## Is Adenoidectomy and/or Tonsillectomy a Risk Factor for Allergic Diseases and Asthma in Adulthood?

Nalan Yurtsever<sup>1</sup>, Sadan Soyyigit<sup>1</sup>, Zeynep Celebi Sozener<sup>1</sup>, Dilsad Mungan<sup>1</sup>, S. Kenan Kose<sup>2</sup>, Zeynep Misirligil<sup>1</sup>





Cite this article as: Yurtsever N, Soyyigit S, Celebi Sozener Z, Mungan D, Kose SK, Misirligil Z. Is Adenoidectomy and/or Tonsillectomy a Risk Factor for Allergic Diseases and Asthma in Adulthood? Eurasian I Med 2018; 50(3): 152-155.

### ORCID IDs of the authors:

N.Y.: 0000-0001-7807-6046 S.S.: 0000-0003-3270-5884 Z.C.S.: 0000-0002-5896-262X D.M.: 0000-0001-8806-2764 S.K.K.: 0000-0002-6734-3847 Z.M.: 0000-0003-4624-4599

<sup>1</sup>Division of Allergy and Immunology, Department of Chest Diseases, Ankara University School of Medicine, Ankara, Turkey <sup>2</sup>Department of Biostatistics, Ankara University School of Medicine, Ankara, Turkey

Received: June 22, 2017 Accepted: December 11, 2017

Correspondence to: Nalan Yurtsever E-mail: nlnyrtsvr@gmail.com

DOI 10.5152/eurasianjmed.2018.17182

©Copyright 2018 by the Atatürk University School of Medicine - Available online at www.eurasianjmed.com

#### **ABSTRACT**

Objective: To determine the relationship between adenoidectomy and/or tonsillectomy in childhood and allergic diseases in adulthood.

Materials and Methods: A survey investigating the history of adenoidectomy and/or tonsillectomy was administered to patients that were followed-up by our department between January and June 2014 with the diagnosis of asthma, allergic rhinitis, urticaria-angioedema, drug allergy, food allergy, and venom allergy; patients willing to participate were included in the study. The relationship and risk ratios were analyzed.

Results: Totally, 510 (female/male: 379/131) patients were included in the study: 248 with asthma, 205 with rhinitis, 82 with drug allergy, 73 with urticaria, 24 with food allergy, and 14 with venom allergy. Of these, 65 (12.7%) had undergone adenoidectomy and/or tonsillectomy. Of these 65 patients, 41 had asthma, 33 had allergic rhinitis, and 28 had other allergic diseases. No relation between the history of atopy and adenoidectomy and/or tonsillectomy (p=0.129) was detected; however, there was a positive correlation between asthma and patients aged < 15 years having a history of tonsillectomy and/or adenoidectomy (p=0.020). The risk of asthma was determined to be increased by 1.96 fold among the patients, provided the patient had undergone adenoidectomy and/or tonsillectomy (confidence interval [CI]:1.14-3.36). No connection was observed between atopic and non-atopic asthmatic patients in relation to adenoidectomy and/or tonsillectomy (p=0.46). No relationship was observed between allergic rhinitis and adenoidectomy and/or tonsillectomy.

Conclusion: Adenoidectomy and/or tonsillectomy in childhood increase the risk of asthma in adulthood, whereas it does not increase the risk of atopy. This result signifies the criticality of adenoidectomy or tonsillectomy in the pathogenesis of asthma.

Keywords: Asthma, chest diseases, pulmonology, allergy, dermatology, immunology, internal medicine

## Introduction

Adenoids and tonsils have significant roles in cellular and humoral immune systems. They are also essential organs of mucosal immune defense system, which balances Th1 and Th2 cells [1]. Adenoidectomy and tonsillectomy are commonly performed in childhood; however, these procedures might cause an immunologic imbalance and increase atopy or allergic diseases [2]. The mechanism of adenoidectomy and tonsillectomy affecting allergic responses is unknown, and different studies show contradictory results. In a review by Kohli et al [3], data compilation suggests a definitive association. Contrarily, in the database analysis by Bhattacharjee et al [4], children experienced relief from asthma after adenotonsillectomy. None of the studies report long-term outcomes or acknowledge the progress of asthma in adulthood. It is crucial to determine whether there is a relationship between the removal of these organs in childhood and a gradual increase in allergy in adulthood.

The present study aimed to determine whether previous adenoidectomy and/or tonsillectomy is associated with allergic diseases, later in life.

## Materials and Methods

#### **Study Subjects**

The present study was a retrospective cohort study. We recruited 510 patients who were admitted to the Department of Allergy and Immunology at Ankara University School of Medicine between January and June 2014. All patients were requested to complete a questionnaire.

#### Questionnaire

This questionnaire included information regarding age, occupation (officer, housewife, student, or other); existence of allergic diseases (asthma, allergic rhinitis, drug hypersensitivity, food allergy,

urticaria-angioedema, or venom allergy); and the age at diagnosis: if tonsillectomy was performed. at what age and the reason of removal: if adenoidectomywas performed, at what age and the reason of removal; presence of other diseases (nasal polyp, sinusitis, or upper respiratory tract infection); history of atopy; and any relative suffering any allergic diseases. The final section of the questionnaire comprising the following was completed by a physician: asthma severity (using the Global Initiative for Asthma Management and Prevention [5] guidelines), rhinitis severity (using Allergic Rhinitis and its Impact on Asthma guidelines [6]), and skin prick test results.

All subjects provided written consent. The study was approved by the Local Ethics Committee at Department of Allergy and Immunology at Ankara University School of Medicine.

## Statistical Analyses

Statistical analyses were performed using the Statistical Package for Social Sciences for Windows (SPSS Inc.; Chicago, IL, USA) version 16. Descriptive statistics were expressed as mean±standard deviation (SD) and numbers with percentages. Categorical data were analyzed using the Chi-square and Fisher's exact tests; and p<0.05 was considered statistically significant. The relationship between adenotonsillectomy and asthma and allergic rhinitis was analyzed using a univariate analysis with chi-

Table 1. Patient characteristics	
n	510
Age (mean±SD), years	42.5±13.8
Female/male, n (%) (74.3–25.7)	379/131
History of atopy, n (%)	293 (57.5)
Prick test positivity, n (%)	192 (46.2)
Monosensitized/polysensitized, n (%)	129/63 (31.1/25.1)
Familial history of atopy, n (%)	245 (48)
Adenoidectomy and/ or tonsillectomy, n (%)	65 (12.7)
Allergic diseases	
Asthma	248 (48.6)
Allergic rhinitis	205 (40.2)
Drug allergy	82 (16.1)
Food allergy	24 (4.7)
Venom allergy	14 (2.7)
Chronic urticaria and angioedema	73 (14.3)
Others	
Nasal polyp	37 (7.3)
Chronic sinusitis	113 (22.2)
Frequent upper respiratory tract infections	222 (43.5)

square tests and univariate odds ratio and their 95% confidence intervals.

#### Results

#### Characteristics of the Study Population

Totally, 510 patients were included in the study. The mean age was 42.5±13.8 years (range. 17-85 years). The male to female ratio was 131:379. Patient occupations were as follows: 30 officers (5.9%), 141 housewives (27.6%), 45 students (8.8%), and 294 others (57.6%); 57.5% patients had a history positive for atopy. According to skin prick test results, 46.2% patients had positive results: 31.1% were monosensitized. and 25.1% were polysensitized. Among the 510 subjects, 65 (12.7%) had a history of adenoidectomy and/or tonsillectomy (Table 1).

## Allergies and Other Diseases

The most common allergy was asthma (48.6%). followed by allergic rhinitis (40.2%). The number of patients with other allergic diseases was lower compared with asthma and allergic rhinitis. The prevalence of accompanying upper-airway diseases was 7.3%, 22.2%, and 43.5% for nasal polyp, chronic sinusitis, and frequent upper respiratory tract infection, respectively (Table 1).

#### Patients with Adenotonsillectomy

Sixty-five patients underwent adenoidectomy and/or tonsillectomy. The mean patient age was 44.4±14.7 years. Twenty-four patients underwent surgery before 15 years of age, whereas 35 underwent surgery after 15 years of age. Six patients did not remember their age at surgery. Further, 66.2% patients mentioned a history of atopy. The distribution of allergic diseases of patients with adenoidectomy and/or tonsillectomy is presented in Table 2.

No statistical significance was observed between the history of atopy and adenoidectomy and/or tonsillectomy (p=0.129).

#### Asthmatic Patients with Adenotonsillectomy

Forty-one patients underwent adenoidectomy and/or tonsillectomy. The mean age was  $21.6\pm16.5$ years. Eleven patients underwent surgery before 15 years of age, whereas 25 underwent surgery after 15 years of age. Five patients did not remember their age at surgery. Twenty-nine (70.7%) patients mentioned a history of atopy. The skin prick

Table 2. Demographic characteristics of pat   tonsillectomy	ients with or without histo	ry of adenoidectomy and/or
	Previous tonsillectomy and/ or adenoidectomy	No previous tonsillectomy and/ or adenoidectomy
n	65	445

11	03	113
Age (mean±SD)	44.4±14.7	42.7±13.7
Age at adenoidectomy and/ or tonsillectomy (mean±SD), years	21.6±16.5	
0–15, n (%)	24 (36.9)	
Age (mean±SD)	9.2±3.8	
>15, n (%)	35 (53.8)	
Age (mean±SD)	31±16.3	
Female/male, n (%), (min–max)	53/12 (81.5–18.5)	326/119 (73.3–26.7)
History of atopy, n (%)	43 (66.2)	250 (56.2)
Prick test positivity, n (%)	22 (33.8)	170 (38.2)
Monosensitized/polysensitized, n (%)	14/8 (63.6–36.4)	115/55 (25.8–12.4)
Familial history of atopy, n (%)	36 (55.4)	209 (47)
Allergic disease		
Asthma	41 (63.1)	207 (46.5)
Allergic rhinitis	33 (50.8)	172 (38.7)
Drug allergy	14 (21.5)	68 (15.3)
Food allergy	3 (4.6)	21 (4.7)
Venom allergy	I (I.5)	13 (2.9)
Chronic urticaria/angioedema	10 (15.4)	104 (23.4)
Others		
Nasal polyp	5 (7.7)	32 (7.2)
Chronic sinusitis	22 (33.8)	91 (20.4)
Frequent upper respiratory tract infections	44 (67.7)	178 (40.0)

test results were positive for 39.0% of the subjects. The commonest group in terms of severity was mild persistent asthma (24.4%; Table 3).

relationship between adenoidectomy and/or tonsillectomy before 15 years of age and the development of asthma.

There was a significant relationship between asthma and adenoidectomy and/or tonsillectomy (p=0.013). We also found asignificant

No relationship has been detected between severity of asthma and adenoidectomy and/or tonsillectomy (p=0.91). No significant differ-

ence was observed between atopic and non-atopic patients in terms of adenoidectomy and/or tonsillectomy (p=0.46). There was no significant relationship between the age of surgery and the age at which asthma was diagnosed in patients who underwent adenoidectomy and/or tonsillectomy before 15 years of age (p=0.05).

The risk of asthma was determined to be increased by 1.96 fold in adenoidectomies and/or tonsillectomies among the allergic patients (CI: 1.14–3.36).

# **Table 3.** Demographic characteristics of patients with asthma with or without history of adenoidectomy and/or tonsillectomy

tomy and/or tonsillectomy		
	Previous adenoidectomy and/or tonsillectomy	No previous adenoidectomy and/or tonsillectomy
n (%)	41 (63.1)	207 (46.5)
Age (mean±SD), years	21.6±16.5	44.9±13.2
Age at adenoidectomy and/ or tonsillectomy (mean±SD), years	21.6±16.5	
0–15, n (%)	11 (26.8)	
Age (mean±SD)	8.9±3.7	
>15, n (%)	25 (61)	
Age (mean±SD)	32.6±17.7	
Female/male, n (%)	35/6 (85.4–14.6)	166/41 (80.2–19.8)
Atopic/non-atopic (%)	29/12 (70.7–29.3)	134/73 (64.7–35.3)
Prick test positivity, n (%)	16 (39)	73 (35.3)
Monosensitized/polysensitized, n (%)	10/6 (62.5–37.5)	48/25 (23.2–12.1)
Asthma severity, n (%)		
Mild intermittent	8 (19.5)	46 (22.2)
Mild persistent	16 (39)	86 (41.5)
Moderate persistent	10 (24.4)	41 (19.8)
Severe persistent	7 (17.1)	34 (16.4)

## **Table 4.** Demographic characteristics of patients with allergic rhinitis with or without history of adenoidectomy and/or tonsillectomy

,		
	Previous adenoidectomy and/or tonsillectomy	No previous adenoidectomy and/or tonsillectomy
n	33	172
Age (mean±SD), years	44.1±15.5	38.06±12.2
Age of adenoidectomy and/ or tonsillectomy (mean±SD), years	21.7±15.2	
0-15, n (%)	11 (45.8)	
Age (mean±SD)	9.2±4.0	
>15, n (%)	19 (54.3)	
Age (mean±SD)	29.7±14.3	
Female/male, n (%)	23/10 (69.7–30.3)	127/45 (73.8–26.2)
History of atopy (%)	30 (90.9)	158 (91.9)
Prick test positivity, n (%)	18 (54.5)	112 (65.1)
Monosensitized/polysensitized, n (%)	11/7 (61.1–38.9)	77/35 (44.8–20.3)
Rhinitis severity, n (%)		
Mild intermittent	14 (42.4)	79 (45.9)
Severe intermittent	10 (30.3)	35 (20.3)
Mild persistent	5 (15.2)	33 (19.2)
Severe persistent	4 (12.1)	25 (14.5)

#### Allergic Rhinitis Patients with Adenotonsillectomy

Thirty-three patients with a mean age of  $44.1\pm15.5$  years underwent adenoidectomy and/or tonsillectomy. Eleven patients underwent surgery before 15 years of age and 19 underwent surgery after 15 years of age. Three patients did not remember their age at surgery. Thirty (69.7%) patients had a history of atopy. Skin prick tests were positive in 54.5% patients. Mild intermittent rhinitis was the most frequent severity form (42.4%; Table 4).

No relationship was found between allergic rhinitis and adenoidectomy and/or tonsillectomy (p=0.063). A relationship between other allergic diseases and adenoidectomy and/or tonsillectomy could not be evaluated because of inadequate number of patients.

## Discussion

In the present study, we found a significant relationship between asthma and the history of adenoidectomy and/or tonsillectomy, particularly if the surgery had been performed before 15 years of age. A patient with a history of adenoidectomy and/or tonsillectomy had 1.96 times-increased risk of developing asthma among our allergic patients.

There has been a global increase in the prevalence of atopic diseases such as asthma and allergic rhinitis. Both genetic predisposition and environmental factors play a role in the pathogenesis of allergic diseases. Particularly, changes in the ThI-Th2 balance establish an important cause for the development of atopic diseases in the immune system [7].

The Waldeyer ring is a significant part of the immune system [1]. Adenotonsillectomy is one of the most common pediatric operations [8]. The removal of the adenoid and/or tonsillar tissue may cause a decrease in the humoral or cellular immune response. In correlation with the hygiene hypothesis, a decrease in this immune response may cause an increased risk of atopic diseases in the long term [1]. Some studies have reported a minor decrease of serum immunoglobulin levels after adenoidectomy and tonsillectomy [9, 10]. After adenoidectomy and tonsillectomy, a change in the response has been reported in not only the humoral, but also in the cellular immune system. Some authors stated changes in B and T cells particularly in different T cell subtypes [10-13]. Do such short-term changes

in the immune system continue in the long term? Data on this subject are limited. To date, immunologic consequences of surgical removal of the Waldeyer ring and its relationship with allergic diseases has been studied and contradictory results have been found [3, 4, 7, 14]. There are no data related to the immune system defects in the long term. In a longitudinal cohort study, adenotonsillectomy surgery performed in childhood was found not to cause an increase in the atopy frequency in early adulthood [7]. In a study by Suvilehto et al [9], allergy and asthma diagnosis was determined to be greater for patients who had recurrent respiratory infections before 7 years of age and had adenoidectomy. In a cross sectional study in Turkey, a history of tonsillectomy was proven to increase the eczema risk by 2.10 fold [14]. In a similar study by Akcay et al [15], adenoidectomy and tonsillectomy were associated with an increased risk of asthma.

In 1989, Strachan proposed a hypothesis called "hygiene hypothesis" stating that a hygienic environment increases the development of atopic diseases. Facing allergens or viral and bacterial infections in childhood shifts the immune system from Th2 to Th1 [16]. Moreover, lower respiratory infections in early childhood, such as respiratory syncytial virus and measles, increase the risk of asthma [17-19]. What if the increase in risk of asthma arises from frequent upper respiratory infections and not because of adenoidectomy? Mattila et al [14] investigated this question in their study and detected the risk of asthma to be higher in children that underwent surgery because of recurrent otitis media. In a survey study conducted with 209 children aged 3-8 years having a history of chronic or recurrent otitis media, an increase in the asthma frequency, nasal eosinophilia, and skin test positivity was found [20]. In another study, the development of atopy and sensitivity was found to be positively correlated with adenoidectomy or tonsillectomy, the history of recurrent upper respiratory infection, and frequent use of antibiotics [21]. We planned and encouraged further studies in larger patient populations to reveal the predicted results on particularly the effect of adenoidectomy on atopy.

Considering these results, children must be attentively evaluated before deciding on adenoidectomy and tonsillectomy, because there aresome arguments in literature on whether adenoidectomy or tonsillectomy is essential. In a study by Van Staaij et al [22], despite healing within 6 months after adenoidectomy and/or tonsillectomy performed because of recurrent upper respiratory infections, no difference was observed in the control group in the 24-month recovery period. Moreover, the long-term effects of these surgeries are unknown.

Our study, contrary to other studies in literature, is a retrospective cohort study. Hence, the most important limitation in our study is the lack of a

control group and retrospectively questioning the ratio of adenotonsillectomy in patients admitted to our allergy clinic. However, this study aimed to determine the ratio of patients with adenotonsillectomy in the allergic patient population. Moreover, we detected that undergoing adenoidectomy and/or tonsillectomy increased the risk of asthma by 1.96 fold. We detected a marginally significant relationship between undergoing adenoidectomy and/or tonsillectomy before 15 years of age and the age at which asthma developed. Does adenotonsillectomy at an early age increase the risk of asthma? To answer this question, multicenter prospective cohort studies in larger patient groups are warranted.

In conclusion, our findings reveal the ratio of adenoidectomy and/or tonsillectomy to be higher in allergic patient populations, particularly in asthmatic patients, and indicate that if these surgeries are performed at an early age, they increase the risk of developing asthma. The underlying mechanisms must be evaluated to understand this relationship.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Ankara University School of Medicine.

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – N.Y., S.S., Z.C.S., Z.M.; Design – S.S., Z.M.; Supervision – Z.M., D.M.; Resources – S.S., Z.C.S., Z.M., D.M.; Materials – N.Y., S.S., Z.C.S.; Data Collection and/or Processing – N.Y., S.S., Z.C.S.; Analysis and/or Interpretation – S.S., S.K.K., Z.M.; Literature Search – N.Y., S.S., Z.M.; Writing Manuscript – N.Y., S.S., Z.M.; Critical Review – Z.M., D.M.; Other – Z.C.S., S.K.K.

**Conflict of Interest:** Authors have no conflicts of interest to declare.

**Financial Disclosure:** The authors declare that this study has received no financial support.

#### References

- van Kempen MJ, Rijkers GT, Van Cauwenberge PB. The immune response in adenoids and tonsils.Int Arch Allergy Immunol 2000; 122: 8-19. [CrossRef]
- Friday GA Jr, Paradise JL, Rabin BS, Colborn DK, Taylor FH. Serum immunoglobulin changes in relation to tonsil and adenoid surgery. Ann Allergy 1992; 69: 225-30.
- Kohli N, DeCarlo D, Goldstein NA, Silverman J. Asthma outcomes after adenotonsillectomy: A systematic review. Int J Pediatr Otorhinolaryngol 2016; 90: 107-112. [CrossRef]
- Bhattacharjee R, Choi BH, Gozal D, Mokhlesi B. Association of adenotonsillectomy with asthma outcomes in children: a longitudinal database analysis. PLoS Med 2014; 11: e1001753. [CrossRef]
- 5. Global Initiative for Asthma Management and Prevention. 2016. Available from www.ginasthma.org.

- Allergic Rhinitis and its Impact on Asthma. 2010. Available from http://www.euforea.eu/about-us/aria.html
- 7. van Hattum ES, Balemans WA, Rovers MM, Zielhuis GA, Schilder AG, van der Ent CK. Adenoidectomy and/or tonsillectomy in childhood is not associated with atopic disease later in life. Clin Exp Allergy 2006; 36: 40-3. [CrossRef]
- 8. Böck A, Popp W, Herkner K. Tonsillectomy and the immune system: a long-term follow up comparison between tonsillectomized and nontonsillectomized children. Eur Arch Otorhinolaryngol 1994; 251: 423-7. [CrossRef]
- Suvilehto J, Seppänen M, Notkola IL, et al. Association of allergy, asthma and IgE sensitisation to adenoidectomy and infections in children. Rhinology 2007; 45: 286-91.
- Ikincioğullari A, Doğu F, Ikincioğullari A, Eğin Y, Babacan E. Is immune system influenced by adenotonsillectomy in children? Int J Pediatr Otorhinolaryngol 2002; 66: 251-7. [CrossRef]
- Bussi M, Carlevato MT, Galeazzi E, Morra B. Immunological investigations on tonsillar and peripheral blood lymphocytes after adenotonsillectomy. Possible suggestions for phenotypical and functional differences. Acta Otolaryngol 1991; 111: 379-83. [CrossRef]
- Hofmann T, Lackner A, Berghold A, Lang-Loidolt D. Influence of sensitization to inhalative allergens on adenotonsillar disease. Otolaryngol Head Neck Surg 2003; 129: 11-5. [CrossRef]
- Akcay A, Tamay Z, Ergin A, Guler N. Prevalence and risk factors of atopic eczema in Turkish adolescents. Pediatr Dermatol 2014; 31: 319-25. [CrossRef]
- Mattila PS, Hammarén-Malmi S, Tarkkanen J, et al. Adenoidectomy during early life and the risk of asthma. Pediatr Allergy Immunol 2003; 14: 358-62. [CrossRef]
- Akcay A, Tamay Z, Hocaoglu AB, Ergin A, Guler N. Risk factors affecting asthma prevalence in adolescents living in Istanbul, Turkey. Allergol Immunopathol (Madr) 2014; 42: 449-58. [CrossRef]
- 16. Strachan DP. Hay fever, hygiene, and household size. BMJ 1989; 299: 1259-60. [CrossRef]
- Illi S, von Mutius E, Lau S, et al. Early childhood infectious diseases and the development of asthma up to school age: a birth cohort study. BMJ 2001; 322: 390-5. [CrossRef]
- Stein RT, Sherrill D, Morgan WJ, et al. Respiratory syncytial virus in early life and risk of wheeze and allergy by age 13 years. Lancet 1999; 354: 541-5. [CrossRef]
- Bager P, Westergaard T, Rostgaard K, Hjalgrim H, Melbye M. Age at childhood infections and risk of atopy. Thorax 2002; 57: 379-82. [CrossRef]
- Alles R, Parikh A, Hawk L, Darby Y, Romero JN, Scadding G. The prevalence of atopic disorders in children with chronic otitis media with effusion. Pediatr Allergy Immunol 2001; 12: 102-6. [CrossRef]
- Majkowska-Wojciechowska B, Pełka J, Korzon L, et al. Prevalence of allergy, patterns of allergic sensitization and allergy risk factors in rural and urban children. Allergy 2007; 62: 1044-50. [CrossRef]
- van Staaij BK, van den Akker EH, Rovers MM, Hordijk GJ, Hoes AW, Schilder AGM. Effectiveness of adenotonsillectomy in children with mild symptoms of throat infections or adenotonsillar hypertrophy: open, randomised controlled trial. BMJ 2004; 329: 651. [CrossRef]