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Predictive fiberoptic endoscopic findings of upper airway in children with allergic rhinitis

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ABSTRACT

Objective: To determine predictive fiberoptic findings of upper airway in children with allergic rhinitis.
Method: 129 children had fiberoptic evaluation of nasal cavity, pharynx and larynx. They were divided into allergic rhinitis group and normal group based on skin prick test results. All video recordings were randomly reviewed by three independent national board-certified otolaryngologists who were blinded to the clinical details and outcomes of the participants' allergy testing. Each physician assessed and documented 10-item questionnaire. Intra-rater, inter-rater reliability and correlation between items and allergic status was calculated.
Results: Intra-rater reliability was moderate to perfect for all physicians on all items (kappa = 0.578–0.962). Inferior turbinate hypertrophy ($\kappa = 0.714$, $p = 0.02$), middle turbinate hypertrophy ($\kappa = 0.728$, $p = 0.01$), discoloration of inferior turbinate ($\kappa = 0.685$, $p = 0.01$), adenoid hypertrophy ($\kappa = 0.662$, $p = 0.02$) had good inter-rater reliability and these findings were predictive of allergic rhinitis. Adenoid hypertrophy was less encountered in allergic rhinitis. All other endoscopic findings beyond the nasal cavity were not predictive for allergic rhinitis in children.
Conclusion: Nasal cavity findings including inferior turbinate hypertrophy, middle turbinate hypertrophy, discoloration of inferior turbinate and adenoid tissue assessment rather than pharyngolaryngeal findings are predictive of allergic rhinitis in children.

1. Introduction

Allergic rhinitis (AR) is the one of the most common chronic conditions in industrialized nations. Nasal obstruction is the main symptom of the disease' with watery runny nose, sneezing and itching frequently observed [1]. These symptoms may result in emotional problems, sleep disorders, as well as deterioration in school performance and daily activities [2]. Thus, AR is a chronic condition that can have a significant impact on the patients' quality of life. Skin tests based on IgE-mediated hypersensitivity are commonly used tools for AR, but their relatively limited availability and cost may restrict their practical use.

History and physical examination may provide information regarding the diagnosis of AR. Ideally, otolaryngologists should look for some specific findings suggesting AR. However, there is no consensus about the otolaryngologic physical examination properties related with AR. Clear rhinorrhea, inferior turbinate hypertrophy, pale discoloration of inferior turbinate, postnasal drip, and allergic salute sign are major signs but not only the physical findings of the nasal cavity in patients with AR [3]. Moreover, there are no universally accepted definitions of AR based on nasal findings. There are published articles showing inter-rater discrepancies about nasal physical findings of AR, with some authors arguing that pale discoloration of the inferior turbinate is an anecdotal judgment about AR prediction [4]. Hypertrophy of the most anterior part of the middle and inferior turbinates is considered as a reliable factor for the prediction of AR in children [4]. However, a unified airway concept offers that allergic disease is not limited to the nasal passages, it also includes the aerodigestive tract and lower airways [5,6]. Often, patients with AR have more laryngeal problems such as vocal nodules, laryngitis than controls [7] and typically, have a higher prevalence of dysphonia [8]. In recent years, evidence has emerged that nonspecific pharyngeal and laryngeal symptoms may also be attributed to allergic diseases. This nonspecific nature of symptoms may result with the underdiagnosis of allergic disease in the pediatric population. Endoscopic judgments beside the nasal cavity is not very well discovered in children with AR. There can be some findings in nasopharynx, oropharynx and larynx that should alert the physician

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about the diagnosis of AR in children. This is the first study evaluating the predictive nasal, nasopharyngeal, oropharyngeal and laryngeal findings together in the pediatric population with AR.

2. Material and methods

This study was performed between January and October 2018 in the University of Health Sciences Umraniye Training and Research Hospital Otolaryngology Department. After approval from the local institutional ethical board, 129 consecutive participants who had a skin prick test were recruited in the study. All participants were referred from the Pediatric Allergy and Immunology Clinic. Participants using nasal, inhaled or systemic steroids, antihistamines or any anti-reflux medication for at least 3 months before the examination were excluded from the study. Patients with a history of nasal, pharyngeal or laryngeal surgery, inadequate visualization of examination areas, or current upper airway infection were also excluded.

A fiberoptic endoscopy system with a diameter of 2.5 mm (Karl Storz 11101 SK; Karl Storz, Tutlingen, Germany) was used. Cotton wool soaked with anesthetic solution was introduced into the nasal cavity bilaterally before the examination. The inferior turbinate and middle turbinate, nasopharynx, oropharynx and larynx were endoscopically visualized and recorded as previously described [3]. All video recordings were randomly reviewed by three independent national board-certified otolaryngologists who were blinded to the clinical details and outcomes of the participants' allergy testing. Each physician assessed and documented the degree of inferior turbinate hypertrophy, middle turbinate hypertrophy, discoloration of inferior turbinate, polypoid degeneration of posterior part of inferior turbinate, torus tubarius mucosal anomalies, adenoid hypertrophy, cobblestone appearance of the posterior pharyngeal wall, laryngeal edema, excessive/thick nasopharyngeal secretion and excessive/thick laryngopharyngeal secretion. Each item was scored on a scale as none, mild, moderate or severe. After video recording assessment and scoring, based on the findings of these video records, physicians were asked to answer the question "Due to the assessment of the patient, how likely do you think it is that patient has allergic rhinitis?" Physicians answered this question as one of the following: not likely, somewhat likely, very likely, extreme likely.

All participants had a skin prick test and allergy was determined by the presence of positive results to the most common allergens which included: mites (Dermatophagoides pteronyssinus, Dermatophagoides farina), cats, dogs, chickens, trees (olive, birch, oak, alder, poplar), grasses (cocksfoot, timothy, meadow grass, ryegrass, wheat), weeds, and molds (*Alternaria, Aspergillus, Cladosporium* species). A histamine solution (histamine phosphate 10 mg/ml) was used as a positive control and saline solution was used as a negative control. Skin reactions were evaluated after 15 min and compared with the wheal given by the positive and the negative controls. A wheal diameter of at least 3 mm was considered as a positive response.

Forty-five video records were reassessed for each item, each question and each physician to create a kappa value for intra-rater reliability three weeks after the first evaluations. Multi-rater inter-rater reliability with Fleiss kappa was calculated. A Mann-Whitney *U* test used to compare the median scores in each item between the allergic and nonallergic group to evaluate differences. SPSS version of 22 (Corp., Armonk, NY) was used for statistical analysis.

3. Results

One hundred and twenty-nine participants (65 boys and 64 girls) with a mean age of 7.5 years, ranging from 5 to 16 years of age, were included in the study. Sixty-four (49.6%) participants had a positive skin prick test and comprised the AR group. Sixty-five (50.3%) participants had a negative prick test and formed the normal group. Upper airway fiberoptic evaluation of all 129 participants were assessed. The questions are presented in Table 1. Intra-rater reliability of the findings for the three physicians was evaluated by the kappa test. Inter-rater reliability of the examination findings of all participants was assessed by the Fleiss kappa test (Table 2).

Table 1
Questionnaire used to evaluate video records of all participants.

Inferior turbinate hypertrophy	None	Mild	Moderate	Severe
Middle turbinate hypertrophy	None	Mild	Moderate	Severe
Discoloration of Inferior turbinate	None	Mild	Moderate	Severe
Polypoid degeneration of inferior turbinate	None	Mild	Moderate	Severe
Torus tubarius mucosa	None	Mild	Moderate	Severe
Adenoid hypertrophy	None	Mild	Moderate	Severe
Cobblestoning of posterior pharyngeal wall	None	Mild	Moderate	Severe
Laryngeal edema	None	Mild	Moderate	Severe
Nasopharyngeal secretions	None	Mild	Moderate	Severe
Laryngopharyngeal excessive/thick ecretions	None	Mild	Moderate	Severe

The comparison of the examination findings of the AR and normal groups showed that inferior turbinate hypertrophy ($p = 0.001$), middle turbinate hypertrophy($p = 0.01$), discoloration of the inferior turbinate ($p = 0.001$) and adenoid hypertrophy($p = 0.04$) were predictive for AR (Fig. 1). Adenoid hypertrophy was inversely related with AR. The predictive value of torus tubarius mucosal anomalies, nasopharyngeal secretions, cobblestoning of the posterior pharyngeal wall, thick endolaryngeal mucus, and laryngeal edema was not statistically significant for the diagnosis of AR.

All intra-rater values were in the limits for all physicians on all repeated assessments (kappa (k) = 0.578–0.962) (Table 2). Inter-rater reliability among the three physicians' regarding inferior turbinate hypertrophy ($\kappa = 0.714$, $p = 0.02$), middle turbinate hypertrophy ($\kappa = 0.728$, $p = 0.01$), discoloration of the inferior turbinate ($\kappa = 0.685$, $p = 0.01$) and adenoid hypertrophy ($\kappa = 0.662$, $p = 0.02$) was significant. Polypoid degeneration of the posterior part of the inferior turbinate ($\kappa = 0.285$, $p = 0.67$), torus tubarius mucosal anomalies ($\kappa = 0.532$, $p = 0.07$), nasopharyngeal secretions ($\kappa = 0.363$, $p = 0.12$), cobblestoning of the posterior pharyngeal wall ($\kappa = 0.278$, $p = 0.25$), thick endolaryngeal mucus ($\kappa = 0.166$, $p = 0.23$), and laryngeal edema ($\kappa = 0.315$, $p = 0.12$) did not reach significance for inter-rater agreement.

4. Discussion

Diagnosis of AR is still clinically challenging, specifically in the pediatric population. Consequently, a detailed medical history, complete otolaryngologic examination and allergen tests should be utilized together for an AR diagnosis. Routine examination should include upper aerodigestive tract beyond the nasal cavity covering the nasopharynx, oropharynx and larynx, as determining abnormalities may help in making a precise diagnosis. If there are any specific physical findings during fiberoptic otolaryngologic examination that alerts the physician to the presence of AR, this would prevent unnecessary procedures. It would also be of benefit to the health care system by reducing the financial burden and avoiding time-consuming additional procedures. There are numerous reports showing the coexistence of AR with other upper or lower respiratory tract disorders such as laryngitis, and asthma [6,9,10].

In our study, clinicians assessed inferior and middle turbinate hypertrophy as having a contact point with lateral nasal wall and uncinate process respectively, finding that both inferior and middle turbinate hypertrophy were more common in the AR group; there was good inter-rater reliability between these findings. We believe that this is due to more anterior nasal blockage in the level of the most anterior part of turbinates, as this area is the very first contact point of the inspired airflow, hence, allergens in the nasal cavity. In another study, clinicians also stated that localized edema of inferior turbinate and middle turbinate head may be due to allergen exposure in pediatric patients with

Table 2
Intra-rater and Inter-rater Kappa Values of Each Physician, Question 1 (Q1): Inferior Turbinate Hypertrophy, Q2: Middle Turbinate Hypertophy, Q3: Discoloration of Inferior Turbinate, Q4: Polypoid degeneration of posterior part of inferior turbinate, Q5: Torus Tubarius mucosal anomalies, Q6: Adenoid Hypertophy, Q7: Cobblestone appearance of posterior pharyngeal Wall, Q8: Laryngeal edema Q9: Excessive/thick nasopharyngeal secretions, Q10: Excessive/thick laryngeal secretions, Q11: Atopic Diagnosis.

	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11
Intrarater 1	0.771	0.823	0.79	0.781	0.578	0.777	0.852	0.898	0.916	0.923	0.714
Intrarater 2	0.782	0.789	0.83	0.611	0.695	0.832	0.932	0.893	0.818	0.831	0.812
Intrarater 3	0.744	0.812	0.814	0.883	0.723	0.844	0.861	0.765	0.771	0.962	0.734
Inter-rater scores	0.714	0.728	0.685	0.285	0.532	0.662	0.278	0.315	0.363	0.166	0.316

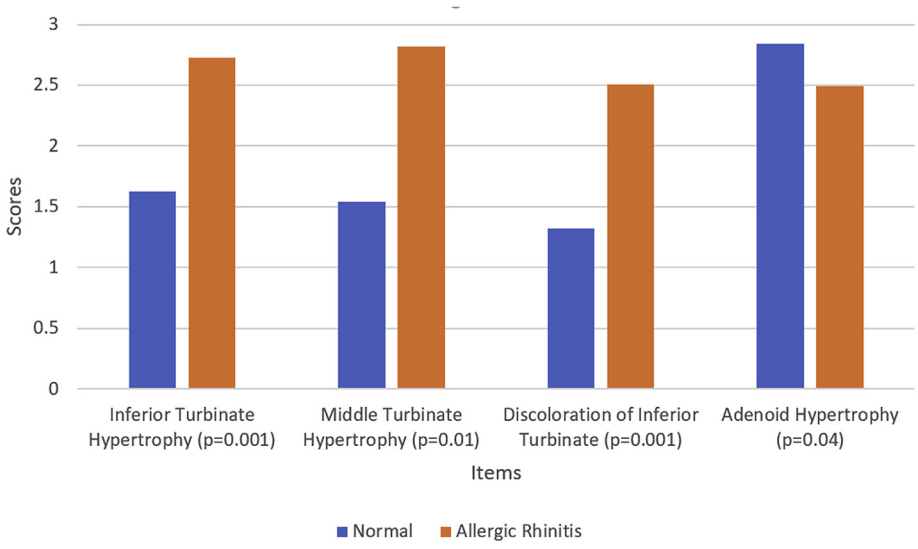

Fig. 1. Comparison of predictive findings of inferior turbinate hypertrophy, middle turbinate hypertrophy, discoloration of inferior turbinate and adenoid hypertrophy between normal and allergic group. Scores ranged from 1 to 4 (1 correlating to normal, 4 correlating to severe changes). These items significantly different between groups. Adenoid hypertrophy was significantly higher in normal group.

AR, but they did not report the inter-rater variability of these findings [4]. The main problem about nasal findings is the difference in interpretation, nonetheless, we were able to show that the physical findings were reliable among physicians in this study. Pale discoloration of nasal mucosa, particularly the inferior turbinate, is another important finding in patients with AR [3], which we found to be statistically significantly present in the AR group compared to the normal group. This finding also had good inter-rater variability.

Another superiority of our study may be the assessment of inferior and middle turbinates hypertrophy and discoloration of the inferior turbinate in four categories as none, mild, moderate and severe. Ameli et al. only considered these three parameters as either present or absent [4], while Eren et al. did not find any nasal findings that were predictive of AR, including turbinate hypertrophy, in adults [11]. Turbinate hypertrophy and turbinate color showed high inter-observer reliability in this study, so physical examination of patients with suspected AR should focus on the anterior part of nasal cavity, specifically inferior and middle turbinate hypertrophy and discoloration of the inferior turbinate. Ameli et al. found an inverse relationship between adenoidal hypertrophy and allergic rhinitis [12], children with a higher volume of adenoidal tissue were less prone to AR, which is consistent with our study. There was reverse relation between adenoidal tissue hypertrophy and allergic rhinitis, thus nasal obstruction in children with AR was not due to adenoidal hypertrophy.

The cobblestone appearance of the posterior pharyngeal wall is one of the main findings of allergy in examination [10]. However, Brook et al. did not find that the cobblestone appearance was a predictive finding in allergic patients and we did not find any difference in cobblestone appearance between groups [13]. Nonetheless, it can be easily misdiagnosed when the laryngeal examination is performed by transoral rigid 70° endoscopy, so fiberoptic endoscopic evaluation of the posterior nasopharyngeal and pharyngeal wall is crucial. Brook et al. found that mucosal abnormalities around the torus tubarius were significant in atopic patients. However, the inter-rater kappa score for torus tubarius findings was quite low, meaning there was highly variable interpretation between physicians [13]. In our study, we did not find any difference between the atopic and normal groups according to assessment of torus tubarius.

In recent years, there has been increased interest regarding the unified airway concept. Upper and lower respiratory tracts consist of pseudostratified columnar epithelium and similar epithelial tissues may demonstrate almost identical responses to stimulation with different agents. Allergic rhinitis, chronic allergic laryngitis and asthma basically induce Th2 cytokines, such as interleukin (IL)-4, IL-5, and IL-13, which induce inflammation [10]. There is also cellular mediated inflammation, mainly by eosinophils. Indeed, Dworkin et al. showed that direct inhalation of an aerosolized antigen form of house dust mite in increasing concentrations induced increased mucus production in the larynx [14]. In the allergic involvement of the larynx, one may expect to find thick mucus often bridging the vocal folds [10]. Indeed, authors of different studies have reached a consensus that the thick laryngeal mucus is one of the main findings in patients with allergy [6,9], but it may be attributed to laryngeal findings of AR or allergic laryngitis. However, Brook et al. showed that this finding was not predictive of allergic status in adults [14], whereas Eren et al. reported that thick endolaryngeal mucus was the only laryngeal examination finding that can predict AR in a logistic regression model. It also had a high inter-rater agreement in an adult population [15]. Despite the discrepancies regarding inter-rater assessment and prediction of endolaryngeal mucus in an adult population, our study is the first to evaluate this in a pediatric population. There was no difference in endolaryngeal mucus production between groups, but there was strong inter-observer variability, suggesting that endolaryngeal mucus is not predictive for the allergic status of pediatric patients. Thick endolaryngeal mucus production may be related with the duration of the disease, which would explain its presence in an adult population with AR rather than

pediatric patients. But clinician must be aware of cooccurence of mucus in the nasal cavity other than pharyngeal and laryngeal secretions with inferior turbinate hypertrophy can predict AR (3).

Laryngeal mucosal edema is another common finding for laryngopharyngeal reflux and an allergic airway, but no study has showed that it would help the diagnosis of AR. There was no difference between groups in laryngeal mucosal edema in the present study, indicating that laryngeal edema cannot be used as a physical finding for the detection of allergy in a pediatric population.

5. Conclusion

To the best of our knowledge, this is the first study evaluating all nasal, pharyngeal and laryngeal findings in children with AR, showing that inferior and middle turbinate hypertrophy, discoloration of the inferior turbinate and adenoidal hypertrophy were associated with the disease. However, torus tubarius mucosal abnormalities, cobblestoning of the posterior pharyngeal wall, laryngeal mucosal edema, nasopharyngeal secretions and laryngeal mucus secretion were not predictive of the disease. Precise history taking, fiberoptic evaluation of upper airway and skin prick test results should be evaluated together for a correct diagnosis.

Conflicts of interest

None.

Financial disclosure

Nothing to disclose.

References

[1] G. Ciprandi, I. Cirillo, C. Klersy, G.L. Marseglia, D. Caimmi, A. Vizzaccaro, Nasal obstruction is the key symptom in hay fever patients, Otolaryngol. Head Neck Surg. 133 (2005) 429–435 https://doi:10.1016/j.otohns.2005.05.049.

[2] J.L. Brożek, J. Bousquet, I. Agache, et al., Allergic rhinitis and its impact on asthma (ARIA) guidelines-2016 revision, J. Allergy Clin. Immunol. 140 (2017) 950–958 https://doi:10.1016/j.jaci.2017.03.050.

[3] M.D. Seidman, R.K. Gurgel, S.Y. Lin, et al., Clinical practice guideline: allergic rhinitis, Otolaryngol. Head Neck Surg. 152 (2015) S1–S43 https://doi:10.1177/0194599814559898.

[4] F. Ameli, F. Brocchetti, M.A. Tosca, A. Signori, G. Ciprandi, Nasal endoscopy in children with suspected allergic rhinitis, The Laryngoscope 121 (2011) 2055–2059 https://doi:10.1002/lary.22156.

[5] J.H. Krouse, The unified airway–conceptual framework, Otolaryngol. Clin. 41 (2008) 257–266 https://doi:10.1016/j.otc.2007.11.002.

[6] J.H. Krouse, Allergy and laryngeal disorders, Curr. Opin. Otolaryngol. Head Neck Surg. 24 (2016) 221–225 https://doi:10.1097/MOO.0000000000000244.

[7] J.H. Hah, S. Sim, S.-Y. An, M.-W. Sung, H.G. Choi, Evaluation of the prevalence of and factors associated with laryngeal diseases among the general population, The Laryngoscope 125 (2015) 2536–2542 https://doi:10.1002/lary.25424.

[8] R. Turley, S.M. Cohen, A. Becker, C.S. Ebert, Role of rhinitis in laryngitis: another dimension of the unified airway, Ann. Otol. Rhinol. Laryngol. 120 (2011) 505–510 https://doi:10.1177/000348941112000803.

[9] R.J. Stachler, J.P. Dworkin-Valenti, Allergic laryngitis: unraveling the myths, Curr. Opin. Otolaryngol. Head Neck Surg. 25 (2017) 242–246 https://doi:10.1097/MOO.0000000000000354.

[10] J.H. Krouse, K.W. Altman, Rhinogenic laryngitis, cough, and the unified airway, Otolaryngol. Clin. 43 (2010) 111–121 https://doi:10.1016/j.otc.2009.11.005.

[11] E. Eren, A. Aktaş, S. Arslanoğlu, et al., Diagnosis of allergic rhinitis: inter-rater reliability and predictive value of nasal endoscopic examination: a prospective observational study, Clin. Otolaryngol. 38 (2013) 481–486 https://doi:10.1111/coa.12171.

[12] F. Ameli, F. Brocchetti, M.A. Tosca, A. Signori, G. Ciprandi, Adenoidal hypertrophy and allergic rhinitis: is there an inverse relationship? Am J Rhinol Allergy 27 (2013) 27 e5-10 https://doi:10.2500/ajra.2013.27.3854.

[13] C. Brook, J.P. Noordzij, K. Russell, A. Aliphas, M. Platt, Predictive findings of allergic disease in fiberoptic nasolaryngoscopy, The Laryngoscope 125 (2015) 286–290 https://doi:10.1002/lary.24880.

[14] J.P. Dworkin, P.M. Reidy, R.J. Stachler, J.H. Krouse, Effects of sequential Dermatophagoides pteronyssinus antigen stimulation on anatomy and physiology of the larynx, Ear Nose Throat J. 88 (2009) 793–799.

[15] E. Eren, S. Arslanoğlu, A. Aktaş, et al., Factors confusing the diagnosis of laryngopharyngeal reflux: the role of allergic rhinitis and inter-rater variability of laryngeal findings, Eur. Arch. Oto-Rhino-Laryngol. 271 (2014) 743–747 https://doi:10.1007/s00405-013-2682-y.