The correlation between adenoid hypertrophy and chronic otitis media with effusion in children

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THE CORRELATION BETWEEN ADENOID HYPERTROPHY AND CHRONIC OTITIS MEDIA WITH EFFUSION IN CHILDREN

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TABLE OF CONTENTS:

I would like to foremost express my gratitude towards my wonderful mentor, Assist. Prof. Marisa Klančnik, MD, PhD. It was a joy working with her on this symbolic project.

1. INTRODUCTION

Otitis media with effusion (OME) is a disease defined by the persistence of serous or mucous fluid in middle ear without signs of an acute infection (1). It is amongst the most common pediatric diseases, and is the most common cause of hearing loss in children (2). It is pertinent that the medical community continuously adds to its knowledge of this consequential disease. Thus, in order to form a complete standardized approach towards the diagnosis and treatment of OME, its significant risk factors must be elucidated as well.

1.1 Anatomy of the middle ear

The anatomy of the ear is divided into three distinct parts: the external, middle, and inner ear. The middle ear (tympanic cavity) begins at the tympanic membrane, where sound wave vibrations from the external ear are formed into mechanical vibrations, and are transferred into the middle ear, and onto the three present ossicles (*malleus, incus*, and *stapes*) (3). As the mechanical vibrations travel through the ossicles towards the oval window (the entry point of the inner ear), pressure is greatly amplified. This amplification is the primary function of the middle ear, which prevents acoustic energy loss that would have occurred as the sound traveled from the low resistance medium (air) to the high resistance medium (inner ear liquid). In simpler terms, the middle ear prevents "impedance mismatch." The pressure within the cavity must be equalized to that of the normal atmospheric pressure to maintain physiologic functioning and tympanic membrane mobility (4). It is the role of the Eustachian tube, via its connection to the nasopharynx, to ensure a passage way for air and secretions in order to maintain a well ventilated and pressure regulated tympanic cavity. The slight negative pressures in the Eustachian tube encourage flow from the enclosed tympanic cavity towards the nasopharyngeal opening. Additionally, the continuous opening and closing of the tube and its mucociliary clearance enforces the physiological gradient (5). A schematic view of the anatomy of the middle ear is presented in Figure 1.

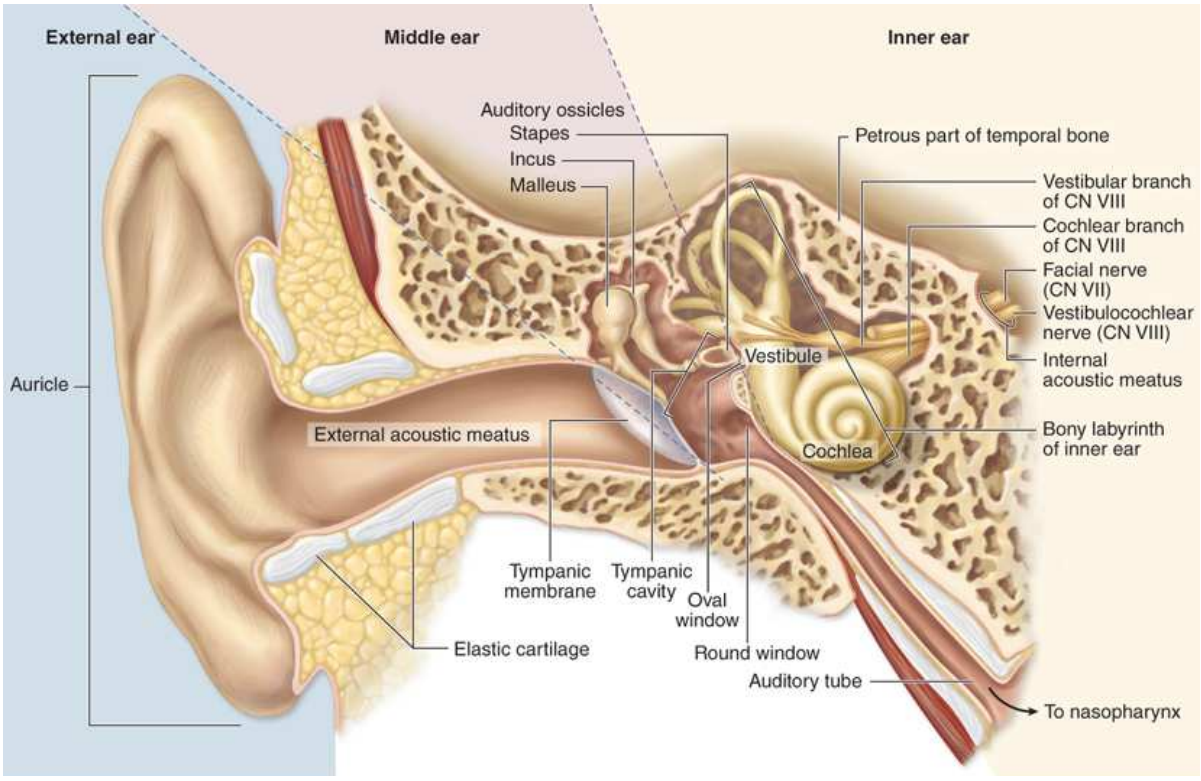


Figure 1. Schematic view of the ear.

Source: Mescher AL. Junqueira's Basic Histology Text & Atlas.14th edition. New York: McGraw-Hill;2016.

1.2 Otitis Media

Otitis media is a collection of middle ear inflammatory diseases which includes acute otitis media (AOM), chronic suppurative otitis media, chronic otitis media epitympanalis (also known as chronic otitis media with cholesteatoma), and otitis media with effusion (OME) (6).

It is estimated that roughly more than 50% of children had a case of OME by their first year, and up to 90% of children by the time they have reached school age (7,8). It is characterized by mucosal hyperplasia and an increase in goblet cells within the epithelial layer. These histologic changes lead to the overproduction of mucoid or serous fluids which accumulate within the middle ear and reduce sound transmission (2). If the ear fluid has lasted for more than three months, it is then diagnosed as chronic OME, and roughly 30-40% of OME cases become as such (1).

AOM, of either bacterial or viral etiology, is presented with ear pain, fever, difficulty sleeping, and an erythematous/bulging tympanic membrane (7). In contrast, OME lacks abrupt inflammatory symptoms, and may go unnoticed as seemingly asymptomatic (9). However, auditory symptoms such as fullness of the ear or hearing troubles may occur (10). Additionally, differences between AOM and OME are noted when observing the tympanic membrane on otoscopy. In AOM, the tympanic membrane generally appears red and bulging outwards, while in OME, it may appear retracted

(caused by the negative pressures) and opacified. Furthermore, in normal conditions, the tympanic membrane moves upon the *valsalva maneuver*, but in cases when OME is present, it remains immobile (7,11). The following three images are of an otoscopic viewing of the tympanic membrane. The first image (Figure 2) is of a normal, healthy tympanic membrane as a thin, semi-translucent membrane with a pearly grey color. Figures 3 and 4 are images are of OME. An evident visualization of fluid behind the tympanic membrane is seen in Figure 3, and air fluid levels are seen in Figure 4.

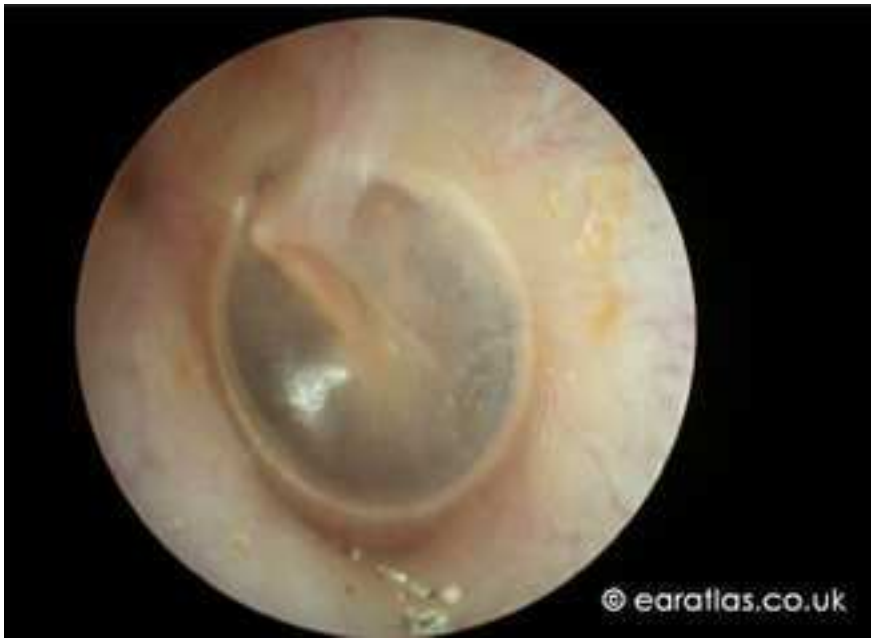


Figure 2. Healthy tympanic membrane
Source: http://www.earatlas.co.uk/1699big.htm

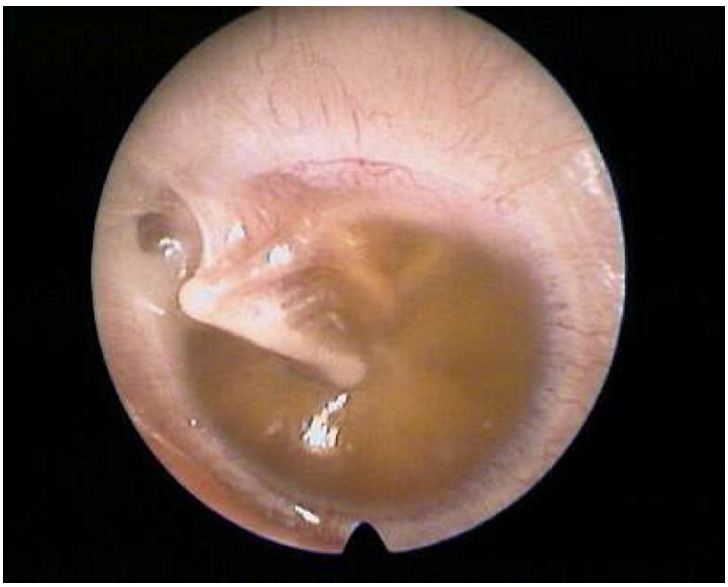


Figure 3. Otoscopic image of otitis media with effusion

Source: Datta D. Otitis Media in Winter: Acute Otitis Media or Otitis Media with Effusion? [internet]. Medicine…Life [updated 2010 Nov 2; cited 2019 Feb 10]. Available from:https://nrsmedic.blogspot.com/2010/11/otitis-media-in-winter-acute-otitis.html.

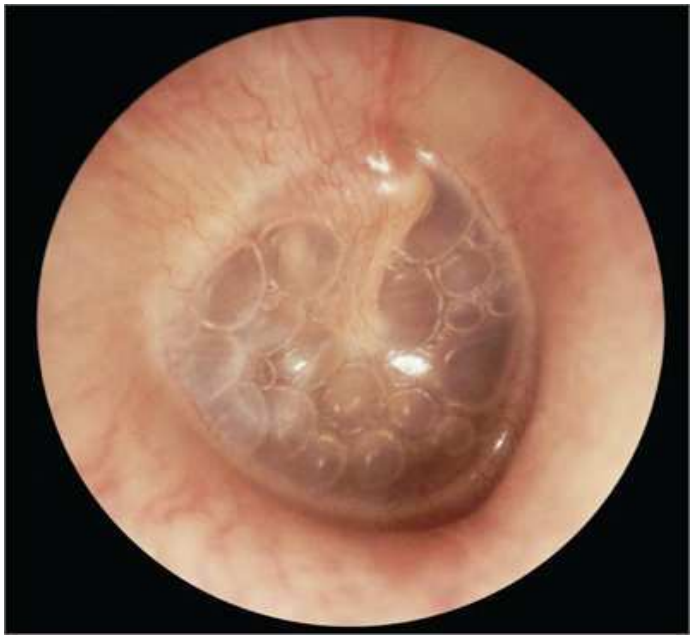


Figure 4. Otoscopic image of otitis media with effusion with air fluid levels

Source: Usatine R, Smith M, Mayeaux EJ, et al, eds. Color Atlas of Family Medicine. 2nd ed. New York, NY: McGraw-Hill; 2013:170-179.

Chronic suppurative otitis media is defined by a continuous inflammatory reaction with suppuration, usually including a perforated tympanic membrane. It most often is a result of a preceding AOM where a perforation occurred. In comparison, OME does not have a persisting acute inflammation, nor is the tympanic membrane injured (12). Cholesteatoma is recognized by the aggregation of keratinized squamous epithelium first grown from the tympanic membrane, and then invading in all directions within the middle ear (13). It may be either a congenital or an acquired disease. In its acquired form, it is also a consequence of a preceding inflammation, whose proliferation was a result of hyperactive mucosal cells. Cholesteatoma also shows to have a continuing inflammation, which, if left untreated, can lead serious adverse affects such as erosion of the middle ear ossicles from the released lytic enzymes (14).

OME is the most common cause of hearing loss in the children that are younger than 12 years old (15). The persisting fluid impairs conductive hearing, diminishing a child's perception in both noisy and quiet environments. The measurable changes range from 18-35dB measured by pure tone audiometry (16). Furthermore, not only is hearing affected, but also the vestibular system, leading to poor balance. All of these conditions lead to poor speech development, intellectual lag, and difficulties in overall school performance (7).

1.3 Eustachian Tube Dysfunction and Adenoid Hypertrophy

1.3.1 Anatomy and pathophysiology of Eustachian tube dysfunction

It is important to recognize the associated risk factors and attributing conditions to aid in the timely diagnosis and treatment of OME. Although the exact pathogenesis is not clearly understood, it has been acknowledged that the etiology is multifactorial. However, two very significant and interrelated factors are identified: adenoid hypertrophy and Eustachian tube dysfunction (17).

As mentioned previously, the Eustachian tube permits pressure equalization in the middle ear via its opening in the nasopharynx. If there are obstructions, patency abnormalities, or poorly function cilia, gasses become absorbed and the physiological pressures become more negative, resulting in the pathognomonic transudate of OME (15).

Additionally, the epidemiology denotes a much higher prevalence amongst children than amongst adult. To explain this epidemiological trend, both anatomical and physiological factors must be discussed. Children, compared to adults, have both a narrower, more horizontally placed Eustachian tube and underdeveloped neuromuscular function. These anatomic differences in children allow for easier infection transference and an inclination towards pressure dysfunction (18). Indeed, up to 35.8% of children have difficulties in pressure equalization, compared to only 5% of adults (19). Younger aged children (3-8 years) also tend to have more difficulties than older children (9-14years)

(18). Thus, OME and age are inversely related. As a person matures, the Eustachian tube function improves, and the incidence of OME declines (19).

1.3.2 Adenoid hypertrophy and risk factors towards its development

It is accepted that adenoid hyperplasia is related to the incidence of OME, potentiated by a chronic obstruction leading to the aforementioned Eustachian tube dysfunction (19). The adenoid, or, the pharyngeal tonsil, is an antibody producing lymphatic tissue located in the superior part of the nasopharynx posteriorly, near the choana and the opening of the Eustachian tube. It, along with the lingual and palatine tonsils, forms the Waldeyer tonsillar ring (20). The adenoid grows during childhood, appearing largest in size in children between ages three and seven, and begins to regress in adolescence (21). The incidence of adenoid hypertrophy (the pathological enlargement of the adenoids) follows the physiological growth and regression patterns of the adenoid (22). However, children younger than seven are prone to more symptomatic effects of enlarged adenoids. This is due to the relatively smaller volume of the nasopharynx and the choanal opening in that age group. Such symptoms may be a nasal sounding voice, difficulty breathing through the nose, night time snoring, and sleep disturbances. Such children rely on breathing through the mouth, thus maintain a constantly ajar mouth for airflow (20). This chronic mouth breathing may later cause cranio-facial deformities and create the facial appearance called "*adenoid facies*," presented as a "long face" with an ajar mouth (23).

The etiology of adenoid hypertrophy itself is not well known, but allergies, upper respiratory infections, and chronic sinusitis have been recognized as preceding factors (20). These recurring infections lead to a hypertrophied and chronically infected adenoid, which then contributes to the pathogenesis of OME. Its influence on the pathogenesis of OME is thus two-fold: it may mechanically obstruct the Eustachian tube and its vegetations may serve as a reservoir for biofilm forming bacteria causing retrograde infections towards the Eustachian tube and the middle ear (24). This biofilm increases bacterial adherence and survival, and decreases response to antibiotic treatment (25). Such biofilm forming bacteria that have been most commonly isolated from the adenoid, and thus in OME, are *Haemophylus influenzae, Streptococcus pneumonia*, and *Moraxella catarrhalis* (24). The local immunity responds to the present pathogens exemplified by a statistically significant increase in T helper cells found within adenoidal tissue of a concomitant OME (26).

There is sufficient evidence to prove that indeed adenoid hypertrophy is an important co-factor in the development of OME. The intention of this article is to delve deeper into the matter, and to further investigate the correlation between the relative sizes of adenoid hypertrophy and the incidence of OME.

Other predisposing risk factors to OME include environmental factors, such as living in lower socioeconomic conditions or exposure to smoke, and genetic factors, such as cleft palate, ciliary dysfunction, and gastroesophageal reflux (19,1). Furthermore, those with a history of allergies have an increased prevalence of OME. Some studies show that up to 59.2% of children with OME have known allergies (1). Studies show that mast cells may be present with an increase in number, whose secretions of histamines and inflammatory mediators influence both adenoid hypertrophy and the mucociliary transport system (27).

1.4 Diagnosis and treatment of OME associated with adenoid hypertrophy

1.4.1 Diagnostic procedures

A thorough history and physical examination is sufficient for an accurate diagnosis of OME. For a non-invasive diagnostic procedure, pneumatic otoscopy and tympanometry are two efficient methods both used to observe changes of movement on the tympanic membrane due to the disturbance within the middle ear. Pneumatic otosocopy requires a physician to blow air onto the tympanic membrane to elicit movement. If fluid is present, as in the case of OME, then the mobility of the tympanic membrane will be compromised (28). Similar results can be attained by asking the patient to elicit the *Valsalva maneuver.* Normally, the membrane should move when this maneuver is performed. However, in cases of OME, an immobile tympanic membrane is visualized (11). Tympanometry is similar to pneumatic otoscopy by the fact that it observes the tympanic membrane movement, but it also quantifies the pressure within the middle ear. It is an objective measurement of compliance of the tympanic membrane and of the middle ear compartment. It involves the administration of varying air pressures (from -400 to +200 daPa) to the external ear canal and measurement of the reflected energy (29).

Tympanocentesis is another diagnostic approach. In contrast to the previously mentioned methods, this is an invasive procedure. It is considered both a diagnostic and a therapeutic method in which a small incision of the tympanic membrane is performed in order to both confirm the presence of fluid and to allow for its drainage (28). Since this is an invasive procedure, it is not the standard method of diagnosis. The gold standard for the diagnosis of OME is a clinical examination and tympanometry (29).

Once the diagnosis of OME is established, then conductive hearing loss can be recorded through pure tone audiometry. A child with normal hearing should not have a hearing threshold above 15dB within the normal speech range. The average hearing loss caused by OME includes a threshold of 25dB, and 20% have above 35dB (28).

1.4.2 Non-surgical interventions

The treatment for OME is categorized into non-surgical or surgical interventions. The non-surgical (or conservative) methods include watchful waiting and medical therapy, and these are the approaches first pursued. Watchful waiting is first used when the diagnosis of OME is established, and is continued normally for the first three months, until the diagnosis is changed to chronic otitis media with effusion (30). During this period of watchful waiting, otoscopy is continued to observe for any color changes, opacifications, retractions of the tympanic membranes, or for fluid levels or air bubbles behind the membrane (6). Watchful waiting is indicated because cases of spontaneous resolutions may occur in the early course of the disease (31). Intranasal steroids may be considered for a period of six weeks in patients with additional allergic rhinitis and adenoid hypertrophy (30). Alternatively, the use of nasal balloon auto-inflation for one to three months could be considered, for studies show that its use reduces the total number of children that require surgical interventions. As the child blows into a specialized balloon through each nostril three times a day, the pressure in the nasopharynx increases and opens the Eustachian tube, which allows for ventilation and drainage of the middle ear (32). Thus, measures that permit middle ear pressure equalization may be considered during the watchful waiting period, which may include the mentioned nasal balloon auto-inflation, or even simpler measures such as chewing gum.

1.4.3 Surgical interventions

A surgical intervention is considered in cases of a persisting OME with hearing loss. Indications includes patients with hearing thresholds of 21-40dB. Any patients with a threshold of over 40dB, the severity of OME has increased to such an extent that it has most likely evolved into a chronic inflammation with adhesions, described as tymapnosclerosis or tympani adhesiva. The surgical interventions include a myringotomy with ventilation tube insertion and an adenoidectomy. Myringotomy is similar to tympanocentesis in its incision of the tympanic membrane, but this procedure additionally inserts a ventilation tube. An image of the inserted tube is found in Figure 5. The ventilation tube is naturally expelled within 9-12 months (31). This procedure has immediate results by decreasing symptoms of hearing loss and aural fullness, and decreases recurrence rates. However, it does not have any affects on long-term outcomes such as speech, language, and Eustachian tube function (31,33).

Adenoidectomy is considered as an important addition to the treatment of OME. According to systematic reviews, resolution rates of OME are significantly higher with the combination of myringotomy with a ventilation tube and adenoidectomy than with myringotomy alone (28).

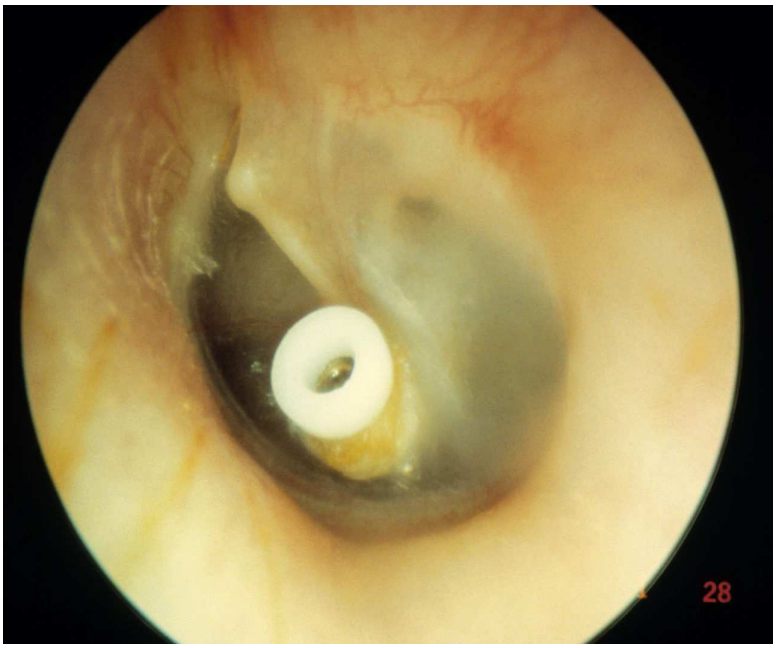


Figure 5. Inserted ventilation tube

Source: Nieto, H, Dearden J, Dale S, Doshi J. Paediatric hearing loss. *BMJ*. 2017;356:j803.

2. OBJECTIVES AND HYPOTHESES

2.1 Objective

The objective of this study is to confirm whether there is a correlation between adenoid hypertrophy and the incidence of otitis media with effusion in children that are of school age or younger. Additionally, this study aims to clarify which age groups are at a greater risk towards having high grade adenoid hypertrophy associated with OME, and which are the most common presenting symptoms among those patients.

2.2 Hypotheses

1. Children that are of school age or younger with higher grade adenoid hypertrophy have an increased incidence of otitis media with effusion.
2. Children younger than 10 years old, compared to those older, are at an increased risk towards having high grade adenoid hypertrophy.
3. The most common presenting factors of adenoid hypertrophy include mouth breathing and nasal obstruction.

3. SUBJECTS AND METHODS

This retrospective study, was performed at the Otorhinolaryngology department of the University Hospital of Split, Croatia between July 2018 and April 2019, and was approved by the hospital's Ethics Committee. This study selected 65 children (37 boys and 28 girls; average age 6 years; range 2-12 years) who had definite indications for an adenoidectomy with a myringotomy with ventilation tube insertion between April 2016 and April 2018.

3.1 Inclusion Criteria

Patients below the age of 13 years old with chronic otitis media with effusion (proven by a B type tympanogram) and with symptoms of adenoid hypertrophy. The children were all initially treated conservatively for 3 months prior to any surgical intervention.

3.2 Exclusion Criteria

Children younger than 2 years old or older than 12 years old were not included. Additionally, those with cleft palate, Down's syndrome, septal deviation, primary ciliary dyskinesia (Kartagener Syndrome), previous head or ear trauma, or previous myringotomy with ventilation tube insertion were excluded from this study.

3.3 Diagnostic and pre-operative tests

Patient data was gathered from pertinent diagnostic and pre-operative tests, and from the surgical database. The initial screening consisted of the standard otolaryngological workup: history, otoscopy, rhinoscopy, and oropharyngoscopy. During the history, focus was put on questioning both the children and their parental figures for any complaints, such as hearing disturbances, difficulty sleeping, nasal obstruction, allergies etc. Diagnostic workup included, tympanometry, audiometry, and flexible nasofiberendoscopy (NFE), accordingly.

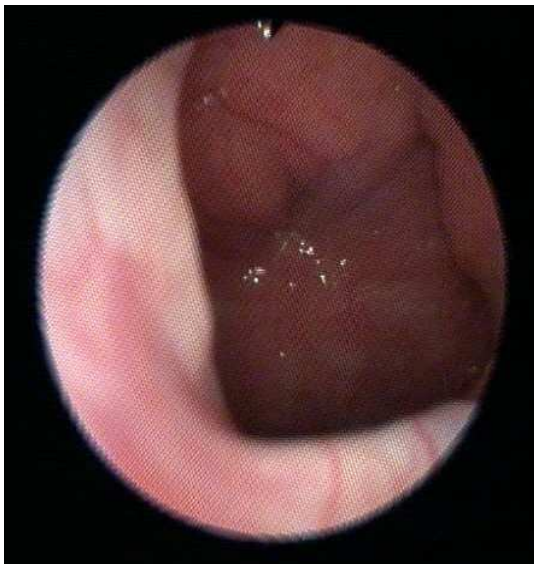
Tympanometry provides critical information about the function and potential pathology of the middle ear system, including presence and quantity of fluid, the degree of middle ear mobility, and the overall volume of the ear canal. Results are recorded as a graphed curvature. Tympanogram type A implies normal middle ear function. A type B (a flattened curve) results when there is fluid present, suggesting OME with a positive predictive value of up to 99%. Finally, a type C tracing indicates presence of a pathologic negative pressure (Eustachian tube dysfunction) (29). The pure tone audiometry test asses hearing loss by recording thresholds (usually 15-20dB for children) across a spectrum of frequencies (500-4,000 Hz; frequencies where speech is audible) (34). In audiometry testing, one of its limiting factors is patient cooperation, in which the patient provides a signal when a tone is heard. Thus, in this study, most children younger than seven years old did not have accompanying audiometry results. Children in that age group do not have enough concentration and

patience for the audiometric test (35). NFE is a trans nasal endoscopic examination, and is the "gold standard" method for diagnosing and quantifying AH. In this study, the degree of AH is recorded according to a subjective adenoid classification, which grades the percentage of choanal opening obstruction by the adenoid. According to literature, this is the recommended classification method. The grading is thus: 1) grade I, adenoid obstructs less than 25% of the choanal opening; 2) grade II, adenoid occupies 25-50% of the choanal opening; 3) grade III, adenoid occupies 50-75% of the choanal opening; 4) grade IV, adenoid obstruction 75-100% of the choanal opening (36). Images of the endoscopic viewings of the grades of AH is seen in the Figure 6. These are original images from the patients used in this study.

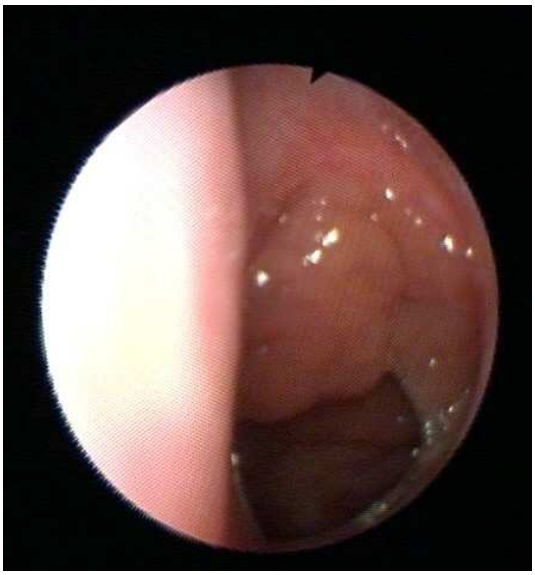
3.4 Statistical Analysis

Data analysis was performed by using the MedCalc 18.2.1 program version (MedCalc Software, Ostend, Belgium). Statistical significance was set to $P < 0.05$. The mean ± SD, median, and ranges were used to describe the numeric variables. In order to analyze any statistical differences between the numeric variables among the study groups, the Kruskal Wallis test was performed. Analysis between two groups was done by the Mann-Whitney U test. Statistical analysis of association of categorical variables was calculated by the chi-square test ($\chi 2$). The chi-square test gave us overall $\chi 2$ and P. The Spearman coefficient correlation rho was also used to measure statistical dependence between two variables.

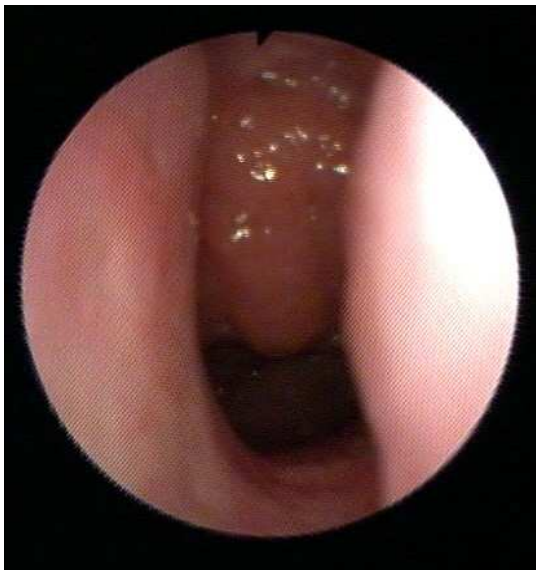
Grade I



Grade II



Grade III



Grade IV

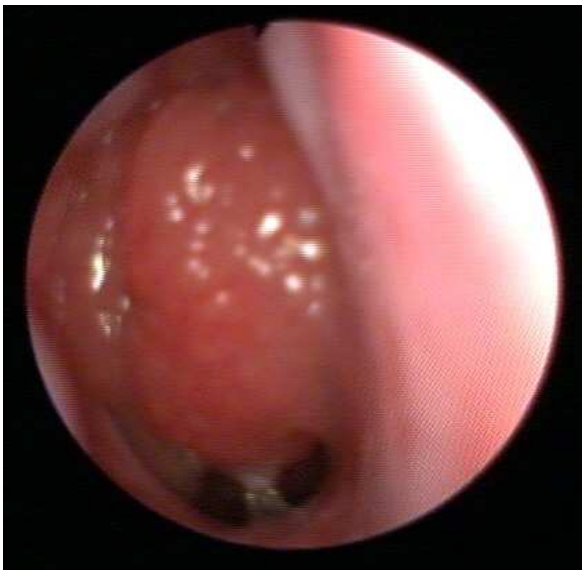


Figure 6. Original images of AH grading I-IV taken from patients used in this study.

4. RESULTS

Sixty-five pediatric patients, who underwent surgery at the University Hospital of Split, from 04/2016 to 04/2018, are included in this study. Their ages ranged from 2-12 years old, average age being 6 years old (Q1-Q3: 4-7 years; min-max: 2-12 years). All of the patients undertook an adenoidectomy and a myringotomy with ventilation tube insertion in both ears. The group included 37 boys with a median age of 5 years old (Q1-Q3: 4-7 years; min-max: 2-12 years), and 28 girls with a median age of 6 years old (Q1-Q3: 4-7 years; min-max: 3-10 years). The boys and girls did not have a statistically significant difference in ages (Z=1.08; P=0.281).

During the clinical examination, otoscopic findings noted the presence of a retracted and opacified tympanic membrane. On tympanometry, all of the patients had B type recordings, and the tonal audiograms showed a conductive hearing loss of 25-35dB. Audiogram results were only available for children aged seven or older.

The pediatric patients were divided into 3 age groups (2-5 years, 6-9 years, and 10-12 years). In Table 1, the age and gender distribution is shown. In the first age group, 32 children were reported (2-5 years), 30 in the second age group (6-9 years), and 3 in the oldest age group (10-12 years) (Table 1). In each age group, the number of males and females was balanced, so no statistical difference was noted ($x2$ = 0.352; P=0.839). The highest incidence of OME with AH occurred in the first and second age groups, with a frequency of 49.23% and 46.15%, respectively (Figure 7).

Table 1. Age and gender distribution of patients. (N=65)

AGE GROUPS (YEARS)	TOTAL	MALE	FEMALE	*P**
2-5	32 (49%)	19 (51%)	13 (46%)	0.839
6-9	30 (46%)	16 (43%)	14 (50%)	
10-12	3 (5%)	2 (2%)	1 (4%)	
TOTAL	65 (100%)	37 (100%)	28 (100%)	

Data are presented as absolute numbers. In parenthesis, data are presented as percentages (%).
*$\chi 2$ test

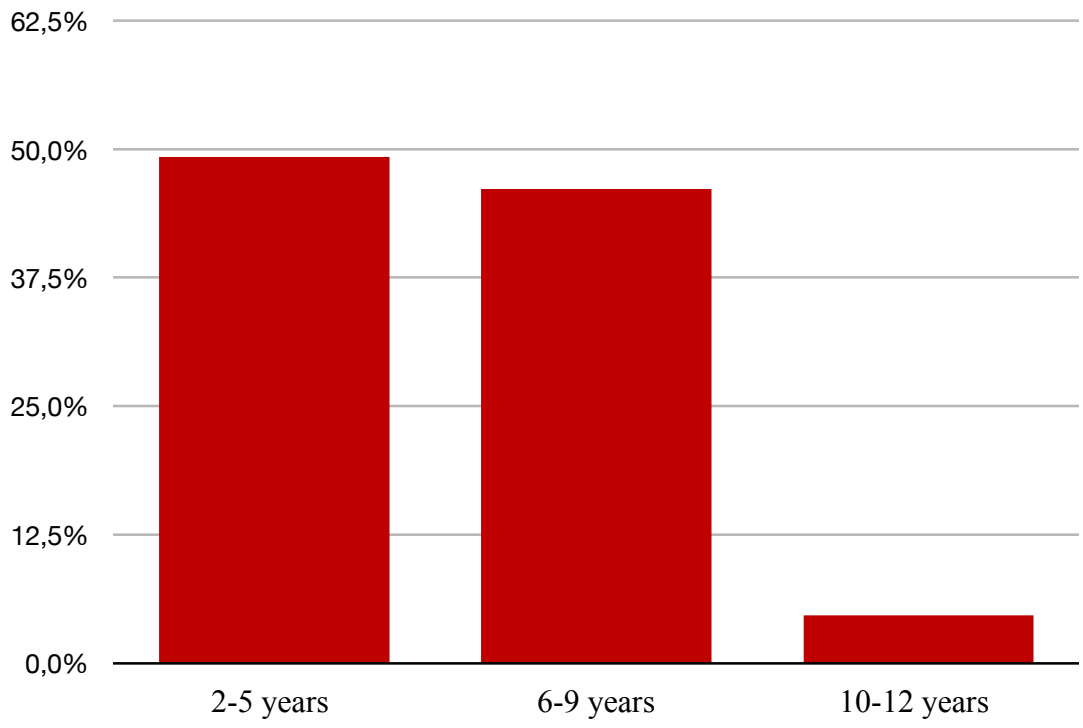


Figure 7. Age distribution

Table 2 shows the distribution of AH grade according to our samples. It is shown that grade I was recorded in 2 patients, which totals to only 3.08% of all measured AH grading. Grade II was recorded 23 tines (35.38%), grade III was recorded 33 times (50.77%), and grade IV was recorded 7 times (10.77%). This shows that the most frequent grades were grades II and III (a total of 84.6%). In order for the distribution to be uniform, the expected number of children per grade would need to be 16. Thus, according to the chi-square analysis, the observed versus expected data resulted in a statistically significant difference ($x2$ =35.9; P<0.001).

Table 2. Grading of adenoid tissue by flexible endoscopy.

Grade	Frequency	Percentage
I	2	3.08%
II	23	35.38%
III	33	50.77%
IV	7	10.77%

Table 3 compares the age groups of the patients to the grade of AH. In the age group 2-5 years, recorded grades from I-IV were 1, 11, 18, and 2, respectively. While in the group 6-9 years, the grades from I-IV were 0, 10, 15, and 5, respectively. Finally, in the age group 10-12, the grades recorded were only 1 patient with grade I, and 2 patients with grade II. According to Spearman's rho coefficient, the correlation between the age groups and the AH grade was not statistically significant (r_s= 0.013; P=0.921). In Table 4, the median ages of the patients (Q1-Q3; min-max) are compared to the grade of adenoid hypertrophy. In the results, no statistical difference was found between the age groups in terms of the grade of AH ($x2$=2.15; P=0.542). When comparing the genders (Figure 8), excluding the groups of 2 patients with grade I AH, there was no statistically significant difference in distribution of grades II, III, and IV between males and females ($x2$=1.45; P=0.484).

Table 3. Relationship between age groups and grade of AH.

AGE GROUPS	GRADE I	GRADE II	GRADE III	GRADE IV	TOTAL
2-5 years	1	11	18	2	32 (49.23%)
6-9 years	0	10	15	5	30 (46.15%)
10-12 years	1	2	0	0	3 (4.62%)
TOTAL	2 (3.08%)	23 (35.38%)	33 (50.77%)	8 (12.31%)	65 (100%)

Data are presented as absolute numbers. In parenthesis, data are presented as percentages (%).

Table 4. Median ages (Q1-Q3; min-max) according to grade.

Grade	Age (years) Median (Q1-Q3; min-max)	*P**
I (n=2)	8 (4 and 12)	0.542
II (n=22)	5.5 (3.7-7; 2-12)	
III (n=33)	5 (4-7; 2-9)	
IV (n=8)	6.5 (5.3-7; 5-7)	

*Kruskal Wallis test.

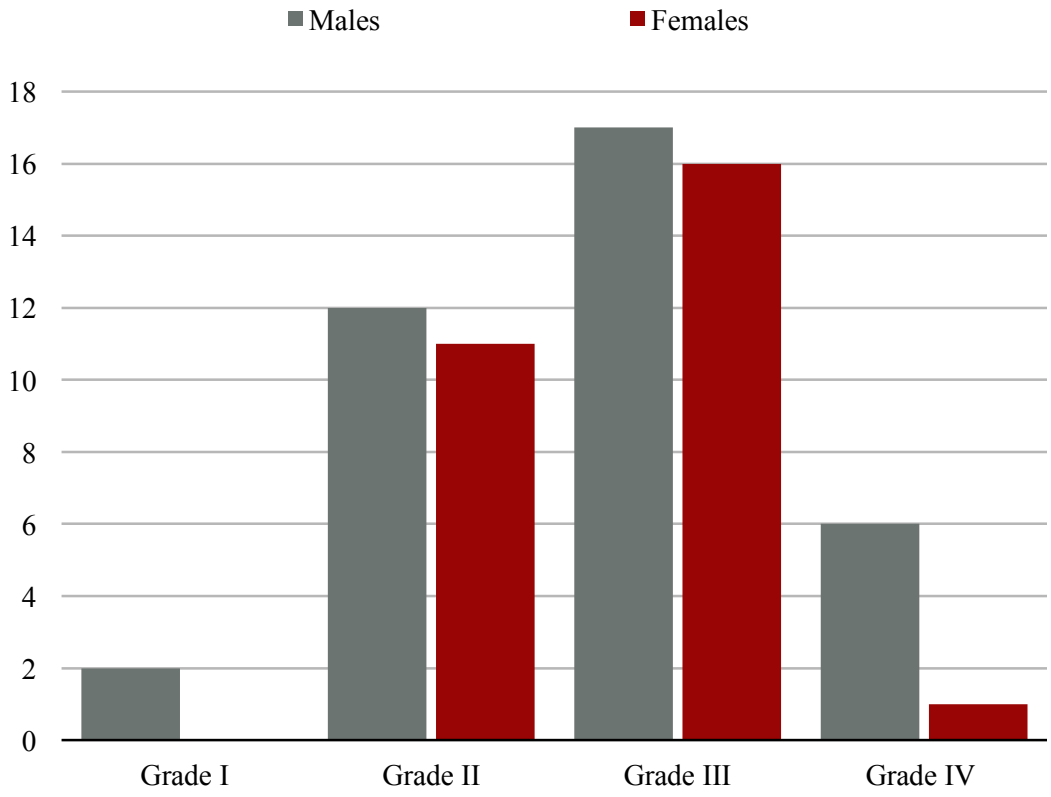


Figure 8. Number of patients found in each grading category.

In respect to the data gathered from the patient histories, all of the patients presented with hearing impairment. Additional to the hearing concerns, the most frequently presenting symptoms of AH were snoring (64.62%), nasal obstruction (60%), and mouth breathing (56.92%) (Table 5). The remaining presenting symptoms reported include: sleep disturbances, voice changes, headache, and epistaxis.

Table 5. Presenting symptoms among the patients with AH. (N=65)

PRESENTING SYMPTOMS	NUMBER	PERCENTAGE
Hearing impairment	65	100%
Mouth breathing	37	56.92%
Nasal obstruction	39	60%
Snoring	42	64.62%
Sleep disturbances	28	43.08%
Voice changes	21	32.31%
Headache	14	21.54%
Epistaxis	8	12.31%

5. DISCUSSION

Otitis media with effusion is a very common childhood disease of the middle ear in which the chronic presence of fluid causes both acute and long term hearing impairments. Therefore, this disease is of considerable interest. This study correlated not only incidence of OME with the level of adenoid hypertrophy, a known risk factor, but also studied which ages were at a higher risk factor, and which were the most common presenting signs.

The results identified that children aged 2-9 years had a higher prevalence of OME than did children in the age group 10-12 years. The first two age groups (group 2-5 years and group 6-9 years) totaled 95.34% of the patient study group, with 49.23% in the first age group and 46.15% in the second. In a similarly conducted study in Kochi, India, which sample included children aged 3-12 years old, its results showed similarly that OME was most prevalent in ages 5-7 years, which included 59.5% of the study sample ($P<0.01$) (15). However, the results of the above mentioned study contrasted in its results of the youngest age group (3-5 years) having a prevalence of only 13.33%, compared to the present study which had a 49.23% prevalence rate. Overall, these statistics show that patients of a younger age distribution are more likely to have OME. These results support the accepted belief that in children the adenoid grows at a faster rate relative to the nasopharyngeal area, thus leading to even a physiological "hypertrophy." This is especially predominant between ages 2 and 5 (37).

Our results did not show a statistically significant difference between the prevalence of OME in males or females ($P=0.281$). This is comparable with the study by Khayat *et al.*, which showed no statistical difference between genders (20). This also correlates with another study conducted by Dewey *et al.,* which concurs with the conclusion that there is no significant difference of OME incidence and gender (38). However, the study conducted by da Costa *et al.*, which used a significantly greater number of cases (4157 patients), concluded that there is indeed a significant increase in prevalence amongst males (37.6%) than amongst females (29.8%) ($P<0.001$) (39). An additional study also concluded a male predominance with a ratio of 7:1 (22). Thus, the significance of gender and incidence cannot yet be ascertained with certainty.

This study observed a statistically significant incidence of patients, who were at the stage of requiring interventional treatment, with adenoid hypertrophy grades II and III. 35.38% of the patients had grade II AH, and 50.77% had grade III AH, totaling a significant 84.6% of all of the patients with OME having a high grade of AH. The observed distribution was in fact statistically different from the expected uniform distribution ($x2 =35.9$; $P<0.001$). This lead to the conclusion that those children with failed conservative treatment for OME, and are thus indicated for an adenoidectomy and myringotomy, are most likely suffering from a grade II or III adenoid hypertrophy. These endoscopic grading classified by the method of Cassano *et al.* indicates an occupation of 25% or more of choanal opening. Those with grade II have 25-50% obstruction, and those with grade III have 50-75%

obstruction (36). It is important to clarify the method of grading classification, because other studies conducted with similar inquiries may have used different classification methods of adenoid hypertrophy. Grading conducted by flexible nasopharyngoscopy (as this study had used) is not only considered more accurate with precise results for levels of adenoid enlargement, but also avoids unnecessary exposure to radiation, an important factor for consideration especially for childhood exposure. However, in cases when endoscopy is unavailable or impractical, then plain radiographs are commonly used as a very reliable substitute (40). Such cases include hospitals which do not have sufficient resources to attain the nasopharyngeal endoscope, or in situations where the child is uncooperative during the invasive diagnostic procedure (37). In the study conducted by Khayat *et al.*, adenoid size was graded by an A/N ratio (adenoidal nasopharyngeal ratio) measured by key distances found on lateral plain X-ray of the nasopharynx. Its results showed 16.7% of cases with grade II (A/N ratio 25-50%) and 54.2% of grade III (A/N ratio 50-75%). These results are fairly similar and concur with the results found in this study. The study by Khayat *et al.* also shows that in patients requiring interventional treatment such as an adenoidectomy, the child is most likely having a higher grade adenoid hypertrophy (20).

Another study more similarly followed the methods of this study by conducting endoscopic grading, but classified the adenoids via a method by Clemens and McMurray. This method compares the enlargement with the vertical height rather than choanal opening area. Grade I indicates adenoid filling a third of the vertical height of the choana. Grade II indicates two thirds height filling, grade III indicates subtotal obstruction, and grade IV is total choanal obstruction. Its results had a majority of patients with grade III AH (15). By Acharya *et al.*, both an endoscopic grading and the Cassano classification was used. This makes that study very similar, and thus an ideal comparison to the present study conducted. Of the 32 patients studied with OME, they found 12 patients with grade III (37.5%) and 13(40.63%) patients with grade IV (41). These results are very similar to the results attained in this study: 35.38% had grade II AH and 50.77% had grade III AH.

All of our patents included in this study presented with hearing impairment, and upon further investigation, conductive hearing loss of 25-35dB was found. This closely relates to statistics found by a recent systematic review conducted in 2017, titled “Hearing loss in children w otitis media with effusion: a systematic review,” which stated that patients with OME have a hearing loss of 18-35dB (16). The other most common presenting signs of AH were mouth breathing (56.92%), nasal obstruction (60%), and snoring (64.62%). The remaining presenting symptoms reported were: sleep disturbances, voice changes, headache, and epistaxis. In a study by Farhad J. Khayat, all of the patients had nasal obstruction, 86% presented with mouth breathing, and 84% had complaints of snoring. These results closely followed our results, but with an increase in overall incidence (42). Additionally, another study also approached our results with manifestations of adenoid hypertrophy

with hearing impairment (58%), mouth breathing (50%), nasal obstruction (50%), and snoring (46.7%) (21). However, in one study, the presenting signs did not seem to correlate with our results, with cough and catarrh being most common signs (73.1% and 69.2%, respectively), and mouth breathing being one of the least common signs (15.4%) (22). Kubba and Bingham concluded in their study that there is no single sign found within the history that could predict the severity of findings on endoscopic evaluations (43).

Thus, although there are different signs that are repeatedly observed in association with adenoid hypertrophy, it can not be concluded here that there exists a specific combination of symptoms that can be used exclusively to diagnose the severity AH. Rather, any practicing physician who encounters a child with any of the above mentioned complaints, he or she must have adenoid hypertrophy added to the differential diagnosis and proceed to further investigations into the matter. Such diagnostic investigations should be conducted by the otorhinolaryngologist, and include a complete clinical examination, including flexible nasopharyngoscopy to establish the grade of AH.

The evidence provided by this study leads to a conclusion that is thus twofold. Firstly, as mentioned above, all physicians must remain alert to any signs and symptoms of adenoid hypertrophy, and must send the child for further workup, including a complete clinical examination by an otorhinolaryngologist for assessment of adenoid hypertrophy. Secondly, if the child is then diagnosed with high grade AH, he or she should undergo audiologic screening assessment for hearing loss caused by a potentially undiagnosed OME. This conclusion is supported by this study which shows that there is a correlation between high grade AH and OME which is at the stage requiring surgical intervention. Today, the protocol involving audiologic screening includes only newborns, preschoolers, and the elderly. There is no screening protocol for children who are in fact in the age groups with the highest risk factor for hearing difficulties resulting from undiagnosed OME. A screening program is crucial so that timely treatment could be commenced, decreasing the child's risk towards permanent hearing loss, chronic inflammation with adhesions, poor speech development, intellectual lag, and difficulties in communication and socialization. Thus, through a simple screening method provided to those children with discovered high grade AH, a world of a difference can be made.

Limitations to this study must be considered when interpreting and applying the conclusion. Firstly, this retrospective study did not include a control group, which would have consisted of patients with adenoid hypertrophy, but without otitis media with effusion. This control group would have allowed for better comparison for the strength of the correlation of AH with OME. However, insufficient data was available, so it was not feasible to allocate patients into a control group. Additionally, another limiting factor to this study is the fact that it included only patients with otitis media with effusion already the phase in which surgical treatment was required. This simply means

that conclusion drawn is specifically related to this subpopulation. If the study included non-surgical cases of OME too, then the study's conclusion could have been used to interpret a wider group of patients. Finally, a third limitation to be mentioned is the fact that only endoscopic viewing of the nasopharynx was performed, without having performed a confirmatory X-ray viewing in order to asses the result's accuracy. Although in daily practice either one or the other visualization approach is used, in research, both methods should be used in order to confirm grading accuracy. Additional research is recommended to include these three factor which were omitted in this study.

6. CONCLUSION

- According to these results, we conclude that the size of the adenoid hypertrophy is critical in the development of OME, and that children with a higher grade of AH have a higher risk towards its development.
- This study conclusively shows that the most common grade encountered was grade II and III. This leads to the conclusion that any child who has failed conservative treatment, and is requiring interventional treatment, is most likely suffering from a higher grade of adenoid hypertrophy.
- The results concluded that there is neither a statistically significant difference between genders in all age groups, nor between age groups and the grade of AH. Thus, all children aged between 2-12 years old with any level of AH may risk development of OME.
- The most common presenting symptoms of AH were established, including hearing impairment, snoring, nasal obstruction, and mouth breathing, accordingly.

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8. SUMMARY

Objectives: The purpose of this study is to confirm whether there is a correlation between adenoid hypertrophy and the incidence of otitis media with effusion in children that are of school age or younger. Additionally, this study aims to clarify which age groups are at greater risk in having high grade adenoid hypertrophy associated with otitis media with effusion, and which are the most common presenting symptoms among those patients.

Methods: Sixty- five patients aged 2-12 years old were included, and were placed into three groups according to age (2-5, 6-9, and 10-12). All of the patients were diagnosed with OME and were treated surgically (myringotomy with ventilation tube insertion and an adenoidectomy). Each patient had undergone pre-operative diagnostic procedures, including a detailed hetero-anamnesis and a clinical examination (otoscopy, rhinoscopy, and oropharyngoscopy). The diagnostic examinations included flexible nasofiberendoscopy of the nasopharynx and audiologic evaluations, including tympanometry and tonal audiometry.

Results: There was an observed statistically significant incidence of patients with grades II and III grades of AH ($P<0.001$). Additionally, this study shows that there is neither a statistical significant difference between number of patients according to their gender, nor between the age of the patient and the grade of AH. Additionally, there is no significant difference between the distribution of grade II, III and IV of AH and the gender groups. The most common presenting symptoms include hearing impairment, snoring, and nasal obstruction.

Conclusion: Children with a higher grade of adenoid hypertrophy have a larger risk towards the development of otitis media with effusion. Additionally, it is conclusive that a child who has failed conservative treatment for OME, and is indicated to surgical interventions, a grade of II or III AH is expected. All children who portray the listed presenting symptoms of AH should undergo a detailed workup and should be consulted by an otolaryngologist for a complete clinical examination and audiologic evaluation.

9. CROATIAN SUMMARY

Naslov: KORELACIJA IZMEĐU VELIČINE ADENOIDNIH VEGETACIJA I KRONIČNE UPALE SREDNJEG UHA S IZLJEVOM U DJECE

Ciljevi: Cilj rada je ispitati povezanost veličine adenoidnih vegetacija i kronične upale srednjeg uha s izljevom, potom ispitati u kojoj dobnoj skupini djece s ovom bolesti je najveća prosječna veličina adenoidnih vegetacija te koji su najčešći prezentirajući simptomi od povećanih adenoidnih vegetacija.

Metode: U istraživanje je uključeno šezdeset petero djece između 2 i 12 godina koja su podijeljena u 3 dobne skupine (2-5, 6-9 i 10-12 godina) s dijagnozom kronične upale srednjeg uha s izljevom, koja su podvrgnuta operativnom zahvatu postavljanja aerizacijskih cjevčica i adenoidektomiji. Svoj djeci je urađena preoperativna dijagnostika koja uključuje detaljnu heteroanamnezu, klinički pregled koji uključuje otoskopiju, rinoskopiju, orofaringoskopiju te dijagnostičke pretrage koje uključuju fiberendoskopiju epifarinksa i audiološku obradu– timpanometriju i tonalnu audimetriju.

Rezultati: Rezultati rada pokazuju da su najčešći gradusi AH II i III (P<0.001). Rezultati pokazuju da nema statistički značajne razlike u broju dječaka i djevojčica u svim dobnim skupinama. Nema statistički značajne razlike životne dobi djece u odnosu na gradus AH. Također nema statistički značajne razlike u distribuciji gradusa AH II, III i IV između dječaka i djevojčica isključujući skupinu gradusa 1 koju sačinjavaju samo dvoje djece. Najčešći prezentirajući simptomi su gubitak sluha, noćno hrkanje i otežano disanje na nos.

Zaključak: Zaključujemo da djeca s većim gradusom adenoidne hipertrofije imaju veću mogućnost za nastajanje kronične upale srednjeg uha s izljevom. Zaključujemo da za svako dijete koje je neuspješno završilo konzervativnu terapiju ove bolesti i mora ići na operaciju ugradnje aerizacijskih cjevčica i adenoidektomiju, očekujemo gradus II ili III AH. Također, sva djeca koji imaju prezentirajuće simptome AH trebaju se dalje obraditi i uputiti otorinolaringologu zbog kompletnog kliničkog pregleda i audiološke obrade.

10. CURRICULUM VITAE

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