

# Prevalence and characteristics of gastroesophageal reflux in children with otitis media in Isfahan, Iran

Seyed Hamidreza Abtahi, Azadeh Kazerooni, Nezamodin Brejis, Zahra Abdeyazdan, Hossein Saneian

Department of Otorhinolaryngology, Isfahan University of Medical Sciences, Isfahan, Iran

## Abstract

**Background:** Otitis media (OM) is the most common cause of childhood hearing loss and reason to visit the pediatrician. Furthermore, gastroesophageal reflux (GER) has been associated with a variety of upper aerodigestive tract symptoms or diseases, such as sinusitis, laryngitis, and otitis. The objective of the present study was to determine the frequency of GER in children, aged 3 months to 7 years, with OM.

**Materials and Methods:** This retrospective case-control study was conducted on 50 children with OM and 50 healthy children. Presence of GER as the main variables was diagnosed by clinical examination in all studied children using the questionnaires with 2 age-stratified versions of the pediatric GER disease symptoms for children 2 years old and younger, and children 3–7 years old.

**Results:** The prevalence of GER in children with OM and controls was 58% and 22% respectively ( $P = 0.0005$ ). The frequency of irritability, congestion, and feeding complex in children with OM were significantly more than in control groups. Among children with recurrent acute OM (AOM), and chronic serous OM (CSOM) the prevalence of GER was significantly more than controls (61.1%, vs. 22% for AOM,  $P = 0.004$ , and 72.7% vs. 22%,  $P = 0.003$ ). In children with AOM, regurgitation, vomiting, irritability and congestion were significantly higher than controls included. In children with CSOM, regurgitation, vomiting, and congestion were significantly higher than controls.

**Conclusion:** Results show a significant association between GER and OM, AOM and CSOM in children with OM compares to healthy children. This shows that looking for GER in children with OM may help improving treatments outcomes.

**Key Words:** Acute otitis media, chronic otitis media, gastroesophageal reflux, otitis media

## Address for correspondence:

Dr. Azadeh Kazerooni, Department of Otorhinolaryngology, Isfahan University of Medical Sciences, Isfahan, Iran. E-mail: [azadehkazerooni@gmail.com](mailto:azadehkazerooni@gmail.com)

Received: 24.05.2015, Accepted: 05.07.2015

## INTRODUCTION

Around the world, despite advances in public health and medical care, pediatric middle ear infections are still prevalent.<sup>[1]</sup> Otitis media (OM) is exceptionally common in the pediatric population, is the most common cause of childhood hearing loss, and is among the most common reason to visit the pediatrician.<sup>[2]</sup>

The incidence of OM varies from country to country. Among Europe and the US children aged <1-year is reported that 62% and of those up to the age of three. 83% have suffered from at least one bout of acute OM (AOM).<sup>[3,4]</sup> Also, 90% of children will have one episode of OM with effusion (OME) by 4 years of age.<sup>[5]</sup> In addition, the incidence of this problem in the population seems to be increasing. It infers that,

Access this article online	
Quick Response Code:	Website: <a href="http://www.advbiores.net">www.advbiores.net</a>
	DOI: 10.4103/2277-9175.182212

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

**For reprints contact:** [reprints@medknow.com](mailto:reprints@medknow.com)

**How to cite this article:** Abtahi SH, Kazerooni A, Brejis N, Abdeyazdan Z, Saneian H. Prevalence and characteristics of gastroesophageal reflux in children with otitis media in Isfahan, Iran. *Adv Biomed Res* 2016;5:81.

OM imposes a significant burden on the health care system and families, and the knowledge regarding the cellular and molecular immunologic and inflammatory events in this disease process is very little. Therefore, improvements in understanding the pathophysiology of OM process are vital to advances in prevention and treatment.<sup>[6]</sup>

Gastroesophageal reflux (GER) as the passage of gastric contents into the esophagus is another frequent problem in the newborn and preschool ages.<sup>[7]</sup> Recent researches suggested that the GER disease (GERD) may be an inflammatory cofactor and can result in upper respiratory tract disorders, including OM in adult and pediatric age group and have been implicated in the disease pathogenesis of OM.<sup>[8,9]</sup> The angle of the immature eustachian tube in children may allow reflux of gastric contents from the nasopharynx into the middle ear.<sup>[10]</sup> One study on 54 children aged between 2 and 8 years old, found greater level of pepsin/pepsinogen concentrations than those in serum of the samples and gave an idea that the reflux of gastric content could be a major factor in glue ear in children.<sup>[11]</sup> Therefore, it is necessary to identify the presence or absence of GER in children with OM. The prevalence of GER in children with OM, previously assessed in some clinical studies and vary values were reported between 55.6% and 64% prevalence of GER in children with OM.<sup>[12-15]</sup> Also, some studies reported the prevalence of GER by OM subtype, and the mean ranged between 48% and 57% was reported for chronic OM and 61–65% for recurrent OM (ROM).<sup>[16,17]</sup>

Because of geographical variations between countries, reported the prevalence of GER in children with OM is different and also, the data about the prevalence of GER in children with OM in our area are limited. So, the present study was designed to evaluate the presence of GER in children with OM in Isfahan, Iran, in 2014.

## MATERIALS AND METHODS

In this case-control study, in 2014, 50 cases were recruited of children with OM, aged 6 months to 7 years, from the pediatric otolaryngology clinics at the Al-Zahra Hospital in Isfahan, Iran to assess the frequency of GER in these children. The diagnosis of OM for children in this study was defined as the presence of middle ear effusion for 3 months or greater. Also, OM subtypes included: AOM (the rapid onset of signs [fever, otorrhea, full or bulging opaque tympanogram, impaired tympanogram mobility, tympanogram erythema] and symptoms [otalgia, irritability, insomnia, anorexia] of inflammation of the

middle ear), ROM (at least three episodes of AOM in a 6-month period or four episodes per year with free intervals of at least 1-month), OME (the presence of fluid in the middle ear without signs or symptoms of AOM), chronic OME (persisting for  $\geq 3$  months from the date of onset [if known] or from the date of diagnosis [if onset unknown]).<sup>[18-21]</sup> Other inclusion criterion for cases was no medical history of disorders that are known to be associated with an increased prevalence of OM. Confirming the presence of GER in children in compared to healthy children, 50 children, age younger than 7 years and older than 6 months without OM among who referred to other clinics in our hospital were enrolled as control group. Informed consent was obtained from parents of each participating patient, and the ethics committee of Isfahan University of Medical Sciences investigated and approved the research.

Data collected were age, sex, OM subtype, the presence of middle ear effusion, tympanometry results (types A, B and C), presence of GER, and symptoms of GER. To assess the symptomatic GER, parents of the studied children were asked about current symptoms that may be suggestive of GER, using validated questionnaires. These questionnaires included the two age-stratified versions of the pediatric GERDs symptom for children 2 years old and younger, and children 3–7 years old.<sup>[22,23]</sup>

The collected data were analyzed statistically with SPSS software version 20 (SPSS Inc., Chicago, IL, USA). Descriptive statistics are reported as mean  $\pm$  standard deviation, median (interquartile range [IQR]) or number (percent) as appropriate. Independent sample *t*-test was used to compare quantitative variables, and Chi-square test was used to compare qualitative variables between the two groups. All probability tests used were two-tailed, and alpha was set at 5%.

## RESULTS

Sixty-six children were reviewed to enrolled 50 patients with OM in case group during the study period. Of 66 reviewed children, 10 were not meet eligible criteria and three parents refused informed consent and did not enter to the study. Also, 73 children without OM reviewed to select control group, 9 children did not meet eligible criteria and 14 refused informed consent and were excluded. Finally, 50 children in the case group and 50 children in the control group completed the study and analyzed.

The mean age of studied children was  $30.3 \pm 6.7$  months, 42 (42%) were male and 58 (58%) female. Table 1 shows characteristics of case and control subjects. As shown

mean of age (cases, 31.4 vs. control, 28.8 months), and sex combination between groups were similar and no significant differences were noted between groups ( $P > 0.05$ ). Presenting diagnosis of OM subtypes in cases was, AOM for 36%, OME for 42% and chronic serous OM (CSOM) for 22% of cases. Tympanometry results showed that, most of the cases 48% had type B tympanograms, 24% had type A tympanograms, and 28% had type C tympanograms. The prevalence of GER in children with OM was 58% and which was significantly more than in children without OM with 22% of GER ( $P = 0.0005$ ).

Table 2 shows results of the comparison of the GER symptoms between children with OM and healthy children. Regurgitation, vomiting, irritability, congestion, cough and feeding complex were more frequent symptoms in cases. However, only the differences in the frequency of irritability, congestion and feeding complex between children with OM and healthy children were statistically significant. Also in studied children with OM, stridor, and obstructive apnea had lower frequent than other symptoms. Among controls, irritability and cough were more frequent occur symptoms.

GER symptoms between case and controls were compared by OM subtypes [Table 3]. Among children with AOM the prevalence of GER was 61.1% (11 of 18 children) and was significantly more than in control groups ( $P = 0.004$ ), also most frequent symptoms in these children which were significantly higher than controls included regurgitation (44.4%), vomiting (38.9%), irritability (50%) and congestion (66.7%). The prevalence of GER in children with CSOM was significantly more than in controls (72.2% vs. 22%, respectively,  $P = 0.003$ ). Most frequent symptoms in children with CSOM, which were significantly higher than controls included regurgitation (54.5%), vomiting (45.4%), and congestion (54.5%).

## DISCUSSION

The intermittent application of gastric contents to the middle ear mucosa which led to the Eustachian tube and mucociliary clearance dysfunctions were discussed in some studies.<sup>[24-26]</sup> Some clinical studies reported that GERD has been found in 55.6–64% of the children with OM, also, it is reported that OME frequency has increased in children with GER.<sup>[27,28]</sup> In the present study, children with OM were assessed to determine the prevalence of GER in these children and we found that 58% (29 of 50 children) with OM had GER. The prevalence of GER in children with AOM or CSOM in our study was 61.1% and 72.7%, respectively.

**Table 1: Characteristics of case and control subjects**

	OM (n=50)	Controls (n=25)	P
Age (month)	31.4±8.7	29.8±8.3	0.62*
Sex			
Male/female	19 (38)/31 (62)	23 (46)/27 (54)	0.11†
OM subtype			
RAOM	18 (36)	-	
OME	21 (42)	-	
CSOM	11 (22)	-	
Tympanogram			
Type A	12 (24)	-	
Type B	24 (48)	-	
Type C	14 (28)	-	
GERD	29 (58)	11 (22)	0.0005*

Data are mean±SD or n (%). P values calculated by \*Independent-samples t-test and †Chi-square test. OM: Otitis media, RAOM: Recurrent acute otitis media, CSOM: Chronic serous otitis media, GERD: Gastroesophageal reflux disease, SD: Standard deviation, OME: Otitis media with effusion

**Table 2: GERD symptoms between case and control subjects**

	OM (n=50)	Controls (n=50)	P
Regurgitation	14 (28)	6 (12)	0.08
Vomiting	12 (24)	5 (10)	0.11
Irritability	22 (44)	8 (16)	0.004
Congestion	24 (48)	5 (10)	0.0001
Cough	20 (40)	11 (22)	0.08
Hoarseness	5 (10)	2 (4)	0.43
Arching	4 (8)	3 (6)	0.99
Stridor	2 (4)	1 (2)	0.99
Feeding complex	15 (30)	6 (12)	0.049
Obstructive apnea	2 (4)	0	0.99
Dysphagia	10 (20)	3 (6)	0.07

Data are n (%). P values calculated by Chi-square test. GERD: Gastroesophageal reflux disease, OM: Otitis media

**Table 3: GERD symptoms between AOM, CSOM and control subjects**

	AOM (n=18)	CSOM (n=11)	Controls (n=50)
GERD	11 (61.1)*	8 (72.7)*	11 (22)
Regurgitation	8 (44.4)*	6 (54.5)*	6 (13)
Vomiting	7 (38.9)*	5 (45.4)*	5 (10)
Irritability	9 (50)*	4 (36.4)	8 (16)
Congestion	12 (66.7)*	6 (54.5)*	5 (10)
Cough	8 (44.4)	4 (36.4)	11 (22)
Hoarseness	2 (11.1)	1 (9.1)	2 (4)
Arching	1 (5.5)	1 (9.1)	3 (6)
Stridor	1 (5.5)	0	1 (2)
Feeding complex	5 (27.8)	2 (18.2)	6 (12)
Wheezing	2 (11.1)	0	0

Data are n (%). P values calculated by Chi-square test. \*Significant compare to controls. AOM: Acute otitis media, CSOM: Chronic serous otitis media, GERD: Gastroesophageal reflux disease

The prevalence of GER in children with OM in our study was similar to previous reports. In Velepik et al.,<sup>[28]</sup> study reported 60%, Rozmanic et al.,<sup>[29]</sup> 55.5%, Keles et al.,<sup>[9]</sup> 64%, Serra et al.,<sup>[30]</sup> 54.3% and in a study by Yüksel et al.,<sup>[26]</sup> reported that 54.9% of children with

OM had GER. These studies selected children with chronic OM or recurrent AOM (RAOM) and performed pH monitoring but in our study pH monitoring was not done and our result was similar to other studies. The results of another study by Kotsis *et al.* revealed that 12.24% of children without GERD, 14.1% of children with low to moderate reflux index and 31.67% of children with severe GERD, showed episodes of RAOM.<sup>[25]</sup> In a study by Yüksel *et al.* like our study GERD were reported in 54.9% of studied children with OME.<sup>[26]</sup> In a systematic review by Miura *et al.* a mean prevalence of GERD in children with CSOM was reported to be 48.4% (range, 17.6–64%) which was lower than our finding with prevalence of 72.7% in these children.<sup>[27]</sup> In the other hand in contrast to our study, Abd El-Fattah *et al.*, reported that only three of 17 studied children with OM had GER, this was lower than our results and reports in other studies.<sup>[16]</sup> The differences between these results can be explained by the differences in age of studied children and difference in methodology. The difference in methodology is that they were submitted to ventilation tubes as well as adenoidectomy/tonsillectomy, and after recovery from surgery, pH monitoring was performed. As the effect of these procedures on GER are not well-established, it seems that the most appropriate time for pH monitoring would be before surgical interventions, in the presence of chronic OM. Other studies stratified data of GER prevalence by OM subtype and reported 50% and 56.2% of GER for chronic OME and 61.5% and 64.3% for RAOM, which were similar to our study (72.7% for chronic OME and 61.1% for AOM).<sup>[16,17]</sup>

Most common symptoms in our studied children with OM were regurgitation, vomiting, irritability, congestion, cough and feeding complex, whereas in a study by Yüksel *et al.*,<sup>[26]</sup> most common symptoms were stertor, dysphagia, pyrosis, irritability and choking. Other two studies by Abd El-Fattah *et al.* and Crapko *et al.* have shown that GER is often not associated with the classical symptoms of heartburn, epigastric pain or regurgitation.<sup>[16,17]</sup> But in our study regurgitation was significantly higher in children with OM compare to control group.

One of possible mechanism of GER in the pathogenesis of several common upper respiratory disorders, including OM can be that reflux of gastric contents into the middle ear from the nasopharynx (due to immature anatomy and function of the eustachian tube).<sup>[31]</sup> Also, the nasopharynx caused by the reflux of gastric contents that could eventually lead to the eustachian tube's obstruction and OM can be another possible mechanism of GER in the pathogenesis of OM.<sup>[32]</sup> However, symptom descriptions of GER are nonspecific and unreliable in infants and young

children and esophageal pH monitoring, is a valid and reliable measure of acid exposure to evaluating GER in children with OM, in our study diagnose of GER was based on symptom descriptions of GER and our results in similar to many previous studies show that the prevalence of GER in children with OM is more frequent than healthy children, therefore, more studies seems to be necessary to investigate the exact mechanism of GER in the pathogenesis of OM.

## CONCLUSION

Results of the present study support a potential association between GER and OM, AOM and CSOM in children with OM compares to healthy children. Also, according to our findings, and similar studies looking for GER in children with OM may help improving medical design making and treatments outcomes.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

## REFERENCES

1. Tasker A, Dettmar PW, Panetti M, Koufman JA, P Birchall J, Pearson JP. Is gastric reflux a cause of otitis media with effusion in children? *Laryngoscope* 2002;112:1930-4.
2. Gold BD. Review article: Epidemiology and management of gastro-oesophageal reflux in children. *Aliment Pharmacol Ther* 2004;19 Suppl 1:22-7.
3. Poelmans J, Tack J, Feenstra L. Prospective study on the incidence of chronic ear complaints related to gastroesophageal reflux and on the outcome of antireflux therapy. *Ann Otol Rhinol Laryngol* 2002;111:933-8.
4. Rosenfeld RM, Goldsmith AJ, Tetlus L, Balzano A. Quality of life for children with otitis media. *Arch Otolaryngol Head Neck Surg* 1997;123:1049-54.
5. Kleinman L, Rothman M, Strauss R, Orenstein SR, Nelson S, Vandenplas Y, *et al.* The infant gastroesophageal reflux questionnaire revised: Development and validation as an evaluative instrument. *Clin Gastroenterol Hepatol* 2006;4:588-96.
6. Deal L, Gold BD, Gremse DA, Winter HS, Peters SB, Fraga PD, *et al.* Age-specific questionnaires distinguish GERD symptom frequency and severity in infants and young children: Development and initial validation. *J Pediatr Gastroenterol Nutr* 2005;41:178-85.
7. Carr MM, Nagy ML, Pizzuto MP, Poje CP, Brodsky LS. Correlation of findings at direct laryngoscopy and bronchoscopy with gastroesophageal reflux disease in children: A prospective study. *Arch Otolaryngol Head Neck Surg* 2001;127:369-74.
8. Rosenfeld RM, Bhaya MH, Bower CM, Brookhouser PE, Casselbrant ML, Chan KH, *et al.* Impact of tympanostomy tubes on child quality of life. *Arch Otolaryngol Head Neck Surg* 2000;126:585-92.
9. Keles B, Ozturk K, Arbag H, Gunel E, Ozer B. Frequency of pharyngeal reflux in children with adenoid hyperplasia. *Int J Pediatr Otorhinolaryngol* 2005;69:1103-7.
10. Nelson SP, Chen EH, Syniar GM, Christoffel KK. Prevalence of symptoms of gastroesophageal reflux during infancy. A pediatric practice-based survey. *Pediatric Practice Research Group. Arch Pediatr Adolesc Med* 1997;151:569-72.
11. Phipps CD, Wood WE, Gibson WS, Cochran WJ. Gastroesophageal reflux

- contributing to chronic sinus disease in children: A prospective analysis. *Arch Otolaryngol Head Neck Surg* 2000;126:831-6.
12. Bothwell MR, Parsons DS, Talbot A, Barbero GJ, Wilder B. Outcome of reflux therapy on pediatric chronic sinusitis. *Otolaryngol Head Neck Surg* 1999;121:255-62.
  13. Heavner SB, Hardy SM, White DR, Prazma J, Pillsbury HC 3<sup>rd</sup>. Transient inflammation and dysfunction of the eustachian tube secondary to multiple exposures of simulated gastroesophageal refluxant. *Ann Otol Rhinol Laryngol* 2001;110:928-34.
  14. White DR, Heavner SB, Hardy SM, Prazma J. Gastroesophageal reflux and eustachian tube dysfunction in an animal model. *Laryngoscope* 2002;112:955-61.
  15. Lieu JE, Muthappan PG, Uppaluri R. Association of reflux with otitis media in children. *Otolaryngol Head Neck Surg* 2005;133:357-61.
  16. Abd El-Fattah AM, Abdul Maksoud GA, Ramadan AS, Abdalla AF, Abdel Aziz MM. Pepsin assay: A marker for reflux in pediatric glue ear. *Otolaryngol Head Neck Surg* 2007;136:464-70.
  17. Crapko M, Kerschner JE, Syring M, Johnston N. Role of extra-esophageal reflux in chronic otitis media with effusion. *Laryngoscope* 2007;117:1419-23.
  18. Rosenfeld RM, Schwartz SR, Pynnonen MA, Tunkel DE, Hussey HM, Fichera JS, *et al.* Clinical practice guideline: Tympanostomy tubes in children. *Otolaryngol Head Neck Surg* 2013;149 1 Suppl: S1-35.
  19. Casselbrant ML, Kaleida PH, Rockette HE, Paradise JL, Bluestone CD, Kurs-Lasky M, *et al.* Efficacy of antimicrobial prophylaxis and of tympanostomy tube insertion for prevention of recurrent acute otitis media: Results of a randomized clinical trial. *Pediatr Infect Dis J* 1992;11:278-86.
  20. Bluestone CD, Klein JO. *Otitis Media in Infants and Children*. 4<sup>th</sup> ed. Hamilton (Ontario): BC Decker; 2007.
  21. Rosenfeld RM, Bluestone CD. *Evidence-Based Otitis Media*. 2<sup>nd</sup> ed. Hamilton (Ontario), Lewiston (NY): BC Decker; 2003.
  22. Abd El-Fattah AM, Abdul Maksoud GA, Ramadan AS, Abdalla AF, Abdel Aziz MM. Pepsin assay: A marker for reflux in pediatric glue ear. *Otolaryngol Head Neck Surg* 2007;136:464-70.
  23. O'Reilly RC, He Z, Bloedon E, Papsin B, Lundy L, Bolling L, *et al.* The role of extraesophageal reflux in otitis media in infants and children. *Laryngoscope* 2008;118 Suppl 116:1-9.
  24. Yilmaz MD, Aktepe O, Cetinkol Y, Altuntas A. Does *Helicobacter pylori* have role in development of otitis media with effusion? *Int J Pediatr Otorhinolaryngol* 2005;69:745-9.
  25. Kotsis GP, Nikolopoulos TP, Yiotakis LE, Papacharalampous GX, Kandiloros DC. Recurrent acute otitis media and gastroesophageal reflux disease in children. Is there an association? *Int J Pediatr Otorhinolaryngol* 2009;73:1373-80.
  26. Yüksel F, Dogan M, Karatas D, Yüce S, Sentürk M, Külahli I. Gastroesophageal reflux disease in children with chronic otitis media with effusion. *J Craniofac Surg* 2013;24:380-3.
  27. Miura MS, Mascaro M, Rosenfeld RM. Association between otitis media and gastroesophageal reflux: A systematic review. *Otolaryngol Head Neck Surg* 2012;146:345-52.
  28. Velepich MM, Velepich MS, Starcevic R, Manestar D, Rozmanic V. Gastroesophageal reflux and sequelae of chronic tubotympanic disorders in children. *Acta Otolaryngol* 2004;124:914-7.
  29. Rozmanic V, Velepich M, Ahel V, Bonifacic D, Velepich MJ. Prolonged esophageal pH monitoring in the evaluation of gastroesophageal reflux in children with chronic tubotympanic disorders. *J Pediatr Gastroenterol Nutr* 2002;34:278-80.
  30. Serra A, Cocuzza S, Poli G, La Mantia I, Messina A, Pavone P. Otolologic findings in children with gastroesophageal reflux. *Int J Pediatr Otorhinolaryngol* 2007;71:1693-97.
  31. Klokkenburg JJ, Hoeve HL, Francke J, Wieringa MH, Borgstein J, Feenstra L. Bile acids identified in middle ear effusions of children with otitis media with effusion. *Laryngoscope* 2009;119:396-400.
  32. Galli J, Calò L, Agostino S, Cadoni G, Sergi B, Cianci R, *et al.* Bile reflux as possible risk factor in laryngopharyngeal inflammatory and neoplastic lesions. *Acta Otorhinolaryngol Ital* 2003;23:377-82.