



# Outcome of Gastroesophageal Reflux Therapy in Children with Persistent Otitis Media with Effusion

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## Abstract

**Introduction** Otitis media with effusion (OME) is considered one of the most common disorders that affect children during the first years of life. There are many risk factors of persistent middle ear effusion; one of these risk factors is gastroesophageal reflux. Association between persistent OME and gastroesophageal reflux diseases (GERDs) could be explained by respiratory tract infections, insufficient ciliary clearance, and poor drainage of the Eustachian tube.

**Objective** To investigate whether the control of gastroesophageal reflux plays a role in the management of persistent OME and decreases tympanostomy tube insertion

**Method** A cross-sectional study was conducted on 50 children complaining of persistent OME. Their ages ranged between 5 and 12 years old. All children were subjected to full history taking, audiological assessment and 24-hour esophageal pH monitoring. The study group was divided according to pH results into two groups: GERD positives and GERD negatives.

**Result** The prevalence of GERD in persistent OME was 58%. There were statistically significant differences in the hearing levels and middle ear condition before and after the treatment ( $p < 0.05$ ). The percentage of improvement of children complaining of persistent OME after antireflux treatment was 52%.

**Conclusion** Gastroesophageal reflux disease should be considered in patients with persistent OME. The administration of proton pump inhibitor (PPI) can set aside superfluous surgical treatment (such as tympanostomy).

## Keywords

- ▶ otitis media with effusion
- ▶ gastroesophageal reflux
- ▶ child
- ▶ prevalence

## Introduction

Otitis media with effusion (OME) is considered one of the most common disorders that affect children during the early years of their life.<sup>1</sup> Its true prevalence is difficult to estimate as it is a silent disorder. Moreover, according to a previous study,<sup>2</sup> its prevalence in children is ~ 16.5%, and between 2.2 and 4.8% worldwide.<sup>3</sup> About 90% of children have reported at least one episode of OME by the age of 4 years old. One of the

most common causes of hearing loss in children is persistent middle-ear effusion, which lasts for > 3 months, with no improvement even after treatment.<sup>4</sup>

Many risk factors exist for persistent middle ear effusion, one of them being gastroesophageal reflux (GER),<sup>5</sup> which is the reflux of gastric content beyond the oropharynx, the larynx, and the nasopharynx. Children with GER may complain of different symptoms such as heartburn, vomiting, and regurgitation.<sup>6</sup> The association between persistent OME and

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gastroesophageal reflux diseases (GERDs) can be explained by respiratory tract infections, insufficient ciliary clearance, and poor drainage of the Eustachian tube.<sup>7</sup>

Two studies were conducted on rats, and in the first one, Heavner et al.<sup>8</sup> concluded that the repeated exposure of the Eustachian tube to the main components of gastric juice (hydrochloric acid [HCL] and pepsin) may lead to Eustachian tube dysfunction, followed by OME. In the other study, the authors found that mucociliary clearance was affected in rats exposed to HCL.<sup>9</sup>

A previous study conducted on 54 children, aged between 2 and 8 years old, who complained of glue ear, reported an increase in the level of pepsin/pepsinogen in effusion samples compared with its level in the serum, suggesting that GER may be the cause of persistent OME.<sup>10</sup>

The presence of bothersome symptoms and complications of the reflux of gastric content can be roughly diagnosed as GERD.<sup>11</sup> The diagnosis of GERD can be confirmed by esophageal PH monitoring with a double probe in which acid may pass the anatomical barrier of the upper esophageal sphincter and come into contact with the extraesophageal mucosa.<sup>12</sup> Proton pump inhibitor (PPI) such as lansoprazole or omeprazole is considered the current treatment for GERD.<sup>13</sup> This medication is safe for use in children as young as 2 years old.<sup>14</sup> While the tympanostomy tube (TT) is considered the standard treatment for persistent OME, it is not completely safe. The hazards of TT insertion include otorrhea, perforation of the tympanic membrane, granulation tissue, myringosclerosis, segmental atrophy of the eardrum, and acquired cholesteatoma.<sup>15</sup>

The study of Beyea et al.<sup>16</sup> concluded that TT patients have a higher risk of chronic ear disease surgery than patients with recurrent middle ear disease.

Therefore, the present study aims to investigate whether the control of gastroesophageal reflux plays a role in the management of persistent OME and decreases tympanostomy tube insertion.

## Subject and Method

### Study Design & Subjects

A cross-sectional study was conducted in the Otorhinolaryngology department and Pediatric Gastroenterology Unit in a teaching university hospital. Concerning ethical aspects, the parents and/or those responsible for the children were given an Informed Consent Form (ICF), and so did the children themselves receive the Informed Assent Form. Both documents contained the objectives of the study, the steps in carrying it out, and its risks and benefits. Furthermore, the confidentiality of the data was guaranteed by the signing of the researchers of the Confidentiality Agreement.

The present study assessed 50 children complaining of persistent OME (OME for > 3 months with no improvement even after obtaining medical treatment).<sup>4</sup>

**The eligibility criteria established for the present research were:** 1) children between the ages of 5 and 12 years old; 2) the presence of bilateral persistent OME for at least 3 months with no improvement even after obtaining medical treatment, based on: **a)** clinical history: the history of hearing

loss, aural fullness and/or ear rubbing; **b)** pneumatic otoscopy: observations suggestive of OME include the presence of a dull tympanic membrane, presence of a level of effusion, decrease or nonmotility of the tympanic membrane, retraction of the tympanic membrane; **c)** tympanometry: type B (flat curve tympanogram with normal external ear canal volume) with absent acoustic reflex; **d)** pure-tone audiometry: the conductive hearing loss diagnosed by elevated pure tone threshold with air bone gap (ABG) should be at least 10 dB and bone conduction threshold should be better than 25 dB. **The exclusion criteria were:** **a)** children with a medical history or concurrent conditions known to increase the incidence of OME, including cleft palate, neurologic delay, allergic rhinitis or Down syndrome, were excluded. **b)** patients with structural abnormalities of the tympanic membrane, including atelectasis, or deep retraction pockets, were also excluded.

**All participants in the current study were subjected to the following**

1. Full history taking including

- Personal history (age, name and gender)
- History of hearing loss, tinnitus, discharge, earache, headache
- History of GERD symptoms (heartburn, vomiting)
- Past history of systemic disease, physical trauma, acoustic trauma, ototoxic drug and operations

**2- Otological examination:** preauricular region, ear pinna, postauricular region, and tympanic membrane.

**3- Basic audiological evaluation**

**a- Pure-tone audiometry** using Orbiter 922 GM (Otomotrix, Denmark): This included

- Air conduction: (Air conduction hearing thresholds were determined by the frequency range of 0.250 and 8 KHz)
- Bone-conduction: (bone conduction hearing thresholds were determined by the frequency range of 0.500 and 4 KHz)
- Hearing thresholds > 25dB were considered as hearing loss (HL).

**b- Speech audiometry** Speech Reception Threshold (SRT) using Arabic spondee words and the Word discrimination scores (WDS) using Arabic phonetically balanced words

**c- Immittanceometry** using Amplaid 724 (Amplifon, Italy). This included tympanometry and acoustic reflex threshold measurement.

4- 24-hour esophageal pH monitoring.

Children were assessed for GERD symptoms (acid regurgitation and heartburn) and all those having GERD were clinically referred to the Pediatric Gastroenterology Unit and underwent a prolonged ambulatory 24-hour esophageal pH monitoring.

Diagnosis of GERD was based on the presence of GERD-related complaints and a decrease in esophageal pH to < 4 for at least 15 seconds. Thereafter, the patients were divided into two groups: GERD positive and GERD negative.

## Procedure

The parents were instructed on antireflux precautions, anti-reflux therapy was prescribed by a pediatric Gastroenterology specialist. The antireflux precautions were avoiding

chocolate, acidic or fruit juices, tomatoes, and fatty or greasy foods; avoiding eating before bedtime; and elevating the head of the bed. Also, the parents were instructed to avoid smoking near the child.

The GERD positive group was given the PPI lansoprazole for between 8 and 12 weeks; 2 dosages of lansoprazole were administered based on the weight of the child. Children weighing < 30 kg were given 15 mg lansoprazole per day, while children weighing > 30 kg were given 30 mg per day.<sup>4</sup>

Each month, the children returned to the clinic for a follow-up visit. At each follow-up visit, the physician completed a follow-up data sheet documenting, history taking, GERD symptoms and basic audiological evaluation. After 3 months; children who did not improve were referred to an ear, nose and throat (ENT) clinic for placement of a tympanostomy tube. **Improvement** was defined as improvement in middle ear effusion and audiometric testing.

**Statistical Analysis**

The data were analyzed by IBM SPSS Statistics for Windows, version 24.0 (IBM Corp, Armonk, NY, USA). Continuous variables were presented as the mean ± standard deviation (SD) and range. Numerical variables were presented by the count and percentage. The independent-samples t-test was used to determine if a difference exists between the means of two independent groups on a continuous dependent variable. The chi-squared test of association was used to discover if there was a relationship between two categorical variables. The differences were considered significant at *p* < .05. All statistical comparisons were two-tailed.

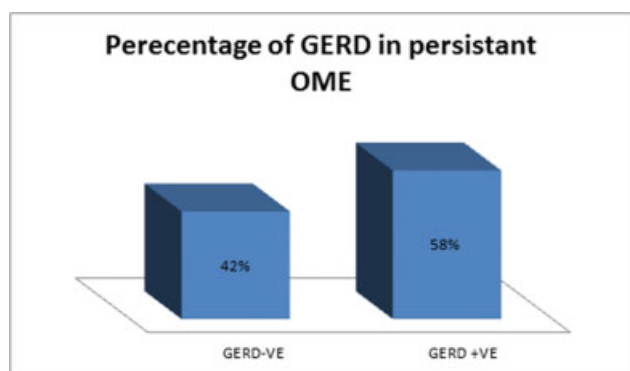
**Results**

**Baseline Characteristics of the Study Groups**

Ages ranged between 5 and 12 years old with a mean age of 8.4 ± 1.2 years old. They were 22 females (44%) and 28 males (56%).

**The Distribution of Study Group According to 24-hour Esophageal pH Monitoring**

The study group was divided into two groups: GERD positives (58%) and GERD negatives (42%). The prevalence of GERD in persistent OME was 58%, as shown in ➤Fig. 1.



**Fig. 1** Percentage of gastroesophageal reflux in persistent otitis media with effusion.

**Basic Audiological Assessment**

➤Tables 1 and 2 show the mean of pure-tone hearing thresholds in the right and left ears of the children with positive GERD before and after treatment with antireflux therapy. There was a statistically significant difference in the hearing levels before and after the treatment (*p* < 0.05).

**Table 1** Mean, Standard deviation range of pure tone thresholds in dB HL in the right ear of 29 patients of the (+) GERD before and after treatment

Frequency (Hz)	Before treatment	After treatment	t	p-value
	Mean ± SD	Mean ± SD		
250	35.5 + 9.5 20-50	16.3 + 6.8 10-40	8.8501	0.0001*
500	33.6 + 9.4 20-50	18.2 + 6.1 10-40	7.4008	0.0001*
1000	32.4 + 5.8 20-40	18.2 + 6.4 10-35	8.8536	0.0001*
2000	31.3 + 4.7 20-40	21.1 + 5.2 10-30	7.6829	0.0001*
4000	32.5 + 4.2 20-40	17.2 + 4.3 10-30	13.7074	0.0001*
8000	33.2 + 6.8 20-40	18.9 + 4.7 10-30	9.3160	0.0001*

Abbreviation: SD, standard deviation.

*p* ≥ 0.05: nonsignificant.

\**p* < 0.05: significant.

(+) GERD Presence of GERD related complaints and a decrease in esophageal pH to < 4 for at least 15 seconds.

**Table 2** Mean, Standard deviation, range of pure tone thresholds in dB HL in the left ear of 29 patients of the (+) GERD before and after treatment

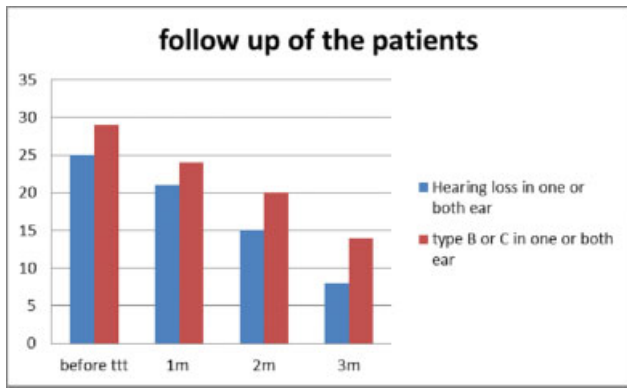
Frequency (Hz)	Before treatment	After treatment	t	p-value
	Mean ± SD	Mean ± SD		
250	35.1 + 8.8 20-50	17.9 + 7.7 10-40	7.6910	0.0001*
500	32.2 + 8.1 20-50	18.4 + 6.4 10-40	7.1988	0.0001*
1000	31.5 ± 5.8 20-40	17.9 + 6.2 10-35	8.6264	0.0001*
2000	30.8 ± 3.3 20-40	20.5 + 5.1 10-30	9.1311	0.0001*
4000	32.7 ± 4.2 15-35	17.5 + 4.4 10-30	13.4568	0.0001*
8000	33.1 ± 6.1 15-35	19.6 + 4.5 10-30	9.5907	0.0001*

Abbreviation: SD, standard deviation.

*p* ≥ 0.05: nonsignificant.

\**p* < 0.05: significant.

(+) GERD Presence of GERD related complaints and a decrease in esophageal pH to < 4 for at least 15 seconds.



**Fig. 2** Follow up of the middle ear condition and hearing loss in the patients

►Fig. 2 shows the follow up of the middle ear condition and the hearing loss in the patients before and after (1–2–3 Months) antireflux therapy. There was a statistically significant difference ( $p < 0.05$ ).

As demonstrated in ►Table 3, the percentage of the improvement of persistent OME after antireflux treatment was 52%, and the percentage of the improvement of the hearing thresholds was 68%. There was a statistically significant difference ( $p < 0.05$ ).

**Discussion**

Otitis media with effusion and GERD are considered two of the most common diseases in children, and this encouraged researchers to prove there is an association between the two diseases and to find a causative relationship between them.<sup>17</sup> A previous study noticed the presence of pepsin in the middle ear effusion among children complaining of OME.<sup>10</sup> Poelmans et al.<sup>18</sup> explained that this association was due to a structural cause, as a horizontal, shorter Eustachian tube in children may increase the reflux of nasopharyngeal contents into the middle ear.

In the present study, ages ranged between 5 and 12 years old with a mean age of  $8.4 \pm 1.2$  years old. The children involved in the present study were 22 females (44%) and 28 males (56%).

The prevalence of GERD in the present study was 58%, as shown in ►Fig. 1. This result was in accordance with a previous study conducted by Yüksel et al.,<sup>7</sup> who reported that 54.9% of children with OME had GERD. Also, Velepici et al.<sup>19</sup> concluded that ~ 60% of the children with tubotympanic disease complained of GERD. The same result was reported by several studies that determined that the prevalence of GERD in children

with OME ranged from 55.6 to 64%.<sup>20,21</sup> On the other hand, Abd El-Fattah et al.<sup>22</sup> found that the percentage of GERD in OME was 17.6%. The different result could be explained by different methodology in the study conducted by Abd El-Fattah et al.<sup>22</sup> In that study, the children complaining of OME were submitted to ventilation tube, tonsillectomy and adenoidectomy, and then assessed pH after recovery from surgery. So, the effects of these procedures on GERD were not well established, as the best time for assessing pH must be before the surgery.

Three mechanisms could explain the increased prevalence of GERD in OME. The first and the most significant one is the harmful effect of acid contents on the mucosa, which results in mucosal swelling, hypersecretion, and ciliary dysfunction. The second mechanism is vagus nerve stimulation. The last one assumed a relation between *Helicobacter pylori* infection and OME. Several studies reported the presence of this bacterium in aspirates of the middle ear.<sup>23,24</sup> The stimulation of *Muc5b* gene expression in the middle ear epithelium by the acidic and proteolytic effect of refluxed pepsin in the middle ear, is considered another possible explanation for the association between the two disorders.<sup>25</sup>

One of the positive confirmations for the role of GERD in the pathogenesis of OME is the improvement of OME with antireflux treatment. According to the previous studies, the percentage of the improvement of the treatment was ~ between 80 and 85% of the studied patients, which resulted in a reduction in the planned surgical procedures.<sup>21,26,27</sup>

In the present study, there is a statistically significant difference in audiometric and tympanometric findings before and after the intake of PPI. The percentage of the improvement of OME in the children with GERD positive are 52%, and the improvement of the hearing thresholds was 68%, as shown in ►Table 3.

The improvement of the middle ear condition and the hearing level of the children occurred gradually. After 1 month of treatment, the OME was improved in 5 patients and the hearing thresholds reached normal levels in 4 patients. The level of improvement increased after 2 months of treatment; 9 patients recovered from OME and 10 patients had normal hearing thresholds. At the end of the study, improvement of OME was found in 15 patients (52%) and improvement of hearing threshold was found in 17 patients (68%). The present study was similar to a previous study conducted by McCoul et al.<sup>17</sup>. They reported statistically significant improvements in hearing loss, tympanometry, and middle ear status after the intake of PPI; progress occurred in 28 of 37 children (76%) at the second visit and in 6 of 10 children (60%) at the third visit.

**Table 3** Middle ear condition and hearing loss in the patients before and after antireflux treatment

Number		Before treatment	After treatment	p-value
Hearing loss	Present	25	8 (32%)	0.00002212*
	Absent	4	21 (68%)	
Tympanometry	Type B/C in one or both ear	29	14 (48%)	0.00002691*
	Type A	0	15 (52%)	

$p \geq 0.05$ : nonsignificant..  
\* $p < 0.05$ : significant.

Also, Dewan et al.<sup>4</sup> demonstrated that lansoprazole administration has a significant enhancement in the pure tone threshold (PTA) and the speech recognition threshold with 33% improvement rate of the middle ear effusion by the end of 3 months of follow-up. In addition, Rosenfeld et al.<sup>28</sup> stated a 28% improvement rate of effusion by the end of 3 months.

## Conclusions

The present study specifies that GERD could have a significant etiologic role in the pathogenesis of OME, as a result of existing statistically significant enhancements in hearing thresholds, and tympanometric results.

One of the important constituents of the effective management of OME in children is the control of GERD. In persistent OME, the administration of PPI can set aside superfluous surgical treatment (as tympanostomy).

### Conflict of Interests

The authors have no conflict of interests to declare.

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