# Characteristics and Progression of Hearing Loss in Children with Down Syndrome

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**Objectives** To evaluate hearing impairment in children with Down syndrome, and to describe the factors that influence the severity of hearing loss or changes in hearing over time.

**Study design** Using the Audiological and Genetic Database (AudGenDB), audiograms of children with Down syndrome were analyzed retrospectively for type, severity, and laterality of hearing loss, as well as changes over time. Medical charts and imaging results were reviewed to identify factors influencing hearing loss.

**Results** Among the 1088 patients with Down syndrome included in the study, 921 had hearing loss in at least 1 ear, 91.1% had bilateral hearing loss, and 8.9% had unilateral hearing loss (1760 total ears with hearing loss). Of the ears with hearing loss, 18.8% (n = 180) had moderate or worse hearing loss. "Undefined" hearing loss and pure conductive hearing loss (CHL) were the most common types, followed by mixed hearing loss and sensorineural hearing loss (SNHL). Three-quarters (75.4%) of the children had experienced chronic otitis media or more than 2 episodes of acute otitis media. Patients with bilateral, mixed hearing loss or a history of seizures were at risk for more severe hearing loss. CHL, absence of cholesteatoma, and placement of first ear tubes before age 2 years were associated with greater improvement in hearing over time, whereas SNHL and mixed hearing loss were associated with progressive decline.

**Conclusion** Children with Down syndrome who have bilateral, mixed hearing loss or a history of seizures are at risk for more severe hearing loss. SNHL and mixed hearing loss should not be overlooked in patients with CHL. All patients with Down syndrome will benefit from serial audiograms, especially those children with SNHL or mixed hearing loss, which is likely to worsen over time. *(J Pediatr 2017;■■:■■-■■).*

**See editorial, p ••• and related article, p •••**

Children with Down syndrome display a wide spectrum of clinical signs and symptoms affecting multiple organ systems,[1,2] most commonly characterized by intellectual disability, hypotonia, typical facies, congenital heart anomalies, and growth delays.[3] Affected children often have narrowed ear canals and hypotonia of the eustachian tubes, possibly contributing to eustachian tube dysfunction, otitis media with effusion, and hearing loss.

Hearing loss of both conductive and sensorineural origin is prevalent in children with Down syndrome. Several previous studies have reported otologic and audiologic findings in children with Down syndrome[4-10]; however, those studies involved relatively few patients, and although they provided a fairly thorough audiologic analysis, their conclusions were limited by the small sample sizes. We used the Audiological and Genetic Database (AudGenDB) to analyze hearing outcomes in children with Down syndrome and identify the factors influencing hearing loss and change in hearing over time.

## Methods

The Institutional Review Board of the Medical University of South Carolina approved this study. The AudGenDB, a publicly available online database funded by the National Institutes on Deafness and Other Communication Disorders, contains information on approximately 105 000 pediatric patients, drawn from the electronic medical records at Children's Hospital of

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| ABR | auditory brainstem response |
| AudGenDB | Audiological and Genetic Database |
| CHL | Conductive hearing loss |
| ICD-9 | *International Classification of Diseases, Ninth Revision* |
| PTA | Pure-tone average |
| SNHL | Sensorineural hearing loss |

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Philadelphia.[11] The database is HIPAA compliant and draws information from electronic health records, audiologic instruments, radiology reports, and clinical genetics results.

The patients in the present series were drawn from a database query of children up to age 21 years who had received a diagnosis of Down syndrome under the diagnosis and/or problem list sections, based on *International Classification of Diseases, Ninth Revision* (ICD-9) codes. Subjects enrolled in the database as of July 7, 2016, were included in the present study. Patient data were organized by age, sex, ethnicity, availability of audiometric data, and detection of hearing loss on audiograms. Ethnicity was categorized into 5 groups: white, Black or African American, Hispanic, Asian, and other (including "other," unknown, Indian, Native Alaskan, American Indian, Native Hawaiian, and Pacific Islander).

Our database analysis approach was adapted from previous studies performed by this group.[12,13] Pure-tone air and bone conduction audiometry and sound field testing were used to evaluate hearing outcomes. The most complete audiogram that demonstrated the earliest evidence of hearing loss was used to characterize the type, severity, and laterality of hearing loss. Throughout the text, *n* is used to denote number of ears, and *N* is used to denote the number of patients.

When available, ear-specific air-conduction thresholds were collected at octave frequencies of 0.25-8.0 kHz and at interoctave frequencies of 3.0-6.0 kHz. Both masked and unmasked bone conduction thresholds were analyzed when available at octave frequencies of 0.25-4.0 kHz and at an interoctave frequency of 3.0 kHz. Audiograms were categorized based on the presence of hearing loss, type of hearing loss, severity of loss, and ear(s) affected (right, left, or bilateral). Hearing loss was defined as a threshold >15 dB for pure-tone audiometry or 20 dB for sound field audiometry at any frequency, or >25 dB at any frequency for infants aged <1 year.[14] In general, we classified hearing loss as conductive hearing loss (CHL), with an air conduction threshold of >15 dB hearing loss and an air-bone gap of ≥10 dB at any recorded frequency; sensorineural hearing loss (SNHL), with an air conduction threshold of >15 dB hearing loss and an air-bone gap of <10 dB at any recorded frequency; mixed, with an air conduction threshold of >15 dB hearing loss and an air-bone gap of >10 dB at the same recorded frequency; combined, with both CHL and SNHL present but at different frequencies; or undefined, with insufficient data to determine the type of loss (eg, audiograms without bone conduction testing or non–ear-specific sound field audiograms).

The pure-tone average (PTA) was calculated for air conduction bilaterally using the frequencies 0.5, 1.0, 2.0, and 4.0 kHz (or 3.0 kHz if values at 4.0 kHz were not available), in accordance with the American Academy of Otolaryngology–Head and Neck Surgery guidelines for PTAs. A PTA based on 3 values (0.5, 1.0, and 2.0 kHz) was used in the minority of cases in which PTA could not be calculated from 4 thresholds. The severity of the hearing loss was established based on the PTA as normal (PTA ≤15 dB), slight (16-25 dB), mild (26-40 dB), moderate (41-55 dB), moderately severe (56-70 dB), severe (71-90 dB), or profound (90+ dB). Tympanometry data, including middle ear pressure, static compliance, and external canal volume, were used to determine tympanogram type (A, B, or C), based on guidelines from the American Speech and Hearing Association.

For each patient with hearing loss, common medical and otologic ICD-9 diagnoses were noted. These included heart defects, gastrointestinal problems, neurologic disorders, developmental or communication disorders, number of acute and chronic otitis media diagnoses, eustachian tube dysfunction, cholesteatoma, and tympanostomy tubes, among others. Radiographic reports were reviewed as available in AudGenDB. The appearance of the external auditory canal, ossicles, semicircular canals, vestibule, cochlea, internal auditory canal, vestibular aqueduct, vestibulo-cochlear nerve, and mastoid air cells were recorded based on the written reports of the radiologist.

### Statistical Analyses

All statistical analyses and graphs were performed with R version 3.2.4 (R Institute for Statistical Computing, Vienna, Austria).[15] Categorical variables were summarized by frequency and percentage. Continuous variables were summarized by mean ± SD, range, or median and IQR as appropriate. All continuous variables were assessed for normality using the Shapiro-Wilk test. To analyze changes in hearing loss over time, the change in PTA from each patient's first audiogram to the last audiogram was calculated. Cases were also stratified by PTA outcome (improved, no change, or worse) with no change defined as an absolute change in PTA ≤10 dB. Comparisons of baseline characteristics and outcomes (categorical variables) were performed using the Fisher exact test or $\chi^2$ test. For continuous variables, the independent *t* test or Mann-Whitney test was used to compare 2 groups, and 1-way ANOVA or the Kruskal-Wallis test was used to compare 3 or more groups. Post hoc comparisons using the Tukey honest significant difference test were used to compare multiple times between groups. In addition, a correlation model was used to determine the relationships among all outcome variables. All independent variables that showed a significant correlation with dependent variables were entered into a regression model. Adjusted ORs or $\beta$ values and their 95% CIs were obtained from the final model as measures of the associations between the independent predictors and the dependent responses. A *P* value <.05 was considered to indicate a statistically significant difference for all statistical tests.

## Results

The AudGenDB includes 1318 children with a diagnosis of Down syndrome, 1088 of whom (82.5%) had available audiometric data. Among these 1088 children, 921 had hearing loss in at least 1 ear on at least 1 audiogram; 91.1% (n = 839) had a bilateral hearing loss and 8.9% (n = 82) had a unilateral hearing loss, for a total of 1760 ears with hearing loss (**Table I**). Among these 1760 ears, 1180 (67.0%) had hearing deficits that persisted across all available audiograms (**Figure 1**). The median number of audiograms performed per child was



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