RESEARCH ARTICLE

Age and Other Factors Affecting the Outcome of AABR Screening in Neonates

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ABSTRACT

BACKGROUND: Although the utility of universal newborn hearing screening is undisputed, testing protocols vary. In particular, the impact of the infant's age at the time of automated auditory brainstem response (AABR) screening has not been well studied.

METHODS: We conducted a retrospective review of newborn hearing screening data in 6817 low-risk, term and late-preterm newborns at our large, urban, academic medical center for a 1-year period to analyze the impact of age and other factors on the screening failure rate and referral for diagnostic testing.

RESULTS: AABR screening failure rates decreased with postnatal age over the first 48 hours; 13.3% failed at <24 hours versus 3.8% at ≥48 hours (P < .0001). Infants who were initially tested at ≥36 hours failed repeat testing more often than those who were tested at <36 hours (11.5% vs 18.9%; P = .03). Other factors that were associated with failure included being a boy and of a race other than white. Sensorineural hearing loss (SNHL) was diagnosed in 18.6% of infants who failed their final screening at ≥48 hours compared with 2.8% of those whose final screening occurred earlier (P = .03). SNHL was more likely in infants who failed their first screening bilaterally (21.2%) than unilaterally (4.4%); P = .03.

CONCLUSIONS: Among healthy newborns, delaying AABR screening in the first 48 hours minimized failure rates. SNHL was 6 times as likely in infants who failed their final screening at ≥48 hours compared with those who were screened at <48 hours of age. In our study, we offer guidance for nursery directors and audiologists who determine hearing screening protocols and counsel families about results.

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The Centers for Disease Control and Prevention's Joint Committee on Infant Hearing (JCIH) has endorsed universal hearing screening before nursery discharge for more than 1 decade.[1] The JCIH has established broad standards for newborn hearing screening, including the use of otoacoustic emissions (OAE) and automated auditory brainstem response (AABR) as the only screening methods.[1] State Early Hearing Detection and Intervention programs further provide more specific screening protocol guidance in the areas of program management, personnel, and adherence to best practice rescreen policies, limiting rescreens before discharge to 1 or 2 only. Typically, however, individual birthing centers determine the specifics of where and when screenings will take place on the basis of their own nursery protocols, available personnel, discharge policies, and community resources.

Screening protocols must be used to strive to identify hearing loss while avoiding false-positives to the greatest extent possible. Maintaining a low rate of false-positive screening failures reduces parental anxiety[2–4] and significantly decreases costs[5] by avoiding unnecessary rescreens at the birthing center as well as referrals to diagnostic facilities for further testing.

Factors that are most likely to increase false-positive failure rates in young neonates are related to commonly occurring conditions of the ear that can cause temporary conductive hearing loss, which improves steadily over the first few days of life.[6–10] Studies have revealed that older infants pass OAE screening at higher rates than younger infants.[11–18] This age effect has not been as extensively studied for AABR screening.[18]

Our primary purpose in the current study was to examine our hospital's AABR hearing screening protocol by reviewing hearing screening data from a 1-year period and to retrospectively analyze the impact of age at the time of screening on outcomes.

METHODS

In this study, we included the hearing screening results for all 6817 infants ≥35 weeks' gestation born in 2013 who were screened in and discharged from the well-newborn nursery at a large, tertiary-care hospital. Our study was approved by the hospital's institutional review board for human subject research.

Screening was accomplished by using the Natus Algo 5 AABR screener. A pass result was achieved when there was a >99% likelihood that an auditory brainstem response had been detected.

Infants were screened according to the hospital's established program protocol. Screenings were performed in the newborn nursery or a quiet room adjacent to the nursery by trained and experienced newborn hearing screening technicians, with the program audiologist being available on-site during weekdays and by pager on weekends and holidays to answer questions and troubleshoot problems. Infants who were born vaginally typically received their first screening at 12 to 36 hours of age, whereas screening for infants born by cesarean was usually delayed until 36 to 48 hours of age. Infants who did not pass the first screening were rescreened 24 to 48 hours later, before discharge. Infants who failed the second screening were scheduled for full diagnostic audiologic evaluation at an outside facility according to our state's Department of Public Health guidelines. Both the first and second screenings were conducted bilaterally according to the current screening recommendations of the JCIH 2007 Position Statement.[1]

We separately examined the factors associated with the following: (1) failing the initial screening, (2) the need for referral for diagnostic audiological evaluation, and (3) the results of diagnostic testing. Our primary question was whether there was an association between the timing of the initial screening test and its results. For the entire cohort of 6817 infants, we divided the variable "age at time of test" into 4 categories: <24 hours, 24 to 36 hours, 36 to 48 hours, and >48 hours. To maintain a reasonable number of infants in each cell when analyzing the impact of age for the 633 infants who required a second screening, we chose to dichotomize the variable at 36 hours of age, combining the lower 2 and upper

2 categories that were used for the entire cohort. We also examined the infant characteristics that commonly influence newborn outcomes because they might confound any association between age at screening and screening failure. Factors examined included sex, gestational age (GA), race and/or ethnicity, and birth weight as well as whether a birth was vaginal or by cesarean. The classification of race and/or ethnicity was based on maternal self-report according to the categories established by the hospital. The crude association of these factors with screening results was determined by using χ^2 tests or Fisher's exact tests, as appropriate, with $P < .05$ being considered statistically significant.

We performed logistic regression analyses to evaluate the association between timing and screening outcomes while controlling for potentially confounding factors. Separate analyses were performed to assess the results of the initial and final screening. For each logistic regression analysis, we initially included all factors that were associated with screening outcomes at a level of $P \leq .1$. We then did a step-down analysis, sequentially eliminating the least significant factor until all factors in the model were significantly associated with an outcome. We also retained any variable that confounded the association of age at testing with screening outcome (which was defined as a change in the point estimate of the odds ratio [OR] of at least 10%) even if that factor was not itself significantly associated with the screening outcome. Results are reported as ORs and 95% confidence intervals (CIs). All analysis was done with SAS 9.4 (SAS Institute, Inc, Cary, NC).

RESULTS

Of the 6817 newborns screened, 636 (9.3%) failed the first screening. Of those, 633 (99.5%) received a second screening before discharge, and 3 were discharged after failing the first screening only. In total, 85 newborns (1.3%) did not pass the in-hospital screening and were referred for full diagnostic audiologic evaluations.

Predictors of Failing the Initial Screening Test

As shown in Fig 1, failing the first screening test was significantly associated with age at
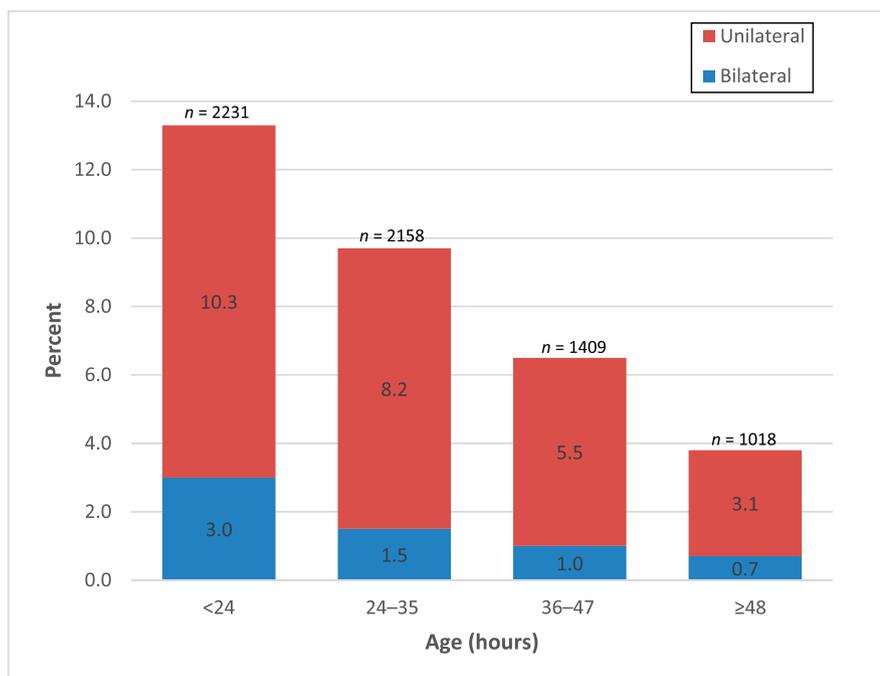
FIGURE 1 Percent of infants who failed the initial AABR screening according to age at screening.

impact of screening at <12 hours of age because there were only a small number of infants who were tested during this time frame (*n* = 104). Infant race and/or ethnicity was also associated with the likelihood of passing the first hearing screening (Table 1). African American infants had the highest rate of screening failure (13.4%), white infants had the lowest (8.1%), and Asian American and Hispanic infants had intermediate rates (10.2% and 9.3%, respectively; *P* < .001). Infants who were born vaginally were more than twice as likely to fail the first screening test as those who were born by cesarean (11.1% vs 5.1%; *P* < .001).

A multivariate logistic regression that was controlled for potential confounders revealed that age at the time of testing remained a significant predictor of failing the initial screening (Table 2). The likelihood of failing for infants who were screened at <24 hours of age was 3.2 times that of infants who were screened at ≥48 hours of age (95% CI = 1.9–5.2). Infants who were screened between 36 and 48 hours of age had a likelihood of failing the initial screening that was 1.7 times that of those who were screened after 48 hours of age (95% CI = 1.1–2.5).

Other factors in the logistic model (Table 2) also remained significant predictors of failing the initial screening. African American infants had a likelihood of failing the initial screening that was nearly twice that of white infants (OR = 1.8; 95% CI = 1.5–2.3). Infants weighing >4000 g were also more likely to fail the initial screening (OR = 1.6; 95% CI = 1.2–2.1). The difference between the failure rates of infants who were born vaginally versus by cesarean in the crude analysis was no longer significant in the regression.

Predictors of Referral for Postdischarge Diagnostic Testing

Eighty-five infants were referred for diagnostic testing (82 who failed the second screening attempt and 3 who failed the single in-hospital screening). As shown in Table 1, race and/or ethnicity was a significant predictor of referral, with African American infants having the highest rate

the time of screening. When screening was delayed beyond 24 hours, failure rates decreased: 9.7% for infants who were screened between 24 and 36 hours of age, 6.5% for those who were screened between 36 and 48 hours of age, and 3.8% for those who were screened at ≥48 hours of age (*P* < .0001). We were unable to evaluate the

TABLE 1 Percent Failure of In-Hospital Screenings and Diagnostic Testing in the Overall Study Population

Characteristic	Initial Screening			Final In-Hospital Screening			Final Hearing Loss[a]		
	%	n/N	P	%	n/N	P	%	n/N	P
Sex									
Girl	9.9	330/3343	.13	1.0	32/3343	.03	0.12	4/3341	.99
Boy	8.8	306/3474		1.5	53/3474		0.14	5/3470	
GA, wk									
35–36	8.1	30/371	.40	1.9	7/371	.23	0.00	0/371	.99
37–42	9.4	606/6444		1.2	78/6444		0.14	9/6438	
Race and/or ethnicity									
African American	13.4	143/1066	< .001	3.0	32/1066	< .001	0.38	4/1064	.10
Asian American	10.2	71/695		1.4	10/695		0.14	1/695	
Hispanic	9.3	102/1100		1.5	16/1100		0.18	2/1098	
White	8.1	293/3623		0.6	23/3623		0.06	2/3621	
Birth wt, g									
<2500	7.1	20/283	.06	0.7	2/283	.69	0.35	1/283	.40
2500–3999	9.2	547/5945		1.3	75/5945		0.13	8/5939	
≥4000	11.7	69/589		1.4	8/589		0.00	0/589	
Route of delivery									
Cesarean	5.1	104/2040	< .001	0.8	17/2040	.04	0.20	4/2040	.47
Vaginal	11.1	532/4776		1.4	68/4776		0.10	5/4770	

[a] Results of posthospital diagnostic testing were unavailable for 6 infants.

TABLE 2 Logistic Regression Analysis of Factors Associated With Failure of the Initial In-Hospital Screening

Characteristic	OR (95% CI)	P
Age, h		
<24	3.2 (1.9–5.2)	< .001
24–35	2.1 (1.3–3.5)	.002
36–47	1.7 (1.1–2.5)	.02
≥48	Reference	—
Race and/or ethnicity		
African American	1.8 (1.5–2.3)	< .001
Asian American	1.3 (1.0–1.7)	.06
Hispanic	1.2 (0.9–1.5)	.25
White	Reference	—
Route of delivery		
Cesarean	0.7 (0.5–1.1)	.11
Vaginal	Reference	—
Birth wt, g		
<2500	1.0 (0.6–1.6)	.91
≥4000	1.6 (1.2–2.1)	< .001
2500–3999	Reference	—

—, not applicable.

(3.0%), white infants having the lowest rate (0.6%), and Hispanic and Asian American infants having intermediate rates of referral (1.5% and 1.4% respectively; $P < .001$). Boy infants were also more likely to require referral (1.5% vs 1.0% for girls; $P = .03$). In the crude analysis, infants who were born by cesarean were less likely to fail the final screening than those who were born vaginally (0.8% vs 1.4%; $P = .04$).

In the multivariate logistic regression model (Supplemental Table 5), being a boy remained a significant predictor of referral for diagnostic evaluation (OR = 1.6; 95% CI = 1.0–2.5), as did infant race and/or ethnicity. The likelihood of being referred for African American infants was almost 5 times that of white infants (OR = 4.8; 95% CI = 2.8–8.3). Hispanic infants were also significantly more likely to be referred for evaluation than white infants (OR = 2.3; 95% CI = 1.2–4.3), as were Asian American newborns (OR = 2.2; 95% CI = 1.1–4.7). Infants who were born by cesarean delivery remained less likely to be referred for diagnostic testing, but the difference did not meet statistical significance (OR = 0.6; 95% CI = 0.3–1.01).

Characteristics Associated With Failure of Second Screening Among Those Who Failed the First Screening

Clinicians who counsel the parents of infants who have failed the first hearing screening may find it helpful to understand those factors that are associated with an increased risk of failing the second hearing screening among this group. Of the 633 infants in our study group who had a second screening test while in the hospital, 82 (13.0%) failed and required referral for additional diagnostic evaluation (Table 3). The proportion of infants who failed the second screen was associated with the age of the infant at the time of the first screening test. Infants who were initially tested at ≥36 hours of age were significantly more likely to fail the repeat test than those who were initially tested at <36 hours of age (fail rate of 11.5% vs 18.9%, respectively; $P = .03$). Failure on the second screening test was also more common among boys and among infants of African American, Hispanic, and Asian American race and/or ethnicity. Infants who had failed the first screening in both ears were >3 times as likely to fail the second screening as those who failed the first screening in 1 ear (30.3% vs 9.0%, respectively; $P < .001$).

All of the factors that were found to be significant in the crude analysis except for Asian American race remained significant in a logistic regression analysis (Table 4). Infants who were initially screened at ≥36 hours of age had an OR of failing the repeat screening that was nearly twice that of those who were initially screened at <36 hours of age (OR = 2.0; 95% CI = 1.1–3.5). The likelihood of failing the second screening for those who failed the first screening bilaterally was >4 times that of those who failed unilaterally on the first screening (OR = 4.6; 95% CI = 2.7–7.9). Compared with girls, boys had more than twice the likelihood of failing the second screening (OR = 2.3; 95% CI = 1.4–4.0). Compared with white infants, African American (OR = 2.7; 95% CI = 1.5–5.1) and Hispanic (OR = 2.3; 95% CI = 1.1–4.8) infants were significantly more likely to fail the second screening.

TABLE 3 Percent Failure of Second Screening Test Among Those Who Failed First Screening Test ($n = 633$)

Characteristic	Failed Second Screening		
	%	n/N	P
Age at first test, h			
<36	11.5	58/506	.03
≥36	18.9	24/127	
Result of first test			
Failed unilateral	9.0	46/514	< .001
Failed bilateral	30.3	36/119	
Sex			
Girl	9.2	30/328	.003
Boy	17.1	52/305	
GA, wk			
35–36	23.3	7/30	.09
37–42	12.4	75/603	
Race and/or ethnicity[a]			
African American	21.3	30/141	< .001
Asian American	14.1	10/71	
Hispanic	15.7	16/102	
White	7.5	22/292	
Birth wt, g			
<2500	10.0	2/20	.86
2500–3999	13.2	72/544	
≥4000	11.6	8/69	
Route of delivery			
Cesarean	15.5	16/103	.39
Vaginal	12.5	66/530	

[a] Data for race and/or ethnicity were missing for 4 infants.

Results of Audiologic Testing

Diagnostic audiologic test results were available for 79 of the 85 infants who were referred for further testing (data not shown). Of those infants, 9 (11.4%) were found to have sensorineural hearing loss (SNHL). SNHL on diagnostic evaluation was found in 18.6% of the infants who failed the final screening at ≥48 hours of age compared with 2.8% in those whose final screening occurred at younger ages ($P = .03$). Hearing loss was also more likely in those infants who had failed the first screening in both ears compared with those who had failed in 1 ear (21.2% both ears and 4.4% 1 ear; $P = .03$). Similarly, the proportion of infants with SNHL was higher among those who failed the second

TABLE 4 Logistic Regression Analysis of the Factors Associated With Failure of the Final Screening Among Those Who Had Failed the Initial Screening (n = 633)

Characteristic	OR (95% CI)	P
Age of first test, h		
≥36	2.0 (1.1–3.5)	.02
<36	Reference	—
Result of first test		
Failed bilateral	4.6 (2.7–7.9)	< .001
Failed unilateral	Reference	—
Sex		
Boy	2.3 (1.4–4.0)	.002
Girl	Reference	—
Race and/or ethnicity		
African American	2.7 (1.5–5.1)	.001
Asian American	1.7 (0.8–4.0)	.19
Hispanic	2.3 (1.1–4.8)	.02
White	Reference	—

—, not applicable.

screening in both ears (26.7% vs 7.8% in 1 ear), although this difference did not reach statistical significance (P = .06). Sex, race, GA, and birth weight were not significantly associated with SNHL (Supplemental Table 6).

DISCUSSION
Timing of Hearing Screening

We found a significant increase in the first screening pass rate with older age at the time of screening over the first 48 hours of life. Furthermore, infants who failed the first screening test at ≥36 hours of age were more likely to also fail the second screening test, suggesting fewer false-positive test results in that group. Similarly, among infants who were referred for diagnostic testing, those who were 48 hours of age or older at the final in-hospital screening test were more likely to be diagnosed with SNHL than those who failed the final screening at an earlier age. Clinicians who counsel families on the implications of a failed hearing screening may find it helpful to have this information as they nuance discussions to emphasize the importance of diagnostic testing without causing undue worry.

Our findings are consistent with those in numerous studies in which researchers examine the effect of screening timing on the results of OAE.[15] However, there have been only a few small studies in which researchers primarily examined the timing of AABR as a factor in hearing screening results.[6,18,19] A focus on AABR protocols is particularly valuable given that multiple studies have revealed lower rates of failure with the use of AABR compared with OAE, particularly at young ages[5,6,18–21] and with no increase in cost.[5,19]

Substantial evidence points to transient conductive hearing impairment in some neonates in the first hours and days that is contributory to hearing screening failure. Stuart et al[22] demonstrated a significant relationship between age and the AABR threshold to air-conducted stimuli but not bone-conducted stimuli. Others have documented the presence of both external canal vernix and debris[6,23] and middle-ear amniotic fluid[6–10,24] in the early neonatal period that resolve in the first hours and days after birth. Taken together, these data reveal a likely explanation for our finding of the impact of timing on AABR screening results over the course of the first 2 days of life.

The relationship between AABR pass rates and age has implications for screening protocols during the birth hospitalization. Although practical considerations may vary among institutions, our data reveal that protocols that defer AABR screening as long as possible in the first 48 hours of life will minimize the number of infants who require a second screening before discharge, reducing both cost and parental anxiety.[2,4,25] Recent recommendations to test for cytomegalovirus infection in infants who fail newborn hearing screening only increase this financial and emotional cost, adding further incentive to minimize false-positive results. Pragmatically, it is usually possible to delay screening attempts to beyond 48 hours of age in infants who are born by cesarean. In contrast, given the typical hospital lengths of stay for infants who are born vaginally in the United States, there is limited ability to delay hearing screening while allowing for 2 screening attempts during the hospital stay. Nevertheless, our data reveal that even modest delays within the period of 24 to 48 hours of life may improve pass rates. In our study population, 87% of the 633 infants who were screened a second time passed the second screening, supporting the existing literature on the value of including a second screening before hospital discharge to minimize the rates of referral for diagnostic testing.[2,26,27]

Other Factors Associated With Hearing Screening Failure

In our study population, newborns who failed the first screening test bilaterally were much more likely to fail the second screening test compared with those who failed in only 1 ear on the first test. Those with bilateral failure on the second screening also had a higher rate of SNHL, although the association did not meet statistical significance, perhaps because of the small number of infants in our study with SNHL. These results are consistent with state-wide data collected by the Massachusetts Universal Newborn Hearing Screening Program.[28]

Although not our primary outcome of interest, we found that African American infants in our cohort were at a significantly higher risk of failing both the first and second hearing screenings but were not significantly more likely to have SNHL. The reason for this finding is not entirely clear. One possible explanation may relate to the lower rates of breastfeeding among African American infants compared with those of other races.[29] Researchers in previous studies have identified that breastfed infants have a lower risk of failing the newborn hearing screening, postulated to be due to breastfeeding's favorable impact on middle-ear status.[30,31] Compared with bottle-fed infants, breastfed infants may suckle more frequently and vigorously and may be less likely to have milk leak into the middle-ear space, as is known to occur during feeding in the supine position. Unfortunately, we did not have the data to examine this question in our population. Future researchers should examine the impact of breastfeeding in the first hours and days of life on AABR hearing screening results and on the presence of middle-ear fluid in the neonatal period.

Similar sex differences were seen in Smolkin et al's[15] and Sequi-Canet et al's[30] OAE screening studies, with these authors suggesting differences in the maturation of OAEs in boys versus girls. Because we saw a male disadvantage in our AABR screenings as well, this appears worthy of further study. It may be useful to explore possible sex-based maturational differences in the auditory system that could impact both OAE and ABR screening results.

Counter to previous studies,[10,14] we did not find lower rates of screening failure among infants who were born vaginally compared with those who were born by cesarean. However, researchers in both of the cited studies examined hearing screenings in the first 48 hours of life, and OAE was the screening method. In a separate article, Smolkin et al[15] noted a decreased screening failure among infants who were born by cesarean when screening was delayed beyond 48 hours. This is consistent with our results because our protocol delays the testing of infants who were born by cesarean until at least 36 hours of age, with many being tested when they are ≥48 hours old. Our finding that infants with birth weights ≥4 kg were more likely to fail the initial screening compared with smaller infants is curious and difficult to explain. Given that this association did not persist in second screenings or diagnostic testing, it may be a spurious result.

Strengths and Limitations

The current study has multiple strengths. Because our study took place at a busy birthing hospital, our sample size was relatively large. Furthermore, testing in our hospital is performed by a small number of trained individuals who are closely supervised by an on-site audiologist, which minimizes the impact of interoperator variability in testing. Our overall referral rates for diagnostic testing are consistently <2%, which is well within the generally accepted range that is indicative of a high-quality screening program. Of course, the fact that our hospital has trained technicians and an audiologist on-site may limit the generalizability of our results because many smaller and rural hospitals do not have an audiologist on-site. In

addition, our results apply only to hospitals that use only AABR for screening. Finally, although many states limit the number of screenings to 2, some permit a third screening attempt after discharge. In both cases, the advantages of protocols that minimize the number of infants who are referred for outpatient testing, whether screening or diagnostic, remain.

Another limitation of our study is the small number of infants who were born by cesarean and were screened in the first 24 hours of life, which impacted our ability to examine screening during the early hours after birth in this subgroup. We also did not have data regarding breastfeeding, which may be an interesting and meaningful variable that influences the outcome of screening. We were unable to study the impact of the timing of the second screening because of the small number of infants who failed this screening ($n = 82$) and the dependence of the results of the second screening on the timing of the first screening. Also, we were unable to examine the impact on screening results of known risk factors for congenital hearing loss, including family history and the presence of genetic mutations that are associated with SNHL, congenital cytomegalovirus and other intrauterine infections, craniofacial anomalies (including cleft palate), and syndromes that are associated with congenital hearing loss. Finally, because true congenital hearing loss occurs in only 2 to 3 per 1000 individuals, even the large sample size of our study resulted in relatively small numbers of infants who were referred for diagnostic testing, allowing for a limited analysis of this group.

Finally, our study was not designed to ascertain false-negative rates of hearing screening in newborns in terms of the ascertainment of SNHL. Such a study would require the capacity to manage a large population of newborns over time. Even if this were possible, it would be extremely challenging to distinguish progressive SNHL that was not present at birth from SNHL that was present but not detected at birth.

CONCLUSIONS

In this study of 6817 low-risk term and late-preterm newborns, we found that older

postnatal age at the time of testing in the first 48 hours of life was associated with decreased false-positive results in terms of the diagnosis of congenital SNHL. Delaying the first screening as long as possible within this time frame helps reduce false-positive rates on in-hospital rescreens and reduces the rate of referrals for audiological evaluation. Other factors that were associated with referral for diagnostic audiological testing included race and/or ethnicity and sex, whereas the only factor associated with SNHL on diagnostic testing was bilateral failure on the first screening. Our study helps provide guidance for nursery directors and audiologists, who determine the timing of newborn hearing screening during the birth hospitalization. Further study is needed to determine the optimal time interval between the first and second hearing screening attempts and the role of race and/or ethnicity and sex in screening, diagnostic evaluation, and the prevalence of childhood hearing impairment.

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