Tonsil volume and allergic rhinitis in children

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ABSTRACT

Tonsil hypertrophy (TH) is very common in children. Previously, it has been reported that an inverse relationship exists between adenoid hypertrophy (AH) and allergic rhinitis (AR). This study aimed to investigate the possible relationship between tonsil volume and AR diagnosis in a group of children complaining of upper airways obstruction. Globally, 171 children (91 boys; mean age, 6.6 years) were studied. Clinical visit, nasal endoscopy, and skin-prick test were performed in all patients. TH and anterior nasal obstruction were graded using the Friedman's classifications. Adenoid volume was graded using the Parikh's classification. Fifty-eight children (33.9%) had relevant TH (grades 3–4); 77 children (44.94%) had AR. There was a strong correlation (gamma = 0.564; p < 0.001) between TH and AH. Tonsil volume was inversely associated with AR diagnosis (odds ratio [OR], 0.314). Risk factors for TH were intense mucosal inflammation (pale mucous membranes) and AH (OR, 3.54 and 2.856, respectively). This study shows that large tonsils are negatively associated with allergy, whereas intense inflammation is a risk factor for TH; AH may be frequently associated with TH.

The palatine tonsils are part of the lymphoid tissue that surrounds the pharynx: collectively defined as the Waldeyer's ring. Tonsils physiologically serve as a defense against inhaled antigens (microbes, allergens, *etc.*). Therefore, tonsils are deeply involved in the innate and adaptive immune response because of their peculiar position at the entry of the upper aerodigestive tract. As consequence of chronic stimulation (result of prolonged antigenic exposure associated with chronic inflammation), palatine tonsils may enlarge so they may almost fill the space in oropharynx, limiting the airflow passage. Tonsil hypertrophy (TH) is detected in approximately one-third of the general pediatric population and constitutes the most frequent otorhinolaryngological indication for surgical intervention.[1] TH has been associated with recurrent respiratory infections, respiratory dysfunction, and sleep disorders. However, measurement of tonsil volume is not well standardized, but a good way to evaluate TH is during nasal endoscopy using the Friedman grading.[2]

On the other hand, allergic rhinitis (AR) is the most common immune-mediated disorder because it may affect up to 40% of the general population. AR is characterized by an inflammatory reaction after allergen exposure. AR is also frequently associated with relevant comorbidities, including other allergies, rhinosinusitis, recurrent respiratory infections, otitis, and adenoid hypertrophy (AH). In this regard, there is firm belief that children with AR may have lymphoid hypertrophy of the upper airways, mainly concerning the adenoids. The possible correlation between AR and AH has been investigated by some studies that reported a positive association between the two disorders.[3–6] On the contrast, a recent study reported that AH, visualized and measured during endoscopy, is not associated with AR, whereas large turbinates may be associated with small adenoids.[7] Because tonsil volume is frequently consistent with adenoid volume, an unmet question concerns the possible relationship between TH and AR. In fact, there are only three studies that addressed the attention on this issue.[8–10] Unfortunately, the findings were conflicting and the methodology sometimes inaccurate. Therefore, the relationship between tonsil volume and AR diagnosis has not been sufficiently elucidated until now. Therefore, this real-life study aimed at investigating the possible relationship between tonsil volume and AR diagnosis in a group of children complaining of upper airways obstruction.

MATERIALS AND METHODS

Patients

Globally, 171 children (80 girls and 91 boys; mean age, 6.61 ± 2.31 years), complaining of persistent upper airway obstruction, were consecutively referred to the Ear, Nose, and Throat Unit of Villa Montallegro (Genoa, Italy) during 2012. They were prospectively enrolled into the study. Inclusion criteria were (i) age between 4 and 12 years and (ii) to have complaints of

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upper airway limitation (mouth breathing, with or without snoring). Exclusion criteria were (i) a craniofacial syndrome, (ii) recent facial trauma, (iii) significantly deviated septum, (iv) concomitant acute rhinosinusitis, (v) previous adenotonsillectomy, and (vi) current use of intranasal corticosteroids. The study was approved by the local review board and an informed consent was obtained by the parents.

Study Design

All children were evaluated by clinical visit, nasal endoscopy, and skin-prick test.

Endoscopy

It was performed with a pediatric rigid endoscope diameter of 2.7 mm with 30° angle of vision (Karl Storz cod 7207 ba; R Storz, Milan, Italy) with a 300-W cold light source (Storz Xenon Nova, cod. 20134001; R Storz) and a light cable of 1.8-mm length. Endoscopy was video recorded by a microcamera connected to digital recorder set (Karl Storz Tele Pack, cod. 20043002–020; R Storz). A flexible endoscope (3-mm diameter) was used in restless children and in those with narrow nasal fossa due to anatomic abnormalities. The child lay supine with his/her head bent by ~45°. Some cotton wool soaked with anesthetic solution (ossibuprocaine 1%) was placed into the nose for 5 minutes. The complete description of the procedure was previously described in detail.[11]

Nose Obstruction Assessment by Endoscopy

Inferior turbinate was evaluated during endoscopy: the volume was graded from I to III according to the Friedman's classification.[12] Grade I was defined as mild enlargement with no obvious obstruction. Grade III was complete occlusion of the nasal cavity. The turbinate in between was graded as II.

Tonsils Volume Assessment

Tonsil volume was classified according to validated criteria[2] as follows: grade 1, tonsils in the tonsillar fossa barely seen behind the anterior pillar; grade 2, tonsils visible behind the anterior pillar; grade 3, tonsils extended three-quarters of the way to medline; grade 4, tonsils completely obstructing the airway (also known as kissing tonsils).

Adenoids Volume Assessment

The patients were evaluated by nasal endoscopy for AH. The adenoids were graded according to Parikh's classification that was created based on the anatomic relationships between the adenoid tissue and the following structures: vomer, soft palate, and torus tubarius.[13] The grading is based on the relationship of the adenoids to adjacent structures when the

patient is at rest (*i.e.*, when the soft palate is not elevated). Specifically, grade 1 adenoids are nonobstructive and do not contact any of the previously mentioned anatomic subsites; subsequently, grades 2, 3, and 4 adenoids contact the torus tubarius, vomer, and soft plate (at rest), respectively.

Skin-Prick Test

Allergy was assessed by the presence of sensitization to the most common classes of aeroallergens by performing a skin-prick test. It was performed as stated by the European Academy of Allergy and Clinical Immunology.[14] The allergen panel consisted of the following: house-dust mites (*Dermatophagoides farinae and Dermatophagoides pteronyssinus*), cats, dogs, grasses mix, *Compositae* mix, *Parietaria judaica*, birch, hazel trees, olive trees, cypress, *Alternaria tenuis*, *Cladosporium*, and *Aspergillus* mix. The concentration of allergen extracts was 100 immune reactivities per milliliter (Stallergenes Italia, Milan, Italy). A histamine solution in distilled water (10 mg/mL) was used as positive control and the glycerol buffer diluent of the allergen preparations was used as negative control. Each patient was skin tested on the volar surface of the forearm using 1-mm prick lancets. The skin reaction was recorded after 15 minutes by evaluating the skin response in comparison with the wheal given by the positive and the negative control. A wheal diameter of at least 3 mm was considered as a positive reaction.

The AR diagnosis was made if nasal symptom history was consistent with sensitization, such as the presentation of symptom occurrence after exposure to the sensitizing allergen.

Statistical Analysis

Normality of continuous variables was checked by histograms and confirmed by the Shapiro–Wilk normality test. For all enrolled patients, descriptive analysis of each characteristic was indicated as mean (m) with SD (±SD) or frequencies (percentages). Goodman and Kruskal test were used to correlate adenoid volume with tonsil volume.

A stepwise forward logistic regression was performed in two consecutive steps. First, a univariate logistic regression was used to compare categorical variables, in particular, to determine if the tonsil volume was associated with other clinical characteristics. Then, statistically significant variables at univariate analysis were fitted in a multivariate ordinal logistic regression model, with adjustment for potential confounding factors, such as age and gender. Data were expressed as odds ratio (OR) and 95% confidence interval (CI). OR indicates an increment or decrement of probability to have higher tonsil volume depending on the predictive variable considered.

Table 1 Demographic and clinical data (*n* = 171)

	Total Mean ± SD or *n* (%)	Not AR (*n* = 95) Mean ± SD or *n* (%)	AR (*n* = 76) Mean ± SD or *n* (%)	*p* Value
Age (yr)	6.61 ± 2.31	6.44 ± 2.35	6.83 ± 2.25	0.28
Sex				
Female	80 (46.8)	35 (36.8)	45 (59.2)	0.006*
Male	91 (53.2)	60 (63.2)	31 (40.8)	
Tonsils volume				
0	12 (7.0)	6 (6.3)	6 (7.9)	<0.001*
1	40 (23.4)	11 (11.6)	29 (38.2)	
2	61 (35.7)	31 (32.6)	30 (39.5)	
3	52 (30.4)	42 (44.2)	10 (13.2)	
4	6 (3.5)	5 (5.3)	1 (1.3)	
Nasal obstruction value				
1	15 (8.8)	8 (8.4)	7 (9.2)	0.09
2	82 (48.0)	39 (41.1)	43 (56.6)	
3	74 (43.2)	48 (50.5)	26 (34.2)	
Inferior turbinate contact				
No	32 (18.7)	28 (29.5)	4 (5.3)	<0.001*
Yes	139 (81.3)	67 (70.5)	72 (94.7)	
Middle turbinate contact				
No	38 (22.2)	30 (31.6)	8 (10.5)	0.002*
Yes	133 (77.8)	65 (68.4)	68 (89.5)	
Pale mucous membranes				
No	83 (48.5)	39 (41.1)	44 (57.9)	0.042*
Yes	88 (51.5)	56 (58.9)	32 (42.1)	
Nasal discharge				
No	56 (32.7)	39 (41.1)	17 (22.4)	0.015*
Yes	115 (67.3)	56 (58.9)	59 (77.6)	
Adenoids volume (*n* = 161)				
1	44 (27.2)	16 (18.0)	28 (38.9)	<0.001*
2	54 (33.5)	21 (23.6)	33 (45.8)	
3	51 (31.7)	41 (46.1)	10 (13.9)	
4	12 (7.5)	11 (12.4)	1 (1.4)	
Sensitization (*n* = 76)				
Mites	57 (75.0)	—	57 (75.0)	
Pollen	9 (11.8)	—	9 (11.8)	
Polysensitization	10 (13.2)	—	10 (13.2)	

*p values with statistical significance.

All *p* values were two tailed, with statistical significance set at 0.05. The SPSS (v.20; IBM Corp.), Stata (v.11; StataCorp. LP, College Station, TX), and MedCalc (v.11.3.0; MedCalc Software bvba, Ostend, Belgium) were used for computation.

RESULTS

One hundred seventy-one children (91 boys and 80 girls) with a mean age of 6.61 ± 2.31 years (range, 2–13 years) were prospectively enrolled in the study. Demographic and clinical characteristics are shown in Table 1.

Seventy-six children had a diagnosis of AR (44.4%).

Tonsil and Adenoid Volume

Globally, 159 (93.0%) children had extravelic tonsil: 40 (25.2%) had volume 1, 61 (38.4%) had volume 2, 52 (32.7%) had volume 3, and 6 (3.8%) had volume 4.

Globally, 161 (94.2%) children had AH: 44 (27.2%) had volume 1, 54 (33.5%) had volume 2, 51 (31.7%) had volume 3, and 12 (7.5%) had volume 4.

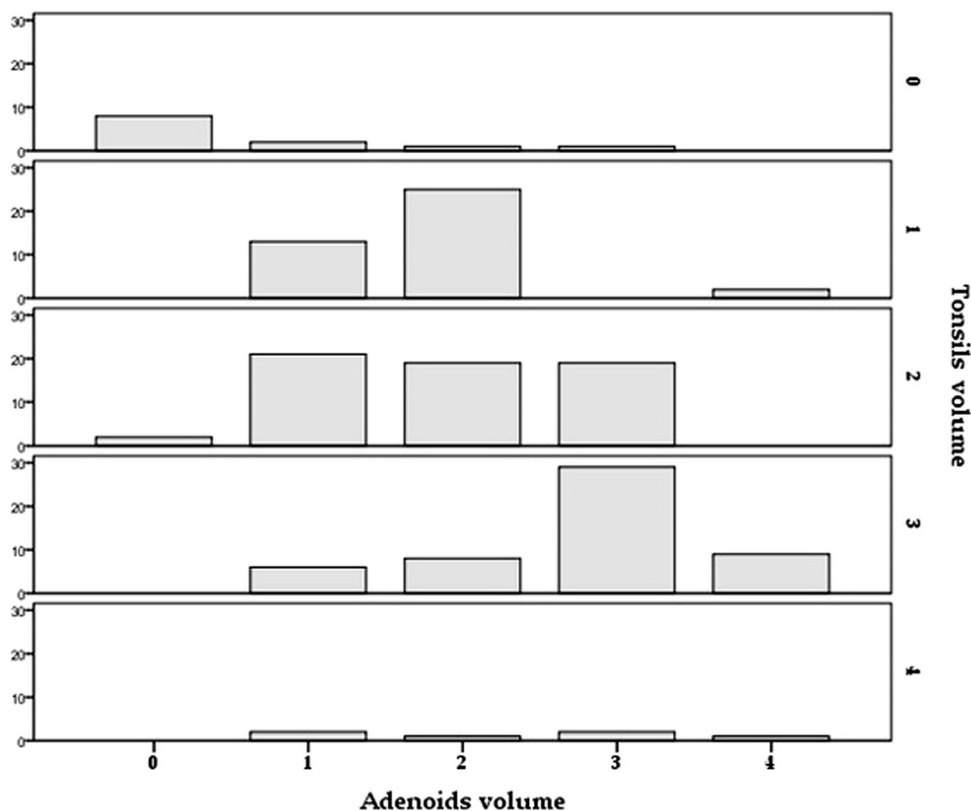There was a strong correlation between tonsil volume and adenoid volume (γ-coefficient by Good-

Figure 1. Relationship between tonsil volume and adenoid volume.

man and Kruskal = 0.564; $p < 0.001$) as shown in Fig. 1.

Nose Data

Seventy-four (43.2%) patients had total nasal obstruction (categorized by Friedman), whereas 97 (56.8%) had partial obstruction. The inferior turbinate was in contact with the lateral wall in 139 patients (81.3%), and the medium turbinate was in contact with the lateral wall in 133 (77.8%). In addition, 88 (51.5%) children had pale mucous membranes; 115 (67.3%) children had nasal discharge.

Fifty-seven children (75%) had sensitization to *Dermatophagoides*, 9 (11.8%) to pollens, and 10 (13.2%) subjects showed polysensitization.

Statistical Data

Table 1 reports the comparison between children with a diagnosis of AR and children without a diagnosis of AR. There were significant differences between children with and without an AR diagnosis. Girls had a more frequent AR diagnosis than boys ($p = 0.006$). There was a significant difference ($p < 0.001$) between the two groups about the tonsil volume as well as for adenoid volume ($p < 0.001$). The contact of the inferior and middle turbinate with the lateral wall was more frequent in children with AR ($p < 0.001$ and $p = 0.002$, respectively). Pale mucous membrane was

Table 2 Multivariate logistic regression—dependent variable: Volume of tonsils ($n = 159$)

	OR	95% CI	p Value
AR (diagnosis)	0.319	1.34–7.62	0.009
Pale mucous membranes (absence)	3.540	1.572–7.969	0.002
Adenoid volume	2.856	1.788–4.563	<0.001

CI = confidence interval; OR–odds ratio.

more frequent in children without an AR diagnosis ($p = 0.042$), whereas nasal discharge was more frequent in children with AR ($p = 0.015$).

In addition, considering 159 children with tonsil grade ≥1, univariate analysis revealed an association between tonsil volume (1–2 versus 3–4) and the following factors: nose obstruction value ($p = 0.008$), inferior turbinate contact ($p = 0.048$), medium turbinate contact ($p = 0.095$), pale mucous membranes ($p = 0.004$), presence of nasal discharge ($p = 0.136$), volume of adenoids ($p < 0.001$), and diagnosis of AR ($p < 0.001$).

The results from the multivariate logistic regression model (Table 2) showed absence of AR ($p = 0.009$), presence of pale mucous membranes ($p = 0.002$), and adenoid volume ($p < 0.001$) as significant predictors of
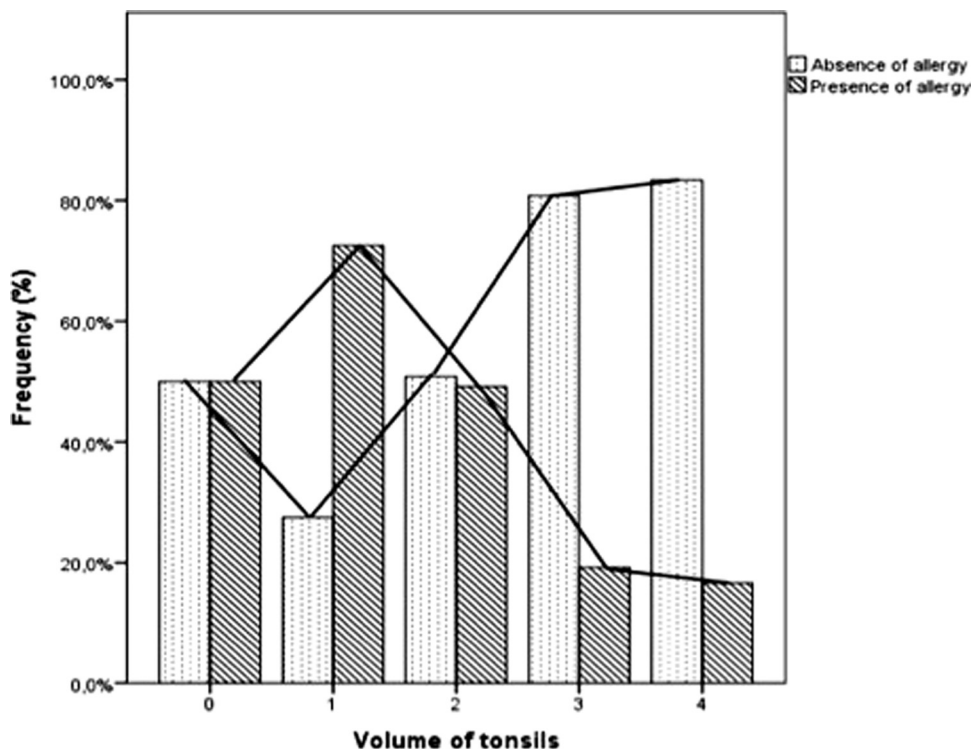
Figure 2. Association between volume of tonsils and presence of allergic rhinitis (AR).

tonsil volume. In particular, the largest adenoids had the highest probability to have hypertrophic tonsils (OR, 2.86; CI 95%, 1.79–4.56). Children with pale mucous membranes were 3.5 times more likely to have TH than those without this clinical characteristic (OR, 3.54; CI 95%, 1.57–7.97). Patients who were not allergic were approximately three times more likely to have hypertrophic tonsils than subjects with AR (OR, 3.19; CI 95%, 1.34–7.62), as reported in Fig. 2.

DISCUSSION

Upper airways symptoms are very common in the pediatric population. Airflow limitation during childhood is frequently attributed to enlarged adenoids, but also other causes must be considered. AR is frequent in children, affecting up to 40% of the general population, and may cause the open-mouth posture.[15] Rare causes of nasal obstruction include choanal atresia, polyps, and tumors.[16]

A well-established opinion assumes that children with AH also frequently may have AR.[17] However, few studies rigorously investigated the relationship between these two disorders, mainly concerning the possible influence of AR on adenoid enlargement.[3–6] A recent study, conducted performing nasal endoscopy, provided conflicting findings as an inverse relationship between adenoid volume and presence of allergy was reported.[7]

On the other hand, tonsil volume is frequently related to adenoid volume so that the term adenotonsillar hypertrophy is commonly used.[18] Unfortunately,

only three studies addressed the possible relationship between AR and TH with contrasting results. Yumoto and colleagues investigated the influence of TH on nasal disorders in 7190 pupils of elementary schools in nine different areas in Japan.[8] These authors concluded that there were no apparent relationships between TH and AR.[8] Sadeghi-Shabestari and colleagues compared 117 children with adenotonsillar hypertrophy, assessed by lateral neck radiography, with 100 healthy children.[9] Findings showed that 70.3% of children with adenotonsillar hypertrophy were sensitized, whereas in the control group showed only 10%. Thus, these authors concluded that allergy is an important risk factor for adenotonsillar hypertrophy. However, the volume of adenoids and tonsils was not measured and graded and endoscopy was not performed. More recently, Olusesi recruited 434 cases of adenotonsillectomy in Nigerian children.[10] They observed that family history of allergy and presence of clinical allergy are related to early onset of symptoms in children with adenotonsillar hypertrophy. However, the methodology was poor because AR diagnosis was made on symptom history alone, AH and TH were not separately considered, and endoscopy was not performed.

The present study provided some interesting findings. First, about one-half of children had AR, but relevant TH, such as grade 3 and 4, was present only in on-third of children. Furthermore, the volume of tonsils was strongly related to volume of adenoids ($\gamma = 0.564$). On the contrary, the volume of tonsils was

inversely associated with AR diagnosis. The multivariate ordinal regression underlines these concepts: absence of AR diagnosis may "protect" (OR, 0.314) from severe TH. On the other hand, AH predicts that TH (OR, 2.85) as well as mucosal edema (such as pale mucous membranes) is the main risk factor (OR, 3.54) for TH. These findings confirm the observation of Yumoto[8] and, indirectly, our previous experience on AH.[7]

TH could depend on exaggerated antigenic stimulation because Waldeyer'r ring represents the first barrier toward the antigens entering the body.[19] When a sustained antigenic exposure persists, TH may occur. Tonsils may be also reservoirs of pathogenic organisms, maintaining chronic hyperstimulation of immune response. Thus, recurrent respiratory infections could result in an increased function of pharyngeal lymphatic tissue, so inducing TH.

On the other hand, airborne allergens may overstimulate the immune system at the tonsil level. In fact, allergic patients have a different distribution of mast cells, the main effective cell in allergic inflammation, into tonsil tissue in comparison with normal subjects so mast cells in the interfollicular area might be promptly activated by direct contact with $CD4^+$ T cells.[20] Children with AH are characterized by impaired immunologic parameters, persisting also after adenotonsillectomy for a long time.[21]

The present study, based on a real-life setting, such as the studied cohort, was comprised of children complaining of upper airways obstruction. They were visited at an ear, nose, and throat office undergoing nasal endoscopy and further evaluated at an allergy office. The results show that severe TH is not associated with AR diagnosis, whereas intense mucosal inflammation (detected by mucosal edema) is associated with TH. A possible interpretation might be that AR, characterized by turbinate enlargement, could affect the passage of antigens able to stimulate tonsil tissue to enlarge. On the other hand, TH is associated with important inflammation reactive to antigen stimulation. In addition, AH and TH seem to be frequent coexisting phenomena.

The main limitations of the present study are (i) the absence of immunologic investigation, able to clarify pathogenic mechanisms; (ii) the lack of symptoms severity assessment; (iii) no information about medications. Therefore, further immunologic studies should be performed to address these issues, mainly concerning the impact of symptom severity on the link between TH and AR, as well as the possible role of undertreatment on these variables.

CONCLUSION

This study shows that large tonsils may be inversely associated with allergy, whereas intense inflammation is a risk factor for TH; and AH may be frequently associated with TH.

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