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Risk Indicators for Congenital and Delayed-Onset Hearing Loss

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Objective: To evaluate risk indicators for congenital and delayed onset hearing loss in a cohort of newborns who underwent newborn hearing screening, and to evaluate the impact of use of the Joint Committee on Infant Hearing (JCIH) recommendations on requirements for ongoing monitoring of infants identified as at risk for hearing loss.
Patients and Methods: Cohort of 26,341 newborns entered in a prospectively collected database as part of the University of Michigan Universal Newborn Hearing Screening program, with 90 patients identified. Logistic regression analysis was used to evaluate putative risk indicators for congenital and delayed onset hearing loss. An estimate of the cost burden of ongoing monitoring imposed by the use of differing risk indicators was performed.
Results: After controlling for the impact of other risk indicators, intensive care unit length of stay greater than 5 days and exposure to loop diuretics are not associated with an increased risk of congenital or delayed onset hearing loss. Inclusion of these risk indicators as a requirement for ongoing audiologic monitoring results in a high monitoring cost per additional case identified.
Discussion: This study confirms that the majority of the risk indicators currently recommended by the JCIH are effective at identifying infants at increased risk of congenital and delayed onset hearing loss. However, use of neonatal intensive care unit length of stay greater than 5 days and exposure to ototoxic medications are associated with small gains in the number of infants correctly identified as at risk of hearing loss. Further evaluation of the utility of these risk indicators, preferably with a diversity of patient population and healthcare settings, is warranted. **Key Words:** Hearing loss—Neonatal screening—Risk factors.

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With approximately 3 out of every 1,000 newborns affected, hearing loss is one of the most common congenital defects (1–3). Before the advent of newborn hearing screening programs, children with moderate to severe hearing loss were often not identified until delays in speech and language acquisition became apparent. This delay has been associated with adverse effects on speech and language development, academic achievement, and social-emotional development (4). Newborn hearing screening on the basis of risk factors alone is only able to identify approximately 50% of infants with significant hearing loss (5,6). Partially in response to the inefficiency of risk factor based screening, interest in establishing programs of universal newborn hearing screening (UNHS) began to build throughout the 1990s (7–9). Implementation of such programs has proceeded rapidly, such that by 2005 every state had a UNHS program and approximately 95% of newborn infants were screened for hearing loss before hospital discharge (4).

UNHS programs are part of broader early hearing detection and intervention (EHDI) programs, whose goals as set forth by the Joint Committee on Infant Hearing (JCIH) include screening of all infants by 1 month of age, a comprehensive audiological evaluation for all infants who do not pass screening by 3 months of age, and appropriate intervention at no later than 6 months of age for infants with confirmed hearing loss. Despite the successes in initial screening, significant challenges remain, as almost half of infants who do not pass the initial screen do not have appropriate follow-up to obtain diagnostic evaluation or appropriate intervention (4). In addition, UNHS programs will fail to detect children affected by delayed-onset hearing loss, a situation estimated to account for between 10% and 50% of all permanent childhood hearing loss (10). Ongoing monitoring of infants deemed at risk for congenital, delayed-onset, or progressive hearing loss poses several logistical, technical, and economic challenges for EHDI programs. These challenges were acknowledged in the 2007 position statement from the JCIH with regard to changes in the risk

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indicators and recommendations for monitoring (4). These risk indicators relevant to UNHS programs are listed in Table 1 (left column).

Beginning in 2001, the University of Michigan established a UNHS program. As part of this program, information on risk indicators (right column Table 1) were prospectively collected on every newborn admitted to the C.S. Mott Children's Hospital at the University of Michigan. This risk indicator information has been used by the program to guide ongoing monitoring. Important differences in risk indicators used in the program, compared to the recommendations by the JCIH, are highlighted in Table 1. We were interested in evaluating the impact of use of these alternative risk factors on identification of children with hearing loss and on requirements for ongoing monitoring.

PATIENTS AND METHODS

Institutional review board approval was obtained to review the records of all newborns admitted to the C.S. Mott Children's Hospital at the University of Michigan from 2001 to 2007. Beginning in 2001, with the advent of the UNHS program at the University of Michigan, a prospectively collected database has been maintained for quality control purposes. The database includes information on location of the infant (mother-baby unit or special care nursery), results of hearing screening, risk indicators for hearing loss (see Table 1), and results of rescreening and ongoing audiologic monitoring, as well as demographic and other data necessary for program administration.

Query of this database yielded a cohort of 26,341 infants eligible for inclusion in the UNHS program. Of these infants, information on a completed screen was available for 25,400 infants (96.4%). Reasons for lack of screening results included parent refusal, transfer to another hospital, patient expiration, and missed opportunities. A query of hospital administrative and billing systems was used to identify infants with risk indicators not routinely collected by our program. This information was used to create categorical risk indicator variables for neonatal intensive care unit (NICU) length of stay, and exposure to aminoglycosides and loop diuretics. The dataset was then transferred to the statistical software package Stata 10 for analysis (StataCorp, College Station, TX, USA). The α level was set at 0.05 for statistical significance for all statistical testing.

Logistic regression was used to estimate the odds ratios and 95% confidence intervals of congenital and delayed hearing loss for each of the risk indicators identified in Table 1. All risk indicators associated with the outcome of interest with a p value of less than 0.2 were included in multiple logistic regression models to evaluate the association between individual risk indicators and the outcomes of interest, while controlling for the effects of other risk indicators.

To estimate the economic impact of changes in monitoring requirements, the average costs of monitoring were estimated by using 2008 Medicare reimbursement rates, which were the current rates at the time the recommendations were formed (United States Department of Health and Human Services, Center for Medicare and Medicaid Services, 2008 Reimbursement Schedule). Hospital charges are not an appropriate measure of true economic cost because of the peculiarities of the medical marketplace. Medicare reimbursement rates are generally considered to more accurately reflect true economic costs than hospital charges. Current procedure terminology (CPT) code 92557 was used for a comprehensive audiologic evaluation, CPT code 92567 was used for tympanometry, CPT code 92585 was used for auditory brainstem response testing, and CPT code 92588 was used for otoacoustic emissions (OAE) testing. The Medicare reimbursement rate in 2008 was $52.94 for CPT code 92557, $21.71 for CPT code 92567, $102.45 for CPT code 92585, and $70.88 for CPT code 92588.

As a sensitivity analysis for the potential cost implications of changes in monitoring, two monitoring scenarios were envisioned: a repeated monitoring protocol calling for monitoring every 6 months until 3 years of age and a monitoring protocol consisting of a single audiologic evaluation around age 2. The repeated monitoring protocol is estimated to include five audiometric evaluations, five tympanograms, one auditory brainstem response, and one OAE. At a minimum, the single evaluation protocol would include a single audiometric evaluation, tympanogram, and OAE evaluation. The average cost of the repeated screening evaluation would then be estimated at $621.23. The average cost of the single evaluation would be estimated at $145.53.

TABLE 1. *Risk indicators*

JCIH 2007 risk indicators	University of Michigan risk indicators
Family history of permanent childhood hearing loss	Family history of permanent childhood hearing loss
NICU stay of more than 5 days or any of the following:[a]	
ECMO	ECMO
Assisted ventilation	Assisted ventilation >14 days
Exposure to ototoxic medications (loop diuretics, aminoglycosides)[a]	Ototoxic medication exposure >7 days[a]
Hyperbilirubinemia requiring exchange transfusion	Hyperbilirubinemia requiring exchange transfusion
In utero infections	In utero infections
Craniofacial anomalies	Craniofacial anomalies
Syndromic condition associated with hearing loss	Syndromic condition associated with hearing loss
Meningitis	Meningitis
	CDH[a]
	Low birth weight (<800 g)[a]

ECMO, extracorporeal membrane oxygenation; CDH, congenital diaphragmatic hernia.

[a]Indicates difference in risk indicator use.

RESULTS

Figure 1 presents a flow diagram of the subjects included in the study. Of the 26,341 infants eligible for inclusion in the UNHS program, 25,440 (96.7%) underwent screening at our hospital. Reasons for lack of screening data included parent refusal (n = 10), transfer to another hospital (n = 381), patient expiration (n = 323), and missed opportunities (n = 187). Initial screening results indicated referral for 940 infants, a rate of 3.7%. An adequate rescreening and/or diagnostic evaluation was documented for 567 of the 940 infants referred on initial testing, amounting to a 40% loss to follow-up. A permanent hearing loss was documented in 90 infants, including 16 infants with delayed-onset hearing loss, for a prevalence rate of 3.4 per 1,000.

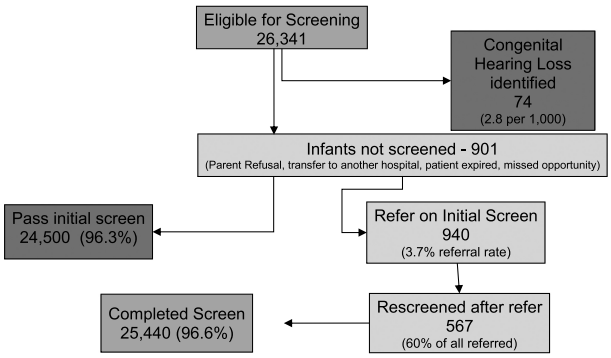

FIG. 1. Flow diagram of the study subjects.

Table 2 presents the results of simple logistic regression to estimate the odds ratio of hearing loss for each of the risk indicators included in Table 1. For this analysis, the presence of hearing loss was used as the response variable, with the categorical risk indicator as the explanatory variable. This analysis shows that with the exception of congenital diaphragmatic hernia, all of the risk indicators are statistically significantly associated with identification of hearing loss. However, these risk indicators are not exclusive of one another, with many infants having more than one risk indicator. To assess the impact of each risk indicator, while controlling for the impact of other risk indicators, multiple logistic regression analysis was performed. For this analysis, the regression model predicts the occurrence of hearing loss based on the risk indicators. All of the risk indicators were included in this model as the p value for each risk indicator was less than 0.2 on univariate analysis. The results of this model are also displayed in Table 2 as the adjusted odds ratios. After controlling for the other risk indicators, NICU stay of more than 5 days, loop diuretic exposure, low birth weight, and congenital diaphragmatic hernia are not associated with increased odds of identification of hearing loss.

A similar analysis was performed, examining the relationship between the risk indicators in Table 1 and identification of delayed-onset hearing loss. Table 3 presents estimates of the odds of delayed-onset hearing loss for each of the risk indicators from Table 1. No estimates are provided for risk indicators which were not present in any infant with delayed-onset hearing loss. From the unadjusted analysis, aminoglycoside exposure, hyperbilirubinemia requiring exchange transfusion, in utero infections, syndromic conditions associated with hearing loss, and meningitis were all statistically significantly associated with delayed-onset hearing loss. All of the risk indicators associated with delayed-onset hearing loss with a p value of less than 0.2 were entered in to the multiple logistic regression model, the results of which are also shown in Table 3 as the adjusted odds ratios. After controlling for other risk indicators, family history of permanent childhood hearing loss, aminoglycoside exposure, hyperbilirubinemia requiring exchange transfusion, in utero infections, syndromic conditions associated with hearing

TABLE 2. *Results of simple logistic regression*

Odds of hearing loss by risk indicator		
Risk indicator	Unadjusted odds ratio (95% confidence interval)	Adjusted odds ratio (95% confidence interval)
Family history of permanent childhood hearing loss	10.5 (5.1–21.4)[a]	11.2 (5.0–25.1)[b]
NICU stay of more than 5 days	6.8 (4.5–10.3)[a]	0.61 (0.29–1.3)
ECMO	12.8 (4.8–34.3)[a]	2.9 (0.79–10.3)[b]
Assisted ventilation >14 days	14.2 (8.3–24.1)[a]	5.6 (2.5–12.4)[b]
Loop diuretic exposure	3.9 (2.4–6.2)[a]	0.64 (0.31–1.3)
Aminoglycoside exposure	4.8 (3.2–7.3)[a]	2.9 (1.7–5.1)[b]
Hyperbilirubinemia requiring exchange transfusion	58.3 (23.5–144.3)[a]	38.4 (10.2–144.7)[b]
In utero infections	19.7 (2.9–132.5)[a]	25.7 (3.2–206.8)[b]
Craniofacial anomalies	34.5 (18.5–64.6)[a]	29.1 (13.3–63.6)[b]
Syndromic condition associated with hearing loss	26.2 (13.9–49.4)[a]	18.0 (8.2–39.4)[b]
Meningitis	28.4 (10.9–74.1)[a]	15.6 (4.8–50.4)[b]
Congenital diaphragmatic hernia	5.8 (0.8–40.8)	1.4 (0.13–14.0)
Low birth weight (<800 g)	16.1 (6.1–42.7)[a]	1.9 (0.50–7.3)

[a]Statistically significant at $p < 0.05$ for unadjusted analysis.
[b]Statistically significant at $p < 0.05$ for adjusted analysis.

TABLE 3. *Estimates of the odds of delayed-onset hearing loss*

Odds of delayed-onset hearing loss by risk indicator		
Risk indicator	Unadjusted odds ratio (95% confidence interval)	Adjusted odds ratio (95% confidence interval)
Family history of permanent childhood hearing loss	7.2 (0.95–54.1)	9.4 (1.2–75.5)[b]
NICU stay of more than 5 days	0.76 (0.10–5.8)	
ECMO	—	
Assisted ventilation >14 days	4.5 (0.59–33.7)	
Loop diuretic exposure	1.7 (0.38–7.4)	
Aminoglycoside exposure	5.7 (2.1–15.3)[a]	3.2 (1.1–9.4)[b]
Hyperbilirubinemia requiring exchange transfusion	83.1 (11.5–600.9)[a]	72.4 (8.1–645.7)[b]
In utero infections	124.7 (17.6–880.9)[a]	125.1 (13.9–1123.5)[b]
Craniofacial anomalies	—	
Syndromic condition associated with hearing loss	52.3 (15.1–181.2)[a]	41.2 (10.2–167.0)[b]
Meningitis	40.5 (5.5–300.2)[a]	13.6 (1.4–134.9)[b]
Congenital diaphragmatic hernia	—	
Low birth weight (<800 g)	—	

[a]Statistically significant at $p < 0.05$ for unadjusted analysis.
[b]Statistically significant at $p < 0.05$ for adjusted analysis.

loss, and meningitis were all statistically significantly associated with delayed-onset hearing loss.

To assess the potential impact of inclusion of risk indicators recommended by the JCIH, but not in the University of Michigan's current pool of risk indicators, we examined the number of infants for whom ongoing audiologic monitoring would be recommended for each set of risk indicators. The primary differences between the risk indicators currently in use in our program and those recommended by the JCIH are the use of NICU length of stay greater than 5 days, and exposure to ototoxic medications (aminoglycosides and loop diuretics, regardless of duration of use). Presence of congenital diaphragmatic hernia and very low birth weight (<800 g) are currently used as risk indicators in our program but are not recommended by the JCIH. The risk indicators in use in our program identified 1,136 infants for whom ongoing audiologic monitoring was recommended, and identified 56 of the 90 infants with hearing loss, including eight with delayed-onset hearing loss. Inclusion of NICU length of stay greater than 5 days and exposure to ototoxic medications would lead to recommendations for monitoring an additional 4,314 infants. Of these additional 4,314 infants, 1,350 would be included for additional monitoring on the basis of exposure to potentially ototoxic medications, 1,769 due to ICU length of stay, with the remaining 1,195 included due to the presence of both risk indicators. Of these 4,314 infants, an additional 10 were identified with hearing loss, of which only one was identified with delayed-onset hearing loss. Of these 10 additional infants, five were included on the basis of exposure to potentially ototoxic medications, three due to ICU length of stay, and the remaining two included due to the presence of both risk factors.

The results of cost estimates for identification of each additional case of hearing loss overall, and of delayed-onset hearing loss by type of monitoring protocol, are presented in Table 4. A sample calculation of the cost associated with a single monitoring protocol per case of hearing loss is provided here:

Annual monitoring costs/additional case of hearing loss identified = [$145.53 (cost of repeated monitoring protocol) × 4,314 (additional patients requiring monitoring)/6 years (study period)]/10 (new cases identified). The annual cost of a single monitoring protocol per additional infant identified with hearing loss is estimated to be just over $62,000. The annual cost of a repeat monitoring protocol per additional infant identified with hearing loss is estimated to be in excess of $267,000. A single evaluation protocol is estimated to cost in excess of $600,000 per additional case identified with delayed-onset hearing loss. For a repeated monitoring protocol, the cost per additional case of delayed-onset hearing loss identified is estimated to be as high as $2.6 million.

TABLE 4. *Results of cost estimates*

Estimated monitoring costs per additional case identified		
Monitoring protocol	Hearing loss overall	Delayed-onset hearing loss
Repeated monitoring	$267,998	$2,679,986
Single evaluation	$62,781	$627,816

DISCUSSION

This study confirms the increased risk of congenital and delayed-onset hearing loss associated with many of the risk indicators recommended by the JCIH. The most notable exceptions were the findings that, after adjusting for other risk indicators, NICU length of stay greater than 5 days and exposure to loop diuretics were not associated with an increased risk of either congenital or delayed-onset hearing loss. Additionally, use of extracorporeal membrane oxygenation, assisted ventilation greater than 14 days, and craniofacial abnormalities were associated with congenital hearing loss, but not delayed-onset hearing loss. The finding with regard to NICU length of stay is perhaps not surprising. Although NICU length of stay has been identified as a risk indicator in other studies, the utility of using a length of stay of greater than 5 days has not (11). The rationale for this use of NICU stay of greater than 5 days, as given in the 2007 JCIH position statement, comes from unpublished data from the National Perinatal Information Network. This data is reported to have shown that 52% of infants discharged from NICUs in 2005 were discharged before 5 days, and that these infants were significantly less likely to have identified risk indicators. Data on hearing loss is not available in this dataset.

The absence of an association between NICU length of stay greater than 5 days or exposure to potentially ototoxic medications and hearing loss is very significant at a programmatic level, as monitoring the additional infants with these risk indicators but without other risk indicators increases the monitoring burden in our population nearly fivefold. The proportion of the increase in monitoring burden attributable to NICU length of stay is 41%, with 31% attributable to exposure to potentially ototoxic medications, and the remainder due to infants with both risk factors. These increases in monitoring burden are accompanied by only a small increase in the number of cases of hearing loss identified. This inefficiency contributes to a high cost for screening per case identified. Although the estimated costs of screening are noted to be quite high, it is important to bear in mind estimates of cost savings from special education when children with hearing loss are identified early and given appropriate educational, medical, and audiological services. These cost savings have been estimated to be as high as $400,000 over the course of primary and secondary education (12).

The risk indicators of low birth weight and congenital diaphragmatic hernia are currently in use in our program, but are not included in the JCIH recommendations. Based upon this data, this exclusion seems appropriate, and we are considering eliminating these conditions from our list of risk indicators. The impact of this exclusion would be

small, removing only 58 infants from the group for whom we recommend ongoing monitoring.

The very low incidence of delayed-onset of hearing loss makes accurate identification of risk indicators difficult, even from a relatively large population such as the one included in this study. This is reflected by the breadth of the confidence intervals in Table 3. The retrospective nature of data collection for the risk indicators of NICU stay and administration of exposure to loop diuretics and aminoglycosides is also a potential weakness of the current study design. The risk of bias introduced by this method of data collection is low, as the data collected retrospectively is objective and carefully maintained as a requirement for accurate billing. Additionally, these results reflect outcomes of a single academic medical center with a tertiary NICU population. Further research is required to determine if similar associations between risk indicators and hearing loss are observed in other geographic locations, among different patient populations, and within different health care settings. To improve the effectiveness of efforts at ongoing follow-up, identification of risk indicators which more efficiently identify children at risk of delayed-onset hearing loss is needed. Efforts to identify such risk indicators will be improved by increasing integration of data collection efforts of EHDI programs at the state and national levels. This integration could also reveal previously unidentified risk factors for even more effective identification of infants and children at risk for congenital and delayed-onset hearing loss.

CONCLUSION

This study confirms that the majority of the risk indicators currently recommended by the JCIH are effective at identifying infants at increased risk of congenital and delayed onset hearing loss. However, in our patient population, use of NICU length of stay greater than 5 days and exposure to loop diuretics are associated with small gains in the number of infants correctly identified as at risk of hearing loss. Inclusion of these risk indicators greatly increases the volume of infants for whom ongoing audiologic monitoring is recommended, and therefore do not appear to be efficient risk indicators in this study population for congenital and delayed-onset hearing loss. Further evaluation of the utility of these risk indicators, preferably with a diversity of patient population and healthcare settings, is warranted.

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