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# Otolaryngology Manifestations of Primary Ciliary Dyskinesia: A Multicenter Study

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Author Contributions

**Faisal Zawawi**, conceptualized and designed the study, designed the data collection instruments, coordinated and supervised data collection, drafted the initial manuscript, reviewed and revised the manuscript; **Adam J. Shapiro**, conceptualized and designed the study, designed the data collection instruments, coordinated and supervised data collection, drafted the initial manuscript, reviewed and revised the manuscript; **Sharon Dell**, coordinated and supervised data collection, critically reviewed the manuscript for important intellectual content; **Nikolaus E. Wolter**, coordinated and supervised data collection, critically reviewed the manuscript for important intellectual content; **Cinzia L. Marchica**, collected data, reviewed and critically revised the manuscript for important intellectual content; **Michael R. Knowles**, analyzed and interpreted data, reviewed and revised the manuscript for important intellectual content; **Maimoona A. Zariwala**, analyzed and interpreted data, reviewed and revised the manuscript for important intellectual content; **Margaret W. Leigh**, analyzed and interpreted data, reviewed and revised the manuscript for important intellectual content; **Mariana Smith**, collected data, reviewed and critically revised the manuscript for important intellectual content; **Pilar Gajardo**, collected data, reviewed and critically revised the manuscript for important intellectual content; **Sam J. Daniel**, conceptualized and designed the study, designed the data collection instruments, coordinated and supervised data collection, drafted the initial manuscript, reviewed and revised the manuscript.

**Competing interests:** None.

Supplemental Material

Additional supporting information is available in the online version of the article.

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## Abstract

**Objective.—**This project aims to prospectively and objectively assess otolaryngological manifestations and quality of life of children with primary ciliary dyskinesia (PCD) and compare these findings with healthy pediatric controls.

**Study Design.—**Cross-sectional.

**Setting.—**Two high-volume pediatric PCD specialty centers.

**Methods.—**Standardized clinical assessment; Sino-Nasal Outcome Test 22 (SNOT-22); Hearing Environment and Reflection Quality of Life (HEAR-QL); Reflux Symptom Index (RSI); standardized physical examination of the sinonasal, laryngeal, and otological systems; and investigations including pure-tone audiograms (PTAs) and sinonasal cultures were collected.

**Results.—**Forty-seven children with PCD and 25 control participants were recruited. Children with PCD had more upper airway symptoms than healthy children. They had significantly higher scores in both SNOT-22 and RSI, indicating worse sinonasal and reflux symptoms, with worse quality of life on the HEAR-QL index compared to healthy children ($P < .05$). Fifty-two percent of children with PCD-related hearing loss were not aware of their hearing deficit that was present on audiological assessment, and only 23% of children who had ventilation tubes had chronic otorrhea, most of which was easily controlled with ototopic drops. Furthermore, although all children with PCD had chronic rhinosinusitis, only 36% of them were using topical nasal treatment. The most common bacteria cultured from the middle meatus were *Staphylococcus aureus* in 11 of 47 (23%), followed by *Streptococcus pneumoniae* in 10 of 47 (21%).

**Conclusion.—**This multisite cohort highlights the importance of otolaryngology involvement in the management of children with PCD. More rigorous otolaryngological management may lead to reductions in overall morbidity and improve quality of life for children with PCD.

### Keywords

PCD; otolaryngology; quality of life; otological; sinonasal

Primary ciliary dyskinesia (PCD) is a mostly autosomal recessive disorder with a prevalence of 1 in 15,000 to 30,000.[1] PCD is frequently not diagnosed in children for multiple reasons, including its overall rarity, its phenotypic overlap with other common childhood respiratory issues, and the need for specialized diagnostic testing procedures to confirm it.[1–3]

Recent advances in PCD research have revealed genotype-phenotype trends in pulmonary function and lower respiratory tract disease, yet knowledge of the upper airway disease burden in PCD is lacking.[2] To date, only retrospective, singlecenter studies have explored sinonasal and otologic disease manifestations in PCD, and these report conflicting results in children with PCD. For example, the incidence of chronic otorrhea postventilation tube placement has varied from less than 10% to over 70%, and the ability to control chronic otorrhea with ototopic drops is not well documented.[4–8] In addition, the prevalence of

sinonasal disease and complications, including anosmia and polyposis, is poorly defined in PCD.[9]

To further our understanding of upper airway disease manifestations in PCD, this study performs a cross-sectional analysis of otolaryngological issues in children with a definitive diagnosis of PCD, followed in 2 high-volume pediatric tertiary care institutions with specialized PCD clinics. Using standardized medical histories, physical examination findings, and quality-of-life questionnaires, this is the first multisite, prospective study of the sinonasal and otologic systems in children with definite PCD.

## Methods and Materials

This cross-sectional study was conducted from January 2016 to January 2020 in the PCD clinics of the McGill University Health Centre in Montreal, Quebec, Canada, and The Hospital for Sick Children in Toronto, Ontario, Canada. Ethics approval was granted from both institutional review boards, and all participants were consented prior to participating in this study. All PCD cases were definitively diagnosed through at least 1 of 3 approved diagnostic criteria as per the American Thoracic Society guidelines: (1) two pathogenic or likely pathogenic mutations in 1 known PCD gene, (2) presence of a disease-causing ciliary ultrastructural defect on transmission electron microscopy (TEM, including outer dynein arm defect, outer plus inner dynein arm defect, or absent inner dynein arm with central apparatus defect and microtubule disorganization), or (3) nasal nitric oxide (nNO) values <77 nL/min, by exhalation against resistance, on at least 2 separate occasions, with cystic fibrosis ruled out via sweat chloride or cystic fibrosis transmembrane conductance regulator (CFTR) genetic testing in children aged ≥5 years. Children who did not meet these criteria were excluded from the study. We also excluded any child who had other systemic comorbidities or craniofacial dysmorphic features. All participants, whether PCD or controls, were in their baseline state of health. We postponed recruitment of any child who had an active upper respiratory tract infection until back to clinical baseline for 6 weeks. Children with PCD and their accompanying family members participated in this study in the PCD group. The control participants were healthy siblings of other children being seen in the hospital for a variety of reasons, including hernia repairs, neck masses, and orthopedic diseases, or they comprised healthy children who were attending the hospital as visitors. These healthy controls specifically lacked chronic medical issues and chronic ear, nose, and throat conditions and were in their baseline state of health at time of recruitment. None of the controls were directly related to the PCD participants. Any control patients with systemic morbidity or craniofacial dysmorphism were excluded.

### Study Questionnaires

The participant or parent filled out 3 validated quality-of-life questionnaires addressing sinonasal-, otologic-, and gastroesophageal reflux–related symptoms: the Sino-Nasal Outcome Test 22 (SNOT-22), the Hearing Quality of Life Questionnaire (HEAR-QL), and Reflux Symptom Index (RSI). Each of these questionnaires has been previously employed or validated in pediatric populations.

### SNOT-22.

The SNOT-22 is a validated patient-based quality-of-life and outcome measure applicable to sinonasal conditions and surgery. The theoretical score ranges between 0 and 110, with higher scores implying a worse health-related quality of life. It is commonly used for either comparing groups or comparing the impact of treatment on the patient's reported sinonasal symptoms.[10]

### HEAR-QL

The HEAR-QL is a validated pediatric quality-of-life and outcome measure that is applicable to all patients attending otolaryngology clinics to determine their "self-described hearing problems." It consists of 26 items with a theoretical range of 0 to 2600, with higher scores implying a better health-related quality of life.[11]

### RSI.

The RSI is a validated 9-item outcome instrument for patients with laryngopharyngeal reflux that is easily administered, is highly reproducible, and exhibits excellent construct-based and criterion-based validity. A result of RSI of >13 is considered abnormal.[12,13]

### Clinical Assessment

A comprehensive and standardized clinical assessment was performed by 1 of 4 pediatric otolaryngologists on each participant, including (1) standardized otolaryngological clinical history (see Appendix 1 in the online version of the article), (2) physical examination focused on the otolaryngological-related disease manifestations, and (3) flexible fiber-optic nasolaryngoscopy. Standardized examination scales included the Brodsky grading scale for tonsils, and the adenoid size was assessed using 4 grades (<25%, <50%, <75%, and >75% obstruction of the posterior nasal choana).[14] The Nasal Polyps Grading Scale by Meltzer et al[15] and the Reflux Finding Score (RFS)[12,16] were used for polyposis and reflux scoring, respectively. Standardized otologic examination findings included external auditory meatus (swollen, discharge, normal) and tympanic membrane (retracted, perforated, fluid, tube, cholesteatoma, normal). Based on American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS) clinical practice guidelines, recurrent otorrhea was defined as ear discharge on more than 4 separate episodes annually and chronic otorrhea when the episodes lasted longer than 8 weeks despite appropriate medical therapy.[17] The presence of chronic rhinosinusitis (with or without polyposis) was also diagnosed per AAO-HNS guidelines.[18]

All patients with PCD underwent endoscopically guided middle meatus nasal culture swabs, which were processed for standard bacterial culture and sensitivities. None of the control participants had nasal cultures performed as part of this protocol. In addition, all participants received tympanograms and pure-tone audiograms.[19]

### Data Analysis

The data were analyzed with SPSS v24 software (SPSS, Inc). Fisher exact test and $\chi^2$ test were used for nominal data while *t* test for means was used to determine significance. A *P* value <.05 was considered significant.

# Results

## Demographics and Genetics

Forty-seven children with PCD (n = 22 from Montreal, n = 25 from Toronto) and 25 healthy children were recruited from both institutions. The mean age of children with PCD was 10.4 years (range, 0.8-18 years) vs 10.1 years (range, 1.5-18 years) in the healthy children ($P = .62$). Additional demographic data are available in Table 1. The PCD diagnosis was verified through positive genetic testing in 40 (85%) of cases, while TEM defect without positive genetic testing was diagnostic in 3 (6%) of cases. The remaining 4 (9%) cases were diagnosed through repeatedly low nNO levels and negative or inconclusive TEM and genetic testing (with negative cystic fibrosis and immunodeficiency testing, n = 0 with laterality defects, n = 2 with prolonged neonatal respiratory distress, n = 2 with bronchiectasis). The most common PCD-causing genetic mutations were DNAH5 (n = 12, 26%) and DNAH11 (n = 5, 11%), and the remaining genetic diagnoses were from disease-causing variants in 14 other PCD-associated genes (Table 2). Despite being followed in specialized PCD clinics at tertiary care institutions, only 12 of 47 (26%) had regular follow-up with otolaryngology every 6 to 12 months, per PCD Foundation consensus recommendations.[2]

## Otologic Manifestations

The most common patient-reported otologic symptom in the children with PCD was hearing loss in 18 of 47 (38%), which was only reported in 2 of 25 (8%) in the control group ($P = .02$). Chronic or recurrent otorrhea was also significantly more common in 11 of 47 (23%) children with PCD compared to 1 of 25 (4%) controls ($P = .04$). None of the participants in the control group complained of vertigo or balance impairment, whereas 9 of 47 (20%) in the children with PCD endorsed balance impairment symptoms ($P = .02$). Despite only 40% of children with PCD reporting hearing loss, documented hearing loss on audiogram was present in 29 of 47 (62%) children with PCD, most of whom had mild to moderate conductive hearing loss. While only 1 participant had severe hearing loss on audiogram, this child had mixed hearing loss. Of those participants who did not report any hearing loss on history, 15 of 29 (52%) actually had measurable hearing deficits on audiogram.

Overall, children with PCD required 4 times the number of tympanic membrane ventilation tubes compared to controls ($P < .01$). Multiple sets of ventilation tubes were placed in 27 of 47 (58%) children with PCD, while multiple sets of ear tubes were only required in 2 of 25 (8%) controls ($P < .01$). The mean frequency of annual reported acute otitis media episodes per participant was not significantly higher in the children with PCD (1.6 episodes) compared to the control group (0.96 episodes) ($P = .09$). On physical exam, the presence of middle ear fluid (30/47; 79%) or ventilation tubes (6/47; 13%) was much more frequent in the children with PCD ($P < .01$) (Table 3). When looking at HEAR-QL results, the PCD group had a significantly lower mean score compared to the control group ($P < .01$) (Table 4).

## Sinonasal Manifestations

The most frequently reported sinonasal symptoms in children with PCD were nasal congestion in 39 of 47 (83%) and nasal discharge in 36 of 47 (77%), which were

significantly more prevalent than in the control group ($P < .01$, Table 1). Diminished sense of smell was reported by 11 of 47 (23%) children with PCD, whereas no participants in the control group reported this symptom. The most common bacteria cultured from the nasal middle meatus were *Staphylococcus aureus* in 11 of 47 (23%), followed by *Streptococcus pneumoniae* in 10 of 47 (21%), *Haemophilus influenzae* in 5 of 47 (11%), and *Moraxella catarrhalis* in 3 of 47 (6%). Negative meatus cultures were found in 18 of 47 (39%).

Although 100% of children with PCD met the AAO-HNS clinical practice guidelines criteria to diagnose chronic rhinosinusitis, only 12 (26%) children with PCD used topical nasal steroids, and only 17 (36%) used nasal irrigation on a regular basis (Table 1). Chronic rhinosinusitis with polyposis was present in 3 children with PCD (6%), and none in the control group had polyps or met the criteria for chronic rhinosinusitis.

Children with PCD also had a significantly higher mean score on the SNOT-22 questionnaire compared to the mean score of the control group (36.4 in PCD vs 5 in controls, $P < .01$) (Table 4). Only 3 children with PCD underwent endoscopic sinus surgery, and all of them for chronic rhinosinusitis with polyposis.

Sleep-disordered breathing symptoms, reported in the standardized medical history questions, were present in many of the children with PCD. Mouth breathing was significantly more prevalent in children with PCD (33/47 [70%] vs 2/25 [8%] in the control group, $P < .01$), as well as snoring in 23 of 47 (49%) of children with PCD compared to 2 of 25 (8%) in the control group ($P < .01$) (Table 1).

### Laryngopharyngeal Manifestations

Although the RSI questionnaire score was significantly higher for gastroesophageal reflux symptoms in the children with PCD (mean 11.5 vs 2 in controls, $P < .01$), the mean RFS scores on laryngeal examination were similar between both groups (mean 8.2 vs 7.2 in controls, $P = .20$). Furthermore, 23 of 47 (49%) children with PCD scored higher than the recognized cutoff of 7 on the RFS compared to 8 of 25 (32%) in the control group ($P = .12$).

## Discussion

Children with PCD have significantly higher sinonasal and otologic disease burdens and worse quality of life compared to pediatric controls. The PCD Foundation consensus statement recommends otolaryngological assessment every 6 to 12 months in children with PCD, with audiology at the first clinical visit and as needed thereafter.[2] Despite being followed in PCD specialty centers by caregivers who are extremely familiar with upper airway disease manifestations of PCD, most of the children in this PCD population did not have regular visits with otolaryngologists. Although the exact reason for this lack of regular ear and sinus care is unclear, poor patient awareness of effective therapies may have contributed to this finding. More in-depth otolaryngology education may empower patient and families to advocate for themselves when institutional practices fail to secure adequate follow-up. However, many of the parents and children in this study tended to underreport their otolaryngological symptoms, despite these symptoms being easily identified on standardized examinations and questionnaires. Thus, care providers should

routinely employ scoring questionnaires in children with PCD, and these patients may benefit from prophylactic and tailored therapies based upon preemptive questionnaires as opposed to more symptom-directed therapies based upon direct patient or family report.

Children with PCD in this study had consistently worse scores on the SNOT-22 questionnaire and on clinical sinonasal history compared to the control group, and 6% had nasal polyposis. This prevalence of nasal polyposis in PCD is much lower than prevalence of nasal polyps in cystic fibrosis- related chronic rhinosinusitis (up to 48%).[20,21] In addition, nearly 23% of children with PCD complained of diminished sense of smell, which is a novel finding that warrants further investigation. All of the participants with PCD had chronic rhinosinusitis as defined by the AAO-HNS,[18] yet only 26% of this population regularly uses topical nasal treatments for chronic rhinosinusitis (saline rinses and topical intranasal corticosteroids). Compliance and adherence to routinely using intranasal therapies is often a challenge in younger children. In a cross-sectional study looking into various factors related to nonadherence to intranasal corticosteroids, the number of dependent children per caregiver was the main factor associated with low adherence to intranasal therapy.[22] Acceptance of regular nasal irrigation with larger fluid volumes often seems even more difficult in smaller children and frequently complicated in those with ear tubes, given the propensity for saline rinses to enter the eustachian tube and middle ear space. However, once most parents overcome their hesitation to try nasal irrigation, it seems well tolerated.[23] Thus, the lack of regular intranasal therapies in this PCD cohort is concerning as these therapies are mainstays of treatment in other populations with chronic rhinosinusitis and have been shown to improve quality of life and possibly to improve lower respiratory tract inflammation.[24–27]

Functional endoscopic sinus surgery (FESS) is often performed in children with PCD as they reach adolescence, and 6% of patients in our population received a previous FESS procedure. In a case series of adult patients with PCD, FESS results in a significant reduction of chronic sinonasal symptoms.[28] Despite a complete lack of evidence for FESS in children with PCD, this procedure is being frequently performed, and further study on surgical techniques, benefits, and outcomes of this therapy should be pursued in pediatric PCD.

Children with PCD suffer from mouth breathing and sleep-disordered breathing (snoring), which was found to be significantly higher than our control group. One past case series has also documented an elevated obstructive apnea hypopnea index on polysomnography of children with PCD.[29] Although our cohort was not systematically tested with polysomnography, the case series is in agreement with our population's reported symptoms of possible sleep-disordered breathing on standardized history reporting. It is quite possible that more aggressive and universal therapies for chronic rhinosinusitis in children with PCD could improve this sleep-disordered breathing.

Laryngopharyngeal reflux (LPR) is a common condition in both children and adults, and our PCD population has significantly higher RSI mean symptom scores compared to controls, but only 38% had scores >13, which is the cutoff score for diagnosing LPR. Positive responses on some of the RSI questions may reflect a poorly controlled sinonasal condition

and chronic lung disease rather than uncontrolled gastroesophageal reflux. Thus, further validation is required before relying on results of the RSI for diagnosing LPR in children with PCD.

Retrospective literature reports children with PCD have a high incidence of hearing loss that is mostly conductive in nature. In our cohort, almost 60% had moderate conductive hearing loss due to middle ear effusion (MEE).[6] The hearing loss is predominantly conductive in nature and can be treated with either ventilation tubes (VTs) or hearing aids.[7,17,30,31] The appropriate management of MEE and recurrent otitis media in children with PCD remains controversial, and VTs have historically been avoided in some European centers due to the risk of developing chronic and recurrent otorrhea in children with PCD.[17,30,31] In past literature, up to 50% of children with PCD can have otorrhea post-VT placement.[17,30,31] Wolter et al[7] retrospectively studied a population of children with PCD after VT insertion, and they concluded >40% develop otorrhea, but only 20% have either recurrent or chronic otorrhea. Furthermore, most of these episodes of otorrhea were easily controlled with ototopic drops. This is in agreement with our results showing 23% of the PCD population had either chronic or recurrent otorrhea, and most of our PCD group participants reported these episodes were controllable with ototopic drops. For this reason, we argue that placing VTs should always be discussed as an option of management of MEE in children with PCD and not routinely avoided for risk of chronic otorrhea.

Another novel finding this study highlights is the balance impairment and vertigo reporting by the parents and children with PCD. Over 19% of the PCD participants reported dizziness, vertigo, or balance impairment. This is an important finding that warrants further investigation, as some children with PCD have received antibiotics and medications during their early childhood that are ototoxic (eg, aminoglycosides) and could lead to vestibular impairment. Another potential cause of this balance impairment could be related to sensory (nonmotile) cilia deficits in kinocilium of the inner ear, but the overlap of these 2 different cilium classes is poorly understood at present.

Although this is the first multicenter study of otolaryngology issues in PCD, there are some limitations. First, the sample size was too small for some of the analyses on the population. In addition, 4 participants who were younger than 6 years required the help of their parents to complete the study questionnaires, which may have influenced their responses. Next, pathogenic variants in *CCDC39* or *CCDC40* genes are known to result in worse outcomes for lower airway disease, but the effects on upper airway disease are unknown. Unfortunately, we did not have enough PCD cases with *CCDC39* or *CCDC40* variants to perform meaningful genotype-phenotype correlations in this project.

## Conclusion

This cohort highlights the need for a focused management of chronic rhinosinusitis and ear disease in patients with PCD, which could lead to reduction in morbidity and improvement in quality of life. Placement of ventilation tubes to address middle ear effusion is a valid treatment option, and future research should focus on identifying subsets of patients with PCD in whom this therapy may have worse complications.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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**Table 1.**

Items Included in the Standardized Clinical History and Their Reporting.[a]

| Characteristic | Primary ciliary dyskinesia (n = 47) | Control (n = 25) | *P* value [95% CI] |
|---|---|---|---|
| Age, mean ± SD, y | 10.4 ± 4.92 | 10.1 ± 4.56 | .72 |
| Male sex | 25 (53.2%) | 14 (56%) | .82 |
| Nonwhite ethnicity | 22 (46.8%) | 10 (40%) | .58 |
| Organ laterality defect | 23 (48.9%) | 0 (0%) | <.01[b] |
| Otologic reported symptoms | | | |
| Hearing loss | 18 (38) | 2 (8) | <.01[b] |
| Vertigo and imbalance | 9 (19) | 0 (0) | .02[b] |
| Otalgia | 6 (13) | 4 (16) | .71 |
| Ear fullness | 10 (21) | 1 (4) | .05 |
| Chronic or recurrent otorrhea | 11 (23) | 1 (4) | .035[b] |
| Mean No. of acute otitis media annually | 1.6 ± 2.75 | 0.96 ± 1.59 | .62 [−0.55 to 1.8] |
| Mean No. of ear tube insertions | 2.04 ± 1.93 | 0.44 ± 0.65 | <.01[b] [0.8 to 2.39] |
| Sinonasal and airway reported symptoms | | | |
| Congestion | 39 (83) | 0 (0) | <.01[b] |
| Pain or pressure | 9 (19) | 0 (0) | .02[b] |
| Obstruction | 31 (66) | 3 (12) | <.01[b] |
| Postnasal drip | 35 (74) | 0 (0) | <.01[b] |
| Anosmia | 11 (23) | 0 (0) | <.01[b] |
| Rhinorrhea | 35 (74) | 0 (0) | <.01[b] |
| Epistaxis | 11 (23) | 5 (20) | .74 |
| Cough | 40 (85) | 0 (0) | <.01[b] |
| Snoring | 23 (49) | 2 (8) | <.01[b] |
| Mouth breathing | 33 (70) | 2 (8) | <.01[b] |
| Mean No. of acute sinusitis in past 2 years | 0.04 ± 0.2 | 0.12 ± 0.43 | .04[b] [0.0736 to 0.22] |

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| Characteristic | Primary ciliary dyskinesia (n = 47) | Control (n = 25) | P value [95% CI] |
|---|---|---|---|
| Mean No. of acute tonsillitis in past 2 years | 0.1 ± 0.6 | 0.4 ± 0.65 | .056 [−0.6 to 0.01] |
| Chronic medical therapy | | | |
| Nasal steroids | 11 (23) | 0 (0) | <.01[b] |
| Saline spray or drops | 16 (34) | 1 (4) | <.01[b] |
| Nasal decongestants | 1 (2) | 0 (0) | .46 |
| Proton pump inhibitors | 1 (2) | 0 (0) | .46 |
| Surgical history | | | |
| Adenoidectomy | 15 (32) | 4 (16) | .15 |
| Past sinus surgery | 3 (6) | 0 (0) | .20 |

[a] Values are presented as number (%) unless otherwise indicated.

[b] Statistically significant; 95% CI is provided for t test results.

**Table 2.**

Positive Tests That Diagnosed Children With Primary Ciliary Dyskinesia (PCD).

| Diagnostic method | No. (%) |
|---|---|
| Electron microscopy defect alone (negative genetics) | 3 (6) |
| ODA defect | 3 |
| Two disease-causing variants in known PCD genes | 40 (85) |
| *DNAH5* | 12 |
| *DNAH11* | 5 |
| *CCDC114* | 3 |
| *CCNO* | 3 |
| *CFAP221* | 3 |
| *CCDC39* | 2 |
| *CCDC40* | 2 |
| *HYDIN* | 2 |
| *ARMC4* | 1 |
| *CFAP300* | 1 |
| *DNAAF1* | 1 |
| *DNAAF2* | 1 |
| *DNAI1* | 1 |
| *LRRC6* | 1 |
| *RSPH1* | 1 |
| *RSPH4A* | 1 |
| nNO <77 nL/min[a] | 4 (9) |

Abbreviations: nNO, nasal nitric oxide; ODA, outer dynein arm defect.

[a]nNO <77 nL/min on at least 2 separate visits, with negative cystic fibrosis and immunodeficiency testing, as well as nondiagnostic transmission electron microscopy and genetic testing.

**Table 3.**

Items Included in the Standardized Clinical Examination and Their Findings.[a]

| Characteristic | PCD (n = 47) | Control (n = 25) | *P* value [95% CI] |
|---|---|---|---|
| Tympanic membrane | | | |
| Normal | 9 (19) | 22 (88) | <.01[b] |
| Fluid | 30 (64) | 3 (12) | <.01[b] |
| Tube | 6 (13) | 0 (0) | <.01[b] |
| Perforation | 2 (4) | 0 (0) | <.01[b] |
| Nasal exam | | | |
| Thick discharge | 38 (81) | 0 (0) | <.01[b] |
| Polyps presence | 3 (6) | 0 (0) | .44 |
| Tonsil size[c] | | | .56 |
| Grade 0 | 6 (13) | 4 (16) | |
| Grade 1 | 22 (47) | 12 (48) | |
| Grade 2 | 11(23) | 6 (24) | |
| Grade 3 | 8 (17) | 2 (8) | |
| Grade 4 | 0 (0) | 1 (4) | |
| Adenoid size[d] | | | |
| Grade 1 | 33 (70) | 21 (84) | .21 |
| Grade 2 | 9 (19) | 2 (8) | |
| Grade 3 | 5 (11) | 1 (4) | |
| Grade 4 | 0 (0) | 1 (4) | |
| Fiber-optic laryngeal assessment | | | |
| RFS, mean ± SD | 8.2 ± 4.12 | 7.2 ± 2.07 | .20 [−0.42 to 2.49] |

Abbreviations: PCD, primary ciliary dyskinesia; RFS, Reflux Finding Score.

[a]Values are presented as number (%) unless otherwise indicated. The 95% CI is provided for t test results.

[b]Statistically significant.

[c]Brodsky grading scale for tonsil size.

[d] Grading scale by Cassano et al[14]: grade 1, <25%; grade 2, <50%; grade 3, <75%; grade 4, >75%.

**Table 4.**

Mean Scores of 3 Validated Questionnaires for Children With Primary Ciliary Dyskinesia (PCD) and Healthy Children (Control).[a]

| Characteristic | PCD (n = 47), mean ± SD | Control (n = 25), mean ± SD | *P* value [95% CI] |
|---|---|---|---|
| Hearing Quality of Life Questionnaire | 2236 ± 469.8 | 2550 ± 61.5 | <.01[b] [−502.60 to −124.97] |
| Sino-Nasal Outcome Test 22 | 36.4 ± 46.98 | 5 ± 6.15 | <.01[b] [12.5 to 50.27] |
| Reflux Symptom Index | 11.5 ± 8.86 | 2 ± 1.9 | <.01[b] [5.86 to 13.04] |

[a]The 95% confidence interval is provided for *t* test results.

[b]Statistically significant.