Hypothyroidism in Children with Serous Otitis Media

Seröz Otitis Mediali Çocuklarda Hipotiroidi

Original Investigation Özgün Araştırmalar	Öztürk Aktaş ¹ , Ahmet Adnan Cırık ² , Ömer Erdur ³ , Lütfi Kanmaz ¹ , Alper Yenigün ⁴ , Kamil Hakan Kaya ⁵ , Fatma Tülin Kayhan ⁵ ¹ Clinic of Otorhinolaryngology, Erzincan State Hospital, Erzincan, Turkey ² Clinic of Otorhinolaryngology, Dr. Ersin Arslan State Hospital, Gaziantep, Turkey ³ Clinic of Otorhinolaryngology, Konya Training and Research Hospital, Konya, Turkey ⁴ Clinic of Otorhinolaryngology, Karaman State Hospital, Karaman, Turkey ⁵ Clinic of Otorhinolaryngology, Bakırköy. Dr. Sadi Konuk Training and Research Hospital, İstanbul, Turkey		
Abstract ►	Objective: In this study, we aimed to evaluate the co-ex- istence and prevalence of hypothyroidism in patients with otitis media with effusion (OME) and to determine the possible relationship between OME and hypothyroidism. Methods: The subject group consisted of 46 paediatric patients (26 boys, 20 girls), ranging in age from 4 to 14 years (mean age±SD 7.78±2.86 years), who were treated in the department of otorhinolaryngology for OME; the control group composed of 30 healthy children (20 boys, 10 girls), ranging in age from 3 to 14 years (mean age±SD 7.20±2.86 years). Triiodothyronine (Free T3), thyroxin (free T4), and thyroid-stimulating hormone (TSH) values of 46 children who were treated for OME, in addition to 30 healthy children, were evaluated.	 Results: Seven patients (15.2%) in the OME group, and one patient (3.3%) in the control group had subclinical hypothyroidism marked only by serum TSH elevations. All of the children in this study, regardless of whether from the subject or control group, had normal serum free T3 and free T4 levels. There was no significant difference between subject and control groups (p>0.05). Conclusion: Although there was no statistically significant difference between subject and control groups in this study, further studies with larger patient groups are needed to investigate the role of hypothyroidism in the aetiology of OME. Key Words: Hypothyroidism, otitis media, effusion 	
Özet ▶	 Amaç: Bu çalışmada, seröz otitis media (SOM) olan hastalarda hipotiroidi birlikteliğinin saptanması ve SOM ile hipotiroidi arasındaki olası ilişkinin belirlenmesi amaçlanmıştır. Yöntemler: Çalışma grubu, SOM nedeniyle Kulak Burun Boğaz Kliniğinde tedavi edilen 4-14 yaşlarında (ortalama yaş±SD, 7,78±2,86 yıl) 46 çocuk (26 erkek, 20 kız) hastadan oluşuyordu. Kontrol grubu ise 3-14 yaşlarında (ortalama yaş±SD, 7,20±2,86 yaş) 30 sağlıklı çocuk hastadan (20 erkek, 10 kız) oluşuyordu. SOM nedeniyle tedavi edilen 46 çocuk hasta ve 30 sağlıklı çocukta serum serbest T3, serbest T4 ve TSH seviyeleri değerlendirildi. 	 Bulgular: SOM grubunda yedi hastada (%15,2) ve kontrol grubunda bir hastada (%3,3) sadece TSH yüksekliği olan subklinik hipotiroidi izlendi. Çalışma grubu ve kontrol grubu olmak üzere çalışmadaki tüm çocuklarda, serum serbest T3 ve serbest T4 seviyeleri normal olarak izlendi. Çalışma ve kontrol grubu arasında anlamlı bir fark izlenmedi (p>0,05). Sonuç: Bu çalışmada, çalışma ve kontrol grubu arasında anlamlı bir fark bulunmamakla birlikte hipotiroidinin, SOM etyolojisindeki rolünü araştırmak için daha büyük hasta gruplarında çalışmalara ihtiyaç vardır. Anahtar Kelimeler: Hipotiroidi, otitis media, efüzyon 	



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Introduction

Otitis media with effusion (OME) is characterised by fluid retention behind the eardrum without general or local infection symptoms. OME is a common disease in children with an incidence of 15% to 20% and may lead to hearing loss or surgical intervention (1). In most children, otitis media improves spontaneously and has a good prognosis, but approximately 10% of paediatric patients experience repeated or chronic OME (2). With few exceptions, it is difficult to predict which children with OME will develop the chronic form. Otitis media with effusion is multifactorial. There are many epidemiologic factors that increase the risk of OME development; these include upper respiratory tract infections, allergic rhinitis, Eustachian tube dysfunction, cigarette smoking (passive), bottle fed rather than breast fed, male sex, immunological deficiency, cilia dysfunction, and cleft palate disease.

The diagnosis of OME is difficult. Since most cases of OME are silent, the diagnosis is often delayed months or years, sometimes resulting in an impairment of speech and language development. Some of the patients are infants who are brought to the attention of a physician because of inattentiveness, suspected

hearing loss, or delayed speech. Many other children are found to have OME by their primary care physician.

The physical diagnosis of OME depends on a careful otoscopic evaluation. While combinations of different tympanic membrane findings (colour, position, and mobility) are the most reliable indicators of the presence or absence of OME, variables such as tympanic membrane redness and the presence or absence of light reflex alone are not reliable predictors for OME (3, 4). The assessment of the mobility of the tympanic membrane can be best achieved with pneumatic otoscope. The middle ear may contain some gas within the fluid which appears as bubbles or an 'air/fluid' level. The tympanic membrane may be retracted, or the ear may be atelectasis with the tympanic membrane assuming the contour of the medial wall of the middle ear.

Tympanometry, when used to complement the otologic examination, is the most accurate diagnostic test for establishing an OME diagnosis. Tympanometry can be performed in almost any child and does not require a voluntary response.

Middle ear effusion is known as one of the symptoms and signs of hypothyroidism and conductive losses may also occur as a result of oedema of the Eustachian tube mucosa (5). Several authors have reported certain cases where hypothyroidism has played a role in the OME pathogenesis (6, 7). Hypothyroidism increases thyrotropic hormone release which results in mucopolysaccharid-acid production causing an increase in turgor and oedema, resulting in congestion and hypertrophy in mucosal glands (8).

This study aimed to evaluate the co-existence and prevalence of hypothyroidism in patients with OME and to determine the possible relationship between these two diseases.

Methods

This is a retrospective study, approved by the local Clinical Research Ethics Committee, and patient consent was obtained in 2009. The subject group consisted of 46 paediatric patients (26 boys, 20 girls), ranging in age from 4 to 14 years (mean age±SD 7.78±2.86 years), who were treated for OME at the department of otorhinolaryngology; the control group consisted of 30 healthy children (20 boys, 10 girls), ranging in age from 3 to 14 years (mean age±SD 7.20±2.86 years). There was no significant difference between the subject and control groups in terms of age and gender (p>0.5). This shows us that both groups are suitable for study (Table 1).

Otitis media with effusion was diagnosed with anamnesis, pneumatoscopy, microscopy, and tympanogram. The pneumatoscopic and microscopic criteria applied for OME diagnosis were: retracted tympanic membrane with good outward mobility and abnormal mobility (hypomobile, immobile, air-fluid level). Tympanometry was performed by a certified audiologist using an Interacoustics Impedance Audiometer AZ26 tympanometry. Tympanograms were coded according to Jerger's (9) 1970 classification: type A: compliance ≥ 0.2 mL and pressure $\geq -99d$ Pa; type C1: compliance ≥ 0.2 mL and pressure between -100 and -199 dPa; type C2: compliance >0.2 mL and pressure between -200 and -399 dPa: type B: compliance <0.2 mL or pressure \leq -400dPa. Type B and type C2 tympanograms were considered to indicate OME. Children with congenital anomalies in the head and neck, Down syndrome, systemic diseases, or those suspected to have congenital or acquired immune deficiency were excluded from this study. The patients were questioned about OME risk factors such as adenoid vegetation, allergic rhinitis and recurrent otitis media. Allergic skin tests, serum Ig-E levels and nasopharyngeal endoscopy were applied when necessary. The triiodothyronine (Free T3), thyroxin (free T4), and thyroid-stimulating hormone (TSH) values of 46 children who were treated against OME, and those from 30 healthy children, were evaluated (Advia Centaur Immunassay system, Bayer Health Care, USA). Total blood samples were collected by needle and syringe from peripheral veins. None of the children, from either the subject or control group, had any known thyroid illness, or hypo- or hyperthyroid symptoms. Blood TSH values >5.5 micro IU/mL (normal range: 0.35-5.5 micro IU/mL) were considered to be hyperthyrotropinemic (10).

Statistical analysis

We used Statistical Package for Social Sciences (SPSS) for Windows 15.0 programmed for statistical analysis, Student's t test for descriptive statistical methods (average, standard deviation, frequency), and quantities datum, chi-square test, and Fisher's Exact chi-square test for qualitative data. Statistical significance was defined as a *p* value less than 0.05. The study protocol was fully explained to patients or their guardians, and written informed consent was obtained from each patient.

Results

Of the 46 patients in the OME group, type B tympanogram was found in 81 ears (44 right, 37 left), type C2 was found in 6 ears (2 right, 4 left), and type A in 5 ears (all are left). All of the children in control group had type A tympanogram. There was no type C1 tympanogram (Table 2).

In the OME group, recurrent otitis media was found in 24 patients (52.2%), whereas only two children (6.7%) in the healthy group had recurrent otitis media (Table 3). This difference was statistically significant (p<0.01).

Adenoid vegetation was found in 25 (54.3%) patients in the OME group. Allergic rhinitis was found in 7 (15.2%) patients in OME group. Adenoid vegetation and allergic rhinitis comorbidity was found in 16 (53.3%) and 3 (10%) children in the

Table 1. Age, gender of the cases with OME and	l control group
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		Gr		
		Subject (n=46) Mean±SD	Control (n=30) Mean±SD	р
Age		7.78±2.86 n (%)	7.20±2.86 n (%)	0.389
Gender	Girls	20 (43.5%)	10 (33.3%)	0.376
	Boys	26 (56.5%)	20 (66.7%)	

Student t test was used for age, and X² test for gender

		Group		
		Subject (n=46) n (%)	Control (n=30) n (%)	р
Right ear tympanometry	Type A Type B Type C1 Type C2	0 (0.0%) 44 (95.7%) 0 (0.0%) 2 (4.3%)	30 (100.0%) 0 (0.0%) 0 (0.0%) 0 (0.0%)	0.001*
Left ear tympanometry	Type A Type B TypeC1 Type C2	5 (10.9%) 37 (80.4%) 0 (0.0%) 4 (8.7%)	30 (100.0%) 0 (0.0%) 0 (0.0%) 0 (0.0%)	0.001*

Table 2. Tympanometry findings in subject and control group

Chi-square test, *p<0.01

Table 3. Risk factors for the subject and control group

		Group		
		Subject (n=46) n (%)	Control (n=30) n (%)	р
Recurrent acute otitis media	Present Not present	24 (52.2%) 22 (47.8%)	2 (6.7%) 28 (93.3%)	0.001*
Adenoid Vegetation	Present Not present	25 (54.3%) 21 (45.7%)	16 (53.3%) 14 (46.7%)	0.931
Allergic Rhinitis	Present Not present	7 (15.2%) 39 (84.8%)	3 (10.0%) 27 (90.0%)	0.511

Chi-square test, *p<0.01

patient and control groups, respectively. There was, however, no significant difference (p>0.05) (Table 3).

Seven patients (15.2%) in the OME group and one patient (3.3%) in the control group had subclinical hypothyroidism marked only by serum TSH elevations. All of the children in this study, from both the subject and control group, had normal serum free T3 and free T4 levels. There was no significant difference between the subject and control groups (p>0.05) (Table 4).

The hyperthyrotropinemic patients were referred to a paediatric endocrinology clinic. Anti-thyroglobulin (TgA), anti-thyroperoxidase (TPOA) antibodies (evaluated by fluorescence enzymatic immunoassays), and urinary iodine concentration were studied in a total of 8 hyperthyrotropinemic patients (7 patients in the OME group, 1 patient in the control group). Thyroid ultrasonography was applied to all 8 patients. Two hyperthyrotropinemic patients in the OME group were diagnosed with Hashimoto thyroiditis. One patient in control group, and 5 patients in OME group were diagnosed with iodine deficiency.

Discussion

Although frequently seen in children, the pathophysiology of OME remains controversial. The most frequent aetiological reasons are infections, inflammation and impaired aeration in the middle ear. Based on these aetiological reasons, a lot of risk factors described above were suggested to be causatives of OME. Among these, some were shown to be related to OME, while some are still being discussed.

Table 4. The comparison of the TSH, free T3, free T4 values among
the subject and control group

		Group		
		Subject (n=46) n (%)	Control (n=30) n (%)	р
FT3	Normal	46 (100.0%)	30 (100.0%)	-
FT4	Normal	46 (100.0%)	30 (100.0%)	-
TSH	Normal	39 (84.8%)	29 (96.7%)	0.137
	High	7 (15.2%)	1 (3.3%)	

Free T3: Triiodothyronine, free T4: Thyroxin, TSH: Thyroid-stimulating hormone, Fisher's exact test

The function of the thyroid gland is regulated by TSH hormone, which is secreted from the frontal lobe of the pituitary gland, and by inner thyroid auto-regulatory mechanisms. Thyroid hormones (thyroxine-T4, triiodotronin-T3) are necessary for growth and differentiation and have significant effects on metabolic processes of all tissues in the body. Only the free forms of thyroid hormones can penetrate into the cells and cause a biological effect. Free T3 and T4 levels are regulated through negative feedback.

Thyroid hormones have effects on growth and development, oxygen usage, and regulation of body temperature, neuronal functions, and lipid, carbohydrate, nucleic acid, vitamin, and inorganic ion metabolisms. They also affect the metabolism of other hormones. The largest effect is achieved by binding to the nuclear T3 receptor.

The metabolism slows down as a result of hypothyroid disease and metabolic pathologies such as oedema develop in tissues. Other symptoms such as hypothermia, constipation, anorexia, brittle skin, hair thinning, and hyporeflexion may develop.

Hypothyroid disease onset might occur at any age in children, but it is more common in girls. The most common reason for acquired hypothyroid disease is chronic autoimmune thyroid disease (Hashimoto disease). Other acquired hypothyroid disease causes are goitrogen matter affect, sub-acute thyroid disease, infiltration of the thyroid tissue as a result of cystinosis or histiositosis X, and hypothalamic glandular diseases. Thyroid dysgenesis, such as ectopy, hemiaplasia and biosynthesis disorders, result in natal hypothyroid condition.

In our study, we searched for the aetiological causes of OME, such as recurrent otitis media, allergic rhinitis, and adenoid vegetation. Although all of these are believed to be risk factors of OME, we only found a significant relationship between recurrent otitis media and OME (11, 12).

Some researchers believe that hypothyroid disease may play a role in the pathogenesis of OME. There are, however, a limited number of papers on this subject and it has been suggested that hypothyroid disease may also play a role in the pathogenesis (6, 7). It was stated that Eustachian tube functions changes and effusions may occur in the middle ear in patients with hypothy-

roid disease (5). Hypothyroid patients intrinsically develop an obstruction originating from Eustachian tube mucosa as well as an extrinsic oedema of pharyngeal ostium. As a result, both tubal function disorder and oedema in the middle ear and mastoid mucosa may play a role in OME pathogenesis.

The clinical picture in which serum free T3 and T4 levels are normal, while serum TSH concentrations are high without any symptoms of hypothyroid disease, is called subclinical hypothyroid disease. There are a small number of studies on the prevalence of hypothyroidism in children. Paoli-Valeri et al. (13) reported that the frequency of hypothyroidism in children was 15% in Merida state. In our study, 15.2% of children with OME were diagnosed with subclinical hypothyroid disease, and these patients were referred to endocrinology clinics. Only one child (3.3%) in the control group had subclinical hypothyroid disease.

Conclusion

Although there was no statistically significant difference between subject and control groups in this study, further studies with larger patient groups are needed to investigate the role of hypothyroidism in the aetiology of OME.

Conflict of Interest

No conflict of interest was declared by the authors.

Peer-review: Externally peer-reviewed.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Dr. Sadi Konuk Education and Research Hospital (2009).

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

Author Contributions

Concept - Ö.A.; Design - A.D.Ç.; Supervision - H.K.; Funding - Ö.E.; Materials - L.K.; Data Collection and/or Processing -Ö.A.; Analysis and/or Interpretation - H.K.; Literature Review - A.Y.; Writer - A.Y.; Critical Review - F.T.K.

Çıkar Çatışması

Yazarlar herhangi bir çıkar çatışması bildirmemişlerdir.

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Hasta Onamı: Yazılı hasta onamı bu çalışmaya katılan hastalardan alınmıştır.

Yazar Katkıları

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References

- 1. Zielhius GA, Rach GH, Bosch AV, Broek P. The prevalance of otitis media with effusions: a critical review of the literature. Clin Otolaryngol 1990; 15: 283-8. [CrossRef]
- 2. Rovers MM, Schilder AG, Zielhuis GA, Rosenfeld RM. Otitis media. Lancet 2004; 363: 465-73. [CrossRef]
- Karma PH, Sipila MM, Kataja MJ, Penttila MA. Pneumotic otoscopy and otitis media. Value of different tympanic membrane findings and their combinations. In:Lim DJ, Bluestone CD, Klein JO, Nelson JD, Ogra PL, eds. Recent advances in otitis media. Proceedings of the Fifth International Symposium. Hamilton, Canada: Decker periodicals, 1993; 41-5.
- Karma PH, Penttilä MA, Sipilä MM, Kataja MJ. Otoscopic diagnosis of middle ear effusion in acute and non-acute otitis media. I. The value of different otoscopic findings. Int J Pediatr Otorhinolaryngol 1989; 17: 37-49. [CrossRef]
- Moosa M, Mazzaferri EL. Disorders of the thyroid gland. In: Cummings CW, Fredrickson JM, Harker LA, Krause CJ, Schuller DE, Richardson MA, editors. Otolaryngology head and neck surgery. St. Louis: Mosby-Year Book; 1998.p.2456.
- Pohjola-Sintonen S. Secretory otitis as the initial sign of hypothyroidism. Duodecim 1988; 104: 1478-80.
- Gruter L. Hypothyroidism and tympanic effusion. A contribution to the diagnosis and therapy and mucotympanum the elderly. HNO 1986; 34: 305-6.
- 8. Settipane GA. Nasal polyps; epidemiology, pathology, immunology and treatment. Am J Rhinol 1987; 1: 119-26. [CrossRef]
- 9. Jerger J. Clinical experience with impedance audiometry. Arch Otolaryngol 1970; 92: 311-24. [CrossRef]
- National Comittee for Clinical Laboratory Standarts. How to define, determine, and utilize reference intervals in the clinical laboratory; approved guideline. NCCLS Document C28-A. Wayne (PA): nccls; 1995; 59.
- 11. Fireman P. Otitis media and nasal disease: A role for allergy. J Allergy Clin Immunol 1988; 82: 917-24. [CrossRef]
- Gates GA, Avery CA, Prihoda TJ, Cooper JC. Effectiveness of adenoidectomy and tympanostomy tubes in the treatment of chronic otitis media with effusion. N Engl J Med 1987; 317: 1444-51. [CrossRef]
- Paoli-Valeri M, Maman-Alvarado D, Jimenez-Lopez V, Arias-Ferreira A, Bianchi G, Arata-Bellabarba G. Frequency of subclinical hypothyroidism among healty children and those with neurological conditions in the state of Merida, Venezuela. Invest Clin 2003; 44: 209-18.