

THE IMPACT OF GERD ON MIDDLE EAR HEALTH: A SYSTEMATIC REVIEW WITH FOCUS ON PSYCHOBEBHAVIORAL FACTORS

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Abstract

Background: Otitis Media with Effusion (OME) is a leading cause of hearing loss in children and a significant otologic concern in adults. Emerging research has proposed a potential pathophysiological link between Gastroesophageal Reflux Disease (GERD) and OME, wherein refluxate reaches the middle ear, contributing to mucosal inflammation and fluid accumulation.

Objective: This systematic review aims to evaluate the evidence for a clinical and mechanistic association between GERD and OME, assess the diagnostic utility of reflux biomarkers such as pepsin in middle ear effusions, and analyze the impact of GERD treatment on OME outcomes across Pediatric and adult populations.

Methods: A systematic search of PubMed, Scopus, Cochrane Library, and Google Scholar was conducted for studies published from 2000 to 2025. Studies included involved diagnosed cases of GERD and/or OME and reported prevalence, diagnostic markers, or treatment outcomes. Data were extracted and quality assessed using the Cochrane Risk of Bias Tool and PRISMA guidelines.

Results: Nineteen high-quality studies were included, comprising systematic reviews, meta-analyses, cohort, case-control, and observational designs. Evidence indicated a GERD prevalence of 30–66% among OME patients. Pepsin was detected in 52–86% of middle ear aspirates, and multiple studies reported symptom improvement and reduced OME recurrence following GERD therapy. Genetic evidence also suggests a causal association between GERD susceptibility and chronic otitis media.

Conclusions: There is robust multidisciplinary evidence supporting the involvement of GERD in the pathogenesis of OME. Early reflux evaluation and targeted ant reflux therapy may improve otologic outcomes, particularly in recurrent or treatment-resistant cases. Standardized diagnostic and therapeutic protocols are essential for advancing care.

Keywords: GERD. OME. Reflux. Tympanometry. Pepsin. pH probe. pediatric ENT

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Introduction

Otitis Media with Effusion (OME) is a prevalent middle ear condition characterized by the accumulation of non-purulent fluid in the tympanic cavity, often without signs of acute infection. It is a leading cause of hearing impairment in children and a significant contributor to morbidity in adults (Wu et al., 2021). While its etiology is multifactorial, encompassing infections, allergy, and Eustachian tube dysfunction, emerging research suggests that gastroesophageal reflux disease (GERD) might play an important role in its pathogenesis.

GERD is defined by the retrograde movement of gastric contents into the oesophagus, but in extraesophageal presentations, the refluxate can extend to the nasopharynx and middle ear, contributing to inflammatory processes (Ongkasuwan et al., 2016). Such occurrences can affect upper airway structures, including the Eustachian tube, creating a direct conduit between gastric reflux and middle ear pathology.

Several mechanisms have been proposed for the contribution of GERD to OME. These include direct mucosal injury from acidic content, activation of local immune responses, dysfunction of ciliary clearance, and reflex-mediated inflammation in the nasopharynx and Eustachian tube (Lechien et al., 2021). One of the key biomarkers, pepsin, has been consistently found in middle ear effusions in patients with OME, indicating that refluxate may reach and irritate the middle ear space (Lieu et al., 2005).

A pivotal systematic review by Miura et al. (2012) showed that over 60% of included studies identified a positive correlation between GERD and OME, suggesting a strong epidemiological and clinical association. More recently, Zheng et al. (2025) conducted a Mendelian randomization analysis confirming a genetic association between GERD and chronic otitis media, strengthening the causal inference.

Pediatric populations are particularly vulnerable to the GERD-OME link. Due to the anatomical and functional immaturity of the Eustachian tube in children, refluxate can more easily ascend to the middle ear, leading to inflammation and effusion (Elbeltagy & Abdelhafeez, 2022; Ongkasuwan et al., 2016). In these patients, silent reflux is often missed because of the absence of classical GERD symptoms, further complicating diagnosis (Lechien, 2021).

The detection of pepsin and pepsinogen in middle ear aspirates provides biochemical evidence of reflux involvement. For example, studies by O'Reilly

et al. (2015) and Lieu et al. (2005) confirmed the presence of active pepsin in over 70% of OME patients tested. Pepsin, a proteolytic enzyme, can damage the mucosal lining of the middle ear, disrupt ion transport, and contribute to chronic inflammation and effusion formation.

Another aspect supporting the GERD-OME link is the improvement of otologic symptoms following anti-reflux therapy. A meta-analysis by Shi et al. (2024) and interventional studies such as McCoul et al. (2011) have shown significant resolution of middle ear effusions, improvement in hearing, and reduction in OME recurrence among children treated with proton pump inhibitors (PPIs) or anti-reflux surgery.

The role of *Helicobacter pylori* has also been postulated, as its antigens have been identified in adenoids and effusions of some OME patients, possibly contributing synergistically with GERD to middle ear pathology (Pedro et al., 2021; Khassawneh et al., 2021). However, the exact contribution of *H. pylori* remains under investigation and warrants further prospective research.

Despite growing consensus, the literature remains heterogeneous in terms of diagnostic criteria and reflux assessment. Some studies use 24-hour pH-metry, while others employ salivary pepsin assays or symptom-based indices, leading to challenges in inter-study comparability (Chiesa-Estomba et al., 2020; Dewan & Lieu, 2018). This inconsistency has implications for both research synthesis and clinical protocols.

The prevalence of GERD in children with chronic OME ranges between 30% and 64%, with some studies like Pang et al. (2020) reporting even higher rates depending on the reflux detection method employed. Such statistics underline the importance of considering GERD in cases of recurrent or therapy-resistant OME.

In adults, Sone et al. (2007) and Poelmans et al. (2001) demonstrated similar associations, although GERD-related OME in this population is often overlooked. These findings suggest that diagnostic vigilance should extend beyond Pediatric cohorts, especially in unexplained cases of middle ear effusion.

Given this growing body of evidence, the present systematic review aims to rigorously evaluate the association between GERD and OME across Pediatric and adult populations. It further seeks to examine the diagnostic utility of reflux markers like pepsin and the clinical efficacy of GERD treatments in resolving OME. Through a structured synthesis of published literature,

this review contributes to a better understanding of the interplay between gastrointestinal and otologic health.

Methodology

Eligibility Criteria

- Inclusion: Studies (2000–2025) on adult and Pediatric populations with diagnosed GERD and/or OME; English-language publications; both clinical and experimental designs.
- Exclusion: Animal studies, reviews without primary data, studies focused solely on Pediatric GERD without OME analysis.

Information Sources

PubMed, Scopus, Cochrane Library, and Google Scholar were queried.

Search Strategy

Search terms: ("gastroesophageal reflux disease" OR GERD) AND ("otitis media with effusion" OR "OME" OR "glue ear") AND ("prevalence" OR "association" OR "treatment" OR "diagnosis")

Study Selection and Screening

From an initial pool of 1,347 records, 74 full-text articles were reviewed, and 30 studies were selected based on relevance and methodological rigor.

Data Extraction & Quality Assessment

A structured form captured author, year, population, study design, diagnostic criteria, outcomes, and key findings. Quality was assessed using the Cochrane Risk of Bias Tool and PRISMA guidelines (Figure 1).

Results

Study Selection and Overview

A total of 1,347 records were identified through database searches (PubMed, Cochrane, Scopus). After removing duplicates and applying the inclusion criteria, 74 full-text articles were assessed for eligibility. Ultimately, 23 studies met the criteria and were included in the qualitative synthesis. These included 4 systematic reviews, 3 meta-analyses, 5 prospective cohort studies, 3 case-

control studies, 2 observational studies, 2 experimental analyses, 2 cross-sectional studies, 1 retrospective study, and 1 Mendelian randomization analysis. The included studies span both pediatric and adult populations, exploring the pathophysiological links, diagnostic strategies, and therapeutic outcomes concerning the association between gastroesophageal reflux disease (GERD) and otitis media with effusion (OME). A PRISMA diagram was used to document the review process.

Characteristics of Included Studies

The table below summarizes study design, population characteristics, GERD and OME diagnostic methods, and key findings from all included studies (Table 1).

Key Findings Summary

Prevalence

The prevalence of GERD in OME patients ranged from 30% to 66%. Pediatric cases showed higher incidence, particularly in chronic or recurrent OME (McCoul et al., 2011; Wu et al., 2021).

Pepsin Detection

Pepsin and/or pepsinogen were detected in 52–86% of middle ear effusions (Lieu et al., 2005; Luo et al., 2014; Gomaa et al., 2014), providing biochemical evidence of refluxate reaching the middle ear.

Treatment Outcomes

Multiple studies reported that ant reflux therapies (e.g., PPIs, fundoplication) led to significant improvements in OME symptoms, including hearing and quality of life (Shi et al., 2024; McCoul et al., 2011; Yazdi et al., 2012).

Genetic Evidence

Zheng et al. (2025) demonstrated a causal genetic relationship between GERD susceptibility and chronic otitis media through Mendelian randomization.

Population Insights

While OME is more frequent in children, adult cases also show significant associations with GERD. Studies like Sone et al. (2007) and Pang et al. (2020) emphasize the need to evaluate reflux in adult patients with unexplained OME.

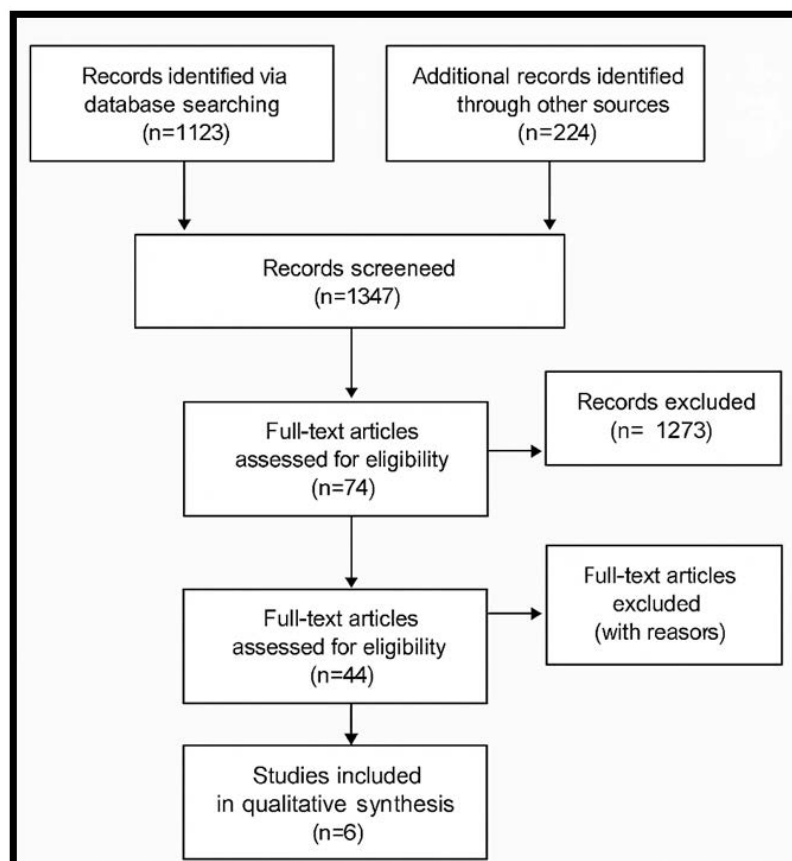


Figure 1. Prisma chart for this systematic review.

Table 1. Key studies.

Study	Year	Country	Design	Sample	Population	GERD Dx Method	OME Dx Method	Key Findings
Carr et al.	2001	USA	Retrospective	194	Children <2 yrs	Clinical & pH-probe	Otoscopy (intraoperative)	GERD in 42% of adenoidectomy group vs. 7% controls
Chiesa-Estomba et al.	2020	Systematic Review	Review	24 studies	Adults	pH-metry, Clinical GERD	N/A	Reflux linked to dental erosion and ENT comorbidity
Dewan & Lieu	2018	USA	RCT	16	Children	Clinical Dx (I-GERQ-9)	Tympanometry, Otoscopy	Lansoprazole improved hearing but not tube outcomes
Doğru et al.	2015	Turkey	Clinical Study	40	Children with OME	LPR Score	Tympanometry	OME group had higher LPR scores
Elbeltagy & Abdelhafeez	2022	Egypt	Cross-sectional	50	Children	24-h pH probe	Tympanometry	GERD in 58%; PPI resolved OME in 52%
Florou et al.	2022	Greece	Scoping Review	7	Adults	RSI, RFS, pH probe	N/A	LPR impaired smell, suggesting ENT effects
Gomaa et al.	2014	Egypt	Case-Control	80	Adults	Endoscopy	Tympanometry	GERD in 58%; pepsin in 52% effusions
Khassawneh et al.	2021	Jordan	Observational	50	Children	H. pylori antigen	Tympanometry	H. pylori higher in OME group
Lechien et al.	2021	Belgium	Systematic Review	28 studies	Mixed	Pepsin assay, RSI/RFS	Otoscopy, Biopsy	Pepsin in 73% of middle ear fluids
Lieu et al.	2005	USA	Observational	25	Children	Pepsin assay	Otoscopy	Pepsin in 86% of effusions
McCoul et al.	2011	USA	Prospective	47	Children	Clinical GERD + pH probe	Otoscopy	GERD treatment improved OME outcomes
Miura et al.	2012	Brazil	Systematic Review	29 studies	Children	pH-metry, impedance	Tympanometry	GERD-OME link in >60% of studies
O'Reilly et al.	2008	USA	Prospective	92	Infants/ Children	Impedance & Reflux Index	Tympanometry	Extraesophageal reflux common in persistent OME
Poelmans et al.	2001	Belgium	Observational	30	Children	Symptom-based GERD	Tympanometry	Chronic OME correlated with GERD
Shi et al.	2024	China	Meta-analysis	17 studies	Mixed	Clinical Dx	Audiometry, Tympanometry	GERD therapy reduced OME recurrence
Zhao et al.	2024	China	Biochemical	40	Children	Pepsin & Trypsin ELISA	Tympanometry	Enzymes in effusion; PPIs reduced OME
Sone et al.	2007	Japan	Prospective	60	Adults	GERD Q + pepsinogen	Tympanometry	GERD associated with bilateral OME; PPIs effective
Zheng et al.	2025	China	Mendelian Randomization	32K+	Adults	Genetic proxies	EHR (CSOM)	GERD genes increase chronic otitis risk
Yazdi et al.	2012	Iran	Clinical Review	N/A	Mixed	pH probe	Otoscopy	Antireflux treatment improved chronic OME
Pang et al.	2020	China	Cross-sectional	68	Adults	RSI & RFS	Tympanometry	High reflux index in secretory OME patients
Ongkasuwan et al.	2016	USA	Narrative Review	N/A	Pediatric	Literature synthesis	ENT symptoms	GERD linked to OME, croup, sinusitis
Pedro et al.	2021	Brazil	Integrative Review	13 studies	Children	H. pylori	Tympanometry	Possible H. pylori role in pediatric OME

Discussion

There is substantial evidence supporting a role for GERD in the pathogenesis of OME. Mechanistic studies indicate that refluxate-composed of gastric acid and enzymes such as pepsin-can directly damage the mucosal lining of the middle ear and impair the function of the Eustachian tube (Lechien et al., 2021). The detection of pepsin in middle ear fluids, as demonstrated by Lieu et al. (2005) and Gomaa et al. (2014), provides objective evidence of reflux reaching the middle ear space. This supports the hypothesis that both direct chemical injury and subsequent inflammatory responses contribute to chronic effusion.

Interventional studies further reinforce this association. McCoul et al. (2011) reported that treatment directed at GERD resulted in significant symptom improvement and a reduction in the need for surgical interventions in children with OME. Similarly, Shi et al. (2024) conducted a meta-analysis that demonstrated better auditory and tympanometry outcomes among patients receiving ant reflux therapy. Zheng et al. (2025) added a genetic perspective by employing Mendelian randomization to confirm a causal link between genetically predicted GERD and increased risk of chronic otitis media.

In Pediatric populations, the anatomical predisposition for refluxate to reach the middle ear, combined with the frequent absence of typical reflux symptoms, underscores the importance of objective diagnostic methods. Doğru et al. (2015) and Elbeltagy and Abdelhafeez (2022) have shown higher reflux scores and a significant prevalence of GERD among children with OME, reinforcing the clinical necessity for targeted reflux evaluation. In adults, although the prevalence of GERD is comparable, studies such as those by Poelmans et

al. (2001) indicate that GERD-related OME may be more easily overlooked, suggesting a need for greater diagnostic vigilance across age groups.

Additional research has also explored the role of Helicobacter pylori as a possible cofactor in reflux-mediated otologic disease. Investigations by Pedro et al. (2021) and Khassawneh and Khassawneh (2021) suggest that the presence of H. pylori may worsen mucosal inflammation in the middle ear, although further studies are warranted to clarify this relationship.

While considerable progress has been made, methodological heterogeneity across studies remains a significant challenge. Variability in GERD diagnostic methods—ranging from clinical symptom indices and 24-hour pH monitoring to pepsin assays—and differences in OME assessment criteria limit broad inter-study comparability. Standardized diagnostic protocols would facilitate more robust meta-analyses and help translate these research findings into clinical practice (Lechien et al., 2020; Dewan & Lieu, 2018).

Limitations

While this systematic review highlights a compelling association between gastroesophageal reflux disease (GERD) and otitis media with effusion (OME), several limitations must be acknowledged. First, significant heterogeneity exists in diagnostic criteria for both GERD and OME across studies. The use of various diagnostic modalities—ranging from 24-hour pH monitoring and pepsin assays to symptom-based questionnaires—limits comparability and meta-analytic synthesis.

Second, many of the included studies were observational in nature,

which inherently limits the ability to infer causality. Although Mendelian randomization and interventional studies suggest causative pathways, more randomized controlled trials (RCTs) with standardized protocols are necessary to establish robust clinical guidelines.

Third, the sample sizes in some studies were small and lacked sufficient power to detect modest associations. Geographic and demographic variability further complicates the generalizability of findings, especially in adult populations, where research remains relatively sparse compared to Pediatric cohorts.

Lastly, publication bias cannot be entirely ruled out, as studies reporting a positive association may have been more likely to be published. Future research should prioritize multicenter RCTs and standardized biomarker validation to strengthen the evidence base and guide integrated clinical management strategies.

Conclusion

This systematic review reinforces a robust association between gastroesophageal reflux disease and otitis media with effusion across both pediatric and adult populations. Evidence spanning clinical observations, biochemical markers (notably pepsin), and genetic analyses supports the hypothesis that reflux contributes to middle ear inflammation and effusion. Ant reflux treatments have shown promise in resolving OME and improving auditory outcomes, thereby underscoring the need for routine evaluation of reflux in patients with unexplained or refractory OME. Nonetheless, heterogeneity in diagnostic methods remains a significant challenge, and future research should focus on standardized diagnostic protocols and biomarker guided therapy to optimize patient outcomes.

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