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Medical Referral Patterns and Etiologies for Children with Mild to Severe Hearing Loss

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Abstract

Objectives: 1) Identify the etiologies and risk factors of the patient cohort and determine the degree to which they reflected the incidence for children with hearing loss and 2) quantify practice management patterns in three catchment areas of the United States with available centers of excellence in pediatric hearing loss

Design: Medical information for 307 children with bilateral, mild to severe hearing loss was examined retrospectively. Children were participants in the Outcomes of Children with Hearing Loss (OCHL) study, a five-year longitudinal study that recruited subjects at three different sites. Children aged 6 months to 7 years at time of OCHL enrollment were participants in this study. Children with cochlear implants, children with severe or profound hearing loss, and children with significant cognitive or motor delays were excluded from the OCHL study and, by extension, from this analysis. Medical information was gathered using medical records and participant intake forms, the latter reflecting a caregiver's report. A comparison group included 134 children with normal hearing. A chi-square test on two-way tables was used to assess for differences in referral patterns by site for the children who are hard of hearing (CHH). Linear regression was performed on gestational age and birth weight as continuous variables. Risk factors were assessed using t-tests. The alpha value was set at $p < 0.05$.

Results: Neonatal intensive care unit stay, mechanical ventilation, oxygen requirement, aminoglycoside exposure, and family history were correlated with hearing loss. For this study cohort, congenital cytomegalovirus (CMV), strep positivity, bacterial meningitis, extracorporeal

membrane oxygenation (ECMO), and loop diuretic exposure were not associated with hearing loss. Less than 50% of children underwent imaging, although 34.2% of those scanned had abnormalities identified. No single imaging modality was preferred. Differences in referral rates were apparent for neurology, radiology, genetics, and ophthalmology.

Conclusions: The OCHL cohort reflects known etiologies of CHH. Despite available guidelines, centers of excellence, and high yield rates for imaging, the medical work-up for children with hearing loss remains inconsistently implemented and widely variable. There remains limited awareness as to what constitutes appropriate medical assessment for CHH.

INTRODUCTION

Pediatric hearing loss affects approximately 1–3 per 1000 newborn children in the United States, earning it status as one of the most common sensory birth conditions (Smith et al., 2005). The incidence of permanent childhood hearing loss, along with the potential to prevent or reduce its consequences on development, served as the impetus for multiple concerted efforts to screen, diagnose, and intervene early on behalf of this patient population. Prior to the implementation of universal newborn hearing screening, infants with mild to severe hearing loss (children who are hard of hearing: CHH) were rarely identified before two years of age, and many were identified even later (Stein et al., 1990; Halpin et al., 2010). In contemporary practice, it is recommended that early identification be followed by early interventions and appropriate medical referrals (Muse et al., 2013). Evidence suggests that early interventions confer developmental benefits for CHH (Tomblin et al., 2014; Tomblin et al., 2015a). However, little is known about the patterns of medical referral for this group of children. An understanding of the etiologies of children in this group and typical referral patterns may provide insights about practice gaps and future needs.

CHH may have complex needs, but their hearing loss is, fortunately, often amenable to early intervention. Thus, efforts from the medical and audiologic communities have focused on screening and timely referrals for diagnostics and intervention. The Joint Committee on Infant Hearing (JCIH) Position Statement in 2007 represents a rich resource for practitioners treating CHH. It advances the “1–3–6” guideline, wherein all newborn/infant hearing screenings should take place by 1 month of age, comprehensive audiologic evaluation should be completed by 3 months, and intervention should commence (when required) no later than 6 months of age (Joint Committee on Infant Hearing, 2007). A consolidated appendix of known risk factors is provided, and strong recommendations are made for medical evaluations by otolaryngology, ophthalmology, and genetics. Nonetheless, there is a lack of consensus in everyday practice as to what constitutes an appropriate medical evaluation after the history and physical are complete. Separately, in 2016, the International Pediatric Otolaryngology Group (IPOG) published consensus guidelines (Liming et al., 2016) targeted for otolaryngologists. This group comprised leaders in the field of pediatric hearing loss, who were queried regarding issues related to work-up and management. Topics included genetics, radiology, ophthalmology, cardiology, and CMV testing. Strong consensus was found in the areas of early CMV testing in the presence of a failed hearing screen, the benefit of ophthalmologic consultation, and the superiority of MRI for peripheral auditory abnormalities. Disagreements persisted about the timing of genetic testing, directed gene

testing versus comprehensive gene testing, and the overall utility of temporal bone imaging in pediatric hearing loss.

As medical assessment can identify etiology and associated conditions that may ultimately impact general health, treatment prognosis and recommendations, and even communication strategy choice, the merit of creating a cost-effective and comprehensive medical work-up scheme is of value (Anand et al., 2012; Hone & Smith, 2002; Jervell & Lange-Nielsen, 1957). For example, some patients with multi-organ disease may present with hearing loss, leading to identification of mutations such as *KCNQ4* or long QT interval. Recognizing such conditions can result in the prevention of sudden death for some children (Jervell & Lange-Nielsen, 1957). Likewise, riboflavin therapy in children with auditory neuropathy resulting from Brown-Vialetto-Van Laere (BVVL) might obviate progressive neurological compromise (Anand et al., 2012). For children with absent cochleas (Michel aplasia) or cochlear nerve deficiency, the choice of an auditory-oral approach to communication may result in persistent and severe language delays, whereas the addition of a manual/visual (or total) mode of communication may be more justified. Conversely, for children expected to lose vision secondary to Usher syndrome, the choice of a primarily sign language approach to communication may result in the loss of communication abilities over time. Numerous other examples exist to justify the need for an early and thorough medical assessment for CHH.

Retrospective analysis of select populations may provide some guidance for management of CHH, given that practitioners continue to wrestle with what constitutes an appropriate, comprehensive medical investigation while remaining sensitive to the cost of such an assessment (Morton & Nance, 2006). The Outcomes of Children with Hearing Loss (OCHL) study was initiated in response to the paucity of studies systematically identifying outcomes in children with mild to severe hearing loss in the context of modern medical practice and resource utilization (Moeller & Tomblin, 2015). The primary sites in the study included Boys Town National Research Hospital (BTRNH), University of Iowa (UI), and University of North Carolina at Chapel Hill (UNC). The primary goal of the study, as described by Moeller and Tomblin (2015), was “to identify factors that influence children’s access to linguistic input, and to determine how these factors may interact over time to exacerbate risk or provide protection” (p. 6S). Several primary findings were released as a supplemental issue in *Ear and Hearing* (Ambrose et al., 2015; McCreery et al., 2015a; McCreery et al., 2015b; Moeller & Tomblin, 2015; Moeller et al., 2015; Tomblin et al., 2015a; Tomblin et al., 2015b; Walker et al., 2015). These included:

- Eighty-four percent of patients with permanent, bilateral hearing loss had stable audiometric thresholds. Additionally, 65% of the children demonstrated adequate aided audibility; the remaining 35% with low audibility are at heightened risk for language delays (McCreery et al., 2015a).
- Provision of well-fit hearing aids reduces risk of and provides protection against language delay. Children with greater aided audibility from their hearing aids had better language outcomes in preschool than children with less aided audibility (Tomblin et al., 2015a).

- Most preschool and school-aged children were wearing hearing aids more than 8 hours per day, but infants and toddlers averaged only 4.36 hours per day. Parents typically overestimated the time hearing aids were worn, on average by 2.34 hours. Additionally, degree of hearing loss and maternal level of education predicted consistency of use for hearing aids. Children with mild hearing loss and children of less educated mothers are at risk for limited hearing aid use. (Walker et al., 2015)
- Caregivers of CHH increased the quality features of linguistic input over time but tended to direct the child more than caregivers of children with normal hearing. Directiveness is a feature that is not optimal for children's language development. Quality of linguistic input from the caregiver at 18 months was related to child language at 3 years (Ambrose et al., 2015).
- Auditory skill development and speech-recognition abilities were influenced by language abilities and audibility with hearing aids. Children with better audibility and stronger language skills had better functional auditory abilities than children with poorer aided audibility and/or language skills (McCreery et al., 2015b).

The OCHL study represented a substantial longitudinal effort and provides continuing insights into CHH (Klein et al., 2017; Koehlinger et al., 2015; Harrison et al., 2017; Walker et al., 2015b; Walker et al., 2016; Walker et al., 2017; Harrison et al., 2017). As CHH are commonly represented within the otolaryngology practices, defining the medical characteristics of the OCHL patient group would allow us to: 1) identify the etiologies and risk factors of the patient cohort and determine the degree to which they reflected the incidence for children with hearing loss and, 2) quantify practice management patterns in three catchment areas of the United States with available centers of excellence in pediatric hearing loss.

PATIENTS AND METHODS

Participants

Medical information for a cohort of 307 children with bilateral, mild to severe hearing loss was examined retrospectively. All children were participants in the OCHL study, a five-year longitudinal study conducted collaboratively by BTNRH, UI, and UNC. Institutional review board approval was granted from each institution. Children were recruited from the home states and surroundings regions of these research teams. Recruitment brochures were sent to parents by the state Early Hearing Detection and Intervention (EHDI) program audiologists, early interventionists, and educators. Additional recommendations for study inclusion came from institutional or community providers. Children qualified for the study if their chronological age was between 6 months and 7 years at the time of recruitment, if they had a four-frequency (500, 1000, 2000, and 4000 Hz) better-ear pure tone average between 25 and 75 dB hearing level, if they had not received a cochlear implant, if English was the primary language spoken at home, and if they did not have significant cognitive or motor delays. There were 317 CHH recruited for the study. While 286 children completed the entire audiometric portion of the OCHL study, 307 of the original 317 children recruited were included in this current study and represent those for whom there was sufficient medical

information for the specific aims. This included 124 (40.4%) from BTNRH, 80 (26.0%) from UI, and 103 (33.6%) from UNC. One hundred and thirty-four children with normal hearing served as a comparison group for a study total of 441 subjects. A complete description of the methods and data collection for the OCHL study can be found in Tomblin et al. (2015b).

Data Collection and Procedure

Medical information was gathered retrospectively using the medical records and intake forms. The primary source of medical information was the subject's medical records (birth hospital discharge summary, pediatrician notes, otolaryngologist notes, imaging reports, etc.). Study intake forms, which included questions regarding risk factors, etiologies, and co-morbidities, among other information such as demographics, were used to supplement medical record information when there were missing or incomplete data in the medical record. When conflicts of information occurred between the medical record and the intake form, data from the medical record were used. Occasionally, conflicting information was observed between intake forms completed by different guardians. In such cases, information from the intake form completed by the mother was used. Imaging reports were completed by the individual radiologists. No repeat evaluation or over-read was performed.

Information included in the data analysis comprised presence of risk factors as identified by the JCIH, etiology of hearing loss, co-morbidities common to CHH, and medical imaging including magnetic resonance imaging (MRI) and computed tomography (CT). Referrals were categorized as neurology, ophthalmology, radiology, genetics, and blood. The latter category represented any referrals for laboratory blood testing (e.g. metabolic panel), excluding blood work for genetic testing.

Analysis

Descriptive statistics were computed using Microsoft Excel. Risk factor analysis was completed using odds ratios as computed in Statistical Analysis System (SAS) software. In the cases where data fields were left blank, this was interpreted as the data being unknown or unavailable (as opposed to assuming a negative response). A chi-square test on two-way tables was used to assess for differences in referral patterns by site. Linear regression was performed on gestational age and birth weight as continuous variables. Risk factors were assessed using t-tests. Alpha was set at $p < 0.05$.

RESULTS

Demographic data have been previously presented (Tomblin et al., 2015a). Patients from UNC were almost exclusively evaluated at their medical center, whereas the patients from UI and BTNRH represented a wide variety of practitioners outside of those institutions.

Individual risk factors, including Neonatal Intensive Care Unit (NICU) stay, mechanical ventilation, oxygen requirement, aminoglycoside exposure, and family history revealed statistical significance for hearing loss compared to the control cohort (Table 1). We could not demonstrate statistical significance between CHH and CMV, strep positivity, bacterial

meningitis, extracorporeal membrane oxygenation (ECMO), and loop diuretic exposure (Table 1) in the current patient sample.

Table 2 demonstrates continuous variable risk factors: gestational age and birth weight. For gestational age, every one day increase in gestational age conveyed a marginal benefit against hearing loss (OR= 0.98, 95% CI [0.97, 0.99]), but with a small effect size. In the case of birth weight, an increase in one gram in birth weight trended to, but did not reach, significance as a protectant against congenital hearing loss.

For NH children, Table 1 demonstrates significantly lower rates of NICU stay (11.5% vs 21.8%, $p = 0.01$), mechanical ventilation (4.6% vs 14.0%, $p = 0.004$), oxygen support (5.3% vs 13.9%, $p = 0.011$) and amnioglycocide exposure (5.3% vs 11.5%, $p = 0.05$) than the CHH. Of note, six NH children tested positive for CMV, though none were positive and there was no statistical difference between NH and CHH groups. Evaluating all infectious etiologies (CMV, Strep, and Meningitis), only one (4.2%) NH child had a positive history compared to 11 (10.4%) CHH. Six NH children had a positive family history of hearing loss compared to 89 among CHH ($p < 0.001$). However, only 34 NH children replied “No” when specifically asked about family history of hearing loss while no CHH confirmed a negative family history. Additionally, Table 2 demonstrates NH children with a smaller range for gestational age (224–294 days vs 168–294 days) as well as a lower limit in birth weight that was much higher than the CHH (1304 g vs 510 g), though this latter statistic was not found to be significant.

Etiologies were recorded for 110 patients: 39 (31.4%) of 124 patients from BTNRH, 39 (37.9%) of 103 from UNC, and 31 (38.8%) of 80 from UI (Table 3). No difference was noted between study sites ($X^2 [3, n=307] = 1.51, p=0.47$). Twenty-seven CHH (9%) were noted to have syndromes. Thirty (10%) had non-syndromic genetic conditions associated with hearing loss. Connexin 26 ($n=18$), non-syndromic EVA (10 subjects), and genes *OTOA* (1 subject) and *OTOF* (1 subject) were specifically identified. Percentages of an etiology per group are listed in the third column of Table 4, while their incidences within the CHH cohort are listed in the fourth column.

Of the 307 CHH patients, 146 (47.6%) had radiology reports available. Sixty had MRI only, 66 had CT only, and 20 had both. Of the 146 patients with radiology reports, 50 (34.2%) had abnormalities found on MRI or CT. Thirty-five (24.0%) of those patients specifically had cochlear and/or vestibular abnormalities (Table 4). Fifteen patients (10.2%), 9 MRI and 6 CT, had no cochleopathic or vestibulopathic findings but displayed other intracranial processes. These included MRI findings of cysts, hemangiomas, cerebellar tonsillar ectopia, gliosis, thalamic astrocytoma, white matter disease, and white matter changes and CT findings of enlarged ventricles, plagiocephaly, and optic nerve atrophy.

Two hundred and twenty-six patients (73.6%) were referred on for specialty services. Aside from radiology, the most referrals were made to ophthalmology ($n=133$), weighed heavily by the referrals through BTNRH (Table 5). This pattern was reciprocated in blood work ($n=132$), where UNC was the predominant source of referrals. These two patterns possibly stem from directed institutional strengths, namely BTNRH's in Usher syndrome and UNC's

streamlined work-up via in-house recruitment. Referral rates across all three sites to neurology, ophthalmology, radiology, and genetics were significantly different. Differences in ordering for blood work were not statistically significant. Evaluating incidence of any referral, 73 patients had one medical referral, 64 had two referrals, 54 had three, 26 had four, and nine patients had five referrals. Eighty-nine patients had three or more referrals; 43 of these were at UNC, 29 at BTNRH, and 17 at UI.

DISCUSSION

Medical assessment of children with mild to severe hearing loss enrolled in the OCHL study from three regions with available tertiary referral centers was investigated. Overall, we found that our radiographic findings and several known risk factors in CHH were congruent with previous literature. Additionally, we found that there was significant variance in referral patterns between regions. While one of the sites (UNC) enrolled patients from their own health system, many of the patients from the other two sites (UI and BTNRH) received their work-up and treatment through outside providers. This represents one of the largest prospectively enrolled cohorts for this patient population.

As a method of affirming the medical congruency with other sample groups, we evaluated risk factors identified by the JCIH. Categorical data including NICU care, ventilator dependence, oxygen requirement of any kind, aminoglycoside exposure, and family history demonstrated statistical significance for hearing loss compared to the control cohort. While other studies have demonstrated associated risks between hearing loss and younger gestational age and birth weights, our study variables showed only small effect size between groups (Beswick et al., 2012; van Dommelen et al., 2015; Dumanch et al., 2017). This may be due to patient stratification schemes in prior studies using birth weight (low, very low, etc.) or prematurity status to evaluate specific subgroups. Additionally, the OCHL study excluded children with significant developmental delay, a condition commonly seen at the low extremes of birth weight and gestational age. This exclusion would create a bias toward healthier infants included in the study.

We assessed congenital CMV, *Streptococcus* positivity, and bacterial meningitis (Kraft et al., 2014; Lasky et al., 1998; Rodenburg-Vlot et al., 2016). Each infectious agent category was significantly underpowered compared to the remaining categorical measures, making the lack of significance unsurprising. The reduction in incidence of *Streptococcus* and bacterial meningitis could reflect aggressive screening and prevention programs across the country, but such interventions are not yet in place for CMV (Ku et al., 2015; Schrag et al., 2016). CMV has emerged as a significant contributor to childhood hearing loss, and universal screening processes are underdeveloped, as evidenced by our 12% testing rate. Of further concern is the reliability of CMV testing, which possesses its highest sensitivity within the first two weeks of life, coupled with the fact that 90% of congenital CMV is asymptomatic (Ross et al., 2011). Nearly 1/3 of children with CMV have hearing loss as their sole clinical manifestation (Kimani et al., 2010). CMV's indolent nature and the delayed onset of hearing loss leaves many children susceptible to its impact (Kimani et al., 2010). Recent programs to detect congenital CMV and facilitate early intervention have emerged across the country, first in Utah, followed by Connecticut and others. The state of Utah has demonstrated the

viability of CMV testing in asymptomatic children who failed their newborn hearing screens. They specifically focused on the first 21 days of life, given that this timeframe separates congenital CMV infection from acquired ex-utero CMV infection (Diener et al., 2017). This depends on prompt collection of saliva, urine, or blood near the time of the original screening. Aggressive screening measures identified an additional 6 children with hearing loss out of 14 who tested positive for CMV, despite being asymptomatic (Diener et al., 2017). While the ultimate cost of universal screening programs is currently under investigation, it is difficult to deny the efficacy of such initiatives (Gantt et al., 2016; Park and Shoup, 2018). Our data demonstrate unreliable implementation within the geographic regions. Until appropriate screening is widespread, interventions for hearing loss due to CMV will remain reactionary instead of preventative.

Genetic causes contribute to at least 50% of cases of childhood hearing loss. Traditionally, 30% have been associated with syndromes (see below), while the remaining 70% are stratified based on inheritance patterns (Grindle, 2014). Autosomal recessive is the most common inheritance pattern of non-syndromic genetic hearing loss, comprising 75–85% of cases. Of these, *GJB2* mutations are a large portion, though this is weighted by higher incidences at increasing hearing loss (Lim et al., 2003). Advancements within the field of genetics have fundamentally changed philosophies of work-up (Smith, Bale, & White, 2005). Several institutions offer a genetic panel screening for known genetic causes of CHH (Brownstein et al., 2011; Shearer et al., 2010; Shearer & Smith, 2012; Tang et al., 2012). A role of the practitioner is to weigh the diagnostic yield of genetic screening against its associated cost. Positive results of genetic testing initiate a process requiring intensive counseling, managing expectations, and family planning. Some parents may defer on such options, opting instead for expectant management of an individual child. Such decisions should be made jointly and with all prognostic information available (Grindle, 2014).

The OCHL cohort contained 27 children with syndromes. We had no known patients with Usher syndrome. Pendred was the most common, representing 2% of our CHH, which is slightly less than the predicted incidence (Fraser, 1965). These results are likely driven by exclusion of children with profound hearing loss in the OCHL cohort. Syndromic patients represent a unique patient subgroup among children with hearing loss. Many suffer from concurrent disease processes that may affect vision or balance, may leave them predisposed for tumorigenesis (e.g., von Hippel-Lindau syndrome, neurofibromatosis type II [Megerian et al., 2002; Asthagiri et al., 2009]), may leave them susceptible to airway compromise (Nowak, 1998, Scott et al., 2012), or may cause dysmorphic features. Aside from genetic counseling interventions, these patients often require more aggressive management programs to ensure proper support measures are in place for them and their families (Jerry & Oghalai, 2011; Toriello et al., 1995). They also intrinsically require more visits with specialty providers and generally convey a higher cost burden.

Radiographically, we noted a 34.2% rate of abnormal findings, consistent with previously reported literature (Fitzgerald & Mark, 1998; Mafong et al., 2002). The division between MRI and CT was equitable, though a substantial minority (14%) underwent bi-modal imaging. Of this latter group, 3 (15%) of 20 had findings on both modalities. The decision to order imaging for a child can be fraught with concerns, including radiation exposure from a

CT and the need for sedation/anesthesia during an MRI. Practitioners must be cognizant of specific pathologies likely to appear on particular imaging, as well as the associated diagnostic yield (Chen et al., 2015). This can be challenging, given accelerated advancements in medical technology. High-resolution CT, functional MRI, and magnetoencephalography have unveiled countless potential investigations for CHH, though not without pitfalls. Assumptions or misinterpretation of data may lead to faulty diagnosis, as in the case of internal auditory canal stenosis and cochlear nerve deficiency (Adunka et al., 2007). Misinterpretation of the findings may lead to errant overconfidence in assigning etiology and may abbreviate the work-up, leaving the child and parents at risk for incomplete treatment and counseling. The necessity of personal radiographic skills or trust in a neuroradiologist is imperative for proper interpretation (Johnson & K. Lalwani, 2000).

Despite the myriad of retrospective analyses evaluating the merits of diagnostic batteries and the accompanying recommendations available in the literature, we found significant practice variations between the participating sites (Brookhouser, 1996; Chan et al., 2011; Kimani et al., 2010; Laury et al., 2009; Lin et al., 2011; Mafong et al., 2002; Preciado et al., 2004). While regional differences in the neurology, ophthalmology, radiology, and genetics referrals are clear, the motivations for the patterns are not. The referrals made by UNC reflect an institutional practice model; the patterns observed at UI and BTNRH represent a heterogeneous referring community. Though many studies have examined national trends in hearing screening and intervention (Harrison et al., 2003; Harrison & Roush, 1996), there is a paucity of literature addressing regional differences in work-up (Rutherford et al., 2011). In our study, without surveying the individual referring providers, it is impossible to surmise the corresponding indications for referral. In general, ophthalmology exams are of uncontested importance for patients with hearing loss, given the incidence of ocular disease among those most severely impacted by hearing loss (Nikolopoulos et al., 2006). In the cases of radiology and genetics, there continues to be debate about if and when such referrals should be made, despite the high rate of positivity for these assessments (Roche et al., 2010). It is also noteworthy that 24% of children imaged in the present study demonstrated pathologic inner ear findings. By contrast, genetic-based testing approaches seek to reserve imaging for children who require cochlear implantation or those who have unilateral, asymmetric, or progressive hearing loss. With the NextGen sequencing, 45–60% of children may be identified as having a pathologic mutation. If practitioners feel that the cause of hearing loss has been properly identified in the genetic work-up, they may defer imaging. For those referred for formal genetic testing, 30 (28.5%) of 105 patients were identified as having mutations that would account for the etiology of their hearing loss. As our data demonstrate, diversity in management continues to be the norm (Jayawardena et al., 2015).

In emphasis of the point, most CHH received 1–2 referrals during medical work-up, while a large contingent ($n=81$, 26.4%) had no documented referral to any of our five categories. This is interesting, given that these patients clearly had access to centers of excellence in treating CHH, even if they were not originally enrolled from that center's health system. It is the prerogative of a provider to develop a management algorithm, which may be based on available resources, practice patterns, and personal preference. However, it remains vital to recognize the regional resources and utilize them to the maximum benefit of the patient. The

technology, both for diagnostics and interventions, evolves at a rapid rate within the audiologic community. Providers interfacing with this vulnerable patient population need to remain current on such developments.

Limitations

There are limitations to this study, several of which have already been highlighted. They include the dependency on family members to accurately convey complex medical diagnoses on intake forms, the necessary vagueness of broad categorizations, and the incongruent nature of referral patterns to the three institutions for the individual regions. As noted previously, 0 CHH had a negative family history of hearing loss. Many of the forms had been left blank by caregivers instead of selecting either “Yes” or “No”. This likely reflects a low response rate” on the intake form rather than a true incidence. These are often inherent in retrospective analyses; we have attempted to offset any detriment to these data by maintaining general application. Children with significant developmental comorbidities were excluded from participation; thus, the results may not generalize to this group. Though we have established contextual bedrock to understand the outcomes of the OCHL cohort, further investigation into the individual subgroups is currently underway.

CONCLUSION

It is imperative to recognize that the end for any diagnostic work-up should be intervention and treatment. This point is emphasized for CHH, especially considering modern technologies and available resources. As eloquently stated in the 2013 JCIH Supplement, “the ultimate goal of [early hearing detection and intervention] is to optimize language, social, and literacy development for children who are [deaf and hard-of-hearing]” (Muse et al., 2013). As evidenced by the OCHL cohort, appropriate, directed interventions for CHH facilitated better language, speech, and audibility outcomes (McCreery et al., 2015a; McCreery et al., 2015b; Tomblin et al., 2015a; Tomblin et al., 2015b). The medical characteristics demonstrate a diverse yet representative population of pediatric patients with mild to severe hearing loss. Typical risk factors, including neonatal intensive care, ventilator use, supplemental oxygen, aminoglycoside use, and family history, were statistically confirmed as risks within this cohort. More critically, it is evident that, despite clinical and scientific advancements and available referral centers, there is still a wide range of practice patterns for the medical management of pediatric hearing loss. Future studies should explore the relationship between these medical data and comprehensive audiometric outcomes of CHH.

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All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Conflicts of Interest and Source of Funding:

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Abbreviations:

BTNRH	Boys Town National Research Hospital
CHH	children who are hard of hearing
CMV	Cytomegalovirus
COME	chronic otitis media with effusion
CT	computed tomography
ECMO	extracorporeal membrane oxygenation
EVA	enlarged vestibular aqueduct
IPOG	International Pediatric Otolaryngology Group
JCIH	Joint Committee on Infant Hearing
MRI	magnetic resonance imaging
NH	normal hearing
OCHL	Outcomes of Children with Hearing Loss
SNHL	sensorineural hearing loss
UI	University of Iowa
UNC	University of North Carolina at Chapel Hill

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Table 1

Presence of Known Risk Factors for Hearing Loss

Risk Factor		NH	CHH	Odds Ratio (CI)	p-value
CMV	Negative	6	35		1
	Positive	0	3	Inf (0, Inf)	
Strep	Negative	10	29		0.659
	Positive	1	7	2.38 (0.25, 119.4)	
Meningitis	Negative	7	31		1
	Positive	0	1	Inf (0.01, Inf)	
NICU *	No	115	236		0.01
	Yes	15	66	2.14 (1.17, 3.92)	
NICU Days	0–5	5	18		
	6–15	5	19	1.05 (0.2, 5.45) ⁺	1
	16+	5	29	1.60 (0.32, 8.03) [!]	0.504
ECMO	No	131	287		0.33
	Yes	0	5	Inf (0.41, Inf)	
Vent *	No	123	252		0.004
	Yes	6	41	3.33 (1.35, 9.86)	
Oxygen *	No	124	247		0.011
	Yes	7	40	2.86 (1.22, 7.80)	
AMG *	No	123	254		0.05
	Yes	7	33	2.28 (0.96, 6.28)	
Diuretic	No	129	295		0.68
	Yes	1	6	2.62 (0.31, 121.5)	
FHX *	No	34	0		<0.001
	Yes	6	89	Inf (90.71, Inf)	

* $p < .05$ ⁺ 6–15 vs 0–5 comparison[!] 16+ vs 0–5 comparison

CMV = cytomegalovirus; NICU = neonatal intensive care unit; ECMO = extracorporeal membrane oxygenation, Vent = any ventilator support; AMG = aminoglycoside exposure; FHX = family history

Table 2

Presence of Non-Categorical Risk Factors for Hearing Loss

Risk Factor	Group	Min	Max	Mean (SD)	Odds Ratio (CI)	p-value
Gestational Age (days)	NH (N = 122)	224	294	272.3 (11.3)	0.98 (0.97, 0.99)	0.01
	CHH (N = 296)	168	294	266.6 (22.4)		
Birth Weight (grams)	NH (N = 92)	1304	4791	3372 (611.2)	1 (0.9, 1)	0.077
	CHH (N = 299)	510	4763	3232 (791.2)		

Table 3

Etiologies of Hearing Loss in Children with Mild-to-Severe Hearing Loss

Etiology	Number	Percent Group	Percent CHL
Syndromic		(n = 27)	(n=307)
Barakat	1	4%	0%
Brachio-oto-renal	4	15%	1%
Charcot-Marie-Tooth	1	4%	0%
Diamond-Blackfan	1	4%	0%
DiGeorge	2	7%	1%
Feingold	1	4%	0%
Goldenhar	3	11%	1%
Pendred	6	22%	2%
Pfeiffer	1	4%	0%
Pierre-Robin Sequence *	1	4%	0%
Stickler	1	4%	0%
Townes-Brocks	1	4%	0%
Treacher-Collins	3	11%	1%
16p11.2	1	4%	0%
Total syndromic	27		9%
Non-Syndromic Genetic		(n=30)	
Connexin 26	18	60%	6%
Non-syndromic EVA	10	33%	3%
<i>OTOA</i>	1	3%	0%
<i>OTOF</i>	1	3%	0%
Total non-syndromic genetic	30		9%
Environmental		(n=21)	
Cisplatin Ototoxicity	1	5%	0%
CMV (Confirmed)	4	19%	1%
Gentamicin exposure	14	67%	5%
Meningitis	2	10%	1%
Total environmental	21		7%
Unspecified Congenital		(n=17)	
Atresia	2	12%	1%
Auditory Neuropathy	7	41%	2%
Mondini Malformation	7	41%	2%
Superior Canal Dehiscence	1	6%	0%
Total Unspecified Congenital	17		6%
No other known etiology or risk factors except history of chronic otitis media with effusion (COME)	15		5%
Unknown etiology	197		64.1%
Total hearing loss	307		

* Not a syndrome, but seen in several syndromes; CMV = Cytomegalovirus; EVA = Enlarged Vestibular Aqueduct

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Table 4

Radiographic Findings

Radiographic Category	Finding (% of Modality Total)	(% of Overall Total)
<i>CT</i>	N = 20	
Cochlear		
Bilateral Dysplasia	3 (15%)	(8.6%)
Bilateral Obstructed	1 (5%)	(2.8%)
Vestibular		
Bilateral EVA	5 (25%)	(14.3%)
Right Dysplastic SCC	1 (5%)	(2.8%)
Left Dysplastic SCC	1 (5%)	(2.8%)
Bilateral Dysplastic SCC	2 (10%)	(5.6%)
Cochlear/Vestibular		
Bilateral Dysplasia + Bilateral Dysplastic SCC**	1 (5%)	(2.8%)
Bilateral Dysplasia + Unilateral EVA	1 (5%)	(2.8%)
Bilateral Dysplasia + Bilateral EVA	5 (25%)	(14.3%)
<i>MRI</i>	N = 15	
Cochlear		
Bilateral Dysplasia**	2 (13%)	(5.6%)
Vestibular		
Bilateral EVA**	7 (47%)	(20.0%)
Unilateral EVA	1 (7%)	(2.8%)
Cochlear/Vestibular		
Bilateral Dysplasia + bilateral EVA	4 (27%)	(11.4%)
Bilateral Dysplasia + bilateral absent SCC	1 (7%)	(2.8%)
Overall Total	35	(100%)

* 3 patients had abnormal findings on both modalities; EVA = Enlarged Vestibular Aqueduct; SCC = Semicircular Canal

Table 5

Referral Patterns for Children who are Hard of Hearing

Specialty	BTNRH (N)	Iowa (N)	UNC (N)	<i>p</i> -value
Neurology	28	10	30	< .0001
Ophthalmology	64	23	46	< .0001
Radiology	34	43	73	< .0001
Genetics	43	20	42	.0053
Blood	33	36	63	.0820

BTNRH = Boys Town National Research Hospital; UNC = University of North Carolina at Chapel Hill