



Spontaneous Tympanic Membrane Perforation in Infants Aged <3 Months with Acute Otitis Media

Üç Aydan Küçük Akut Otitis Medialı İnfantlarda Spontan Timpanik Membran Perforasyonu

Sevgi Yaşar Durmuş¹(iD), Gönül Tanır²(iD), Selçuk Mülazımoğlu³(iD), Ayşe Kaman²(iD), Türkan Aydın Teke²(iD), Rumeysa Yalçınkaya²(iD), Fatma Nur Öz²(iD)

¹ Clinic of Pediatric Infectious Diseases, Kayseri Research and Training City Hospital, Kayseri, Türkiye

² Clinic of Pediatric Infectious Diseases, Dr. Sami Ulus Gynecology and Child Health and Diseases Training and Research Hospital, Ankara, Türkiye

³ Department of Otolaryngology, Ankara University Faculty of Medicine, Ankara, Türkiye

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Abstract

Objective: Acute otitis media (AOM) is among the most common infectious childhood diseases, and during its course, spontaneous tympanic membrane perforation (STMP) can occur. Babies aged <3 months are more vulnerable to complications of AOM than those aged >3 months. This study aimed to determine the clinical course in babies aged <3 months with AOM and STMP.

Material and Methods: The study included babies aged <3 months that were hospitalized for AOM and STMP. Patient medical records, including patient characteristics, clinical and laboratory findings, antibiotic treatment, and organisms isolated from clinical specimens, were retrospectively reviewed.

Results: There were 31 patients with a mean age of 59 ± 19.6 days (d). Mean duration of complaint before hospital admission was 3.7 ± 3.6 d. The most common complaint was ear discharge [n= 16 (51.6%)]. The most common pathogen isolated from pus cultures was *Streptococcus pyogenes* [n= 3 (27%)]. Among the patients, one had *Moraxella catarrhalis* bacteremia, one developed mastoiditis as a complication of AOM.

Conclusion: During the course of AOM and STMP in patients aged <3 months, bacteremia, and mastoiditis can complicate the prognosis. Antibiotics that target the bacteria which cause AOM should be preferred. Clinicians should be aware that *S. pyogenes* can cause STMP in young babies with AOM.

Keywords: Acute otitis media, bacteremia, infant, otorrhea, tympanic membrane perforation

Öz

Giriş: Akut otitis media (AOM) çocukluk çağının en sık enfeksiyon hastalıkları arasındadır ve hastalık sürecinde spontan timpanik membran perforasyonu (STMP) ortaya çıkabilir. Üç ayın altındaki bebekler, üç aydan büyük bebeklere göre AOM'un komplikasyonlarına daha yatkındır. Bu çalışma üç ayın altında AOM ve STMP'li bebeklerde hastalığın seyrini tanımlamayı amaçlamaktadır.

Gereç ve Yöntemler: Çalışmaya AOM ve STMP nedeniyle hastaneye yatırılarak izlenen üç ayın altındaki bebekler dahil edilmiştir. Hastaların özelliklerini, klinik ve laboratuvar bulgularını, antibiyotik tedavilerini ve klinik örneklerden elde edilen mikroorganizmaları içeren hasta kayıtları, geriye dönük olarak incelenmiştir.

Bulgular: Ortalama yaşları 59 ± 19.6 gün olan 31 hasta mevcuttu. Hastaneye başvuru öncesi ortalama yakınma süresi 3.7 ± 3.6 gündü. En sık yakınma kulak akıntısı [n= 16 (%51.6)] idi. Püü kültürlerinden en sık izole edilen etken *Streptococcus pyogenes* [n= 3 (27%)] idi. Akut otitis media komplikasyonu olarak bir hastada *Moraxella catarrhalis* bakteriyemisi ve bir hastada mastoidit gelişmişti.

Sonuç: Üç ayın altındaki hastalarda AOM ve STMP seyrinde bakteriyemi ve mastoidit komplikasyonu görülebilir. Akut otitis mediaya neden olan bakterileri hedef alan antibiyotikler tercih edilmelidir. Klinisyenler *S. pyogenes*'in AOM'lu küçük bebeklerde STMP'ye neden olabileceğinin farkında olmalıdır.

Anahtar Kelimeler: Akut otitis media, bakteriyemi, infant, otore, timpanik membran perforasyonu

Correspondence Address/Yazışma Adresi

Sevgi Yaşar Durmuş

Kayseri Şehir Eğitim ve Araştırma Hastanesi,
Çocuk Enfeksiyon Hastalıkları Kliniği,
Kayseri-Türkiye

E-mail: drsvgyr@gmail.com

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Introduction

Acute otitis media (AOM) is characterized by inflammation of the middle ear and usually presents with fever, ear pain, and otorrhea (1). Acute otitis media is among the most common infectious childhood diseases (2). Acute otitis media may result in otorrhea, perforation of the tympanic membrane, chronic suppurative otitis media, or mastoiditis. During the course of AOM, pus accumulates in the middle ear cavity, increasing the pressure in the cavity and disrupting blood circulation in the tympanic membrane, which can cause spontaneous tympanic membrane perforation (STMP). Afterward, middle ear fluid (MEF) flows out to the external ear canal (3). It has been reported that the incidence rate of AOM associated TM perforation/otorrhea is 3% to 7%. This situation varies depending on the appropriate and timely diagnosis and treatment of AOM, the presence of antibiotic resistance, the vaccination status of the child, and whether non-vaccine serotypes are causative agents for AOM (4,5). The occurrence of STMP at the time AOM is diagnosed may be indicative of late-stage AOM.

Acute otitis media incidence is highest in children younger than two years old. Eustachian tube anatomy and maternal antibodies' waning are predisposing factors of AOM in young children (6,7). Because of the nonspecific nature of the clinical symptoms of AOM, including excessive crying, impaired sleep, and difficulty physically examining the ears, its diagnosis is difficult for pediatricians (1,6,7). Babies aged <3 months are more vulnerable to complications of AOM as well as disseminated infections due to AOM than those aged >3 months (8). Physicians must be aware of AOM and its complications; however, there are few relevant studies on patients aged <3 months (6). The present study aimed to retrospectively determine the clinical characteristics, causative organisms, treatment, and clinical course of AOM and STMP in babies under three months age.

Materials and Methods

This study was conducted at Dr. Sami Ulus Gynecology and Child Health and Diseases Training and Research Hospital, Ankara, Türkiye, a pediatric referral hospital that provides health-care services to >20.000 inpatients and >900.000 outpatients annually. This retrospective descriptive study included babies hospitalized with AOM and STMP between January 2010 and December 2018. The babies included were not on oral and/or parenteral antibiotics before hospital admission. Babies aged >3 months, had AOM without otorrhea, had otorrhea due to otitis externa, had a co-morbid condition, and whose parents declined lumbar puncture (LP) were excluded. As AOM is not limited to the temporal bone, it can disseminate and lead to bacteremia, sepsis, and meningitis in babies aged <3 months (8); therefore, LP is a routine procedure at our clinic for hospitalized patients aged <3 months with AOM and STMP.

Acute otitis media with STMP was diagnosed based on new onset of clinical diagnostic symptoms (irritability and fever) and otorrhea not originating from acute external otitis. Uncomplicated AOM was diagnosed based on mild bulging of the tympanic membrane and new onset of ear pain (holding, tugging, rubbing of the ear) or intense erythema of the tympanic membrane (1). Mastoiditis was diagnosed based on irritability, fever, swelling of the mastoid area, and when opacification was seen in the middle ear cavity, and mastoid air cell with erosion of mastoid bone on temporal bone computed tomography (CT). Patient characteristics, including age, gender, gestational age, duration of complaints before hospital admission, breastfeeding status, vaccination status, physical examination findings, laboratory findings, antibiotic treatment, duration of hospitalization, and organisms isolated from blood, cerebrospinal fluid (CSF), and pus cultures (if obtained), were obtained from medical records and retrospectively evaluated. Diagnosis of AOM and STMP was confirmed by an ear nose throat (ENT) specialist in most patients. The study approved by local Ethical Committee of Dr. Sami Ulus Gynecology and Child Health and Diseases Training and Research Hospital (Date: 15.03.2019, Decision no: 2019-3).

Statistical analysis

Data were analyzed using IBM SPSS Statistics for Windows v.20.0 (IBM Corp., Armonk, NY). The normality of the distribution of numerical variables was tested using the Kolmogorov-Smirnov test. Numerical variables with normal distribution are shown as mean \pm standard deviation, and numerical variables not normally distributed are shown as a median.

Results

During the eight year study period, 53 children were hospitalized with AOM and STMP. The 31 patients who remained after applying the exclusion criteria were included in the study (Figure 1). Patient demographic and clinical characteristics are summarized in Table 1. Of included babies, 24 (77.4%) were admitted to the hospital with ear discharge, and eight had accompanying complaints; the remaining seven children were diagnosed with AOM and STMP by physical examination, although there was no complaint of ear discharge at the admission. The most common presenting complaint was ear discharge [n= 16 (51.6%)], followed by ear discharge and fever [n= 8 (25.8%)], irritability [n= 3 (9.7%)], fever [n= 2 (6.5%)], ear tugging [n= 1 (3.2%)], and fever and irritability [n= 1 (3.2%)]. Upon physical examination, bilateral otorrhea was noted in eight patients and was accompanied by irritability in one patient and a bulging fontanel in one patient. Unilateral otorrhea was observed in 23 patients and was accompanied by irritability in one patient, ipsilateral pinna tenderness in one patient, ipsilateral purulent conjunctivitis in one patient, and tachypnea and crackles on lung auscultation in one patient.

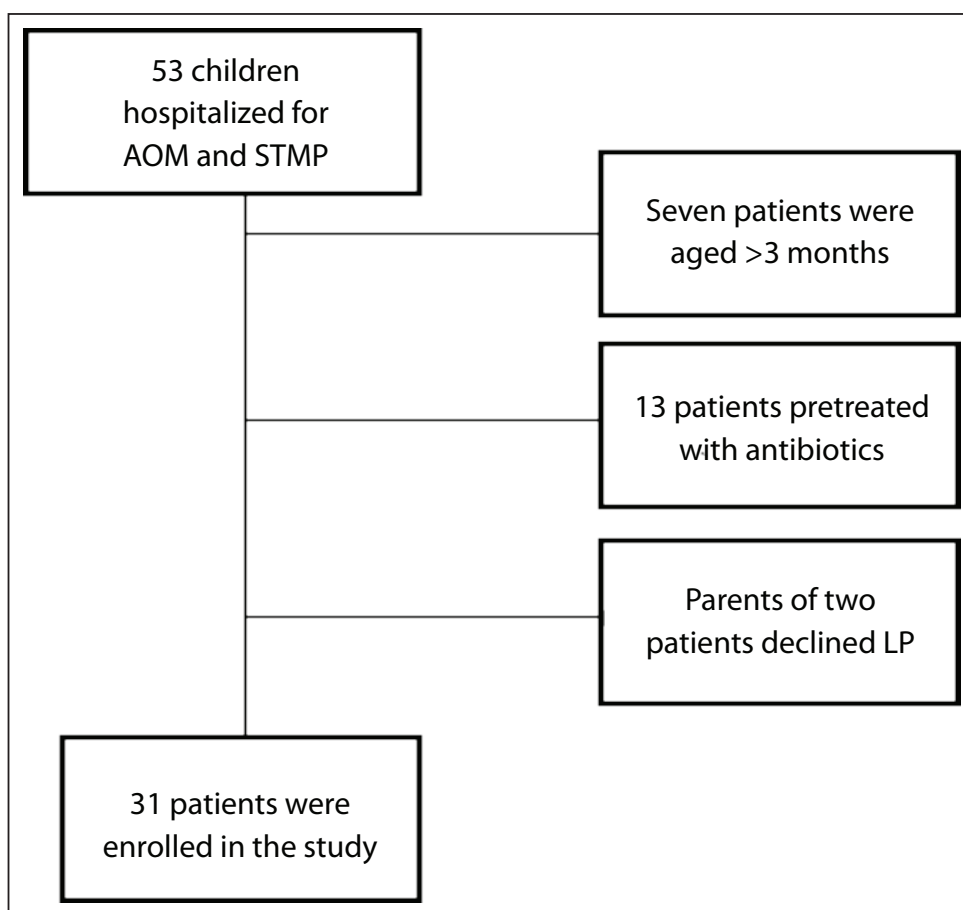


Figure 1. Flow diagram of the patient inclusion process.

AOM: Acute otitis media, LP: Lumbar puncture, STMP: Spontaneous tympanic membrane perforation.

Table 1. Patient demographic and clinical characteristics

Characteristics	
Male, n (%)	20 (64.5%)
Age, day (Mean ± SD)	59 ± 19.6
Gestational age, n (%)	
Term	30 (97)
Preterm	1 (3)
Feeding, n (%)	
Breastfeeding	22 (71)
Breast/Formula feeding	4 (13)
N/A	5 (16)
Cigarette exposure, n (%)	
Yes	13 (41.9)
No	10 (32.3)
N/A	8 (25.8)
Immunization status for babies*, n (%)	
Younger than two months	15 (48.4)
Vaccinated	15 (48.4)
Non-vaccinated	1 (3.2)
Complaint duration before admission, day, (Mean ± SD)	3.7 ± 3.6

*According to actual national vaccination schedule: 1 dose of 7 or 13 valent-conjugated pneumococcal vaccine and 1 dose of *Haemophilus influenzae* type b vaccine.

Laboratory results of the patients, at the admission are demonstrated in Table 2. The CSF cultures of the study population did not yield any microorganisms and one patient, who had 60 leukocytes/mm³ in the CSF, was diagnosed with aseptic meningitis. Pus culture was performed in 11 patients and blood culture was performed in all patients; results are shown in Table 3. Four blood cultures that yielded coagulase-negative *Staphylococci* (CoNS) and pus culture results other than *S. pyogenes* (CoNS, *Pseudomonas aureginosa*, *Staphylococcus aureus*, *Klebsiella pneumoniae*) considered to be due to contamination.

Table 2. Laboratory results of patients

Tests	Mean ± SD
White blood cell count (x10 ³ µL)	11.0 ± 3.3
C-reactive protein (mg/L), median (IQR),	4.1 (3.2-13.7)
Cerebrospinal fluid findings (n= 21)	
Leukocyte count (/mm ³), median (IQR)	1 (0-5)
Glucose (mg/dL)	50 ± 5.8
Protein (mg/dL)	51.4 ± 23.9

IQR: Interquarter ranges.

Table 3. Isolated microorganisms from pus and blood cultures

Microorganisms isolated from pus cultures	n (%)
<i>Streptococcus pyogenes</i>	3 (27)
Methicillin-sensitive CoNS	1 (9)
Methicillin resistant CoNS	1 (9)
<i>Klebsiella pneumoniae</i>	1 (9)
<i>Pseudomonas aeruginosa</i>	1 (9)
Methicillin-sensitive <i>Staphylococcus aureus</i>	1 (9)
Mixed	3 (27)
Microorganisms isolated from blood cultures	
None	26 (84)
Methicillin-sensitive CoNS	2 (6.4)
Methicillin resistant CoNS	2 (6.4)
<i>Moraxella catharralis</i>	1 (3.2)

In a male patient who was on cefotaxime therapy, fever persisted for six d, and then retro auricular swelling and redness developed. Temporal bone CT was performed and showed increased soft tissue density in mastoid cells and the antrum, with concomitant bony erosions, and he was diagnosed with mastoiditis.

All patients were treated with intravenous antibiotics during hospitalization as follows: cefotaxime (n= 27); amoxicillin-clavulanate (n= 4). Patients were discharged following clinical and laboratory amelioration following ≥ 24 h of feverless observation. The mean duration of hospitalization was median= 4 d (range= 3-15 d). The patient with mastoiditis was treated in hospital for 15 d, but surgical intervention was not required because of resolution of the related findings. All of the patients were discharged with oral antibiotics, to complete a 10-d antibiotic course. Post-discharge, all patients were followed-up as outpatients, although long-term follow-up data were not obtained.

Discussion

Babies younger than 90 days are not included in many studies regarded with AOM and there are not sufficient recommendations for AOM management in this age group. In this report, we shared our eight years of experience in babies aged <3 months with AOM and STMP. We detected that bacteremia and mastoiditis may accompany to AOM with STMP in babies younger than three months.

Acute otitis media is common during infancy and childhood. Due to its acute symptoms, including fever, otalgia, and irritability, parents generally present with their children to emergency departments. Timely and accurate diagnosis and appropriate management of AOM are essential for the overuse of antibiotics and the risk of complications of un-

treated AOM. The symptoms and signs used to diagnose AOM include pain, tympanic membrane bulging, and fever and confirmation of middle ear effusion is considered critical for diagnostic accuracy. Based on such findings, the diagnosis of AOM in emergency departments is reasonably accurate, although assessing the tympanic membrane via tympanometry and/or pneumatic otoscopy can improve diagnostic accuracy (9,10). Accurate diagnosis of AOM in babies aged <3 months can be incredibly challenging. Visualization of the tympanic membrane can be difficult in this age group because of the uncommon orientation of the narrow external ear canal. The vernix caseosa or cerumen can block the ear canal (11-13). Furthermore, babies aged <3 months can have nonspecific signs or symptoms. As the present study included AOM patients aged <3 months with otorrhea, the most common presenting symptoms were ear discharge and fever, which facilitated the accurate diagnosis of AOM.

It has been reported that STMP can occur during an episode of AOM and complicate the clinical course of the disease (3). It remains unclear if AOM with STMP is a distinct disease with specific characteristics or a severe form of AOM. According to the American Academy of Pediatrics Clinical Practice and Treatment Guideline, STMP is considered a sign of AOM severity (1). On the other hand, STMP associated drainage of pus results in a rapid and marked improvement in symptoms due to decreased pressure in the middle ear cavity (14). In the present study, there was a wide otorrhea duration range before hospital admission, which might be related to pain relief with STMP. The associated pus drainage also provides an opportunity to collect a culture sample (Figure 2). Ear nose throat specialist consultation is important for the removal of pus from the ear canal and confirmation of the diagnosis of AOM and STMP.

The most common causative microorganisms of AOM are *Streptococcus pneumoniae*, non-typable *Haemophilus influenzae*, *M. catarrhalis* in babies and toddlers and *S. pyogenes* in older children (2,3). Recent studies on the microbiological characteristics of children with AOM presenting with STMP reported that *S. pyogenes* was more frequently isolated from MEF in patients with spontaneous otorrhea than in those without perforation (15,16). One study that included 12,617 AOM patients who provided MEF samples reported that *S. pyogenes* isolation frequency was 5.7% in the children with spontaneous otorrhea and 1% in those with an intact tympanic membrane that underwent tympanocentesis (15). A study from Italy reported that *S. pyogenes* was observed in 17.4% of MEF cultures from children with AOM and STMP. It was suggested that *S. pyogenes* has an important causative role of STMP in the course of AOM (16). Despite small sample size, in our study it has been seen that *S. pyogenes*, which was defined



Figure 2. Image of the left auricle in a typical case of AOM and STMP. Note the pus draining from the external ear canal, and the crusting around the tragus and lobule.

as a causative agent in older children with AOM and STMP in previous studies, can cause STMP during AOM in babies aged <3 months.

Pseudomonas aureginosa and *S. aureus* are both known agents of external ear canal flora, and *Klebsiella pneumoniae* is not a usual causative agent of AOM, despite it may cause chronic suppurative otitis media, these agents were considered as a contaminant, although isolated from pus cultures (17,18). One of the present study's patients had *M. catarrhalis* bacteremia. Although *M. catarrhalis* is a well-known causative agent of AOM, bacteremia is infrequently reported in all age groups from neonates to the elderly. In contrast to adults, many babies with *M. catarrhalis* bacteremia are immunocompetent (19). In a recent multicenter, retrospective study, there was no bacterial meningitis in afebrile babies <90 days of age with AOM. In another study from Israel, in a population of 137 babies younger than two months of age with AOM, three patients with aseptic meningitis were determined (11,20). In our study, one patient was diagnosed with aseptic meningitis, and none of the patients were diagnosed with bacterial meningitis.

Acute mastoiditis in young babies is rarely reported. A Swedish study that included babies aged <6 months reported that during a 15-year period only 17 babies with mastoiditis were observed (21). Among those 17 babies, three had AOM before mastoiditis, and the findings that preceded acute mas-

toiditis were respiratory tract infection or fever for a mean seven d (median= three d). Similarly, the present study's patient with mastoiditis had AOM and fever for the preceding 6 d. The current guidelines recommend systemic antibiotic treatment in children with AOM and STMP due to the severity of the disease (1,3). All patients in the present study underwent septic workup before systemic antibiotic treatment was initiated.

Study limitations

The present study's limitations are its retrospective design, small sample size, and lack of long-term patient follow-up.

Conclusion

Spontaneous tympanic membrane perforation can occur during AOM and complicate its clinical course in patients aged <3 months with bacteremia and mastoiditis. *S. pyogenes* can cause STMP in babies with AOM. Such patients can be successfully treated with antibiotics effective against bacteria that cause AOM.

Ethics Committee Approval: Ethics committee approval was obtained from Ankara Dr. Sami Ulus Gynecology and Child Health and Diseases Training and Research Hospital Medical Education Board before starting the study (Date: 15.03.2019, Decision no: 2019/13). The study was carried out in accordance with the principles of the Declaration of Helsinki.

Informed Consent: Patient consent was obtained.

Peer-review: Externally peer-reviewed.

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