American Journal of Medicine and Medical Sciences 2023, 13(10): 1496-1501
DOI: 10.5923/j.ajmms.20231310.28

A Comprehensive Review of Otitis Media

Fozilova N. I.*, Khushvakova N. J.

Department of Otorhinolaryngology №1 of Samarkand State Medical University, Samarkand, Uzbekistan

Abstract Otitis media encompasses three conditions: acute otitis media (AOM), otitis media with effusion (OME), and chronic suppurative otitis media (CSOM). AOM is common and can lead to severe complications, especially in low-income nations. OME, often following AOM, affects child development and can lead to hearing loss. CSOM is prevalent in low- and middle-income countries and can result in hearing loss and neurological issues. Global efforts, including vaccination and guidelines, have improved otitis media management. Diagnostic approaches contribute to the practical assessment and management of ear conditions, although their specificities and sensitivities vary. The effectiveness of hearing aids and acoustic interventions for OME remains uncertain and requires more robust evidence, especially for high-risk populations. Establishing consensus on OM research standards is vital, and involving parents and children in research planning can improve the quality and relevance of pediatric occupational medicine studies, ultimately benefiting both children and caregivers.

Keywords Otitis media, AOM, CMOS, Treatment, Management, Prevention

1. Introduction

Otitis media comprises three distinct conditions: acute otitis media (AOM), otitis media with effusion (OME), and chronic suppurative otitis media (CSOM) [1]. These conditions are interrelated and share common characteristics. Otitis media is a frequently encountered pediatric condition, particularly in high-income countries, where it constitutes the primary reason for seeking medical attention, antibiotic prescriptions, and surgical interventions [2].

AOM is characterized by the presence of middle ear effusion (MEE) and symptoms associated with acute infection [2]. While some children experience AOM sporadically, others suffer from recurrent episodes, leading to ear discomfort, fever, and general malaise, causing distress for both children and their parents. The heightened prevalence of AOM can give rise to rare but severe complications, including acute mastoiditis, meningitis, and brain abscesses marked by pus formation. Low-income nations are particularly susceptible to these risks [3], resulting in an annual mortality rate of 21,000 individuals due to OM-related issues. Studies have reported a global occurrence of hearing loss associated with OM at a rate of 30 cases per 10,000 individuals, with a range from 0.7 to 95 cases [2]. Tympanic membrane perforation, commonly known as eardrum perforation, can occur as a result of AOM or the use of tympanostomy tubes for treatment.

* Corresponding author:
otorhyno.ssmu@gmail.com (Fozilova N. I.)
Received: Sep. 14, 2023; Accepted: Sep. 27, 2023; Published: Oct. 11, 2023
Published online at http://journal.sapub.org/ajmms

OME is characterized by the presence of MEE behind an intact tympanic membrane. Unlike AOM, OME does not involve acute infection [4]. The primary consequence of OME is a type of hearing impairment known as conductive hearing loss, resulting from the hindrance of sound wave transmission within the middle ear due to the presence of effusion. Repeated occurrences of hearing loss can impact various aspects of a child's life, including language development, behavior, and academic performance. By the age of 10, a significant majority of children, approximately 80%, have experienced OME. OME can develop following a viral infection [3,4] or after an episode of AOM when the inflammatory response subsides, leaving MEE in its wake. It is noteworthy that all children experience OME for a specific duration after an episode of AOM [2,4]. OME is recognized as a risk factor for AOM, emphasizing the interconnectedness of these two conditions.

The persistence or recurrence of ear discharge through a perforated tympanic membrane or ventilation tube is the outcome of chronic infection within the middle ear and mastoid cavity [5]. CMOS is linked to the development of conductive hearing loss and damage to the ossicles in the middle ear. Moreover, it has been associated with an increased risk of cerebral complications and irreversible sensorineural hearing loss [4,5]. This condition is prevalent in low- and middle-income nations [3].

Significant global progress has occurred in the field of OM (OM) since the publication of a seminal study more than a decade ago. These advancements have primarily revolved around pneumococcal conjugate vaccination and the development of updated guidelines for precise diagnosis and appropriate antibiotic use. These initiatives have had a

profound impact on the worldwide epidemiological and clinical landscape of OM. The objective of this Primer is to provide a contemporary assessment of OM, covering its epidemiology, pathophysiology, diagnosis, impact on children and families, as well as strategies for prevention and therapeutic interventions.

2. Epidemiology of OM

The prevalence and incidence of a particular phenomenon are essential measures in epidemiology and public health research. These metrics provide insights into the frequency and occurrence of a specific condition or event.

Recent research on the worldwide burden of OM made a prediction [6]. According to the cited source, there is an annual incidence rate of 8 new incidences of AOM per 100 individuals. The prevalence of AOM exhibits considerable variation across different economic regions, with rates ranging from 3.6 in central Europe to 43.4 in Sub-Saharan West Africa, central Africa, and Asia. Approximately 709 million new episodes of AOM are predicted to occur annually, with 51% of these cases affecting children under 5. The incidence rates of AOM on a global scale exhibit the most significant occurrence in children aged 1-4 years, with 61 new episodes per 100 children annually. Furthermore, the incidence rates reach their maximum during the first year of life, with a rate of 45.3 new episodes per 100 children yearly [6,7].

Ocular melanocytosis is typically devoid of symptoms and can often evade diagnosis, hence posing challenges in accurately determining its frequency and prevalence. The most reliable epidemiological evidence on OME is derived from extensive cohort studies, including children residing in economically disadvantaged nations. These studies, predominantly conducted throughout the 90s, have demonstrated a screening test point prevalence of OME reaching as high as 20% [6,7]. By the age of three, the majority of children have experienced at least one occurrence of OME [18-21]. The highest occurrence rate is observed around the age of one year.

According to a study, CSOM has a global incidence rate of 4.8 new episodes per 1,000 individuals [across all age groups] annually [2]. An estimated annual incidence of around 31 million cases of CMOS has been reported, with approximately 22% of these cases occurring in children under the age of 5. According to research, the initial year of an individual's existence exhibits the highest occurrence of CMOS on a global scale, with a reported incidence rate of 15.4 new cases per 1,000 children [7].

2.1. The Social and Environmental Factors

The risk associated with operational management is influenced by a multitude of host and environmental variables. Several variables have been identified as potential risk factors for OM. These include a young age, male sex, race and ethnicity, genetic factors and a family history of OM, craniofacial defects such as cleft palate, atopy, immunodeficiency, upper respiratory tract infections [URTI] and adenoid hypertrophy, and laryngopharyngeal reflux [8,9]. Several environmental risk factors have been identified for OM, including low socioeconomic status, exposure to tobacco smoke, having older siblings, attending daycare, and using pacifiers [9,10]. According to a study conducted by, it has been found that breastfeeding has a preventive effect on OM. In underdeveloped countries, the presence of malnutrition, filthy water, poor hygiene, overcrowding, HIV infection, TB, malaria, and inadequate health care services contribute to an increased probability of chronicity and complications associated with OM [3,9].

3. Pathophysiology and Mechanisms

In spite of the considerable prevalence of sickness, OM in economically prosperous countries is predominantly characterized by a self-limiting nature and infrequently leads to auditory impairment or developmental setbacks [6]. Hearing loss with long-term consequences is more prevalent among high-risk populations in both emerging and affluent nations. The disease progression of these people is a multifaceted amalgamation of social, environmental, and genetic risk factors. The pathogenesis of OM commences with the initial and extensive colonization of bacteria in the nasopharynx. This is followed by the emergence of early-stage AOM, characterized by an inflammatory process occurring in the middle ear due to persistent exposure to infectious agents. Additionally, the formation of biofilms, viral infections, and the development of severe chronic ear disease contribute to the progression of OM.

3.1. Bacterial Pathogens

The colonization of the nasopharynx by bacterial pathogens at an early stage significantly increases the susceptibility to OM. The three primary bacterial pathogens that prevail globally are Streptococcus pneumoniae [commonly known as pneumococcus], non-typeable Haemophilus influenzae, and Moraxella catarrhalis. However, the prevalence of these species and strains is influenced by geographical location and the utilization of pneumococcal conjugate vaccination (PCV). Research findings indicate that infants of Indigenous Australian descent, aged between 1 and 3 months, exhibit a higher likelihood of harboring two or more nasopharynx otopathogens compared to their non-Indigenous counterparts in Australia. The carriage of non-typeable H in Indigenous Australian children at an early age. The presence of Haemophilus influenzae increases the risk of OM, whereas early carriage of Moraxella catarrhalis in non-Indigenous Australian children decreases the risk. The risk of OM is elevated in the presence of Moraxella catarrhalis. The observed discrepancy between Indigenous and non-Indigenous Australian children can be attributed to many environmental risk factors [12]. There is limited research available that has established a connection between

nasopharyngeal bacterial density or load and OM. Furthermore, the existing studies have primarily concentrated on children who are at a higher risk of developing OM [9-12]. Nevertheless, these analyses provide evidence that there is a correlation between the density of bacteria in the nasopharynx and the likelihood of developing OM.

Bacterial biofilms, known for their ability to shield bacteria from the effects of antibiotics [12] and the host immune response, have been detected in the middle ears of individuals diagnosed with CMOS (CSOM) [13], persistent OME (OME) [10-13], and OM cases that have shown resistance to antibiotic treatment [6]. Biofilms have been observed on the mucosa of the middle ear using MEE. Animals that have been immunized against non-typeable Haemophilus influenzae. The study conducted showed that immunization against influenzae led to a more rapid clearance of biofilm infections, indicating that immunization can elicit immune responses that effectively target pathogens present in middle ear biofilms [13].

3.2. Viral Pathogens

The occurrence of AOM is consistently preceded by the common cold or viral upper respiratory tract infection (URTI). The presence of bacterial otopathogens in the nasopharynx does not result in adverse effects until the occurrence of viral-induced inflammation. AOM can arise due to various upper respiratory tract infection (URTI) viruses. The respiratory viruses of significance, listed in descending order of importance [13], encompass RSV, rhinovirus, adenovirus, coronavirus, bocavirus, influenza, parainfluenza, enterovirus, and human metapneumovirus. The presence of a viral infection leads to modifications in the immunological function of the host [13,14]. This results in the activation of cytokine activity and inflammatory mediators [65], as well as an elevation in bacterial colonization and adherence. This is achieved by the upregulation of host cell surface antigens, which act as receptor sites for bacterial attachment. Viral infection can lead to alterations in the properties of mucus and the process of mucociliary clearance by cells in the Eustachian tube and nasopharynx mucosa. This phenomenon gives rise to tubal dysfunction, which subsequently leads to the occurrence of negative middle ear pressure. It is worth noting that this condition tends to be more pronounced in children who are under 24 months of age as compared to those who fall within the age range of 25-47 months [14]. The presence of negative pressure in the middle ear facilitates the ingress of pathogens, such as germs and viruses [69]. The risk of developing AOM is dependent on the presence of colonized bacterial otopathogens. The absence of colonization carries the lowest risk, while the presence of all three otopathogens carries the highest risk [12,14].

3.3. The Role of Immune System

The heritability estimates for AOM and OME vary between 40% and 70%, with boys exhibiting significantly higher heritability compared to girls [16]. Several genes associated with the innate immune response have been found to be connected to OM [1,4]. Cytokine polymorphisms specific to the otopathogen may enhance the susceptibility to OM. Polymorphisms in IL6, IL10, and TNF have been found to be indicative of OM in both humans and animals when they coincide with respiratory syncytial virus [RSV] and rhinovirus infection [8]. Additionally, polymorphisms in signal transduction pathways, such as TLR signaling have been associated with both the risk and severity of OM [18]. The majority of polymorphisms primarily impact the innate immune response. However, certain variations within the transforming growth factor-p [TGFp] signaling pathway have the potential to disrupt pro-inflammatory responses [17,18]. The presence of cell-mediated dysfunction is increasingly evident in pediatric patients with OM who have deficient antibody responses to specific otopathogens, despite the existence of conflicting findings. The precise genetic factors behind these discoveries remain uncertain, while it is plausible that interactions between pathogens, hosts, and the environment may play a role. Further investigation is required to gain a comprehensive understanding of the mechanisms through which these genetic factors contribute to the occurrence of OM.

4. Screening, Diagnosis, and Prevention

The symptoms reported in a patient's medical history may indicate the presence of OM, but they do not provide sufficient evidence for a definitive diagnosis. For example, symptoms of AOM may be either absent or inconspicuous [3,5]. The symptoms commonly associated with acute ear infection are not observed in OME. However, children with OME may experience hearing difficulties, engage in ear scratching, exhibit clumsiness, have disrupted sleep patterns, demonstrate delays in language development, or exhibit subpar academic performance [7,19].

The prevalence of ear pain is high among individuals diagnosed with AOM, with approximately 50-60% of affected youngsters reporting this symptom [19]. Prelinguistic children may exhibit symptoms of ear pain through behaviors such as tugging, rubbing, or holding their ears, excessive screaming, or alterations in their sleep patterns and behavior [5]. Fever and vomiting are general symptoms that lack specificity in differentiating AOM from Upper Respiratory Tract Infection (URTI) in pediatric patients [17].

The diagnosis of AOM and OME is not possible without the inclusion of MEE, as indicated by a previous study [5]. The challenge associated with validating MEE in primary care settings elucidates the reason behind the frequent occurrence of overdiagnosis of AOM [5,9]. There is evidence to suggest that paediatricians may exhibit a tendency to underdiagnose OME in comparison to otolaryngologists [15,17]. AOM, CMOS are known to be potential causes of observable discharge in the external auditory canal. A significant diagnostic feature of AOM is the identification of

tympanic membrane bulging using otoscopy [2,5].

4.1. Diagnostic Approaches

Otoscopy. Otoscopy serves as the primary diagnostic tool for AOM. In order to achieve an accurate diagnosis, it is imperative to remove earwax that obstructs the tympanic membrane [12,17-19]. During the process of otoscopy, the physician documents various aspects pertaining to the tympanic membrane, including its color, opacity, position, and integrity. The presence of a protruding tympanic membrane, which has been associated with a higher incidence of bacterial infections in MEE, is the most enduring manifestation of AOM [9-10] and serves as the most effective means of differentiating AOM from OME [14]. The tympanic membrane may exhibit a wrinkled appearance when the swelling diminishes [4-7]. The presence of an opaque or hazy tympanic membrane is a reliable indicator of MEE, regardless of its underlying cause. There are a number of image-based scales that have been developed to standardize the process of otoscopic recording and interpretation [15].

Tympanometry. Tympanometry is a diagnostic procedure that provides an objective assessment of middle ear function and the mobility of the tympanic membrane [2]. Tympanometry exhibits comparable sensitivity [ranging from 90% to 94%], but demonstrates lesser specificity in comparison to pneumatic otoscopy for the purpose of diagnosing OME. Tympanometry is a more convenient and valuable method compared to pneumatic otoscopy for the management of children with OM in primary care settings. However, the cost of equipment and the need for training pose significant obstacles [1]. Tympanometry is a diagnostic procedure that provides an estimation of the equivalent volume of the ear canal. This volume refers to the amount of air present in front of the probe and typically ranges from 0.3 to 0.9 ml in children [11]. In the event that the ear canal is obstructed by cerumen or if the probe is applied with pressure against the canal wall, it is possible that a low equivalent volume, measuring less than 0.3 ml, could result in an unreliable measurement. A significant equivalent volume, ranging from 1 to 5.5 ml, suggests the presence of a perforated or ventilation tube, necessitating more investigation if not initially considered. Tympanometry commonly employs a 226 Hz tone, although in the case of toddlers under 6 months, it is recommended to use a 1,000 Hz probe tone due to the limited sensitivity of the 226 Hz tone to MEE [14].

Acoustic reflectometry. A greater degree of sound reflection from the tympanic membrane is indicative of an increased susceptibility to MEE [17]. Parents are able to monitor the middle ear state of their child due to the user-friendly nature, absence of a completely airtight seal, and reasonable cost of an accessible consumer iteration [18]. Reflectometry has been found to exhibit lower sensitivity [19-21] and specificity [20] compared to tympanometry in the diagnosis of MEE in certain investigations. However, its notable high specificity and negative predictive values contribute to effectively exclude MEE in children with URTIs.

4.2. Prevention

The implementation of preventive measures for OM can exhibit variability as a result of its intricate characteristics. Strategies that prioritize the reduction of modifiable risk factors encompass all types of infections, such as bacterial, viral, and environmental. The topic of discussion in management pertains to the utilization of antibiotic and surgical chemoprophylaxis as strategies to mitigate the occurrence of OM in young individuals.

Vaccines targeting bacterial otopathogens. The objective of immunizations is to eradicate S. The phenomenon of nasopharyngeal colonization. The presence of untypeable H. pneumoniae strains is observed. Influenzae and M. The term "catarrhalis" refers to a specific bacterial species. The pneumococcal conjugate vaccine 7 (PCV7) is designed to specifically target seven serotypes of Streptococcus pneumoniae. Pneumonia treatment became accessible in the United States and various European countries starting in the year 2000. The vaccine was incorporated into the standard universal vaccination regimen at 2, 4, and 6 months of age, followed by a booster dose administered at 12-15 months. The administration of PCV7 resulted in a 29% reduction in AOM caused by the serotypes included in the vaccination. Additionally, PCV7 led to a 6-7% decrease in overall AOM cases and a 20% reduction in the use of ventilation tubes for chronic recurrent OM [16,18]. According to the cited source, it was observed that ten years after its introduction, the use of PCV13 resulted in a decrease in the incidence of AOM, mastoiditis, and the need for ventilation tube insertions [21].

4.3. Treatment of OM

Infants with Down syndrome and craniofacial malformations, such as cleft palate, who are particularly vulnerable to the condition, have been excluded from OM trials. There is a pressing need for rigorous academic research to be conducted on the screening and management options for at-risk youth with OME. Further investigation is required to examine the efficacy of topical antibiotics in the treatment of AOM accompanied by spontaneous tympanic membrane perforation-induced ear discharge. The efficacy of the topical antibiotic approach has been demonstrated in pediatric patients with breathing tubes, however, its effectiveness in individuals without tubes remains uncertain [2-5,12].

Additionally, there exists intriguing research pertaining to trans-tympanic medication delivery methods that do not require membrane rupture or the use of a tube. According to a study conducted on chinchillas, the application of ciprofloxacin gel to the tympanic membrane resulted in a significant rise in antibiotic concentrations in the middle ear fluid. This increase was found to be sufficient for the treatment of AOM [6,7]. Further investigation is required to ascertain the most viable and efficient strategies for

implementing human applications. The efficacy of hearing aids and other acoustic interventions, such as soundfield amplification, in the management of OME remains uncertain. There is a need for robust empirical evidence, particularly in the context of children who are at a higher risk for this condition. The utilization of biomolecules to stimulate the formation of perforated edges and the investigation of bioengineered scaffolds have been subjects of research in the field of CMOS with the aim of enhancing the repair of tympanic membrane perforations. Further investigation is required to ascertain the therapeutic efficacy of these medications [2-8].

Across order to facilitate the pooling and comparison of results across future studies, it is imperative for clinicians and researchers to establish a consensus on illness definitions, study techniques, and core outcome measures across all domains of epidemiology, prevention, and treatment within the field of OM. Current recommendations suggest the incorporation of outcome measures in trials evaluating the management of orofacial myofunctional disorders in pediatric patients with cleft palate [18-23]. It is strongly advised that core outcome sets be implemented for all patient groups and manifestations of oral mucosal conditions, encompassing both specific and general impacts. We propose engaging in comprehensive discussions regarding parents and children, ensuring an appropriate level of information, with the intention of involving them in the planning phase as well as all following stages of operations management study. The enhancement of practice can be facilitated by the implementation of high-quality research that possesses statistical power and is devoid of confounding factors. Such research endeavors can effectively add significance to the field of occupational medicine for children and their caregivers.

5. Conclusions

Otitis media encompasses three conditions: acute otitis media (AOM), otitis media with effusion (OME), and chronic suppurative otitis media (CSOM). AOM is common and can lead to severe complications, especially in low-income nations. OME, often following AOM, affects child development and can lead to hearing loss. CSOM is prevalent in low- and middle-income countries and can result in hearing loss and neurological issues. Global efforts, including vaccination and guidelines, have improved otitis media management. Diagnostic approaches contribute to effective assessment and management of ear conditions, although their specificities and sensitivities vary. The effectiveness of hearing aids and acoustic interventions for OME remains uncertain and requires more robust evidence, especially for high-risk populations. Establishing consensus on OM research standards is vital, and involving parents and children in research planning can improve the quality and relevance of pediatric occupational medicine studies, ultimately benefiting both children and caregivers.

REFERENCES

[1] A. G. Schilder et al., "Otitis media," Nature reviews Disease primers, vol. 2, no. 1, pp. 1–18, 2016.

[2] S. M. Parmar, A. Sood, and H. S. Chakkal, "Prevalence of chronic suppurative otitis media in schoolgoing children," Indian Journal of Otology, vol. 24, no. 4, pp. 223–226, 2018.

[3] G. Bowatte et al., "Air pollution and otitis media in children: a systematic review of literature," International Journal of Environmental Research and Public Health, vol. 15, no. 2, p. 257, 2018.

[4] H. Atkinson, S. Wallis, and A. P. Coatesworth, "Otitis media with effusion," Postgraduate medicine, vol. 127, no. 4, pp. 381–385, 2015.

[5] S. Wallis, H. Atkinson, and A. P. Coatesworth, "Chronic otitis media," Postgraduate medicine, vol. 127, no. 4, pp. 391–395, 2015.

[6] K. A. Daly et al., "Epidemiology, natural history, and risk factors: panel report from the Ninth International Research Conference on Otitis Media," International journal of pediatric otorhinolaryngology, vol. 74, no. 3, pp. 231–240, 2010.

[7] R. DeAntonio, J.-P. Yarzabal, J. P. Cruz, J. E. Schmidt, and J. Kleijnen, "Epidemiology of otitis media in children from developing countries: A systematic review," International Journal of Pediatric Otorhinolaryngology, vol. 85, pp. 65–74, 2016.

[8] L. Monasta et al., "Burden of disease caused by otitis media: systematic review and global estimates," PloS one, vol. 7, no. 4, p. e36226, 2012.

[9] Y. Zhang, M. Xu, J. Zhang, L. Zeng, Y. Wang, and Q. Y. Zheng, "Risk factors for chronic and recurrent otitis media–a meta-analysis," PloS one, vol. 9, no. 1, p. e86397, 2014.

[10] A. Sophia, R. Isaac, G. Rebekah, K. Brahmadathan, and V. Rupa, "Risk factors for otitis media among preschool, rural Indian children," International journal of pediatric otorhinolaryngology, vol. 74, no. 6, pp. 677–683, 2010.

[11] P. Vanneste and C. Page, "Otitis media with effusion in children: Pathophysiology, diagnosis, and treatment. A review," Journal of otology, vol. 14, no. 2, pp. 33–39, 2019.

[12] L. O. Bakaletz, "Bacterial biofilms in the upper airway-evidence for role in pathology and implications for treatment of otitis media," Paediatric respiratory reviews, vol. 13, no. 3, pp. 154–159, 2012.

[13] T. Marom, J. Nokso-Koivisto, and T. Chonmaitree, "Viral–bacterial interactions in acute otitis media," Current allergy and asthma reports, vol. 12, no. 6, pp. 551–558, 2012.

[14] S. Skovbjerg et al., "High cytokine levels in perforated acute otitis media exudates containing live bacteria," Clinical microbiology and infection, vol. 16, no. 9, pp. 1382–1388, 2010.

[15] T. M. Wine and C. M. Alper, "Cytokine responses in the common cold and otitis media," Current allergy and asthma reports, vol. 12, pp. 574–581, 2012.

[16] R. Mittal et al., "Role of innate immunity in the pathogenesis of otitis media," International Journal of Infectious Diseases, vol. 29, pp. 259–267, 2014.

[17] A. Leichtle, Y. Lai, B. Wollenberg, S. I. Wasserman, and A. F. Ryan, "Innate signaling in otitis media: pathogenesis and recovery," Current allergy and asthma reports, vol. 11, pp. 78–84, 2011.

[18] A. Leichtle et al., "The role of DNA sensing and innate immune receptor TLR9 in otitis media," Innate immunity, vol. 18, no. 1, pp. 3–13, 2012.

[19] J. Kim, S. K. Park, J. H. Park, D. W. Lee, Y. S. Choi, and S. O. Shin, "Clinical Characteristics of Bilateral Chronic Otitis Media.," Korean Journal of Otorhinolaryngology-Head and Neck Surgery, vol. 57, no. 12, pp. 821–825, 2014.

[20] K. M. Harmes, R. A. Blackwood, H. L. Burrows, J. M. Cooke, R. Van Harrison, and P. P. Passamani, "Otitis media: diagnosis and treatment," American family physician, vol. 88, no. 7, pp. 435–440, 2013.

[21] S. Bakir et al., "Mental health and quality of life in patients with chronic otitis media," European Archives of Oto-rhino-laryngology, vol. 270, pp. 521–526, 2013.

[22] I. Baumann, B. Gerendas, P. K. Plinkert, and M. Praetorius, "General and disease-specific quality of life in patients with chronic suppurative otitis media-a prospective study," Health and Quality of Life Outcomes, vol. 9, pp. 1–6, 2011.

[23] P. Marchisio, E. Nazzari, S. Torretta, S. Esposito, and N. Principi, "Medical prevention of recurrent acute otitis media: an updated overview," Expert Review of Anti-Infective Therapy, vol. 12, no. 5, pp. 611–620, 2014.