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Original articles

Hearing screening analysis in children exposed to the Zika virus

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ABSTRACT

Purpose: to analyze the results of neonatal hearing screening examinations in newborns with and without microcephaly, exposed to the Zika virus, without other risk indicators for hearing loss, and verify the association between screening results, sample characteristics, and the gestational trimester when exposure took place.

Methods: a descriptive cross-sectional study. Subjects included in the study had no risk indicator for hearing loss other than microcephaly, and presented, along with their mothers, positive RT-PCR results, respectively at birth and during pregnancy. The transient evoked otoacoustic emission and brainstem auditory evoked potential examinations were applied by the researcher between March 2016 and December 2017. Newborns failed the screening when they failed at least one retest in at least one ear. The data were descriptively analyzed, using the Fisher exact test; p-values equal to or lower than 0.05 were considered significant.

Results: out of the 45 subjects, 30 (66.7%) were females, 6.7% were likely to have sensorineural hearing loss, with or without auditory neuropathy spectrum disorder – which was possibly present in only one ear of one of these three subjects. Failure in the screening was statistically significant in subjects with at least one of the congenital Zika syndrome characteristics and subjects with subcortical calcification and brain cortex thinning, macular chorioretinal atrophy with focal pigmentary mottling, and hypertonia with symptoms of extrapyramidal involvement. The gestational trimester of exposure was associated with screening results.

Conclusion: the responses in screening point to the possibility of hearing loss in newborns with and without microcephaly, whereas the presence of microcephaly was not significant to examination failures. Exposure in the first gestational trimester indicated a possible relationship with screening failures.

Keywords: Newborn; Hearing Loss; Zika Virus; Microcephaly; Congenital Abnormalities

INTRODUCTION

According to the 2013 National Health Survey in Brazil, 0.9% of the population had hearing loss due to a disease or accident, while another 0.2% had hearing loss from birth[1].

Hearing loss may lead to a poor prognosis, especially regarding language and oral communication development in childhood. However, early diagnosis and intervention may provide a significant sociocognitive improvement to children[2].

The central nervous system is known to have great plasticity, particularly in the first 6 months of life. Hence, early stimulation increases nerve connections, enabling better auditory pathway rehabilitation[3]. Therefore, children who are diagnosed with hearing loss in the first semester of life and begin rehabilitation in that period have better cognitive, speech, and language development than those who undergo this process later[4].

Children presented with hearing loss can be diagnosed early when they have access to neonatal hearing screening (NHS) – which must preferably take place within 24 to 48 hours of life at the maternity hospital or, at the latest, within the first month of life, except when the screening cannot be made due to the child's health[5]. The objective of NHS is to refer infants to diagnosis as early as possible to reach a functional diagnosis and begin intervention before their sixth month of life, providing them a better prognosis[5].

NHS has two quick objective examinations: the evoked otoacoustic emissions (EOAE) and the automated brainstem auditory evoked potentials (A-BAEP). The decision on which examination to apply depends on the presence or absence of risk indicators for hearing loss (RIHL) in each case[6].

A-BAEP should be applied when there are RIHL, as they increase the risk of retrocochlear changes, including auditory neuropathy spectrum disorder (ANSD). These changes are not recorded in the EOAE examination, as it assesses the functionality of the auditory pathway to the region of the cochlea[6].

The 2015 Zika virus epidemic in Brazil increased the cases of microcephaly in children born to women affected by this disease during pregnancy. The Ministry of Health emphasizes that A-BAEP should be the first of the NHS examination options in such cases, as microcephaly is a risk indicator for deafness[6-8].

With the advancement of research on the impact of the Zika virus on the auditory health of newborns exposed to the disease, the studies on the hearing of newborns with and without microcephaly also increased. However, two studies in the literature[9,10] approaching subjects with and without microcephaly did not report having excluded infants with RIHL from their samples[6]. Neither did another two papers that studied only children with microcephaly[11,12] indicate the exclusion of subjects with RIHL[6]. Such non-exclusion of those with RIHL in these studies[9-12] may have led to biased results.

Given the above, the present study aimed at analyzing the auditory responses in NHS examinations of newborns with and without microcephaly exposed to the Zika virus and without any other RIHL and verify the association between screening results, sample characteristics, and gestational trimester when the exposure took place.

METHODS

This is a descriptive cross-sectional study conducted at the Department of Speech-Language-Hearing Therapy at the Hospital of the Fernandes Figueira Institute – FIOCRUZ. This paper originated from the cohort study "Vertical exposure to the Zika virus and its consequences to child neurodevelopment", carried out at the same institute.

The participants' parents/guardians were instructed about the research and, aware of its terms, necessarily signed an informed consent form in the presence of an independent witness. This form was presented in the cohort and approved by the Research Ethics Committee of the Fernandes Figueira Institute under number 52675661600005269.

Demographic variables (date of birth and sex) were collected from the medical records and history surveyed with the parents/guardians, as well as the following clinical outcomes: mother's and child's RT-PCR, made in the laboratory at the Fernandes Figueira Institute; gestational trimester when the infection took place, based on skin rash[8]; the presence of RIHL [13]; and characteristics of congenital Zika syndrome (CZS)[14].

The presence of CZS[14] was characterized using data from the "Vertical exposure to Zika virus and its consequences to child neurodevelopment" cohort database, namely: head circumference (HC); ophthalmological, neurological, and imaging examination results available (transfontanellar ultrasound, computed tomography, magnetic resonance). These criteria were analyzed because they enable the identification of some general signs of the syndrome, such as severe microcephaly (HC < -3 SD) with partial collapse of the skull; thin brain cortex with subcortical calcifications; macular scarring

and focal pigmentary mottling; congenital contracture; and marked early hypertonia with symptoms of extrapyramidal involvement[14].

The HC was analyzed with Intergrowth 21, considering severe microcephaly – i.e., HC < -3 SD with partial collapse of the skull – as characteristic of CZS[14].

The equipment used to examine the transient evoked otoacoustic emissions (TEOAE) and A-BAEP was the Madsen AccuScreen, manufactured by GN Otometrics. The NHS protocol (TEOAE and A-BAEP) verifies the functioning of various areas of the auditory pathway[6], comparing the results of both examinations.

The NHS examinations (TEOAE and A-BAEP) were applied by the speech-language-hearing therapist responsible for the research between March 2016 and December 2017. Newborns and infants of the cohort were assessed, born either at the maternity of this research institute or elsewhere, with or without microcephaly, with suspicion of exposure to the Zika virus. Initial assessments were made mostly during the hospital stay, while the subsequent ones were made in outpatient centers of the research institute, in scheduled follow-up for the other cohort visits.

The TEOAE examination was applied with automatic analysis using binomial statistics of the responses, with nonlinear sequential click stimuli at an approximate speed of 60 Hz and intensity of 70-84 dBSPL (45-60 dBHL), self-calibrated according to the volume of the canal, frequency range from 1.5 kHz to 4.5 kHz, sample rate at 16 kHz, artifact lower than 20%, and probe stability higher than 80%[15]. To pass the TEOAE, the subject needed at least eight valid peaks recorded in alternated directions, counted both above and below the median line. When the recording had less than eight peaks, the subject failed the test[15].

Regarding A-BAEP, after verifying electrode impedance, automatic analysis of the responses was made with binomial statistics, with click stimuli at an approximate speed of 80 Hz, intensity of 35 dBnHL, a sample rate of 16 kHz, and input bandwidth between 70 Hz and 4 kHz. A pass result in A-BAEP indicates the detection of a brainstem auditory response to 35-dBnHL stimuli, particularly between 2 kHz and 4 kHz. Passing the examination ensures that a significant hearing loss at these frequencies can be ruled out with 99.5% certainty. A fail record means that the brainstem auditory response to 35-dBnHL stimuli was not detected, particularly between 2 kHz and 4 kHz[15].

In case of failure in TEOAE and A-BAEP, they were retested[5]. The retests were applied approximately 15 days after the tests.

Infants with abnormal NHS – i.e., who failed at least one of the examinations in the retest – were referred for otorhinolaryngological and audiological diagnostic assessment[6].

The inclusion criteria were as follows: being born to women with positive RT-PCR during pregnancy, from either blood, urine, amniotic fluid, or placental sample; and newborns or infants with positive RT-PCR laboratory test, from either blood, urine, or cerebrospinal fluid sample. In both situations, the only RIHL present was microcephaly.

Subjects that did not conclude the NHS (because of either nonattendance or death), that had a negative RT-PCR and whose mothers also had a negative RT-PCR, who did not obtain the result of the examination, or who had a RIHL other than microcephaly were excluded from the study.

The TEOAE and A-BAEP results were analyzed both separately and in combination. Newborns/infants who passed both tests or both retests in both ears passed the screening, whereas those who failed at least one retest in at least one ear failed the screening. For subjects who needed the retest, the final result was considered – i.e., the results that were included in the study analysis.

Data analysis was made with descriptive analysis of the data and statistical tests, both using the SPSS software. The significance level was set at 0.05.

In the descriptive analysis, the relative frequencies of the variable categories in the study were presented. Then, the Fisher exact test was used to test the association of the study variables with NHS results. The null hypothesis in this test is that the variables are not statistically associated. Thus, the null hypothesis is rejected, concluding that the variables were significantly associated in cases when the p-value was lower than the set significance level.

RESULTS

Altogether, 128 newborns and infants were assessed; 83 of them were excluded from the study for the following reasons: 42 for nonattendance or death, 29 for mother's and subject's negative or unknown RT-PCR laboratory test results, and 12 for having other RIHL. Hence, this study sample comprised 45 subjects – 30 (66.7%) females and 15 (33.3%) males.-

Most subjects born in this institute (n = 25; 55.6%) were submitted to the first NHS examination between the first 24 hours and 30 days of life, except for four individuals, whose first assessment took place between 30 and 60 days of life due to their serious health condition. As for infants born in other maternities in Rio de Janeiro (n = 20; 44.4%), the first NHS examination took place between 48 hours and 90 days of life, except for one subject, who was assessed at 5 months of life due to their clinical conditions.

The median age at the first screening examination was 7 days (IQR 2-32 days).

Chart 1 presents the distribution of sex, number of newborns with and without CZS characteristics[14], and presence of the five general symptoms of the syndrome[14] in relation to NHS results. It also highlights the variables with the greatest frequencies of fails in NHS, verifying a statistically significant association between NHS fails and the presence of at least one CZS characteristic[14], subcortical calcification and brain cortex thinning, macular chorioretinal atrophy with focal pigmentary mottling, and hypertonia and symptoms of extrapyramidal involvement. It is important to highlight that there was a trend toward significance between NHS fail results in Chart 1 and the occurrence of severe microcephaly with partial collapse of the skull – the most studied clinical manifestation of the disease among the CZS characteristics[14]. However, no association was verified between the results of these variables (p-value = 0.059).

The most frequent CZS characteristic[14] in this study was hypertonia and symptoms of extrapyramidal involvement (n = 12; 27%), followed by subcortical calcification and brain cortex thinning (n = 11; 24%), severe microcephaly (HC < -3 SD) with partial collapse of the skull (n = 7; 16%), macular chorioretinal atrophy with focal pigmentary mottling (n = 6; 13%), and lastly, congenital contracture in one infant (2% of the sample).

Chart 1. Overall sample characteristics (n = 45) in relation to neonatal hearing screening results

	NHS fail	NHS pass	p-value
Sex			
Males	1 (2.2%)	14 (31.1%)	0.746
Females	2 (4.5%)	28 (62.2%)	
CZS characteristics			
Without characteristics	0 (0.0%)	32 (71.1%)	0.020*
With at least one characteristic	3 (6.7%)	10 (22.2%)	
Severe microcephaly (< -3 SD) with partial collapse of the skull			
Yes	2 (4.5%)	5 (11.1%)	0.059
No	1 (2.2%)	37 (82.2%)	
Subcortical calcification and brain cortex thinning			
Yes	3 (6.7%)	8 (17.8%)	0.012*
No	0 (0.0%)	34 (75.5%)	
Macular chorioretinal atrophy with focal pigmentary mottling			
Yes	3 (6.7%)	3 (6.7%)	0.001*
No	0 (0.0%)	39 (86.6%)	
Congenital contractures			
Yes	1 (2.2%)	0 (0.0%)	0.067
No	2 (4.5%)	42 (93.3%)	
Hypertonia and symptoms of extrapyramidal involvement			
Yes	3 (6.7%)	9 (20.0%)	0.016*
No	0 (0.0%)	33 (73.3%)	

*Significant at 0.05 level. Fisher's exact test
Captions: CZS = congenital Zika syndrome; SD = standard deviation

Chart 2 describes the TEOAE and A-BAEP results both alone and in combination, according to the presence or not of severe microcephaly (HC < -3 SD) with partial collapse of the skull[14], with NHS failure in 6.7% of the study sample (three infants). The individuals who failed the TEOAE were the same who failed the A-BAEP.

Chart 2. Results of the TEOAE, A-BAEP, and TEOAE + A-BAEP examinations, according to the presence or not of congenital Zika virus syndrome microcephaly

	With microcephaly		Without microcephaly	
	Pass	Fail	Pass	Fail
TEOAE	5	2	37	1
A-BAEP	5	2	37	1
A-BAEP + TEOAE	5	2	37	1

Captions: TEOAE = transient evoked otoacoustic emissions; A-BAEP = automated brainstem auditory evoked potentials.

Chart 3 presents the TEOAE, A-BAEP, and TEOAE + A-BAEP results of the three subjects who failed the NHS (per ear). Each one of them had four out of the five CZS characteristics[14].

Infant 3, without microcephaly, had more ears failing the NHS examinations (TEOAE and A-BAEP) than infants 1 and 2, who had microcephaly (Chart 3).

Chart 3. Results of the TEOAE, A-BAEP, and TEOAE + A-BAEP examinations per ear of infants who failed the neonatal hearing screening

Infants	TEOAE		A-BAEP		TEOAE + A-BAEP	
	RE	LE	RE	LE	RE	LE
1 (with CZS microcephaly)	P	F	P	F	P	F
2 (with CZS microcephaly)	P	F	P	F	P	F
3 (without microcephaly)	F	P	F	F	F	F

Captions: TEOAE = transient evoked otoacoustic emissions; A-BAEP = automated brainstem auditory evoked potentials; RE = right ear; LE = left ear; P = pass; F = fail

Lastly, the results presented in Chart 4 show an association between the gestational trimester when exposure occurred and the NHS results.

Chart 4. Relationship between the gestational trimester when the exposure to the Zika virus took place and neonatal hearing screening results

Gestational Trimester of Exposure	NHS fail	NHS pass	p-value
1st Trimester	2 (4.4%)	13 (28.9%)	0.016*
2nd Trimester	0 (0.0%)	23 (51.1%)	
3rd Trimester	0 (0.0%)	6 (13.4%)	
Undetermined	1 (2.2%)	0 (0.0%)	

*Significant at the 0.05 level. Fisher's exact test
Captions: NHS = neonatal hearing screening

DISCUSSION

The RT-PCR laboratory test is the one indicated by the Ministry of Health to detect the Zika virus, as it is the gold standard to identify the disease[16]. Therefore, the researchers of the cohort at the Fernandes Figueira Institute that originated this study chose this laboratory examination.

One study stands out among those retrieved from the literature, as it studied animals using RT-PCR in 100% of its sample[17]. Other studies used this examination in part of their samples as well[9,18]. Three papers used serology instead of RT-PCR to confirm the disease in their samples[11,19,20], while another two included children of pregnant women that had a skin rash, though without laboratory confirmation of viral infection[10,12].

In the present study, RT-PCR enabled the inclusion of symptomatic and asymptomatic subjects – i.e., newborns or infants with and without clinical CZS characteristics[14]. This provided a better understanding of the disease encompassing those exposed to the virus, instead of only a given group with specific clinical characteristics of the syndrome.

In the study sample, the most common manifestation of the syndrome was hypertonia and symptoms of extrapyramidal involvement, while microcephaly was the third most common of the five characteristics described by Moore et al. (2017)[14]. This finding indicated that health professionals need to take a broader clinical look at all CZS characteristics, rather than only microcephaly.

None of the studies found in the literature described results related to the CZS characteristics. Two studies presented auditory assessment results of infants with and without microcephaly[9,10], while the other studies retrieved from the literature were directed to the impact of the virus on the hearing of subjects with microcephaly[11,12,18-20].

The Zika virus can knowingly occur without presenting symptoms in newborns[21] or manifesting up to five clinical characteristics[14]. Hence, all subjects exposed to the disease must be approached, rather than only those with microcephaly. Also, all CZS clinical manifestations must be analyzed, rather than only microcephaly. Thus, it is possible to know the sample better and establish relationships between clinical manifestations and auditory examination results.

The broader sample description and analysis in this study made it possible to verify statistical significance between the presence of at least one CZS characteristic[14] and NHS failures. They also revealed the significance of certain CZS characteristics with NHS failures, such as subcortical calcification and brain cortex thinning, macular chorioretinal atrophy with focal pigmentary mottling, and hypertonia and symptoms of extrapyramidal involvement.

This and other studies in the literature[9,12,18,19] used the standard concept to characterize microcephaly: HC < -2 SD of the specific mean per sex and gestational age[22]. As for the degree of microcephaly, the methodology in this and other published papers[12,19,20] distinguished microcephaly (HC < -2 SD) from severe microcephaly (HC < -3 SD), both defined based on the specific mean per sex and gestational age[23]. Other studies[10,11,18], however, did not distinguish the degrees of microcephaly and included subjects with microcephaly in their samples. These methodological differences may lead the researcher to mistaken results, as the microcephaly reported in the study may not have the characteristics of CZS-specific microcephaly[14]. Therefore, identifying the different degrees of microcephaly seems to be the best way to understand the impact of disease-specific microcephaly.

Regarding RIHL, two studies were careful to exclude subjects with specific indicators, although they did not exclude 100% of the RIHL[18,20]. The other papers found in the literature did not exclude subjects with RIHL[9-12].

Both the confirmation of exposure to the Zika virus with RT-PCR and the exclusion of all RIHL other than microcephaly (as it was focused on in this study) were essential to avoid confounding biases of this disease with other possible causes of auditory changes. This made it possible to relate potential NHS failures with actual exposure to the Zika virus.

Three subjects (6.7%) in this study failed the NHS, two of whom have microcephaly characteristic of CZS [14]. It was also possible to discriminate each result examination both alone and in combination, according to the presence or not of severe microcephaly (HC < -3 SD) with partial collapse of the skull[14].

Two studies in the literature assessed a mixed population – i.e., subjects with and without microcephaly[9,10]. In the first one[9], the authors did not divide the subjects into two different groups, and the results did not point to auditory changes. In the second study[10], the authors did not inform whether the TEOAE failures (present in 6.6% of the sample) occurred in subjects with or without microcephaly.

It is important to describe auditory examination results of groups with and without microcephaly

separately because CZS-specific microcephaly is the most relevant finding among those that impair the central nervous system of fetuses and newborns infected with the Zika virus at the beginning of pregnancy[24]. However, the present study did not find any association between NHS results and microcephaly.

This paper observed that three infants failed the NHS. The data point to the possibility of sensorineural loss, with or without ANSD, in the left ear of infants 1 and 2 and the right ear of infant 3. The findings also point to a likely presence of ANSD alone in the left ear of infant 3, who passed the TEOAE and failed A-BAEP, which is suggestive of this pathology[25].

Although A-BAEP is less sensitive to detecting changes in the middle ear than TEOAE[5,6], the influence of middle ear changes in the results of infants 1 and 2 could not be completely ruled out. They unilaterally failed both tests (left ear), but neither otoscopy nor acoustic immittance was made before their retest. Infant 3, on the other hand, who bilaterally failed the TEOAE and A-BAEP (except for the left ear in the TEOAE), had a normal otoscopy before the retest. Therefore, in this infant (without microcephaly), NHS examinations may not have been influenced by any conductive component, particularly excluding any physical obstruction in the eternal auditory meatus.

Among the studies presented, only the ones whose subjects had microcephaly and had been demonstrably exposed to the Zika virus[19,20] described the laterality of the auditory changes. In the study with one individual with severe microcephaly, the diagnosis was bilateral sensorineural hearing loss[19]. In the study with 69 subjects, four of them were diagnosed with sensorineural hearing loss – two of them bilateral and the other two unilateral loss[20].

Part of the results in the study by Leal et al. (2016)[20], whose subjects had microcephaly, had values near those in the present study, as 5.8% of the population were diagnosed with sensorineural hearing loss. In this research, 6.7% of the sample had the possibility of having the same type of hearing loss. The results differ when approaching the presence of ANSD. In the present study, one subject without microcephaly may have ANSD, while Leal et al. (2016)[20] verified only sensorineural hearing loss, which impaired the hearing of subjects with severe microcephaly.

The paper by Silva et al. (2017)[11] approached subjects with microcephaly and suspicion of exposure to the Zika virus (based on the mothers' clinical symptom of skin rash during pregnancy). They demonstrate that the screening examination results (TEOAE and A-BAEP) corroborate the findings of the present paper regarding the odds of the sample having sensorineural changes, as well as ANSD.

Silva et al. (2017)[11] also found the risk (4.2%) of a subject having ANSD, as they passed the TEOAE and failed BAEP – which suggests the presence of this pathology[25]. As for the number of failures in the NHS examinations, the results in the studies diverge considerably. This research recorded 6.7% of failure in the sample in at least one of the two screening tests; as for the study in question[11], 79% of those assessed failed at least one of the two screening tests. Also, while this study did not observe any difference between TEOAE and A-BAEP failures – i.e., 6.7% failed the TEOAE and 6.7% failed the A-BAEP –, in the study by Silva et al. (2017)[11] the TEOAE failures reached 75%, while in A-BAEP they were 29%.

A paper[17] studied mice demonstrably exposed to the Zika virus in the uterus with an RT-PCR laboratory test. Its objective was to verify action potentials collected in the promontories with BAEP (with tone-burst at 4 kHz, 6 kHz, and 8 kHz, 85-95 dB, click, and tone-pip at 8 kHz) and study the cochlea of infected rats with hearing loss with histopathological and immunohistochemical analyses. These authors concluded that hearing loss in some mice was transitory, while in others it was long-lasting. This suggests that exposure to the Zika virus during the fetal period may lead to chronic or permanent hearing loss. The study also observed that there was no statistically significant difference in the number of outer hair cells between rats with profound hearing loss and the control group. This indicates that hearing loss associated with the Zika virus infection seemingly does not involve damaged cochlear hair cells, as the cochlea in the rats with profound hearing loss were intact. This situation is not coherent with the definition of sensorineural hearing loss, which is characterized by impaired outer hair cells, possibly affecting the functioning of inner hair cells as well[26].

On the other hand, the present paper demonstrated that 6.7% of the sample possibly had a sensorineural loss with or without ANSD – which is suggestive of impaired cochlear cells, as the failures occurred in both TEOAE and A-BAEP examinations. However, the possibility of having ANSD was observed only in the left ear of subject 3 – which is similar to the results found by Julander et al. (2018)[17], as a profound hearing loss without changes in the outer hair cells of mice may suggest the presence of ANSD.

Three studies found different outcomes from those described in these results[9,10,18]. In the study by Marques Abramov et al. (2018)[18], the results point to normal brainstem functioning. In the paper by Fandino-Cardenas et al. (2018)[9], none of the subjects assessed had hearing loss. Lastly, the study by Borja et al. (2017)[10] concluded that the TEOAE failures may have been caused by conductive problems, although the study presented 6.6% of TEOAE failures – which is close to the percentage found in this research. The authors[10] described that no tests or procedures were conducted to rule out changes in sound transmission and that the nervous conduction had absolute latencies and interpeak intervals adequate to the age, with clear amplitude and response level at 30 dBHL with click-BAEP.

Concerning the gestational trimester, exposure to the Zika virus acquired in the first trimester may be related to failure in NHS examinations.

Another two studies also pointed to auditory problems in children born to mothers who acquired the disease in the first gestational trimester[19,20]. One of these studies is a case report of a woman who was infected in the first trimester of pregnancy and whose infant was diagnosed with bilateral profound sensorineural hearing loss[19]. The other study[20] demonstrated that four out of five children of mothers who had rash skin during the first trimester of pregnancy were diagnosed with sensorineural hearing loss. However, despite this verification, the study concluded that the trimester when the pregnant women had rash skin was not significantly associated with the diagnosis of sensorineural hearing loss.

The conclusion of the abovementioned study[20] differs from that of this paper, as it found a significant association between gestational trimester of exposure and NHS results – i.e., exposure in the first gestational trimester (when the cochlea is being formed)[27] may be related to failures in the TEOAE and A-BAEP examinations.

In contrast with the above results, another paper[28] describes the possibility of the Zika virus infection in the third gestational trimester causing less severe problems in newborns. The milder deformities mentioned by the authors, caused by exposure to the disease at the end of the pregnancy, include sensorineural deafness[28].

Not performing otoscopy in all participants and not performing acoustic immittance were some of the limitations of the present paper. Also, not applying diagnostic BAEP examination made it impossible to visualize the functionality of the auditory pathway and determine the auditory threshold. Nevertheless, it must be emphasized that the diagnostic BAEP assessment was not included in this study methodology.

CONCLUSION

Newborns with and without microcephaly exposed to the Zika virus and without RIHL failed NHS examinations, indicating that 6.7% of this study sample may be presented with hearing loss. Even though severe microcephaly with partial collapse of the skull is the most studied clinical manifestation of the Zika virus disease among all CZS characteristics, no association was found between NHS failures and the occurrence of microcephaly.

As for the gestational trimester of exposure, an association was found between NHS results and the trimester when the pregnant mother acquired the disease, indicating a possible relationship between NHS failures and contamination with the Zika virus in the first gestational trimester.

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