

RESEARCH
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Fatih Alper Akcan¹
Abdullah Belada¹

¹Duzce University Faculty of
Medicine, Department of
Otorhinolaryngology, Duzce,
Turkey

Corresponding Author:

Fatih Alper Akcan
Duzce University Faculty of
Medicine, Department of
Otorhinolaryngology, Duzce,
Turkey
Phone: +90 505 7671113
mail: f.akcan@yahoo.com

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konuralptipdergi@duzce.edu.tr
konuralptipdergisi@gmail.com
www.konuralptipdergi.duzce.edu.tr

Investigation of Risk Factors for Otitis Media With Effusion in Patients with Adenotonsillar Hypertrophy (Risk Assessment in Otitis Media with Effusion)

ABSTRACT

Objective: Sleep Disordered Breathing (USB) is one of the most common childhood disorders ranging from simple snoring to obstructive sleep apnea (OSA), and most common cause of it is the adenotonsillar hypertrophy (ATH). Otitis Media with Effusion (OME) is another important problem in children with USB due to ATH. The aim of this study was to evaluate the possible risk factors for the development of EOM in children with USB due to ATH.

Methods: 171 pediatric patients with ATH-related snoring and sleep apnea complaints were included in the study. The patients were divided into two groups. Group 1: patients with ATH + OME and Group 2: patients with ATH alone. A pre-operative standard questionnaire was used to assess USB severity. Twenty-one different parameters were evaluated for both groups.

Results: Age, sex, exposure to tobacco smoke, cow milk exposure before 12 months, breast milk only for at least 6 months, duration of symptoms, USB symptom scores, history of recurrent tonsillitis, adenoid / nasopharynx (AN) ratio, tonsil size, body mass index (BMI), hemoglobin (Hb) level, hematocrit (Hct) ratio, mean platelet volume (MPV), eosinophil ratio, neutrophil-lymphocyte ratio (NLR), thyroid function tests (TSH, fT4), folate and vitamin B12 levels were evaluated. There was no statistically significant difference between these parameters except BMI. BMI values were 16.08 ± 1.96 in Group 1 and 17.11 ± 2.81 in Group 2, respectively (p: 0.006).

Conclusions: Many different parameters were evaluated for EOM, a multifactorial disease. Among the groups, only BMI was different. Further study is required to identify risk factors for the development of EOM in patients with ATH.

Keywords: Sleep Disordered Breathing, Snoring, Otitis Media With Effusion, Adenotonsillar Hypertrophy, Pediatric.

Adenotonsiller Hipertrofi Hastalarda Efüzyonlu Otitis Media İçin Risk Faktörlerinin Araştırılması (Efüzyonlu Otitis Media'da Risk Değerlendirmesi)

ÖZET

Amaç: Uykuda Solunum Bozukluğu (USB), basit horlamadan obstrüktif uyku apnesine (OSA) kadar uzanan en yaygın çocukluk çağı bozukluklarından biridir ve bunun da en önemli sebepleri arasında ilk sırada adenotonsiller hipertrofi (ATH) gelmektedir. ATH'ye bağlı USB'li çocuklarda karşılaşılan bir diğer önemli sorun ise Efüzyonlu Otitis Media'dır (EOM). Bu çalışmanın amacı, ATH nedeniyle USB olan çocuklarda EOM'nin gelişimindeki olası risk faktörlerini değerlendirmektir.

Gereç ve Yöntem: ATH'ye bağlı horlama ve uyku apnesi şikayetleri olan 171 pediatrik hasta çalışmaya dahil edildi. Hastalar iki gruba ayrıldı. Grup 1: tek başına ATH olanlar ve Grup 2: ATH + EOM olan hastalar. USB şiddetini değerlendirmek için pre-operatif olarak standart bir anket kullanıldı. Her iki grup için yirmi bir farklı parametre değerlendirildi.

Bulgular: Yaş, cinsiyet, tütün dumanına maruz kalma, 12 aydan önce inek sütü maruziyeti, en az 6 ay sadece anne sütü, semptomların süresi, USB semptom skorları, tekrarlayan tonsillit öyküsü, adenoid/nazofarenks (AN) oranı, tonsil büyüklüğü, vücut kitle indeksi (VKİ), hemoglobin (Hb) düzeyi, hematokrit (Hct) oranı, ortalama trombosit hacmi (MPV), eozinofil oranı, nötrofil-lenfosit oranı (NLO), tiroid fonksiyon testleri (TSH, fT4), folat ve B12 vitamini düzeyleri değerlendirildi. VKİ dışında bu parametreler arasında istatistiksel olarak fark yoktu. VKİ değerleri Grup 1'de 16.08 ± 1.96 ve Grup 2'de sırasıyla 17.11 ± 2.81 idi (p: 0.006).

Sonuç: Multifaktöriyel bir hastalık olan EOM için pek çok farklı parametre değerlendirildi. Gruplar arasında sadece VKİ farklı olarak tespit edildi. ATH hastalarında EOM gelişimi açısından risk faktörlerini tanımlamak için daha fazla çalışma gereklidir.

Anahtar Kelimeler: Uykuda Solunum Bozukluğu, Horlama, Efüzyonlu Otitis Media, Adenotonsiller Hipertrofi, Pediatrik.

INTRODUCTION

Sleep-disordered breathing (SDB) is one of the most common childhood disorders, from simple snoring to obstructive sleep apnea (OSA) (1). Approximately 2-3% of children are affected by SDB, which can lead to behavioral, cognitive, and growth abnormalities (1,2). The most common cause of SDB in childhood is upper respiratory tract obstruction due to adeno-tonsillar hypertrophy (ATH).

Another important problem encountered in children with ATH-related USB is otitis media with effusion (OME). OME is an inflammatory condition in the middle ear with no signs and symptoms of acute infection (3). It has been reported that this condition affects 90% of children up to the age of 4 years (3,4). The etiology of EMO is multi-factorial, but the main cause is Eustachian tube dysfunction (ED) (5). Inflammatory processes such as atopy and especially upper respiratory tract infections (URIs) can cause ED. The prevalence of EOM was 5.3% to 9% in different countries (6,7).

Several risk factors have been identified in patients with OME, including daily care, allergic rhinitis, and tobacco smoke exposure (8).

The aim of this study is to evaluate the risk factors in the development of EMO in children with SDB due to ATH.

MATERIAL AND METHODS

This study was conducted in Düzce Faculty of Medicine, Department of Otorhinolaryngology between February 2017 and August 2018. The study was conducted in accordance with the Helsinki Declaration Principles and informed consent was obtained from all cases included in the study together with the ethics committee approval (2018-158). One hundred and seventy three pediatric patients included in the study had snoring and sleep apnea complaints due to ATH. The patients with ATH with nasopharyngeal and oropharyngeal obstruction were evaluated by flexible fiber optic endoscopy and direct observation. Patients were determined to have additional systemic diseases like asthma, allergic rhinitis, chronic rhinosinusitis, etc or not. Adenoid size was graded as grade 1–4 by flexible fiber optic endoscopy (Carl Storz, 2.4 mm) according to the adenoid / nasopharyngeal ratio (9). The tonsil grading scale was graded as: Grade 1, tonsils are only visible in the tonsillar fossa; Grade 2, tonsils can be seen out of the tonsillar fossa; Grade 3, tonsils elongating three-quarters of the midline; and Grade 4, tonsils greater than grade 3 according to the size of the tonsils for (10).

A standard questionnaire was used pre-operatively for SDB; Mouth breathing during sleep, daytime mouth breathing, apnea, snoring, cough, runny nose and restless sleep. Scoring, for each of

the above; 0: never, 1: in the meantime, 2: often, and 3: always (11,12). The patients were divided into 3 subgroups according to this questionnaire score; mild: 1-7, moderate: 8-14 and severe: 15-21.

The patients were divided into two groups: those with ATH + OME (Group 1) and those with only ATH (Group 2). All patients underwent adenoidectomy / adenotonsillectomy under general anesthesia for SDB. A ventilation tube was also applied to patients who had OME before the operation. Twenty-one different parameters (laboratory and physical findings) were evaluated for both groups. Age, gender, tobacco smoke exposure, cow milk exposure before 12 months, exclusive breast milk for at least 6 months, duration of symptoms, SDB symptom scores, recurrent tonsillitis history, adenoid / nasopharynx (A / N) ratio, tonsil grade, body mass index (BMI), hemoglobin (Hb) level, hematocrit (Hct) ratio, mean platelet volume (MPV), eosinophil ratio, neutrophil-lymphocyte ratio (NLR), thyroid function tests (TSH, fT4), folate and vitamin B12 levels were evaluated.

The patients with additional systemic diseases like cranio-facial malformation, asthma, allergic rhinitis, chronic rhino-sinusitis etc. and those who had undergone previous adenotonsil surgery and a history of ventilation tube were excluded from the study.

Independent variables were made with the t test or the Mann-Whitney U test. Individual variables were analyzed using the Pearson chi-square test. The statistical analyzes were made with SPSS v.22 package program and the level of significance was set at 0.05.

RESULTS

During the study, a total of 171 patients were evaluated. There were 62 patients in Group 1 and 109 patients in Group 2. The mean age of the groups was 5.00 ± 2.22 and 5.71 ± 2.83 , respectively, and there was no significant difference ($p = 0.093$). There was no significant difference between the groups in terms of gender, exposure to tobacco smoke, cow milk exposure before 12 months, only breast milk for at least 6 months, duration of symptoms, SD symptom scores, and recurrent tonsillitis history. The demographic distributions of the groups are summarized in Table 1. AN ratio, tonsil size, BMI, Hb level, Hct ratio, MPV, eosinophil ratio, NLR, thyroid function tests (TSH, fT4), folate and vitamin B12 levels were evaluated. There was no statistically significant difference between these parameters except BMI. BMI values were 16.08 ± 1.96 in Group 1 and 17.11 ± 2.81 in Group 1, respectively ($p: 0.006$). Physical examination and laboratory parameters are summarized in Table 2.

Table 1. Features of demographic of groups of study and control. İstatistical level of meaningfulness is accepted value of $p= 0.05$

Variables	Group 1 n=62	Group 2 n=109	P value
Age	5.00±2.22	5.71±2.83	0.093
Median value (min-max)	2 (0-4)	2 (1-4)	0.641
Sex			
Man	29 (%46.8)	56 (%51.4)	0.563
Woman	33 (%53.2)	53 (%48.6)	
Exposed of cigarette smoke			
Yes	24 (%38.7)	47 (%43.1)	0.574
No	38 (%61.3)	62 (%56.9)	
Use of cow milk before 1 age	19 (%30.6)	41 (%37.6)	0.359
Breastfeed just first 6 month	35 (%56.5)	72 (%66.1)	0.212
Time of mean symptom (month)	12 (1-60)	24 (2-84)	0.111
Score of symptom:			
• 1-7	1 (%1.6)	6 (%5.5)	0.234
• 8-14	27 (%43.5)	56 (%51.4)	
• 15-21	34 (%54.8)	47 (%43.1)	
Frequency of recurrence tonsillit	7 (%11.3)	13 (%11.9)	0.901

Table 2. Finding of laboratory and physical of groups of study and control.

Variable	Group 1 n=62	Group 2 n=109	P value
A/N ratio			
0-25%	0 (%0.0)	4 (%3.7)	0.229
25-50%	1 (%1.6)	5 (%4.6)	
50-75%	22 (%35.5)	45 (%41.3)	
75-100%	39 (%62.9)	55 (%50.5)	
Degree of tonsil			
1	27 (%43.5)	43 (%39.4)	0.561
2	28 (%45.2)	45 (%41.3)	
3	7 (%11.3)	19 (%17.4)	
4	0 (%0.0)	2 (%1.8)	
BMI	16.08±1.96	17.11 ± 2.81	0.006
Hemoglobin g/dL	12.64±1.56	12.99±1.01	0.069
Hct %	37.20±3.82	37.98±2.75	0.125
MPV	7.31±0.82	7.50±0.67	0.102
N/L ratio	51.52±13.38	49.90±11.99	0.417
Median ratio of Eosinofil (min-max)	1.65 (0-10.9)	1.90 (0-9.7)	0.336
TSH	2.66±1.45	2.79±1.80	0.624
fT4 median (min-max)	1.06 (1-14)	1.05 (1-11)	0.936
Folate	12.58±4.51	12.94±4.42	0.613
Vitamin B ₁₂	416.06±165.10	381.67±171.47	0.203

A / N ratio: Adenoid / Nazofarenks ratio. BMI: Body Max İndex. Hct: Hematokrit. MPV: Mean Platelet Volume Hacmi. N / L: Nötrofil / Lenfosit ratio. TSH: Tiroid stimulation hormon. fT4: Free T4. İstatistical level of meaningfulness is accepted value of $p= 0.05$.

DISCUSSION

OME is an important health problem affecting the quality of life of children. Although it varies according to the method applied and the regions reported, it is generally seen in young age groups (13). OME prevalence of primary school

children was 7.6% in a study conducted in Turkey (14). Recent studies have shown that ATH is an important risk factor for OME. However, since not every child with ATH has OEM, the results are discussed below in the context of our findings,

along with previous studies examining additional risk factors.

Age is suggested to be one of the most important factors in the development of OME. Zielhuis et al. (15) suggested that the disease peaked at the age of 2 and 5 years. In our study, it was observed that there was no significant difference between the groups and the average age was around 5 in both groups.

In terms of gender; the majority of patients in both the ATH and ATH + OME groups were male. In other studies (4,16). However, studies are available showing that otitis media predominantly affects females (17). In our study, although the rate of women in the OME group was high, the difference was not significant.

Feeding with breast milk is considered to protect newborns from various diseases such as lower respiratory tract infections, nonspecific gastroenteritis, acute otitis media, atopic dermatitis, asthma (young children), obesity, type 1 and 2 diabetes, childhood leukemias, sudden infant death syndrome and necrotizing enterocolitis (18). Although some studies (16,18) found that longer breastfeeding was associated with a lower risk of OME, in our study and others (13,19–21) there was no association between breastfeeding and OME. However, Ip et al. (18) showed that there is a significant difference in the development of OME depending on the duration of breastfeeding.

Some studies have found a relationship between home smoking, particularly parental smoking, and OME (16,22). In our study, no relationship was shown between exposure to tobacco smoke and OME.

When data were evaluated with regard to the size of the adenoid and tonsil; Eliçora et al. (23) showed that there was no difference in OME between patient populations with adenoid size of 75% (Stage 3) and 100% (Stage 4). In our study, all stages were evaluated, but it was observed that there was no difference between the groups in terms of OME. Again, when evaluated according to the size of the tonsil and the history of recurrent tonsillitis, no association was found with OME.

REFERENCES

1. Lumeng JC, Chervin RD. Epidemiology of pediatric obstructive sleep apnea. *Proc Am Thorac Soc* 2008; 15:242-252.
2. Schlaud M, Urschitz MS, Urschitz-Duprat PM, Poets CF. The German study on sleep-disordered breathing in primary school children: epidemiological approach, representativeness of study sample, and preliminary screening results. *Pediatr Perinat Epidemiol* 2004; 18:431-440
3. Tos M. Epidemiology and natural history of secretory otitis. *Am J Otol* 1984; 5:459-462.
4. Teele DW, Klein JO, Rosner B, et al. Epidemiology of otitis media during the first seven years of life in children in greater Boston: a prospective, cohort study. *J Infect Dis* 1989;160:83-94.
5. Ryding M, White P, Kalm O. Eustachian tube function and tympanic membrane findings after chronic secretory otitis media. *Int J Pediatr Otorhinolaryngol* 68 (2004) 197–204.
6. Tong MC, Yue V, Ku PK, Lo PS, van Hasselt CA. Screening for otitis media with effusion to measure its prevalence in Chinese children in Hong Kong. *Ear Nose Throat J* 79 (2000) 626–629.

Neutrophil / lymphocyte ratio is the inflammatory parameter that has been defined in recent years and can be easily calculated from peripheral blood analysis. High NLR correlates with the severity of inflammation. Studies have found higher NLR in OME patients compared to the control group (24,25). However, in our study, no significant difference was observed between the groups.

Mean platelet volume (MPV) acts as an indicator of platelet activation. Large platelets with denser granules are more enzymatically and metabolically active. Increased platelet activation plays an important role in the development of inflammation, and platelets have been found to significantly contribute to chronic inflammation and MPV can be used as a marker of inflammatory disease (26,27). Although Somuk et al. (28) found the MPV value in OME patients to be borderline higher than the control group in their study, the results were statistically insignificant. In our study, MPV values were similar in the study and control groups.

Studies have been investigating the relationship between obesity and EOM in recent years [30-33]. Although it was stated in these studies that childhood obesity may be associated with the presence or development of otitis media with effusion, in contrast to these, BMI was found to be lower in the study group in our study ($p = 0.006$). Although our study is the first study evaluating thyroid function tests, vitamin B12 and folate levels with regard to the relationship with OME, no significant difference was found between the groups in terms of these parameters.

CONCLUSION

Epidemiologic, familial, and environmental factors all appear to play a role in the pathogenesis of OME to some extent, and few can be significantly changed to prevent or cure the disease. In our study, only the BMI was found to be different among groups. More studies are needed to identify the risk factors for developing OME in patients with sleep-disordered breathing due to ATH.

7. Wang Z, Chen P, Xu Z, Wei Y, Hu Y, Zhang B et al. The prevalence of otitis media with effusion of kindergarten children in Wuhan city. *Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi* 23 (2009) 1036–1037, 1043.
8. Daly KA, Giebink GS. Clinical epidemiology of otitis media, *Pediatr. Infect. Dis. J.* 19 (Suppl. 5) (2000) 31–36.
9. Parikh SR, Coronel M, Lee JJ, Brown SM. Validation of a new grading system for endoscopic examination of adenoid hypertrophy. *Otolaryngol Head Neck Surg* 2006;135(5):684–687.
10. Brodsky L. Modern assessment of tonsils and adenoids, *Pediatr. Clin. North Am.* 36 (6) (1989) 1551–1569.
11. Sharifkashani S, Dabirmoghaddam P, Kheirkhah M, Hosseinzadehnik R. A new clinical scoring system for adenoid hypertrophy in children. *Iran J Otorhinolaryngol.* 2015; 27: 55-61
12. Bitar MA, Rahi A, Khalifeh M, Madana LMS. A suggested clinical score to predict the severity of adenoid obstruction in children. *Eur Arch Otorhinolaryngol* 2006; 263:924–928
13. Martines F, Bentivegna D, Maira E, Sciacca V, Martines E. Risk factors for otitis media with effusion: case–control study in Sicilian school children, *Int. J. Pediatr. Otorhinolaryngol.* 75 (2011) 754–759.
14. Okur E, Yildirim I, Kilic MA, Guzelsoy S. Prevalence of otitis media with effusion among primary school children in Kahramanmaraş, in Turkey, *Int. J. Pediatr. Otorhinolaryngol.* 68 (5) (2004) 557–562.
15. Zielhuis GA, Rach GH, Den Bosch V, Den Broek V. The prevalence of otitis media with effusion: a critical review of the literature, *Clin. Otolaryngol.* 15 (1990) 283–288.
16. Apostolopoulos K, Xenelis J, Tzagaroulakis A, Kandiloros D, Yiotakis J, Papafragou K. The point prevalence of otitis media with effusion among school children in Greece, *Int. J. Pediatr. Otorhinolaryngol.* 44 (3) (1998) 207–214.
17. Saim A, Saim L, Saim S, Ruzzymah BH, Sani A. Prevalence of otitis media with effusion amongst pre-school children in Malaysia, *Int. J. Pediatr. Otorhinolaryngol.* 41 (1997) 21–28.
18. Ip S, Chung M, Raman G, et al. Breastfeeding and maternal and infant health outcomes in developed countries, *Evid. Rep. Technol. Assess. (Full Rep)* 153 (2007) 1–186.
19. Bailie R, Stevens M, McDonald E, Brewster D, Guthridge S. Exploring cross-sectional associations between common childhood illness, housing and social conditions in remote Australian Aboriginal communities, *BMC Public Health* 10 (2010) 147.
20. Zielhuis GA, Heuvelmans-Heinen EW, Rach GH, Van den Broek P. Environmental risk factors for otitis media with effusion in preschool children, *Scand. J. Prim. Health Care* 7 (1989) 33–38.
21. Kraemer MJ, Richardson ME, Weiss NS, Furukawa CT, Shapiro GG, Pierson WE, et al. Risk factors for persistent middle ear effusions, *JAMA* 249 (1983) 1022–1045.
22. Iversen M, Birch LM, Lundqvist GR, Elbrond O. Middle ear effusion in children and the indoor environment: an epidemiological study, *Arch. Environ. Health* 40 (1985) 74–79.
23. Eliçora SŞ, Öztürk M, Sevinç R, Derin S, Dinç AE, Erdem D. Risk factors for otitis media effusion in children who have adenoid hypertrophy. *Int J Pediatr Otorhinolaryngol.* 2015 Mar;79(3):374-7.
24. Kum RO, Ozcan M, Baklaci D, et al. Investigation of neutrophil-to-lymphocyte ratio and mean platelet volume in sudden hearing loss. *Braz J Otorhinolaryngol* 2015;81:636–641.
25. Atan D, Apaydin E, Özcan KM, et al. New diagnostic indicators in chronic otitis media with effusion: neutrophil to lymphocyte ratio and thrombocyte lymphocyte ratio. *ENT Updates* 2016;6:12–15.
26. Endler G, Klimesch A, Sunder-Plassmann H, Schillinger M, Exner M, Mannhalter C. Mean platelet volume is an independent risk factor for myocardial infarction but not for coronary artery disease, *Br. J. Haematol.* 117 (2002) 399–404.
27. Mimidis K, Papadopoulos V, Kotsianidis J, Filippou D, Spanoudakis E, Bourikas G. Alterations of platelet function, number and indexes during acute pancreatitis, *Pancreatolgy* 4 (2004) 22–27.
28. Somuk BT, Soyaliç H, Koc S, Gürbüzler L, Doğru S, Eyibilen A. Mean platelet volume as an inflammatory marker of chronic otitis media with effusion. *Int J Pediatr Otorhinolaryngol.* 2014 Nov;78(11):1958-60.
29. Braun T, Dreher A, Dirr F, Reichel O, Patscheider M. Pediatric OSAS and otitis media with effusion. *HNO.* 2012 Mar;60(3):216-9.
30. Kaya S, Selimoğlu E, Cureoğlu S, Selimoğlu MA. Relationship between chronic otitis media with effusion and overweight or obesity in children. *J Laryngol Otol.* 2017 Oct;131(10):866-870.
31. Kim JB, Park DC, Cha CI, Yeo SG. Relationship between pediatric obesity and otitis media with effusion. *Arch Otolaryngol Head Neck Surg.* 2007 Apr;133(4):379-82.
32. Kim SH, Park DC, Byun JY, Park MS, Cha CI, Yeo SG. The relationship between overweight and otitis media with effusion in children. *Int J Obes (Lond).* 2011 Feb;35(2):279-82.