April 2019 and September 2021 were included in the study, and newborns whose mothers had Covid-19 disease during pregnancy were called Group 1, and those who did not have were called Group 2. Statistical difference was studied by comparing these two groups by their birth weight, week of birth, type of delivery, first hearing test result, and referral to a reference center.

Results: A total of 746 newborn babies, 472/746 (63.3%) female and 274/746 (36.7%) males, were included in our study. There were 202/746 (27.1%) newborns in Group 1 and 544/746 (72.9%) newborns in Group 2. There was no statistically significant difference between the two groups in terms of testing age (p>0.05). When the right and left ears were evaluated separately in two groups in terms of passing the first test; no statistically significant difference was found in terms of passing the hearing test for the right and left ears, respectively (p=0.234, p=0.15). There was no statistically significant difference between the two groups in terms of birth weight and referral to a reference center (p>0.05), (p=0.775).

Conclusions: The Covid-19 disease of the mother during pregnancy does not affect the newborn hearing screening results.

Keywords: *Auditory brainstem responses (ABR), Covid-19, hearing, neonatal, pregnancy*

1. Introduction

Congenital hearing loss is accepted as an important congenital pathology and its incidence is 1.64 per 1.000 live births[1]. Detection of hearing loss in newborn children in the first 3 months and appropriate intervention in the first 6 months are important[1-3]. Otherwise, delayed detection and intervention will affect the child's speech, language, and psychosocial development, resulting in a failure in school and social life[1]. Universal newborn hearing screenings is mandatory in most countries for the early diagnosis and treatment of children with moderate to severe hearing loss[2]. The tests used in screening are otoacoustic emission (OAE) and auditory brainstem response (ABR)[3]. Since these screening tests are reproducible and non-invasive, they are very easy to apply in newborns. In these tests, a *refer* result even in one ear may indicate possible hearing loss and therefore these newborns should be retested within 1 month. If the result is *refer* again, it should be evaluated with clinical ABR within 3 months[2].

Various viral diseases can cause congenital or acquired, unilateral or bilateral hearing loss. These viral agents can harm inner ear structures directly or activate inflammatory processes that causing hearing loss. Virus can cause direct destruction to inner ear structures, especially inner ear hair cells and organ of Corti, or via activation of host immune-mediation devastation[4].

In our study, it was aimed to compare the newborn screening ABR (Auditory Brainstem Responses, AABR) results of babies of mothers who had Covid-19 (Coronavirus disease-2019) disease during pregnancy and babies of mothers who did not have Covid-19 disease.

* Corresponding Author: Vedat Delibas
e-mail: delibasvedat.vd@gmail.com
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2. Materials and methods

Data of newborns who were admitted to the ENT clinic audiology unit at Adana City Hospital between April 2019 and September 2021, and screening ABR test results were recorded retrospectively. Madsen Acuscreen brand AABR device was used. The AABR test was recorded by attaching electrodes to the forehead, right and left ears mastoids, and using a 35 dBnHL stimulus. In AABR tests, the result was shown as "pass" or "refer".

In accordance with the national newborn screening program, the first test was conducted within 72 hours of discharge in case the test fails then the second test was conducted within 7-15 days, and in case that test fails then the third test was conducted within 15-30 days. And the who failed the tests were referred to the reference center (Fig. 1).[5] Patients whose file data could not be accessed were excluded from the study. In addition, conditions with congenital hearing loss risk factors such as syndromic diseases, stay in the intensive care unit, use of ototoxic drugs, meningitis, sepsis, intrauterine infections, jaundice, cerebral diseases were accepted as exclusion criteria. Newborn of mothers with Covid-19 and newborn of mothers without Covid-19 were followed up with the same national hearing screening program. There is no difference in practice.

Vaccine information could not be accessed because the mothers' Covid-19 vaccination program and our national newborn screening program are not yet integrated.

Newborns whose mothers had Covid-19 disease during pregnancy were defined as Group 1, and those who did not have were defined as Group 2. Statistical difference was studied between Group 1 and Group 2; by newborns' birth weight, week of birth, type of delivery, first hearing test result, and referral to a reference center.

The diagnosis of Covid-19 was made according to the results of real time PCR test on the swabs taken from the nasopharynx.

Our study was approved by the University of Health Sciences, Adana City Training and Research Hospital clinical research ethics committee with decision number 89/1570 on 30 September 2021. The patient was informed in detail and her written consent was obtained.

2.1. Statistical analysis

Number (n) and percentage (%) as descriptive statistics for categorical variables obtained within the scope of the study and mean±standard deviation as descriptive statistics if parametric test assumptions are provided for numerical parameters, if not, median and minimum-maximum values are given. Normality control for numerical parameters was evaluated with the Shapiro-Wilk Normality test. Comparison of numerical variables in groups was analyzed using the "Student t Test" if parametric test assumptions were met, and "Mann Whitney U Test" if not. Pearson chi-square test was used to compare categorical variables between the two groups. Statistical analysis and SPSS 16.0 software for Windows (SPSS, Inc., Chicago, IL) were used for all statistical analyses, and $p<0.05$ was considered statistically significant.

3. Results

30.921 babies were born between April 2019 and September 2021 in our hospital. Screening ABR test was performed in 30.148 (97.5%) of these newborns. During this period, 1.537 (5.1%) newborns were referred to a reference hearing center. A total of 746 newborn babies, 472/746 (63.3%) females and 274/746 (36.7%) males, were included in our study.

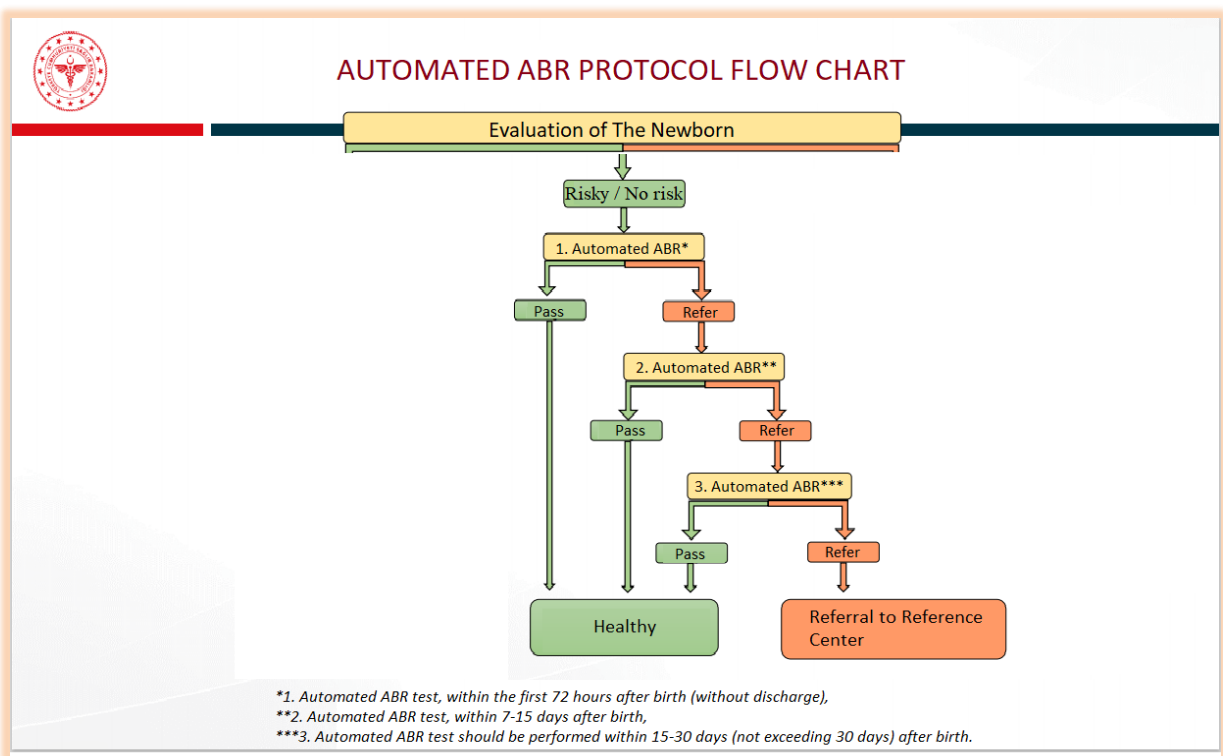

Figure 1
Automated ABR Protocol Flow Chart

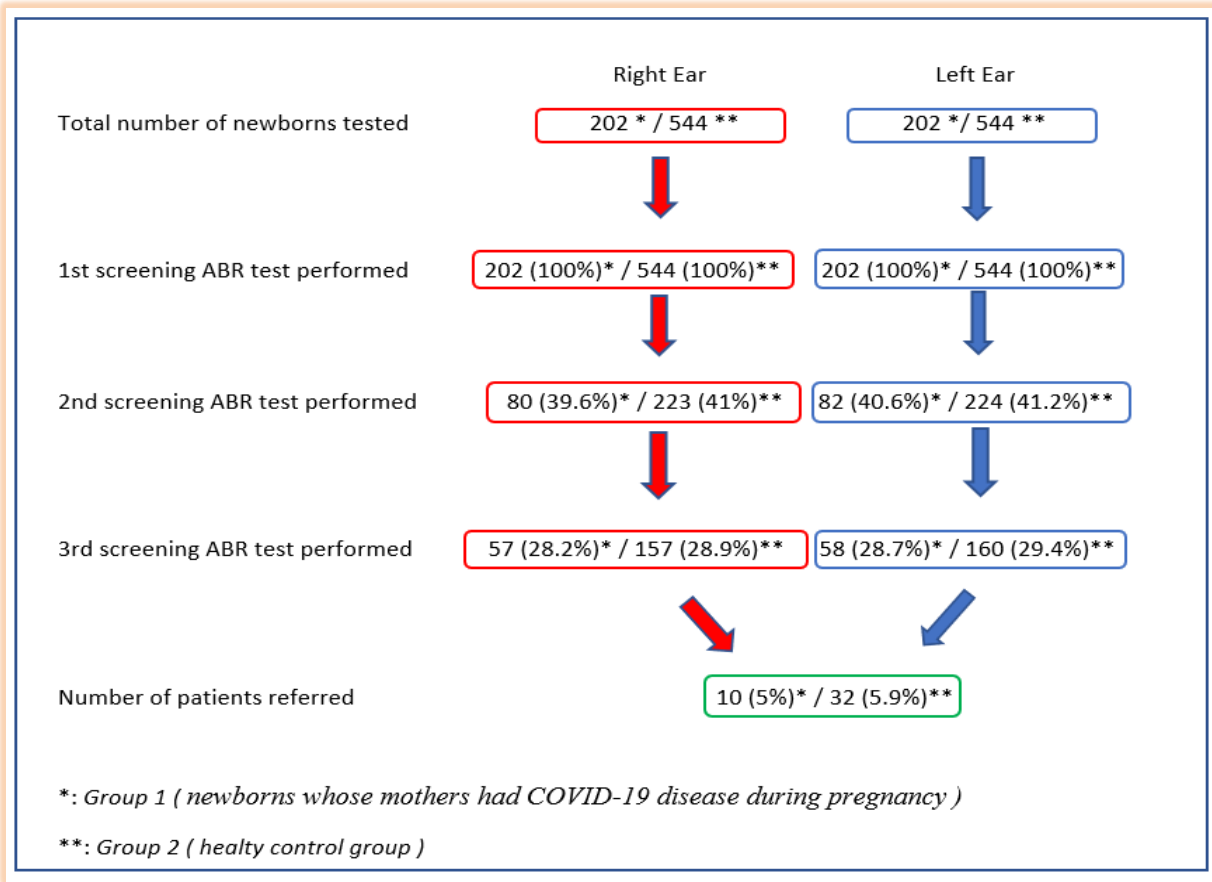

Figure 2
The numbers of passing and referral of newborn in group 1 and group 2

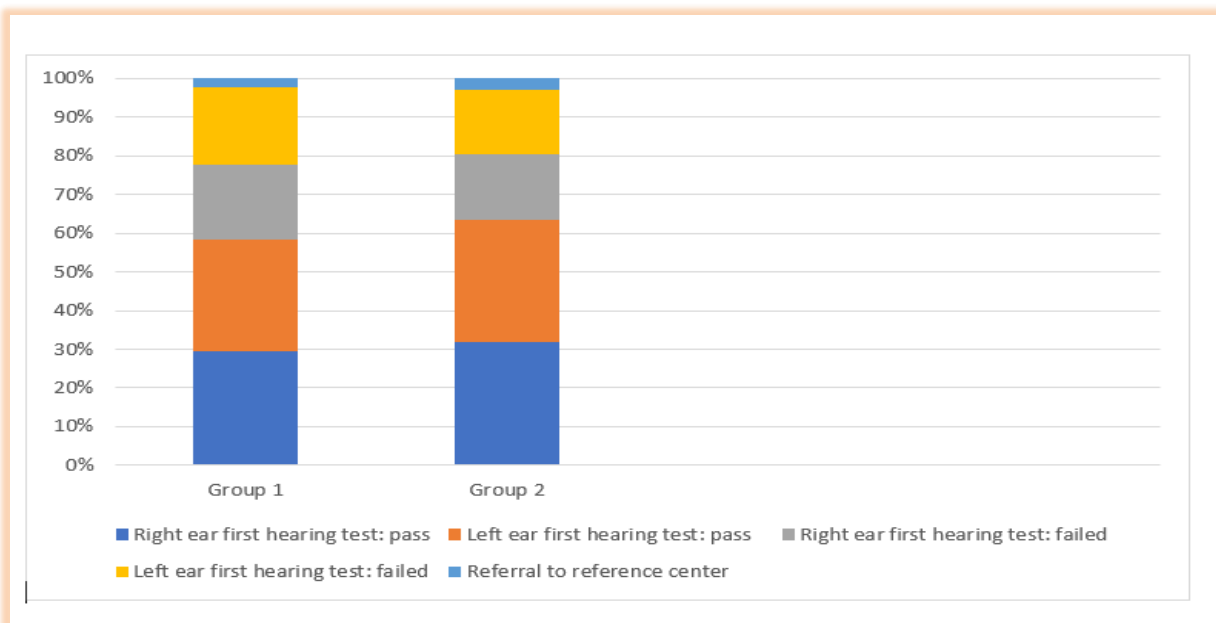

Figure 3
The Schematic view of the right and left ear first hearing test results and referral rates to the reference center between the two groups

Table 1
Categorical variables and screening results of newborns in group 1 and group 2

Variables		Group 1 (Covid-19 positive mothers) n=202	Group 2 (Covid-19 negative mothers) n=544	P value
Birthweight (gr)	min	1340	1180	
	max	5000	4500	
	25	2850	3000	0.746
Percentiles	50(Median)	3190	3100	
	75	3500	3450	
Gestational age (day)	min	0	1	
	max	200	158	
	25	1	2	0.105
Percentiles	50(Median)	5	2	
	75	18	3	
Delivery by C-section		135 (66.8%)	263 (48.3%)	<0.001
NICU stay		173 (85.6%)	462 (84.9%)	0.898
Referred on 1st screen		R=80 / L=82	R=223 / L=224	0.234
Referred on 2nd screen		R=57 / L=58	R=157 / L=160	0.150
Referred on 3rd screen		10	32	0.755

There were 202/746 (27.1%) newborns in Group 1 and 544/746 (72.9%) newborns in Group 2 (Fig. 2). Of all newborns, 398/746 (53.4%) were delivered by cesarean section and 348/746 (46.6%) were delivered by normal delivery. Birth weights are between 1.180 and 5.000 g; the mean was 3.108.1±538.6. There was no statistically significant difference between the two groups in terms of birth weight (p>0.05). Although the week of birth varied between 27 and 42; the mean was 39±1. There was a statistically significant relationship between the mother having Covid-19 during pregnancy and the delivery type of the newborn (p<0.001). While most of the mothers who did not have Covid-19 gave birth naturally 281/544 (51.7%), most of the mothers who had Covid-19 had a cesarean section 135/202 (66.8%). There was no statistically significant relationship between the mother's Covid-19 status and the need for intensive care of the newborn (p=0.898) (Table I). Their ages ranged from 1 to 200 days with a mean of 4.4±1.3. There was no statistically significant difference between the two groups in terms of testing age (p>0.05).

When the first test results of the newborns in Group 1, 80/202 (39.6%) right ears failed the test; 82/202 (%40.6) left ears failed the test. And in Group 2, 188/544 (34.6%) right and left ears failed the test equally. It was observed that a total of 42/746 (5.6%) newborns were referred to a reference center because they could not pass at least 1 of the AABR 3rd test results. There was no statistically significant difference between the two groups in terms of referral to a reference center (p=0.775) (Fig. 3).

4. Discussion

Bilateral permanent severe hearing loss in early childhood may interfere with children's speech, language, and cognitive development; and due to its increasing societal cost, it may cause negative effects on social, emotional, and academic development. However, children with mild or unilateral permanent hearing loss may have speech, language, educational, and psychosocial disorders[6]. Recognition of hearing loss in an infant by the family is generally not possible until the infant is 2-3 years old[3,7]. The ideal approach for the national newborn hearing screening program is to screen all infants before the first month after birth, to diagnose them at 3 months of age, and to provide an appropriate response (audiological, medical, and educational) until 6 months of age[6,8].

National newborn hearing screening is important in terms of reintegrating individuals with hearing loss into society through early rehabilitation and it is accepted as a mandatory screening in most countries.[2] In this screening program, which is also mandatory in our country, the screening is auditory brainstem responses (AABR)[3]. The screening program can be applied in different ways between countries and even in different regions within the same country. In some settings, the first screening occurs in the hospital. An out-patient screening enhances reliability of testing as fluid/vernix has likely resolved but also poses potential increases in losing infants in the follow-through of testing.

There are programs in which only OAE or ABR is used or in combination, and there are studies comparing these programs[6,9-11]. The response obtained in the measurements made with the scanning ABR is evaluated automatically and gives a result as passed or failed.[7] In the analysis performed by Cebulla et al.[10] in 2014, a 2-stage AABR screening program was applied and when the patients who got *passed* results were followed prospectively for 2 years, no permanent hearing loss was found in any of them. In this sense, the sensitivity of screening programs was found to be 100%. In the study conducted by Demir et al.[2] in 7.780 newborns in 2019, they adopted a 3-stage program as a hearing screening test. They used TEOAE in the first stage (on the first 3 days), TEOAE or DPOAE in the second stage (on the 15th day), and AABR in the third stage (1st month). In accordance with the literature, as the 3rd day approaches in the TEOAE test performed in the first 3 days, the infants' *passed* result rate had increased. At the end of the three stages, congenital hearing loss (47 bilateral, 3 unilateral) was detected in 50 newborns, and a ratio of 6/1.000 was obtained. They argued that the three-stage screening program had higher rates of detecting hearing loss in newborns than the other two-stage programs (in which TEOAE and AABR were used). In our study, T-ABR (Scan ABR/AABR) was used in accordance with the national newborn screening program. In our study, it was observed that the screening test of Group 1 and Group 2 babies was performed early enough and there was no difference between the test ages. This result reflects the importance given to the screening program despite all the negative aspects of the pandemic period in

terms of this mandatory testing service, among pregnant women with and without Covid-19.

In the study conducted by Sezer et al.[3] in 2017 with 253 newborns, they emphasized that cesarean section or normal vaginal delivery had no effect on hearing screening test results. In our study, the rate of cesarean section (66.8%) in Covid-19 positive mothers was high, but this did not cause a significant difference between the hearing screening test results in the two groups.

There is no single cause of congenital hearing loss, but it is a multifactorial condition that includes anatomical pathologies in the inner ear, mutations in inner ear endolymph hemostasis and conduction, mechanical-electrical conduction pathologies, and prenatal infections.[12] Cytomegalovirus, which is one of the prenatal infections, is the most common cause of non-genetic congenital hearing loss. Rubella virus, Toxoplasma, Syphilis, and Herpes simplex virus are also other pathogens[13]. The effect of Covid-19 disease, which causes many clinical spectrum and pandemic, during pregnancy on hearing in newborns is unknown.

The presence of ACE-2 receptors in cells belonging to the placenta was investigated in the immunochemical study conducted by Faure-Bardon et al.[14] in 2020 on 8 samples. This receptor was not observed in cytotrophoblasts and syncytioblasts before 7 weeks. There was no difference in ACE-2 receptor levels in the placenta of the Covid-19 positive mother and in the normal placenta, and it was detected at a minimal level. This finding may be compatible with the result of our study. The reason why we could not find a difference in hearing screening results in babies born to Covid-19 positive mothers in our study may be due to the fact that the fetus was not affected by Covid-19 in the intrauterine period. Also one potential protective mechanism suggesting fetuses may not be at greater risk for hearing loss due to maternal Covid-19 vaccine.

As new illnesses arise, it is important to understand if these need to be added to risk factors we consider as important to recognize a higher rate of hearing loss or late onset hearing loss. This data does not suggest that maternal Covid-19 during pregnancy confers a higher refer rate on hearing screening. As far as we searched the literature, there is no article similar to the results of our study. Çelik et al.[15] and Alan et al.[16] results different from our results.

In the study conducted by Çelik et al.[15] in 2021 with babies born to 37 Covid-19 positive pregnant women and 36 healthy (Covid-19 negative) pregnant women, a significant hearing loss in the babies born to Covid-19 positive pregnant women in cooperation with the other group was found. They found low TEOAE amplitudes in patients at high frequencies (3–4 kHz) and weak contralateral suppression activity of patients, especially at higher frequencies (2,3,4 kHz). They argued that there is an insufficiency in the medial olivocochlear efferent system in babies exposed to intrauterine SARS-CoV-2 and emphasized that cochlear functions should be examined in babies whose mothers had Covid-19.

In the study conducted by Alan et al.[16] in 2021 with babies born to 118 Covid-19 positive pregnant women and 118 healthy (Covid-19 negative) pregnant women, their hearing levels were compared with AABR results, and it was found that the number of referrals and hearing loss were statistically higher in babies of pregnant women who were positive for Covid-19 compared to the other group. Alan noted screening "in the first 2 weeks of age" with a rescreen in 2 weeks from the first test (potentially moving to an age of 1 month). But we described screening within 72 hours of discharge followed by a re-screen in 7-15 days. The differences between the results of our study and Alan's study may be due to the difference in scanning times.

In our study, when Group 1 and Group 2 were compared, we did not detect any difference in the amount of stay in the right and left ears in the first test results. In addition, there was no statistically significant difference in terms of referral. Although there is a need for further controlled studies to be conducted with the Clinical ABR test to investigate the effect of Covid-19 disease on hearing, our study did not detect a negative effect of having Covid-19 disease during pregnancy on AABR results.

4.1. Limitation

The limitations of this study are the lack of information about the trimester that mothers were exposed to covid-19 and the hearing status of the referred newborns.

5. Conclusion

It was observed that the Covid-19 disease of the mother during pregnancy does not affect the newborn hearing screening results. Our newborn national hearing screening program continued to be implemented without interruption during the Covid-19 pandemic. We think it would be good to need for more studies as well as some longitudinal data on children pre-natally exposed to maternal Covid-19 to help us ensure there is not a risk for late-onset hearing loss. Current protocols would suggest no further need for testing once the child has passed hearing screening/testing and this may in fact be true.

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Statement of ethics

The study approval was obtained from Adana City Hospital Clinical Research Ethics Committee. (Meeting Number: 89, Decision Number : 1570, Date: 09/30/2021),following the most recent version of the Declaration of Helsinki.

Conflict of interest statement

The authors declare that they have no financial conflict of interest with regard to the content of this report.

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Author contributions

All authors conceptualization, design, supervision, literature review, conduction and writing- original draft preparation. All authors contributed to the final manuscript revisions and approved the final version.

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