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Prevalence of and associations with allergic rhinitis in children with chronic rhinosinusitis☆

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ABSTRACT

Objectives: Chronic rhinosinusitis (CRS) in children has been associated with a variety of disorders including atopic disease, cystic fibrosis, immunologic disorders and ciliary dyskinesia. Although a strong association, or even cause and effect relationship, between allergic rhinitis (AR) and CRS is commonly assumed, the epidemiologic relationship between these disorders has not yet been defined in children.
Methods: A retrospective review of all children diagnosed with CRS on otolaryngology or allergy office evaluation at a large tertiary-care pediatric hospital over a ten-year period was performed. Demographic data and concomitant diagnoses of AR, cystic fibrosis, immunologic disorders and primary ciliary dyskinesia were analyzed for relationships with CRS.
Results: A total of 4044 children with an average age of 8.9 years and a slight male predominance (53.8%) with CRS were identified. Of these children, 0.2% had primary ciliary dyskinesia, 4.1% had cystic fibrosis, 12.3% had an immunologic disorder, and 26.9% had AR. A concomitant asthma diagnosis was positively associated with a diagnosis of AR (OR = 6.24, 95% CI: 5.27–7.39, $P < 0.001$), whereas a concomitant cystic fibrosis diagnosis was negatively associated (OR = 0.12, 95% CI: 0.06–0.26, $P < 0.001$).
Conclusions: AR is more prevalent than the other comorbidities combined in children with CRS, and is independently associated with the presence of asthma. Formal allergy testing, guided by clinical history and regional allergen sensitivity prevalence, should be strongly considered in all children with CRS, in particular those with reactive airway disease.

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1. Introduction

Chronic rhinosinusitis (CRS) can be the ultimate manifestation of various disease processes [1,2] that cause sinonasal inflammation [3]. Whereas acute rhinosinusitis is common in the pediatric population, occurring as the sequela of six to eight percent of viral upper respiratory tract infections [4,5], chronic rhinosinusitis is comparatively rare. CRS in the pediatric population is defined as 90 days or more of persistent purulent rhinorrhea and nasal congestion [6]. The management of CRS in children consists primarily of medical treatment to eradicate bacterial infection and reduce underlying sinonasal inflammation [7]. Surgical interventions, such as adenoidectomy and endoscopic sinus surgery, are reserved for patients who fail medical management. Such interventions are designed to both eradicate potential bacterial reservoirs and enhance sinonasal aeration and drainage [7–9].

Regardless of treatment modality, the management of CRS requires an understanding of the underlying causes of sinonasal inflammation on a patient-by-patient basis. Because of the heterogeneous nature of CRS, clinical evaluation is required to uncover comorbidities that must be addressed, in addition to the specific interventions necessary to eradicate the sinus disease. Cystic fibrosis, immunodeficiency and primary ciliary dyskinesia are distinct conditions which contribute to the development and persistence of CRS symptoms in both children and adults [10,11]. The contribution of allergic rhinitis to the pathogenesis of CRS in children is more difficult to ascertain because, similar to CRS, allergic rhinitis is also characterized by sinonasal inflammation [12–15]. Although allergic rhinitis is commonly assumed to be associated with or a have a cause and effect relationship with CRS, the prevalence of allergic rhinitis in pediatric CRS has not to date been well characterized. In this study, a large cohort of pediatric patients with CRS is evaluated for the prevalence of allergic rhinitis. Moreover, the prevalence of allergic rhinitis is characterized in subpopulations of pediatric CRS who have concurrent cystic

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fibrosis, immunodeficiency or primary ciliary dyskinesia. Characterizing the relative prevalence of allergic rhinitis in comparison to other comorbid conditions associated with the pathogenesis of CRS will hopefully provide a greater understanding of the potential role of AR and inform subsequent treatment strategies [11,16].

2. Materials and methods

2.1. Patient selection

Approval for this study was obtained from the Boston Children's Hospital Institutional Review Board. A consecutive series of patients ($N = 4044$) aged less than or equal to 18 years evaluated in the otolaryngology or allergy and immunology clinic with the diagnosis of chronic rhinosinusitis between August 2002 and August 2012 was identified based on associated ICD-9 code (473.*). ICD-9 codes were also utilized to screen for concomitant diagnoses of allergic rhinitis (477.*), asthma (493.*), immunity disorders (279.*), cystic fibrosis (277.*) and primary ciliary dyskinesia (759.*). Demographic data consisting of age at the time of presentation as well as gender were recorded.

2.2. Statistical analysis

All analysis and descriptive statistics were performed with the statistical software R (www.r-project.org). Statistical significance between the prevalence of binary characteristics between different cohorts of patients was performed using Fisher's exact test, while differences between continuous variables were performed using a Student's t-test. Associations between the presence of allergic rhinitis in the cohort of children with CRS and predictor variables (age, gender, and presence of comorbid conditions including asthma, cystic fibrosis, disorders of the immune system and primary ciliary dyskinesia) were determined by logistic regression using the lrm() function from the Regression Modeling Strategies (rms) package [17]. Univariate logistic regression was performed for each predictor variable. Multivariate logistical analysis was performed using all predictor variables. In the multivariate model, significant predictors were identified via backwards elimination, using a P-value cut-off of 0.100. Cross validation was performed through bootstrapping of the dataset using the validate() function from the rms package over 100 iterations. For each variable retained in the final model, a P-value and a log-odds ratio were calculated. P values less than 0.05 were considered significant in the analysis of associations.

3. Results

Over the ten year span from which patients were screened, 4044 children with the diagnosis of chronic rhinosinusitis (CRS) were identified. The clinical and demographic characteristics of these children are outlined in Table 1. The average age of these children was 8.9 years (SD: 4.9 years, range: 0.3–18.9 years) with a 53.8% male and 46.2% female gender breakdown.

3.1. Prevalence of related comorbidities in children with chronic rhinosinusitis

Of the 4044 children diagnosed with CRS, 165 (4.1%) also carried a diagnosis of CF, 496 (12.3%) a diagnosis consistent with an immune system disorder, and 10 (0.2%) a diagnosis of primary ciliary dyskinesia (PCD). Three children with CRS were found to have a diagnosis of cystic fibrosis (CF) and an immune system disorder. For the purposes of subsequent analyses, these children were considered to be in both the CF and the immune system disorders cohorts.

Children with CRS who also had CF tended to be slightly older with an average age of 10.9 years (SD: 4.7 years) in comparison to those CRS children with PCD (average age 9.6 years [SD: 5.7 years]) or immunologic disorders (average age of 7.7 years [SD: 4.7 years]). The difference in age between the children with CF and immunologic disorders was found to be statistically significant ($P < 0.001$ by ANOVA and $P < 0.001$ by t-test). There were no statistically significant differences in the gender composition of children with these three comorbid conditions.

3.2. Prevalence of allergic rhinitis in children with chronic rhinosinusitis

The prevalence of allergic rhinitis was characterized in various populations of children with CRS (Table 1). Of all children with CRS, 1086 children (26.9%) were diagnosed with allergic rhinitis (AR). The average age of these children with both CRS and AR was 8.9 years (range: 0.7–18.9 years). The gender composition of these children with CRS and AR was similar to those children with CRS who did not have AR, likewise demonstrating a slight male

Table 1
Clinical and demographic characteristics of children with CRS.

	Number	Age	Gender		Asthma
	(%)	Years	Male (%)	Female (%)	(%)
All CRS patients	4044 (100%)[a]	8.9	53.8	46.2	18.1
With AR	1086 (26.9%)	8.9	56.5	43.5	40.7
Without AR	2958 (73.1%)	8.9	52.8	47.2	9.8
CRS patients with Cystic Fibrosis (CF)	165 (4.1%)[a]	10.9	49.7	50.3	4.8
With AR	6 (3.6%)	8.2	33.3	66.7	16.7
Without AR	159 (96.4%)	11.0	50.3	49.7	4.4
Immunodeficiency (ID)	496 (12.3%)[a]	7.7	54.6	44.4	31.7
With AR	184 (37.1%)	8.4	52.2	47.8	41.8
Without AR	312 (62.9%)	7.2	56.1	43.9	25.6
Primary Ciliary Dyskinesia (PCD)	10 (0.2%)[a]	9.6	60.0	40.0	10.0
With AR	1 (10%)	13.7	0.0	100.0	0.0
Without AR	9 (90%)	9.2	66.7	33.3	11.1
Uncomplicated CRS	3376 (83.5%)[a]	8.9	53.9	46.1	16.7
With AR	896 (26.5%)	9.0	57.6	42.4	40.6
Without AR	2480 (73.5%)	8.9	52.5	47.5	8.1

[a] Relative to the total number of children with CRS (4044).

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