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Incidence and factors associated with sensorineural and conductive hearing loss among survivors of congenital diaphragmatic hernia

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ABSTRACT

Purpose: The reported incidence of sensorineural hearing loss (SNHL) in long-term survivors of congenital diaphragmatic hernia varies widely in the literature. Conductive hearing loss (CHL) is also known to occur in CDH patients, but has been less widely studied. We sought to characterize the incidence and risk factors associated with SNHL and CHL in a large cohort of CDH patients who underwent standardized treatment and follow-up at a single institution.

Methods: We retrospectively reviewed charts of all CDH patients in our pulmonary hypoplasia program from January 2004 through December 2012. Categorical variables were analyzed by Fisher's exact test and continuous variables by Mann–Whitney t-test ($p \leq 0.05$).

Results: A total of 112 patients met study inclusion criteria, with 3 (2.7%) patients diagnosed with SNHL and 38 (34.0%) diagnosed with CHL. SNHL was significantly associated with requirement for ECMO ($p = 0.0130$), prolonged course of hospitalization ($p = 0.0011$), duration of mechanical ventilation ($p = 0.0046$), requirement for tracheostomy ($p = 0.0013$), and duration of loop diuretic ($p = 0.0005$) and aminoglycoside therapy ($p = 0.0003$).

Conclusions: We have identified hearing anomalies in over 30% of long-term CDH survivors. These findings illustrate the need for routine serial audiologic evaluations throughout childhood for all survivors of CDH and stress the importance of targeted interventions to optimize long-term developmental outcomes pertaining to speech and language.

Congenital diaphragmatic hernia (CDH) is a severe congenital anomaly affecting 1 in every 2500–3000 live births. Advances in surgical technique and neonatal care have led to improved overall survival rates, with increasing recognition of the substantial risk of secondary morbidities including pulmonary hypertension and gastrointestinal dysfunction in surviving neonates. Neurodevelopmental (ND) sequelae are commonly encountered, and are increasingly recognized as a major limitation of quality of life in long-term survivors [1]. Hearing loss (HL) is one recognized neurodevelopmental complication of CDH, with sensorineural hearing loss (SNHL) described in a number of studies. Several neonatal risk factors for SNHL reported in the literature are encountered at high rates in CDH, including a requirement for extracorporeal membrane oxygenation (ECMO) [2] and exposure to ototoxic medications including aminoglycosides [3] and loop diuretics [4]. However, the actual prevalence of SNHL in this population is unclear, with reported incidence rates varying from 2% to 60% [5–7]. It remains poorly understood whether the occurrence of SNHL in CDH survivors is higher than that observed in graduates from neonatal intensive care units (2–6%) [8]. Conductive hearing loss (CHL) has also been reported to occur in CDH patients [9], but has been less widely studied.

Infants with HL are at risk for delayed speech development and language acquisition, poor social development, and impaired academic achievement. Early identification and appropriate intervention can prevent or minimize adverse effects and optimize developmental outcomes. While a number of studies have investigated a relationship between CDH and HL, few have reported a correlation between HL and cognitive-linguistic development in this population.

We sought to characterize the incidence and risk factors associated with SNHL and CHL in a large cohort of CDH patients who underwent standardized treatment and follow-up at a single institution. In addition to the identification of risk factors associated with HL in this population, we sought to characterize the possible relationship between HL and neurodevelopmental outcomes specific to cognitive-linguistic functioning.

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1. Methods

The records of all CDH survivors treated at the Children's Hospital of Philadelphia and enrolled in the Pulmonary Hypoplasia Program between January 2004 and December 2012 were retrospectively analyzed under institutional IRB approval. Recorded data on patient demographics, prenatal course and imaging, surgical resection and postoperative course, and the results of focused audiologic and neurodevelopmental examinations during regular outpatient follow-up were analyzed. Inclusion criteria included completion of newborn hearing screening in addition to formal audiologic assessment at 6 months of age or older, as well as standardized neurodevelopmental assessment at 2 to 3 years of age. As described previously [1], neurodevelopmental outcomes were evaluated by either the Bayley Scales of Infant Development II (BSID-II) if children were examined prior to 2006 ($n = 10$), or the BSID-III if children were examined after 2006 ($n = 62$). Scores specific to language development, the BSID-II Mental Developmental Index and the BSID-III Language domain scores, were grouped into one of three categories: average (≥ 90), borderline (71–89) and delayed (≤ 70). In 6 patients, scores from both the BSID-II and BSID-III were available, and fell within the same category in all cases.

Patients enrolled in our Pulmonary Hypoplasia Program undergo newborn hearing screening using transient evoked otoacoustic emissions (TEOAEs) and auditory brainstem response (ABR), followed by audiological assessment at scheduled follow-up appointments every 6 months until 3 years of age. Patients are subsequently screened on an annual basis. Outpatient audiologic assessments included behavioral audiometry, OAE testing, and 226 Hz tympanometry. If hearing anomalies were suspected, diagnostic ABR was also performed. Bone conduction threshold evaluation was performed when possible, but was frequently unattainable or difficult to interpret in this population. Certified pediatric-experienced audiologists administered hearing evaluations, with all reports reviewed by a single certified audiologist to ensure correct interpretation of results. Patients were classified into one of the following four categories: 1) normal hearing response — thresholds of 20 dB or better on soundfield testing or 15 dB or better for each ear on ear-specific testing; 2) confirmed SNHL — minimum response level at greater than 20 dB HL for at least two of the octave frequencies from 250 through 4000 Hz with bone conduction responses also at 20 dB or higher; 3) suspected CHL — abnormalities on behavioral audiometry and/or auditory brainstem response testing with abnormal tympanometry, with or without bone conduction results; 4) hearing loss not otherwise defined (HL NOD) — abnormalities on behavioral audiometry and/or auditory brainstem response testing with normal tympanometry.

Statistical analysis was performed using Fisher's exact test for categorical variables and Mann–Whitney test for continuous variables, with p-values < 0.05 considered significant. All data analysis was conducted using GraphPad Prism 6.0 (La Jolla, CA).

2. Results

From January 2004 through December 2012, 225 neonates with CDH were enrolled in the Pulmonary Hypoplasia Program. A total of 91 patients were excluded from further study because of inadequate audiologic assessment, and 22 were excluded because of inadequate ND data. Of the remaining 112 patients, 3 (2.7%) patients were diagnosed with SNHL, 38 (34.0%) demonstrated abnormalities on auditory brainstem response and/or behavioral audiometry consistent with CHL, and 5 (4.5%) were found to have HL NOD.

Table 1 provides a description of the clinical parameters of the entire patient cohort stratified according to hearing status. Most patients were born at term, with no association between birth weight or gestational age and HL. Prenatal diagnosis was made in approximately half of patients, and prenatal predictors of survival including LHR and liver position did not differ significantly between patient cohorts. SNHL was significantly associated with several previously reported risk factors including requirement for ECMO ($p = 0.0130$), prolonged course of hospitalization ($p = 0.0011$), duration of mechanical ventilation ($p = 0.0046$), requirement for tracheostomy (0.0013), and duration of loop diuretic ($p = 0.0005$) and aminoglycoside therapy ($p = 0.0003$). SNHL was also found to be significantly associated with severity of gastroesophageal reflux disease (GERD) as evidenced by an increased requirement for Nissen fundoplication ($p = 0.0337$), as well as reduced APGAR scores at 5 min ($p = 0.0044$). Requirement for tracheostomy was also found to be significantly associated with CHL ($p = 0.0463$), while duration of aminoglycoside therapy was significantly longer in the HL NOD cohort ($p = 0.0299$).

Table 2 provides a description of the neurodevelopmental outcomes of the study population stratified according to hearing status, with a focus on outcomes related to cognitive-linguistic development. There were no significant differences in the categorical BSID-II MDI/Bayley III language domain composite scores, rates of diagnosed developmental delay, language or speech delay, or the use of assistive services including speech and occupational therapy, across all three categories of hearing loss compared to patients with normal hearing.

Of the 3 patients diagnosed with SNHL, all three were diagnosed prior to NICU discharge after abnormal hearing screening results and were fitted for bilateral hearing aids, with one patient subsequently undergoing cochlear implantation. The 5 patients diagnosed with HL NOD continue to be followed, with reevaluation recommended within 6 months. Of the 38 patients diagnosed with suspected CHL, 21 were found to have complete resolution on subsequent audiologic assessment, with spontaneous normalization of testing in 12 and resolution following pressure equalization (PE) tube placement in 9 patients. One patient was found to have a unilateral atresia of the external auditory canal and continues to be followed by otolaryngology (ORL), 6 patients are currently awaiting ENT assessment for possible PE tube placement, while 10 have failed to complete recommended audiologic reassessment.

3. Discussion

Although survival rates for CDH have improved significantly with advances in neonatal care, long-term survivors face numerous morbidities impacting neurodevelopmental function. There is significant variability in the literature with respect to the incidence of HL in CDH survivors. SNHL has been more widely reported, while comparatively fewer studies address CHL in these patients (Table 3). In this retrospective series of 112 patients, the prevalence of SNHL in CDH survivors was 2.7%, a rate comparable to the prevalence of SNHL in the population of infants requiring intensive care [10]. Unexpectedly, we observed high rates of CHL in our study (34%), although in only one case this was because of a fixed atresia. The incidence of CHL in neonatal intensive care graduates ranges from 0.5% to 9.0% in the literature [11,12], suggesting a substantially increased risk in CDH survivors. Importantly, 91 patients were excluded from this study because of inadequate audiologic assessments. While the low rate of adherence to recommended hearing testing is likely to be multifactorial in nature, it may be postulated that a lack of awareness of the risks of hearing loss in this population is a significant contributing factor.

Hearing loss in CDH has been attributed to a number of mechanisms and may be because, at least in part, of side effects of treatment. Table 3 presents a summary of the incidence of HL and identified risk factors of SNHL in CDH survivors in the literature to date, with the most common factors including ECMO, length of mechanical ventilation, and exposure to ototoxic agents including