Does *Helicobacter Pylori* Have a Role in the Etiology of Adenoid Hypertrophy?

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Abstract To investigate whether there is any association between nasopharyngeal reflux and adenoid hypertrophy in children by using 24-h pH monitoring with dual probe and to determine whether *Helicobacter pylori* simply colonises in adenoid tissue or it is present there temporarily due to extraesophageal reflux. A prospective study at a tertiary referral center. Thirty-two patients who underwent adenoidectomy, aged ranged between 4 and 13 were included. All children with adenoid hypertrophy underwent 24-h pH monitoring with a dual probe. Proximal probe was placed in the nasopharynx. The presence of nasopharyngeal reflux and gastroesophageal reflux were investigated by 24-h pH monitoring. The presence of *H. pylori* was investigated in adenoidectomy samples by HP-fast test. Of the 32 patients who underwent adenoidectomy, 5 had nasopharyngeal reflux positivity while 27 patients did not show nasopharyngeal reflux positivity with pH monitoring. *Helicobacter pylori* could not be detected in 5 nasopharyngeal reflux positive children while 3 of 27 nasopharyngeal reflux negative children showed *H. pylori* positivity, one of them in the mucosa and others in the core. This study demonstrated the high incidence of nasopharyngeal reflux and gastroesophageal reflux in adenoid hypertrophy and the

possible colonisation of *H. pylori* in the adenoid tissue. This may change the assessment of children with adenotonsillar hypertrophy in near future. However, more placebo controlled and double blind studies and larger series are still needed to support this hypothesis.

Keywords *Helicobacter pylori* · Adenotonsillar hyperplasia · Extraesophageal acid reflux · pH Monitoring · Child

Introduction

Chronic adenotonsillar hypertrophy is a common cause of upper airway obstruction in children and in severe cases, it may result in cor pulmonale, pulmonary vascular hypertension, and alveolar hypoventilation. Furthermore, adenotonsillar hypertrophy is the most common cause of sleep apnea in children and has become a frequent indication for adenotonsillectomy [1]. The etiology of chronic adenotonsillar hypertrophy is still unclear. Gastroesophageal reflux (GER) or extraesophageal reflux in children are one of the increasingly recognized and defined causes of adenotonsillar hypertrophy in the literature [2–5]. If GER is shown to play a significant contributory role in the etiology of adenoid hypertrophy, medical treatment of GER might obviate the need for adenoid surgery. Recently, *Helicobacter pylori* (HP) has been accused for the colonisation in tonsillary and adenoid tissue, this colonisation may cause HP to spread by oral-oral or fecal-oral route to other persons and make difficult the eradication of gastroduodenal HP infection [6, 7].

Main objective of this study is to investigate whether there is any association between nasopharyngeal reflux (NR) and adenoid hypertrophy in children by using 24-h pH monitoring with dual probe. Secondary objective is to

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determine whether HP simply colonises in adenoid tissue and plays a role in etiology of adenoid hypertrophy or it is present there temporarily due to extraesophageal reflux.

Material and Methods

Fourty-two children who had adenoid hypertrophy with/without tonsillar hypertrophy underwent 24-h pH monitoring with a dual probe. They had chronic mouth-breathing, snoring, and sleep apnea or sleep disturbances. Patients with history of allergic rhinitis, immune deficiency and metabolic disease were excluded.

All subjects underwent cephalometric investigation. Adenoid-nasopharyngeal ratio was calculated and children with greater than 80% adenoid-nasopharyngeal ratio were included. The patients were asked about symptoms of GER such as pyrosis, emesis, dysphagia, and regurgitation. Informed consent from parents were obtained. The study was approved by The Ethic Committee of Ankara Training and Research Hospital (No: 2890). The pH was measured with two-channel antimony probes with one internal reference electrode (Synectics Medical LDA, Portugal). The distance between both sensors was 10 cm, and the probe was connected to a Ohmega device (MMS, Medical Measurement Systems bv, The Netherlands). Before each study, the pH probe was calibrated in buffer solutions of pH 7 and 1. The proximal probe was located in the nasopharynx (just in front of the adenoid). The position of the catheter was measured in centimeters from the ala of the nostril. The location of the catheter was checked by lateral neck graphy. During 24-h pH monitorisation, the subjects were followed as an outpatient and their parents were told to let them to do their daily activities. No advice regarding diet or positioning was given. The changes in pH were continuously recorded over 24 h study. The pH probe results were recorded separately for each probe. The read-out data was performed with an IBM compatible personal computer (Windows XP OP) using MMS Ohmega, software version 8.11.

We recorded the number of episodes $\text{pH} < 4$, reflux index (the percentage of the time when pH was less than 4), the number of reflux episodes longer than 5 min, the longest episode of all reflux. For GER, normal values of these parameters were defined as 50, 4.2, 4.0, and 9.2, respectively and positive GER was accepted as above one of these values. However, any episode under pH 4 in the nasopharynx was accepted as a positive result if it was preceded by an esophageal pH drop of similar magnitude [8].

Mucosal and coral biopsies were taken from the adenoid tissue and the presence of HP was investigated in biopsy samples by HP-fast test (GI Supply, Camp

Hill, PA). Adenoidectomy was performed using curettes. At the end of the operation, 2-mm-diameter wide pieces were cut from adenoidectomy specimen with a sterile blade. The pieces was immediately washed thoroughly with sterile saline and placed in HP-fast test. Previous use of antibiotics, bismuth compounds, antacid drugs, or H₂ receptor blockers were questioned and the patients with the history of these medications were excluded due to the reduced risk of sensitivity of the HP-fast test and increased risk of false-negative results. The HP-fast test was kept in the refrigerator and they were taken out to room temperature 3–4 h before testing. The tests were read and recorded in the prepared forms, first after 15 and 30 min and thereafter at periods of 1, 4, and 24 h. At the end of the 24 h, a yellow/light peach and greenish-yellow color HP-fast test were recorded as negative and a dark green, aqua blue and dark blue color were recorded as positive for HP.

Results

Of the 42 patients, 17 were male and 25 were female. The average age of patients was 7.83 ± 2.84 years (age range, 3–13 years). NR was found in 8 of 42 (19%) children with adenoid hypertrophy whereas esophageal reflux was found in 10 of 42 (23.8%). Results of pH probes were given in Table 1. Data of nasopharyngeal and esophageal probes according to parameters (the number of episodes $\text{pH} < 4$, reflux index, the number of reflux episodes longer than 5 min, the longest episode of all reflux) were shown in Table 2. Age, sex distribution and analysis of symptomatology in NR positive and negative patients were shown in Table 3.

Of the 42 patients, 8 were lost to follow up. Thirty-four patients underwent adenoidectomy (with/without tonsillectomy or ventilation tube insertion) in our clinic. Two of these were excluded due to previous antibiotic use. HP-fast test was performed in 32 patients left (20 female, 12 male, mean age 7.81 ± 2.81 years, age range, 4–13 years). Of the 32 patients, 5 had NR positivity while 27 patients did not show NR positivity with pH monitorisation. HP could not be detected in 5 NR positive children while 3 of 27 NR negative children showed HP positivity, one of them in the mucosa and others in the core. Due to the small size of the NR positive group, statistical analysis could not be able to be done. The data of study group related to NR and HP were summarized in Table 4.

Statistical Analysis

Data analysis was performed by using SPSS for Windows, version 11.5 (SPSS Inc., Chicago, IL, United

Table 1 Results obtained from the proximal and distal pH probe in the study

Patient no.	Nasopharyngeal (proximal)				Esophageal (distal)			
	No. of episodes	% of time with pH < 4.0	No. of episodes > 5 min	Longest episode (min)	No. of episodes	% of time with pH < 4.0	No. of episodes > 5 min	Longest episode (min)
1	103.1	5.7	1.9	18.6	171.8	11	5.8	18.6
2	0	0	0	0	14.7	0.4	0	0.6
3	48.4	3.7	3.2	9.6	82.1	28.6	13.7	101.3
4	2	0.2	0	2.5	17.9	0.9	1	5.6
5	0	0	0	0	12.5	2.2	2.1	8.7
6	1	0.1	0	1	10.4	0.3	0	1
7	0	0	0	0	15.6	0.5	0	2.1
8	1	0.1	0	0.3	13.5	0.8	0	3.6
9	0	0	0	0	6.8	1.2	1.1	10.9
10	0	0	0	0	36.8	2.4	0	3.9
11	0	0	0	0	35.3	1.7	1.1	5.5
12	0	0	0	0	5.5	0.1	0	0.5
13	1.1	0.1	0	0.2	29.4	7.3	6.5	19.2
14	0	0	0	0	14.9	0.8	0	2.6
15	1.1	0.1	0	0.7	2.1	0.1	0	0.7
16	0	0	0	0	46.6	7.4	4.3	24.1
17	0	0	0	0	0	0	0	0
18	1.2	0.2	0	1.5	7.4	0.3	1.1	6.3
19	0	0	0	0	50.7	4.6	2.3	24.2
20	0	0	0	0	53.3	8	2	42.1
21	0	0	0	0	6.3	0.2	0	1.2
22	0	0	0	0	36	1.9	0	2.9
23	0	0	0	0	30.9	2.1	1.1	12.5
24	0	0	0	0	62.8	4.3	1	6.7
25	0	0	0	0	44.5	3.8	3.1	9
26	0	0	0	0	46.8	4.6	1.1	31.1
27	0	0	0	0	27.8	1.5	0	3.3
28	0	0	0	0	17.4	0.6	0	1
29	0	0	0	0	33.3	1.8	0	3.1
30	0	0	0	0	7.1	0.3	0	1.3
31	0	0	0	0	20.5	1.5	0	3.9
32	0	0	0	0	40.7	1.9	0	3.1
33	0	0	0	0	41.3	3.1	0	3.8
34	0	0	0	0	39.4	3.1	2.1	5.5
35	0	0	0	0	22.9	1	0	1.7
36	0	0	0	0	20.2	2.1	1.1	5.4
37	0	0	0	0	14.7	0.6	0	1.7
38	0	0	0	0	24.6	1.5	0	4
39	0	0	0	0	8.1	0.2	0	1.3
40	0	0	0	0	0	0	0	0
41	0	0	0	0	7.3	0.6	0	2
42	0	0	0	0	38.1	1.6	0	4.7

States). While, data were shown as mean $\pm$ standard deviation (minimum–maximum) for continuous variables, otherwise, number of cases and (%) were used for categorical ones.

Discussion

Chronic adenotonsillar hypertrophy is one of the most common surgery ailment in children. Previous attempts at

Table 2 Results obtained from nasopharyngeal and esophageal pH probe in the studyData were shown as mean $\pm$ SD (minimum–maximum)

	Nasopharyngeal	Esophageal
Number of reflux episodes	3.78 $\pm$ 17.38 (0.0–103.1)	29.00 $\pm$ 29.16 (0.0–171.8)
% of Time with pH < 4.0	0.24 $\pm$ 1.03 (0.0–5.7)	2.78 $\pm$ 4.76 (0.0–28.6)
Number of reflux episodes > 5 min	0.12 $\pm$ 0.57 (0.0–3.2)	1.20 $\pm$ 2.51 (0.0–13.7)
Longest episode of reflux (min)	0.82 $\pm$ 3.20 (0.0–18.6)	9.30 $\pm$ 17.14 (0.0–101.3)

Table 3 Age, sex distribution and analysis of symptomatology in NR positive and negative patients

	Age*	Gender** (Female/Male)	Pyrosis	Emesis	Dysphagia	Regurgitation
NR positive (8)	6.5 $\pm$ 3.2	4 (50%)/4 (50%)	1	4	3	4
NR negative (34)	8.1 $\pm$ 2.7	21 (62%)/13 (38%)	0	2	1	0

NR Nasopharyngeal reflux

* $P = 0.141$ ** $P = 0.694$ **Table 4** The data of study group related to NR and HP

Existence of NR	A	B	HP+	HP–
NR positivity	8	5	0	5
NR negativity	34	27	3	24
Total	42	32	3	29

A Number of patients with 24 h dual probe pH monitorisation, B Number of patients both underwent adenoidectomy and HP investigation among patients with 24 h dual probe PH monitorisation, NR Nasopharyngeal reflux, HP *Helicobacter pylori*

identifying the pathophysiologic mechanisms have focused on microbiological and immunologic changes in enlarged tonsils and adenoids [4]. Enlargement of the adenoids during early and middle childhood may occur in response to a variety of antigenic challenges including viruses, bacteria, allergens, foods, and environmental irritants [3].

The exposure of the upper aerodigestive tract to gastric secretions results in numerous pathologic conditions such as chronic rhinosinusitis, recurrent otitis media, chronic cough, and airway abnormalities etc. [9, 10]. GER has recently been a popular cause of chronic adenotonsillar hypertrophy in the literature [2–5]. Reflux into the nasopharynx is unusual in most patients [9] and little is known about the possible role of GER in nasopharyngeal disease [11].

Studies have shown that extraesophageal reflux can cause considerable damage to the less resistant respiratory epithelium of the larynx, trachea, nose, and middle ear [3]. A certain amount of GER is considered normal in infant, but beyond 12 months of age the amount of physiologic reflux approximates that of adults [12].

24-h pH monitoring has become the gold standard for evaluated GER because of its reported sensitivity rate ranged from 79 to 95% and specificity rate from 86 to

100% [12, 13]. In some investigations, pH probe have been also located in the pharynx to further evaluate possible associations with upper airway disease [2, 8, 11, 14].

Recently a few studies related to the relationship between adenoid hypertrophy and reflux were published in the literature. Carr et al. [5] studied the incidence of reflux in children undergoing adenoidectomy and found that 88% of children age 1 year or less and 32% over age 1 had GER disease. By the age of 12 months and thereafter, only 8% of children were thought to have GER. In a study conducted by Monroy et al. [3], among 72 revision adenoidectomy patients, GER was investigated in 29 patients and 28 of these patients showed GER. Keles et al. [2] were investigated frequency of pharyngeal reflux in children with adenoid hyperplasia. In the study ($n = 30$) and control groups ($n = 12$) according to reflux index, positive pharyngeal reflux and GER were found to be 25%, 64.5% and 8.3%, 46.7%, respectively. They located the distal probe just above the lower esophageal sphincter and proximal probe 10 cm above distal probe. Tumgor et al. [14] also reported a study with dual probe by placing proximal and distal probes in the same location and found mean reflux index score 46.7% (proximal probe) and 56.7% (distal probe).

In this study, the possible role of extraesophageal reflux in the etiology of adenotonsillar hypertrophy was investigated with dual probe; one was located in esophagus the other was located in the nasopharynx. According to our knowledge, in previous published English literature, there were no studies which investigated existence of NR by this method with probe placed in the nasopharynx. We also studied that a relationship between nasopharyngeal reflux confirmed 24-h pH monitoring with nasopharyngeal probe and HP existence in adenotonsillar tissue. This report is also first study to focus on this relationship.

In this present study, of the 42 patients undergoing dual pH probe, 8 (19%) were found to have NR, 10 (23.8%) were found to have pathologic esophageal reflux. These values are smaller than those of above mentioned two studies. This may be due to the location of both probes more proximally in our study. However, nasopharyngeal measurements give more accurate results than distally located probe measurements in terms of the presence of reflux. Of the 42 patients undergoing dual pH probe, 10 (23.8%) were found to have pathologic esophageal reflux, indicating a prevalence of GER that was clinically significant and much higher than a 5% prevalence anticipated in the general population [9].

HP is a spiral, microaerophilic, Gram-negative bacterium. HP infection is very common in the population [6]. The prevalence of the disease is 30–40% in developed countries and 80–90% in the underdeveloped countries [15]. HP infection plays an important role in the pathogenesis of other gastroduodenal diseases such as peptic ulceration, gastric lymphoma, and gastric cancer [6]. The presence of HP in gastric mucosa is bound to mucosa-associated lymphatic tissue. Tonsils and adenoid are also its component, participate in the immune function. But they may serve as a reservoir for bacteria [6, 16]. It was hypothesised that carcinoma or lymphoma risk might raise when HP exists in tonsillar or adenoid tissue. For this reason, great interest has recently been focused on detection of HP presence in tonsillar and adenoid tissue [6].

Different methods such as polymerase chain reaction (PCR), rapid urease tests (RUT), culture in order to be identified HP were used in previous studies. The results of studies about the HP presence in adenoid tissue are inconsistent. Moreover, among positive studies, it was not clear that whether this positivity is due to colonisation or temporary passes of HP from the stomach to the nasopharynx. Unver et al. [7] in adenoid tissue and Khademi et al. [17] in tonsillar and adenoid tissue investigated HP by the *Campylobacter*-like organism (CLO) test and found positive results. Cirak et al. [18] and Bulut et al. [19] investigated HP in tonsillar and adenoid tissue by PCR and reported positive results. Bitar et al. [20] found positivity by RUT and histology, but no positivity by nested PCR in adenoid tissue. Contrary to these studies, Yilmaz et al. [21] did not find any positivity in tonsillar and adenoid tissue by the CLO test. Pitkaranta et al. [22] investigated adenoid tissue and middle ear fluid by culture. They found negative results. Eyigor et al. [15] found positivity by RUT and negative by PCR for the *glmM* gene.

In this study, the presence of HP was investigated by a fast urease testing named HP-fast test. HP fast test tests urease activity as in the other urease testings. HP-fast test was preferred because it was fast and practical.

No detection of HP among 5 NR positive patients and only 3 positivity (2 in the core) among NR negative 27 patients supported that nasopharynx may be a colonisation area for HP. Two core HP positivities support the colonisation in the tissue rather than originating from the stomach.

Conclusion

In summary, this study demonstrated the high incidence of NR and GER in adenoid hypertrophy and the possible colonisation of HP in the adenoid tissue. This may change the assessment of children with adenoid hypertrophy in near future. However, more placebo controlled and double blind studies and larger series are still needed to support this hypothesis.

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Conflict of Interest The authors declare that they have no conflict of interest.

References

1. Wiatrak BJ, Woolley AL (1998) Pharyngitis and adenotonsillar disease. In: Cummings CW, Fredrickson JM, Harker LA, Krause CJ, Richardson MA, Schuller DE (eds) *Pediatric otolaryngology head & neck surgery*, 3rd edn. Mosby, St. Louis, pp 198–202
2. Keles B, Ozturk K, Arbag H, Gunel E, Ozer B (2005) Frequency of pharyngeal reflux in children with adenoid hyperplasia. *Int J Pediatr Otorhinolaryngol* 69:1103–1107
3. Monroy A, Behar P, Brodsky L (2008) Revision adenoidectomy—a retrospective study. *Int J Pediatr Otorhinolaryngol* 72:565–570
4. Stapleton A, Brodsky L (2008) Extra-esophageal acid reflux induced adenotonsillar hyperplasia: case report and literature review. *Int J Pediatr Otorhinolaryngol* 72:409–413
5. Carr MM, Poje CP, Ehrig D, Brodsky LS (2001) Incidence of reflux in young children undergoing adenoidectomy. *Laryngoscope* 111:2170–2172
6. Lukes P, Astl J, Pavlík E, Potuzníková B, Sterzl I, Betka J (2008) *Helicobacter pylori* in tonsillar and adenoid tissue and its possible role in oropharyngeal carcinogenesis. *Folia Biol (Praha)* 54:33–39
7. Unver S, Kubilay U, Sezen OS, Coskuner T (2001) Investigation of *Helicobacter pylori* colonization in adenotonsillectomy specimens by means of the CLO test. *Laryngoscope* 111:2183–2186
8. Koufman JA (1991) The otolaryngologic manifestations of gastroesophageal reflux disease (GERD): a clinical investigation of 225 patients using ambulatory 24-hour pH monitoring and an experimental investigation of the role of acid and pepsin in the development of laryngeal injury. *Laryngoscope* 101:1–78
9. Phipps CD, Wood WE, Gibson WS, Cochran WJ (2000) Gastroesophageal reflux contributing to chronic sinus disease in

- children: a prospective analysis. Arch Otolaryngol Head Neck Surg 126:831–836
10. Suskind DL, Zeringue GP III, Kluka EA, Udall J, Liu DC (2001) Gastroesophageal reflux and pediatric otolaryngologic disease: the role of antireflux surgery. Arch Otolaryngol Head Neck Surg 127:511–514
 11. Contencin P, Maurage C, Ployet MJ, Seid AB, Sinaasappel M (1995) Gastroesophageal reflux and ENT disorders in childhood. Int J Pediatr Otorhinolaryngol 32:135–144
 12. Halstead LA (1999) Role of gastroesophageal reflux in pediatric upper airway disorders. Otolaryngol Head Neck Surg 120:208–214
 13. Richter JE, Bradley LA, DeMeester TR, Wu WC (1992) Normal 24-hr ambulatory esophageal pH values. Influence of study center, pH electrode, age, and gender. Dig Dis Sci 37:849–856
 14. Tunggor G, Midilli R, Yuksekkaya HA, Cakir M, Ozgenc F, Yagci RV (2006) Larengopharyngeal reflux in patients with severe adeno-tonsil hyperplasia. Int J Pediatr Otorhinolaryngol 70:761–762
 15. Eyigor M, Eyigor H, Gultekin B, Aydin N (2009) Detection of *Helicobacter pylori* in adenotonsillar tissue specimens by rapid urease test and polymerase chain reaction. Eur Arch Otorhinolaryngol 266:1611–1613
 16. Jelavic B, Bevanda M, Ostojic M, Leventic M, Vasilj M, Knezovic E (2007) Tonsillar colonization is unlikely to play important role in *Helicobacter pylori* infection in children. Int J Pediatr Otorhinolaryngol 71:585–590
 17. Khademi B, Niknejad N, Gandomi B, Yeganeh F (2007) Comparison of *Helicobacter pylori* colonization on the tonsillar surface versus tonsillar core tissue as determined by the CLO test. Ear Nose Throat J 86:498–501
 18. Cirak MY, Ozdek A, Yilmaz D, Bayiz U, Samim E, Turet S (2003) Detection of *Helicobacter pylori* and its CagA gene in tonsil and adenoid tissues by PCR. Arch Otolaryngol Head Neck Surg 129:1225–1229
 19. Bulut Y, Agacayak A, Karlidag T, Toraman ZA, Yilmaz M (2006) Association of cagA + *Helicobacter pylori* with adenotonsillar hypertrophy. Tohoku J Exp Med 209:229–233
 20. Bitar MA, Soweid A, Mahfouz R, Zaatar G, Fuleihan N (2005) Is *Helicobacter pylori* really present in the adenoids of children? Eur Arch Otorhinolaryngol 262:987–992
 21. Yilmaz M, Kara CO, Kaleli I, Demir M, Tümkaya F, Büke AS, Topuz B (2004) Are tonsils a reservoir for *Helicobacter pylori* infection in children? Int J Pediatr Otorhinolaryngol 68:307–310
 22. Pitkaranta A, Kolho KL, Rautelin H (2005) *Helicobacter pylori* in children who are prone to upper respiratory tract infections. Arch Otolaryngol Head Neck Surg 131:256–258