International Journal of Pediatric Otorhinolaryngology 87 (2016) 130–133

Contents lists available at ScienceDirect

International Journal of Pediatric Otorhinolaryngology

journal homepage: http://www.ijporlonline.com/

Prevalence of hearing loss in children with 22q11.2 deletion syndrome

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ARTICLE INFO

Article history:
Available online 7 June 2016

Keywords:
22q11.2 microdeletion syndrome
DiGeorge syndrome
Velocardiofacial syndrome
Hearing loss
Cleft palate
Speech articulation disorder

ABSTRACT

Objective: The purpose of this study was to determine the prevalence and characterize the types of hearing loss in pediatric patients with 22q11.2 deletion syndrome (22q11DS).
Methods: Fifty-eight patients were identified via retrospective chart review performed of patients with 22q11DS between 1996 and 2014. Patient demographics, pertinent family history, associated comorbidities, and degree and type of hearing loss were gathered for each patient. A literature review of the National Library of Medicine's database with a focus on hearing loss and 22q11DS was performed.
Results: 22 patients (38%) were found to have hearing impairment: 68% with conductive hearing loss, 14% with sensorineural hearing loss, and 18% with mixed hearing loss. Patients with hearing loss regardless of type had a higher prevalence of developmental delay (55%), cleft palate (23%), articulation disorders (77%), and a greater need for tympanostomy tubes (73%) compared to patients with normal hearing. Temporal bone computed tomography scans of 5 patients revealed a variety of abnormalities in the middle and/or inner ears.
Conclusion: Hearing impairment occurs in up to 38% of 22q11DS patients of both conductive and sensorineural types, with the conductive type being the most common. These patients have a greater need for tympanostomy tubes and a higher prevalence of developmental delay and speech articulation disorders. Early hearing screening and treatment is warranted in this population.

1. Introduction

The 22q11.2 deletion syndrome (22q11DS), including DiGeorge syndrome and velocardiofacial syndrome, is the most common human microdeletion syndrome, occurring between 1:6000 and 1:2000 live births [1–3]. The deletion results in hypoplasia of the branchial arches *in utero*, leading to abnormalities in the structures derived from them [4]. Consequently, 22q11DS is characterized as a highly variable constellation of findings including but not limited to congenital heart disease, hypoparathyroidism, immunodeficiency, neurocognitive disorders, cleft palate, and velopharyngeal insufficiency [5–8].

Eustachian tube dysfunction due to poor palate function and immunodeficiency due to impaired thymic development predispose these patients to chronic otitis media, leading to significant conductive hearing loss (CHL) [5,9,10]. Sensorineural hearing loss (SNHL) has also been reported in these patients, but the etiology is less clear [8,10]. Funke et al. demonstrated in a murine model that T-box transcription factor 1 (TBX1), expression of which is altered in 22q11DS, is necessary for normal middle and inner ear development [11]. Regardless of type, unrecognized hearing loss can lead to delayed speech and cognitive development in 22q11DS patients.

There is a large discrepancy in the literature regarding the percentage of 22q11DS patients who suffer from hearing loss, ranging from 40% to as high as 75% [5,10,12]. Of the few studies that have attempted to describe this, even fewer have focused on the pediatric population, for whom timely identification of hearing impairment is of particular importance. The purpose of this study was to determine the prevalence and type of hearing loss in pediatric patients with 22q11DS.

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http://dx.doi.org/10.1016/j.ijporl.2016.06.005
0165-5876/

2. Methods

Approval for the study was obtained by an institutional review board. A retrospective chart review of patients with 22q11DS treated at a tertiary pediatric hospital between 1996 and 2014 was performed using an electronic medical record search. Inclusion criteria included all patients under the age of 18 years at time of review with confirmed 22q11DS by either fluorescence in situ hybridization or chromosomal microarray.

Information gathered included demographics, pertinent family history, associated comorbidities, type and degree of hearing loss, and the need for tympanostomy tubes or hearing aids. Severity of hearing loss was categorized as mild, moderate, and severe, corresponding to pure tone averages of 20–40 dB, 41–60 dB, and >61 dB respectively. In cases of bilateral hearing loss, the more affected ear was used for categorization.

A review of pertinent literature regarding hearing loss in the 22q11DS population found in the National Library of Medicine's online database was performed and summarized.

3. Results

Fifty-eight patients (26 male, 32 female) were identified based on the inclusion criteria. Patient demographics, family history, and comorbidities are presented in Table 1. Of these 58 patients, twenty-two patients (38%) suffered from hearing loss based on audiological work-up. Fifteen (68%) had conductive hearing loss, bilateral in nine patients (60%) and unilateral in six patients (40%). Three patients (14%) had sensorineural hearing loss, bilateral in two patients and unilateral in one patient. The remaining four patients (18%) had unilateral mixed hearing loss (Fig. 1).

Of the 22 patients with hearing loss, seventeen (78%) had mild hearing loss, four (18%) had moderate hearing loss, and one (5%) had severe hearing loss. Nine (41%) of these patients required hearing aids (Fig. 2). Sixteen patients (73%) had otitis media and CHL requiring tympanostomy tubes, sixteen (73%) had cardiac disease, twelve (55%) had some degree of developmental delay, five (23%) had cleft palate, and seventeen (77%) had a speech articulation disorder. Of the thirty-six patients with normal hearing, ten (28%) required tympanostomy tube placement, twenty-six (72%) had cardiac disease, fifteen (42%) were developmentally delayed, four (11%) had cleft palate, and eighteen (50%) had a speech articulation disorder (Table 2).

Five patients with hearing loss underwent further assessment with temporal bone computed tomography (CT) scans. Four had speech articulation disorders, but none were developmentally delayed. The CT scan of one patient with unilateral CHL revealed tympanosclerosis in the affected ear, and the CT scan of another patient with bilateral CHL demonstrated poorly formed lateral semicircular canals bilaterally. One patient with bilateral mixed hearing loss was found to have a fused incus and malleus in both ears. The remaining two patients had bilateral SNHL: one was found to have bilateral vestibular dilatation and a left malleus fused to the lateral middle ear wall, while the other had no cochlear or ossicular malformation (Table 3, Fig. 3).

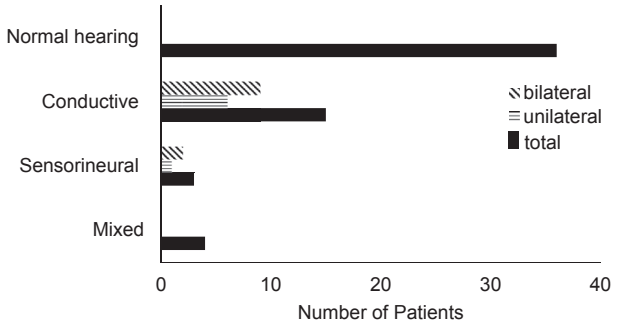

Fig. 1. Type of hearing loss. 22 patients (38%) had hearing loss based on audiological work-up. 15 patients (68%) had conductive hearing loss, bilateral in 9 patients (60%) and unilateral in 6 patients (40%). 3 patients (14%) had sensorineural loss, bilateral in 2 patients (66%) and unilateral in 1 patient (33%). 4 patients (18%) had mixed hearing loss.

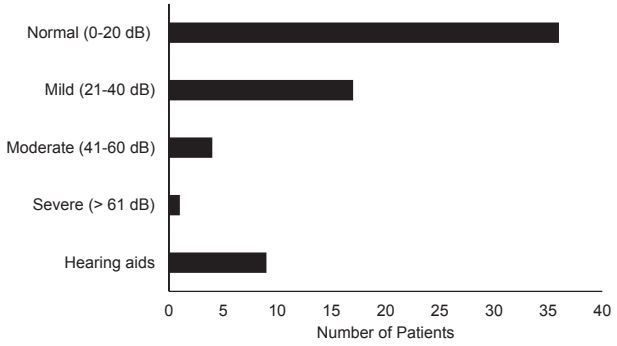

Fig. 2. Degree of hearing loss*. Of the 22 patients with hearing loss, 17 patients (78%) had mild hearing loss, 4 patients (18%) had moderate hearing loss, and 1 patient (5%) had severe hearing loss. 9 patients (41%) required hearing aids. *Degree of hearing loss based on pure tone averages (PTA) and are reported based on the worst ear if the patient had bilateral hearing loss.

Table 1
Demographics.

Patients with DGS	58
Male	26 (45%)
Female	32 (55%)
Age (mean yrs ± stdev)	8.5 ± 5.3
Family history of DGS	2 (3%)
Family history of cardiac disease	16 (28%)
Family history of hearing loss	3 (5%)
Cardiac disease	42 (72%)
None	16 (28%)
Mild[a]	7 (12%)
Severe[b]	35 (60%)
Developmental delay	31 (53%)
Hearing loss	22 (38%)
Cleft palate	9 (16%)
Speech articulation disorder	35 (60%)
Hypocalcemia	12 (21%)
Immunodeficiency	1 (2%)

[a] Mild: PDA, PFO, ASD, VSD.
[b] Severe: TOF, IAA.

Table 2
Characteristics of patients with and without hearing loss.

	Normal hearing	Hearing loss
Number of patients	36	22
Gender		
Male	17 (47%)	9 (41%)
Female	19 (53%)	13 (59%)
Surgery for tympanostomy tube	10 (28%)	16 (73%)
Number of surgeries for tympanostomy tube placement (mean ± stdev)	1.4 ± 0.5	1.4 ± 0.8
Cardiac disease	26 (72%)	16 (73%)
Developmental delay	15 (42%)	12 (55%)
Cleft palate	4 (11%)	5 (23%)
Speech articulation disorder	18 (50%)	17 (77%)
Hypocalcemia	9 (25%)	3 (14%)
Immunodeficiency	0 (0%)	1 (5%)