Websites: http://www.sciencepub.net/nature http://www.sciencepub.net

Emails: naturesciencej@gmail.com editor@sciencepub.net



Tympanometric changes in gastro esophageal reflux disease patients

Dr. Mustafa Shams al-Din Khafaji, MD¹, Dr. Ahmed Sobhi Elsayed, MD², Ahmed Mustafa Abdelmoneim, M.B.B.CH³

¹Professor of Otorhinolaryngology Faculty of Medicine, Al-Azhar University, Egypt ²Lecturer of Otorhinolaryngology Faculty of Medicine, Al-Azhar University, Egypt ³Resident of Otorhinolaryngology, Egypt

Abstract: Background: Multiple studies have questioned about the relationship between GERD and eustachian tube dysfunction. This study was conducted to survey tympanometric changes in GERD patients who presented to the Outpatient otorhinolaryngology clinic at Al-Azhar University hospitals. Patient and methods: Forty-eight cases with GERD scores higher than 8 were included. They were subjected to history taking, clinical examination, and complete otorhinolaryngological examination including anterior rhinoscopy, otoscopy, and tympanometry. Results: The mean age of the cases included in the study was 34.51 ± 14.71 . The mean GERD score of the cases included in the study was 10.69 ± 16.91 . In the right ear, there were 39 cases (81.3%) with type A curve, 3 cases (6.3%) with type A curve, 6 cases with type C curve (12.5%) and 3 cases (6.3%) with type A dcurve. Conclusion: Based on the results of the study, we concluded that GERD causes tympanometric changes mostly unilateral type c mostly secondary to unilateral Eustachian tube dysfunction.

[Mustafa Shams al-Din Khafaji, Ahmed Sobhi Elsayed, Ahmed Mustafa Abdelmoneim. **Tympanometric changes** in gastro esophageal reflux disease patients. *Nat Sci* 2019;17(12):31-38]. ISSN 1545-0740 (print); ISSN 2375-7167 (online). <u>http://www.sciencepub.net/nature</u>. 4. doi:10.7537/marsnsj171219.04.

Keywords: Tympanometric; change; gastro; esophageal; reflux; disease; patient

1. Introduction

Gastro esophageal reflux disease, GERD is a condition where there is repeated backward movement of stomach contents into the esophagus causing damage to the esophageal tissues (*Herregods et al., 2015*).

The esophagus is protected from the harmful effects of refluxed gastric contents by the anti-reflux barrier at the gastro esophageal junction, by esophageal clearance mechanisms, and by epithelial defensive factors (*Vakil et al., 2006*).

The attachment of the lower esophageal sphincter to the crural diaphragm results in increased pressure during inspiration and when intra-abdominal pressure increases disruption of normal defense mechanisms leads to pathologic amounts of reflux *(Eherer, 2014)*.

Signs and symptoms of GERD occur when defective epithelium comes into contact with refluxed acid, pepsin, or other noxious gastric contents, In addition to the direct noxious effects of refluxed acid, pepsin, and bile, refluxed gastric juice stimulates esophageal epithelial cells to secrete chemokines that attract inflammatory cells into the esophagus, thereby damaging the esophageal mucosa (*Larsen et al.*, 2013).

Individuals with a diagnosis of GERD have symptoms of heartburn, regurgitation, upper

abdominal pain within one hour of eating and dysphagia, these symptoms usually worsen when the individual is in a supine position or if the intrabdominal pressure increases (*Herregods et al., 2015*).

Other proposed associations that are not clearly established include pharyngitis, sinusitis, otitis media, and idiopathic pulmonary fibrosis (*Vakil et al., 2006*).

When GERD is associated with typical signs and symptoms, such as heart- burn or acid regurgitation, that are responsive to antisecretory therapy, no diagnostic evaluation is warranted (*Katz et al., 2013*). GERD Questionnaire has been developed as a tool to support the diagnosis of GERD and to assist in the selection of suitable treatment based on response measurement, it has been developed on the basis of evidence and information collected from recent highquality clinical studies (*Dent et al., 2007*).

The term Eustachian tube dysfunction (ETD) describes impairment of ET function and leads to a variety of symptoms and physical findings, the condition does not necessarily lead to detectable middle ear pathologies (*Schilder et al., 2015*). Because the most common cause of obstructive dysfunction is mucosal inflammation within the cartilaginous ET, patients should be questioned about

laryngopharyngeal reflux (LPR) *(Seibert and Danner, 2006)*. ETD has been found to be associated with a higher number of nasopharyngeal reflux events and higher reflux finding score in adult patients *(Brunworth et al., 2014)*.

Tympanometry is one of the most frequently performed and important components of the basic audiologic evaluation, Tympanometry measures how the middle-ear system responds to sound energy and how it reacts dynamically to changes in atmospheric pressure (*Iacovou et al., 2013*).

Tympanometry is an objective, physiological measure of acoustic admittance of the middle ear as a function of air pressure in a sealed ear canal, Normally our ears operate most efficiently at atmospheric pressure, Clinically it is of interest to measure middle ear function at greater and lesser pressures compared to ambient pressure for diagnostic purposes because many conditions can affect pressure within the middle ear, Increases or decreases in air pressure cause the TM and ossicular chain to stiffen, and this change can be seen as a decrease in admittance of sound energy to the middle ear (Iacovou et al., 2013).

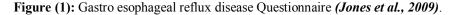
2. Patients and methods Study design

This a cross sectional observational study conducted to survey tympanometric changes in gastro esophageal reflux disease patients who presented to the Outpatient otorhinolaryngology clinic at Al-Azhar University hospitals in the period between December 2018 and August 2019. The study was approved by the local ethical committee.

Patient sample

Forty-eight patients (n = 48) complaining from gastro esophageal reflux disease, with GERD score (figure 1 - developed by jones and his colleagues (*Jones et al., 2009*)) over 8 points were included. Patients having score less than 8, complaining from other orogenic diseases not caused by gastro esophageal reflux disease, or having nasal diseases (congenital, traumatic, inflammatory, neoplastic) were excluded from our study.

| Question | | Frequency score (points) for symptom | | | |
|---|---|--------------------------------------|----------|----------|--|
| | | 1 day | 2-3 days | 4–7 days | |
| 1. How often did you have a burning feeling behind your breastbone (heartburn)? | 0 | 1 | 2 | 3 | |
| 2. How often did you have stomach contents (liquid or food) moving upwards to your throat or mouth (regurgitation)? | 0 | 1 | 2 | 3 | |
| 3. How often did you have a pain in the centre of the upper stomach? | 3 | 2 | 1 | 0 | |
| 4. How often did you have nausea? | 3 | 2 | 1 | 0 | |
| 5. How often did you have difficulty getting a good night's sleep because of your heartburn and/or regurgitation? | 0 | 1 | 2 | 3 | |
| 6. How often did you take additional medication for your heartburn and/or regurgitation, other than what the physician told you to take? (such as Tums, Rolaids, Maalox?) | 0 | 1 | 2 | 3 | |



Patient preparation

All cases were subjected to complete history taking and thorough clinical examination. Moreover, complete otorhinolaryngological examination with anterior rhinoscopy and otoscopy.

Tympanometry

It was performed for all cases. Tympanometry was performed with the middle ear analyzer Impedance Audiometer - AT235h - Interacoustics®, using 226 Hz and 1 kHz probe tones. Two tympanometric measures were analyzed, the compliance and the gradient. The compliance was measured in both types of probe tones and the gradient was evaluated only with the 226 Hz probe tone, both obtained in ml.

Statistical analysis of data

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for

Social Sciences) version 22 for Windows® (SPSS Inc, Chicago, IL, USA). Data of categorical variables were presented as number (frequency) and comparison between two groups containing qualitative data was compared using Chi-Square test (x^2). Quantitative data was checked for normal distribution by using Kolmogorov-Smirnov test. Parametric data was presented as mean \pm SD. Student t-test was used to compare two groups with parametric quantitative data (expressed as t). Non parametric data was presented as median (min – max). Mann-Whitney test (expressed as z) was used for comparison between groups.

The correlation between continuous normally distributed data was performed by Pearson's correlation while Spearman's correlation was used to test the correlation between continuous not normally distributed data (expressed as r). P value < 0.05 was considered to be significant.

3. Results

The mean age of the included cases included in the study was 34.51 ± 14.71 years with minimum age of 13 years and maximum age of 63 years. Among the cases included in the study there were 3 males (6.3%) and 45 females (93.8%).

The mean GERD score of the cases included in

the study was 10.69 ± 16.91 . Regarding the distribution of GERD score in the cases, there were 7 cases (14.6%) with score 9, 18 cases (37.5%) with score 10, 6 cases (12.5%) with score 11 and 17 cases (35.4%) with score 12. These data are illustrated in Table (1).

| Table (| 1): Demographic data and | nd GERD score of the ca | ses included in the study. |
|---------|--------------------------|-------------------------|----------------------------|
|---------|--------------------------|-------------------------|----------------------------|

| Age (years) | | | |
|-------------------------|-------------------|------------|--|
| Mean \pm SD | 34.51 ± 14.71 | | |
| Median (Min-Max) | 32 (13-63) | | |
| Sex | Frequency | Percentage | |
| Male | 3 | 6.3 % | |
| Female | 45 | 93.8 % | |
| GERD score | | | |
| Mean \pm SD | 10.69 ± 16.91 | | |
| Median (Min-Max) | 10 (9-12) | | |
| GERD score (categories) | Frequency | Percentage | |
| 9 | 7 | 14.6% | |
| 10 | 18 | 37.5% | |
| 11 | 6 | 12.5% | |
| 12 | 17 | 35.4% | |

Regarding the analysis the curves of tympanogram detected in the cases, the data are shown in table (2). In the right ear, there were 39 cases (81.3%) with type A curve, 3 cases (6.3%) with type B curve and 6 cases (12.5%) with type Ad curve.

In the left ear, there were 36 cases (75%) with type A curve, 3 cases (6.3%) with type B curve, 6 cases with type C curve (12.5%) and 3 cases (6.3%) with type Ad curve.

| Right ear | | • | |
|-----------|-----------|------------|--|
| | Frequency | Percentage | |
| Type A | 39 | 81.3 % | |
| Type B | 3 | 6.3 % | |
| Type C | 0 | 0 % | |
| Type Ad | 6 | 12.5 % | |
| Left ear | | | |
| | Frequency | Percentage | |
| Type A | 36 | 75% | |
| Type B | 3 | 6.3% | |
| Type C | 6 | 12.5% | |
| Type Ad | 3 | 6.3% | |

Table (2): Tympanometry types in the study cases.

Regarding the comparison of the patients according the types of curves in right ear, the data are illustrated in Table (3). The mean age in cases with type A tympanogram curve was 36.03 ± 15.36 years, in type B was 30 years and in cases with Ad curve it was 27 ± 9.85 with no significant difference between the three groups (p= 0.322).

There were 3 males with and 36 females in cases with group A and in group B and C all the cases were females with no significant difference in the sex distribution between the study groups (p=0.691).

There were 7 cases with score 9, 18 cases with score 10, 3 cases with score 11 and 11 cases with score 12 in cases with type A tympanogram cases. All the cases with type B curves had score 12 and in cases with type Ad curves, there were 3 cases with score 11 and 3 cases with location 3 with statistically significant difference between the three groups (p=0.006).

Table (3): Comparison of items according to groups of tympanogram curves in the right ear.

| Variables | <i>Type A (N=39)</i> | <i>Туре В (N=3)</i> | Type Ad (N=6) | Test of significance |
|-------------------|----------------------|---------------------|---------------|--------------------------------------|
| Age | | | | |
| Mean ± SD | 36.03 ± 15.36 | 30 | 27 ± 9.85 | |
| P1 | | 0.768 | 0.339 | F= 1.164 |
| P2 | | | 0.954 | P = 0.322 |
| Sex | • | | • | |
| Male | 3 (7.7%) | 0 (0%) | 0 (0%) | $\chi 2 = 0.738$ |
| Female | 36 (92.3%) | 3 (100%) | 6 (100%) | P = 0.691 |
| GERD Score | | | · | |
| 9 | 7 (17.9%) | 0 (0%) | 0 (0%) | |
| 10 | 18 (46.2%) | 0 (0%) | 0 (0%) | |
| 11 | 3 (7.7%) | 0 (0%) | 3 (50%) | $\chi 2 = 18.081 \text{ P} = 0.006*$ |
| 12 | 11 (28.2%) | 3 (100%) | 3 (50%) | |

Quantitative data expressed as (mean \pm SD)

Categorical data expressed as (number and percentage within group) F= one-way ANOVA $\chi^2=$ chi-square test P= probability P1= significance in relation to type A group

P2= significance in relation to type B group

*= significant value when $p \le 0.05$

Regarding the comparison of the patients according the types of curves in left ear, the data are illustrated in table (4). The mean age in cases with type A tympanogram curve was 33.69 ± 16.13 years, in type B was 30 ± 1.86 years, in type C it was $41\pm$ 9.85 and in cases with Ad curve it was 36 ± 1.03 with no significant difference between the three groups (p= 0.667).

There were 3 males with and 33 females in cases with group A tympanogram curves and in group B, C and Ad all the cases were females with no significant difference in the sex distribution between the study groups (p=0.785).

There were 7 cases with score 9, 12 cases with score 10, 3 cases with score 11 and 14 cases with score 12 in cases with type A tympanogram curves cases. All the cases with type B curves had score 12, all cases with type C curves had score 10 and all cases with type Ad tympanogram curves had score 11 high level of significance between the three groups (p< 0.001).

| Variables | <i>Type A</i> (<i>N</i> =36) | <i>Туре В</i> (N=3) | Type C (N=6) | Type Ad (N=3) | Test of significance |
|------------|----------------------------------|------------------------|-----------------|------------------|--|
| Age | | | | | |
| Mean ± SD | 33.69 ± 16.13 | 30 ± 1.86 | 41 ± 9.85 | 36 ± 1.03 | |
| P1 | | 0.975 | 0.678 | 0.994 | F = 0.526 |
| P2 | | | 0.917 | 0.959 | P = 0.667 |
| P3 | | | | 0.963 | |
| Sex | | | | | -2 - 1.0(7) |
| Male | 3 (8.3%) | 0 (0%) | 0 (0%) | 0 (0%) | $\chi^2 = 1.067$ P = 0.785 |
| Female | 33 (91.7%) | 3 (100%) | 6 (100%) | 3 (100%) | $\Gamma = 0.783$ |
| GERD Score | | | | | |
| 9 | 7 (19.4%) | 0 (0%) | 0 (0%) | 0 (0%) | |
| 10 | 12 (33.3%) | 0 (0%) | 6 (100%) | 0 (0%) | $\chi 2 = 37.843 \text{ P} < 0.001 **$ |
| 11 | 3 (8.3%) | 0 (0%) | 0 (0%) | 3 (100%) | |
| 12 | 14 (38.9%) | 3 (100%) | 0 (0%) | 0 (0%) | |

| Table (4): Compariso | on of items according | g to groups o | of tympanogram | curves in the right ear. |
|----------------------|-----------------------|----------------|-----------------|---------------------------|
| Tuble (1). Comparise | on or reems accorany | s to si oups (| or cympunosi um | cal ves in the right cart |

Quantitative data expressed as (mean \pm SD)

Categorical data expressed as (number and percentage within group) F= one-way ANOVA χ 2= chi-square test P= probability P1= significance in relation to type A group

P2= significance in relation to type B group P3= significance in relation to type C group

** = highly significant value when $p \le 0.001$

4. Discussion

Eustachian tube connects the tympanic cavity and the nasopharynx. Eustachian tube patency and its proper functioning are highly essential for the normal maintenance of middle ear function. Obstruction of the Eustachian tube will result in negative pressure in the tympanum and lead to retraction, effusion and other complications *(Handzel et al., 2012)*.

Eustachian tube has at least three important functions with respect to the middle ear: Ventilation or pressure regulation of the middle ear, clearance or drainage of middle ear secretions into the nasopharynx and protection from nasopharyngeal secretions and sound pressure. The ventilator function is important since a malfunctioning Eustachian tube hampers the function of tympanum and leads to middle ear effusion *(Choi et al., 2009)*.

Gastro esophageal reflux disease is defined as chronic symptoms due to mucosal damage caused by the reflux of gastric contents into the esophagus. The classical symptoms of GERD are heartburn, regurgitation, chest pain, dysphagia, odynophagia, nausea, dyspepsia, bloating, belching, indigestion, water brash and hiccups (*Bredenoord and Smout*, 2008).

Malfunctioning of eustachian tube opening could be due to GERD besides other causes. Previous studies have established that GERD may cause inflammation of the nasopharyngeal end of Eustachian tube and result in Eustachian tube catarrhal inflammation (*Brunworth et al., 2014*).

The passage of gastric acid and pepsin leads to impaired functioning of the Eustachian tube after constant exposure to pH<4, which favors the onset of average otitis (*Crapko et al., 2007*). This type of change may be common in infants who have GER and undergo newborn hearing screening (NHS), through otoacoustic emissions. This test is sensitive to changes in middle ear, it is imperative to evaluate the same (by tympanometry) in neonates due to the high incidence of GERD aged zero to six months (*Vargas Garcia et al., 2009*)

Tympanometry is the most widely used method in clinical practice to assess functional condition of the middle ear, mobility of the tympanic membrane and dynamic ossicle *(Shanks and Shohet, 2009)*.

This study was conducted to survey tympanometric changes in gastro esophageal reflux disease patients by tympanometry.

The study included 48 patients who were diagnosed to have GERD (score over 8 points at gastro esophageal reflux Disease Questionnaire). All the patients were subjected to tympanometry.

Another study recruited nearly equal number of patients (50 patients) to assess gastroesophageal reflux

disease (GERD) in patients with Eustachian tube catarrh and the effect of proton pump inhibitors on symptoms of Eustachian tube disease (*Bhargava et al., 2015*).

Abtahi et al. conducted a retrospective casecontrol study on 50 children with OM and 50 healthy children to determine the frequency of GER in children (*Abtahi et al., 2016*).

The mean age of the cases included in the study was 34.51 ± 14.71 years with minimum age of 13 years and maximum age of 63 years. Among the cases included in the study there were 3 males (6.3%) and 45 females (93.8%).

This came in agreement with another study where most of the included cases were females (70%) and only 30% were males. Also in that study, the majority were in the age groups of 45 years and above (44%) with minimum age of 18 years (*Bhargava et al., 2015*).

This also came in accordance with Camboim and his colleagues who included 118 infants ranging in age from newborns to 6-month-olds and demonstrated higher prevalence of female cases (*Camboim et al., 2012*).

This disagreed with many results that demonstrated higher prevalence of male cases included in these studies (*Costa et al., 2004; Oliveira and Norton, 2009*).

In another study, the mean age of studied children was 30.3 ± 6.7 months, 42 (42%) were male and 58 (58%) female *(Abtahi et al., 2016)*.

Anwar et al. included 43 males and 20 females and a total 117 ears of 63 patients who underwent myringotomy operation. The M: F ratio was 2.15:1. The age range was 3 to 12 years with mean age of seven years (*Anwar et al., 2016*).

Ulualp et al have done a study to determine the prevalence and the characteristics of pharyngeal acid reflux events in single and multiple otolaryngological disorders. The authors hypothesize that the presence of posterior laryngitis may be an indicator of a causal role for gastroesophageal reflux in other aerodigestive tract lesions, such as chronic rhinosinusitis, vocal cord nodule and laryngotracheal stenosis (Ulualp et al., 1999).

Issing et al did a study in 40 patients to determine the incidence of gastroenterological disease in patients complaining of upper aerodigestive, pulmonary, laryngeal, pharyngeal and oral symptoms. They showed that in man patients suffering from the abovementioned otolaryngological symptoms, occult gastroesophageal disease was present *(Issing et al.,* 2001).

Koufman did a clinical investigation of 225 patients to establish occult (silent) gastroesopshageal

reflux. GERD is an etiological factor in the development of many inflammatory and neoplastic disorders of the upper aerodigestive tract (*Koufman*, 1991).

In our study, the analysis the curves of tympanogram detected in the cases, revealed in the right ear, there were 39 cases (81.3%) with type A curve, 3 cases (6.3%) with type B curve and 6 cases (12.5%) with type Ad curve. While in the left ear, there were 36 cases (75%) with type A curve, 3 cases (6.3%) with type B curve, 6 cases with type C curve (12.5%) and 6 cases (12.5%) with type Ad curve.

The pattern of tympanometric analysis in the study conducted by Anwar and his colleagues was as follows; in the left ear, 3 cases with type A, 47 cases with type B and 13 cases with type C while in the right ear, 8 cases with type A, 43 cases with type B and 12 cases with type C (*Anwar et al., 2016*)

Another study was conducted by Tallat Jabeen and colleagues in the twin cities of Rawalpindi and Islamabad involving 600 children in different schools. Using tympanometry as a screening tool, they found OME in 13% of these children. Type B curve was found in 88.5% and type C curve was obtained in 11.5% of these children (*Jabeen et al., 2013*)

The typmpanomeric curve was type A (normal) in 78% of the cases, type C in 8% of the cases and type Ad in 2% of the cases (*Bhargava et al., 2015*).

In another study, Tympanometric tests were performed to diagnose OME. The tympanometry test results showed type B in 47 (77%) and type C in 14 (23%) of the 61 ears in the OME group (*Doğru et al., 2015*).

McCoul et al. included 36 cases in their study and showed that 83.8% of the cases had type B tympanogram and 8.3% of the cases had type A and type C curves for each type *(McCoul et al., 2011)*.

In another study, tympanometry results showed that, most of the cases 48% had type B tympanogram, 24% had type A tympanogram, and 28% had type C tympanogram. The prevalence of GERD in children with OM was 58% and which was significantly more than in children without OM with 22% of GERD (*Abtahi et al., 2016*).

Regarding the prevalence of GERD in cases with OM in different studies, Velepic *et al.*, study reported 60%, Rozmanic *et al.*, 55.5%, Keles *et al.*, 64%, Serra *et al.*, 54.3% and in a study by Yüksel *et al.*, reported that 54.9% of children with OM had GERD (*Rožmanic et al.*, 2002; Velepic et al., 2004; Keles et al., 2005; Serra et al., 2007; Yüksel et al., 2013).

The results an 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 *(Kotsis et al., 2009)*

In a study by Yüksel *et al.* like our study GERD were reported in 54,9% of studied children with OME *(Yüksel et al., 2013)*

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 *(Miura et al., 2012)*

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 *(Abd El-Fattah et al., 2007)*.

Conclusion

Based on the results of the study, we concluded that GERD causes tympanometric changes mostly unilateral type c mostly secondary to unilateral Eustachian tube dysfunction.

References

- Abd El-Fattah, A M; Abdul Maksoud, G A; Ramadan, A S; Abdalla, A F and Abdel Aziz, M M. (2007). Pepsin assay: a marker for reflux in pediatric glue ear. Otolaryngology—Head and Neck Surgery, 136(3), 464-470.
- Abtahi, S H; Kazerooni, A; Brejis, N; Abdeyazdan, Z and Saneian, H. (2016). Prevalence and characteristics of gastroesophageal reflux in children with otitis media in Isfahan, Iran. Advanced biomedical research, 5.
- 3. Anwar, K; Khan, S; ur Rehman, H; Javaid, M and Shahabi, I. (2016). Otitis media with effusion: Accuracy of tympanometry in detecting fluid in the middle ears of children at myringotomies. Pakistan journal of medical sciences, 32(2), 466.
- 4. Bhargava, A; Cherian, M; Cherian, T A and Gupta, S. (2015). Gastroesophageal Reflux Disease in Patients with Eustachian Tube Catarrh. International Journal of Phonosurgery and Laryngology (2), 61-66.
- 5. Bredenoord, A J and Smout, A J. (2008). Refractory gastrooesophageal reflux disease. European journal of gastroenterology & hepatology, 20(3), 217-223.
- Brunworth, J D; Mahboubi, H; Garg, R; Johnson, B; Brandon, B and Djalilian, H R. (2014). Nasopharyngeal acid reflux and Eustachian tube dysfunction in adults. Annals of Otology, Rhinology & Laryngology, 123(6), 415-419.
- Camboim, E D; Scharlach, R C; Almeida, M C O d; Vasconcelos, D and Azevedo, M F d. (2012). Analysis of compliance and tympanometric gradient in infants with reflux. Revista da

Sociedade Brasileira de Fonoaudiologia, 17(2), 156-160.

- Choi, S H; Han, J H and Chung, J W. (2009). Pre-operative evaluation of eustachian tube function using a modified pressure equilibration test is predictive of good postoperative hearing and middle ear aeration in type 1 tympanoplasty patients. Clinical and experimental Otorhinolaryngology, 2(2), 61.
- Costa, A J; Silva, G A; Gouveia, P A and Pereira Filho, E M. (2004). Prevalência de refluxo gastroesofágico patológico em lactentes regurgitadores. J Pediatr (Rio j), 80(4), 291-295.
- Crapko, M; Kerschner, J E; Syring, M and Johnston, N. (2007). Role of extra - esophageal reflux in chronic otitis media with effusion. The Laryngoscope, 117(8), 1419-1423.
- 11. Dent, J; Vakil, N; Jones, R; Reimitz, P; Schöning, U; Halling, K, et al. (2007). Validation of the reflux disease questionnaire for the diagnosis of gastroesophageal reflux disease in primary care. Gut, 56(Suppl 111), 328.
- 12. Doğru, M; Kuran, G; Haytoğlu, S; Dengiz, R and Arıkan, O K. (2015). Role of laryngopharyngeal reflux in the pathogenesis of otitis media with effusion. J Int Adv Otol, 11(1), 66-71.
- 13. Eherer, A. (2014). Management of gastroesophageal reflux disease: lifestyle modification and alternative approaches. Digestive Diseases, 32(1-2), 149-151.
- Handzel, O; Poe, D and Marchbanks, R J. (2012). Synchronous endoscopy and sonotubometry of the eustachian tube: a pilot study. Otology & Neurotology, 33(2), 184-191.
- Herregods, T; Bredenoord, A and Smout, A. (2015). Pathophysiology of gastroesophageal reflux disease: new understanding in a new era. Neurogastroenterology & Motility, 27(9), 1202-1213.
- Iacovou, E; Vlastarakos, P V; Ferekidis, E and Nikolopoulos, T P. (2013). Multi-frequency tympanometry: clinical applications for the assessment of the middle ear status. Indian Journal of Otolaryngology and Head & Neck Surgery, 65(3), 283-287.
- 17. Issing, W; Gross, M and Tauber, S. (2001). Manifestations of gastroesophageal reflux in the otorhinolaryngology tract. Laryngo-rhinootologie, 80(8), 464-469.
- Jabeen, T; Malik, S N and Chattha, R U. (2013). Frequency of secretory otitis media in children of age 3 to 5 years in Rawalpindi and Islamabad. Rawal Medical Journal, 38(1), 52-55.
- 19. Jones, R; Junghard, O; Dent, J; Vakil, N; Halling, K; Wernersson, B, et al. (2009). Development of the Gerd Q, a tool for the

diagnosis and management of gastro - oesophageal reflux disease in primary care. Alimentary pharmacology & therapeutics, 30(10), 1030-1038.

- Katz, P O; Gerson, L B and Vela, M F. (2013). Guidelines for the diagnosis and management of gastroesophageal reflux disease. The American journal of gastroenterology, 108(3), 308.
- 21. Keles, B; Ozturk, K; Arbag, H; Gunel, E and Ozer, B. (2005). Frequency of pharyngeal reflux in children with adenoid hyperplasia. International journal of pediatric otorhinolaryngology, 69(8), 1103-1107.
- 22. Kotsis, G P; Nikolopoulos, T P; Yiotakis, I E; Papacharalampous, G X and Kandiloros, D C. (2009). Recurrent acute otitis media and gastroesophageal reflux disease in children. Is there an association? International journal of pediatric otorhinolaryngology, 73(10), 1373-1380.
- 23. Koufman, J A. (1991). The otolaryngologic manifestations of gastroesophageal reflux disease (GERD): a clinical investigation of 225 patients using ambulatory 24 hour pH monitoring and an experimental investigation of the role of acid and pepsin in the development of laryngeal injury. The Laryngoscope, 101, 1-78.
- 24. Larsen, M B; Sørensen, A; Crone, K; Weis, T and Boeckstyns, M. (2013). Carpal tunnel release: a randomized comparison of three surgical methods. Journal of Hand Surgery (European Volume), 38(6), 646-650.
- 25. McCoul, E D; Goldstein, N A; Koliskor, B; Weedon, J; Jackson, A and Goldsmith, A J. (2011). A prospective study of the effect of gastroesophageal reflux disease treatment on children with otitis media. Archives of Otolaryngology–Head & Neck Surgery, 137(1), 35-41.
- 26. Miura, M S; Mascaro, M and Rosenfeld, R M. (2012). Association between otitis media and gastroesophageal reflux: a systematic review. Otolaryngology--Head and Neck Surgery, 146(3), 345-352.
- Oliveira, N and Norton, R C. (2009). Relação entre achados video nasolaringoscópicos e pHmetria esofágica em crianças com manifestações clínicas de refluxo extra-esofágico. Arq Int Otorrinolaringol, 13(2), 140-145.
- Rožmanic, V; Velepic, M; Ahel, V; Bonifacic, D and Velepic, M. (2002). Prolonged esophageal pH monitoring in the evaluation of gastroesophageal reflux in children with chronic tubotympanal disorders. Journal of pediatric gastroenterology and nutrition, 34(3), 278-280.
- 29. Schilder, A; Bhutta, M; Butler, C; Holy, C;

Levine, L; Kvaerner, K, et al. (2015). Eustachian tube dysfunction: consensus statement on definition, types, clinical presentation and diagnosis. Clinical Otolaryngology, 40(5), 407-411.

- Seibert, J W and Danner, C J. (2006). Eustachian tube function and the middle ear. Otolaryngologic Clinics of North America, 39(6), 1221-1235.
- Serra, A; Cocuzza, S; Poli, G; La Mantia, I; Messina, A and Pavone, P. (2007). Otologic findings in children with gastroesophageal reflux. International journal of pediatric otorhinolaryngology, 71(11), 1693-1697.
- 32. Shanks, J and Shohet, J. (2009). Tympanometry in clinical practice. Handbook of clinical audiology, 157-188.
- Ulualp, S O; Toohill, R J and Shaker, R. (1999). Pharyngeal acid reflux in patients with single and multiple otolaryngologic disorders. Otolaryngology—Head and Neck Surgery, 121(6), 725-730.
- 34. Vakil, N; Van Zanten, S V; Kahrilas, P; Dent, J

and Jones, R. (2006). The Montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus. The American journal of gastroenterology, 101(8), 1900.

- 35. Vargas Garcia, M; Frasson de Azevedo, M and Testa, J R. (2009). Medidas de Imitância acústica em lactentes com 226Hz e 1000Hz: correlação com as Emissões Otoacústicas e o exame otoscópico. Brazilian Journal of Otorhinolaryngology, 75(1).
- Velepic, M M; Velepic, M S; Starcevic, R; Manestar, D and Rozmanic, V. (2004). Gastroesophageal reflux and sequelae of chronic tubotympanal disorders in children. Acta otolaryngologica, 124(8), 914-917.
- 37. Yüksel, F; Doğan, M; Karataş, D; Yüce, S; Şentürk, M and Külahlı, İ. (2013). Clinical presentation of gastroesophageal reflux disease in children with chronic otitis media with effusion. The Journal of craniofacial surgery, 24(2), 380.

8/27/2019