# The Relationship Between Oxidative Stress and Adenotonsillar Hypertrophy in Children

## Çocuklarda Oksidatif Stres ile Adenotonsiller Hipertrofi Arasındaki İlişki

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## ABSTRACT

**Objective:** In this study, it was aimed to evaluate the preoperative and postoperative oxidative stress levels of children with obstructive adenotonsillar hypertrophy and to compare the obtained data with healthy children.

**Material and Methods:** 25 patients and 25 healthy controls were included in the prospective study conducted between March and September 2015. In the study sample, children who were diagnosed with adenotonsillar hypertrophy due to chronic tonsillitis, snoring and mouth breathing and who were planned for adenotonsillectomy were included in the patient group. Control group included 25 healthy volunteers with the same demographic characteristics. Serum and urine samples were collected from the patient group twice, before and after surgery, and once from the control group. 8-hydroxy-2-deoxyguanosine levels of all samples were determined by EIA method, protein carbonyl levels were determined by ELISA method and malondialdehyde levels were determined by manual spectrophotometric method.

**Results:** In the study, it was found that the serum malondialdehyde levels of children with adenotonsillar hypertrophy were significantly higher than the control group ($p=0.003$) and that there was no difference in terms of other parameters ($p>0.05$). After the operation, it was determined that the levels of all three parameters evaluated significantly decreased compared to before ($p<0.05$). It was determined that there was a statistically significant and weak correlation between malondialdehyde and 8-hydroxy-2-deoxyguanosine values before the operation ($p=0.003$, $r=0.566$).

**Conclusion:** Hypertrophic adenotonsillar, which is common in the pediatric population, causes many clinical conditions and adversely affects the health and quality of life of children. In line with our findings, we can say that serum and urine MDA levels and tissue PCO levels are useful markers in the evaluation of oxidative damage in children with obstructive ATH and may help to elucidate the etiopathogenesis of the disease. Considering the effects of ATH on health, it is recommended to be considered as an important health problem and to examine the clinical, biochemical and histopathological studies of the disease in a larger sample group.

**Key Words:** Adenotonsillar hypertrophy, 8-hydroxy-2-deoxyguanosine, Malondialdehyde, Protein carbonyl

## ÖZ

**Amaç:** Bu çalışmada obstrüktif adenotonsiller hipertrofili çocukların ameliyat öncesi ve sonrası oksidatif stres düzeylerinin değerlendirilmesi ve elde edilen verilerin sağlıklı çocuklarla karşılaştırılması amaçlanmıştır.

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**Ethics Committee Approval / *Etik Kurul Onayı*:** This study was conducted in accordance with the Helsinki Declaration Principles. The study was approved by Atatürk University, Faculty of Medicine, Non-Invasive Clinical Research Ethics Committee (19.02.2015 / B.30.2ATA.0.01.00 / 28).

***Contribution of the Authors / Yazarların katkısı*: *ALYAR G:*** Constructing the hypothesis or idea of research and/or article, Planning methodology to reach the Conclusions, Organizing, supervising the course of progress and taking the responsibility of the research/study, Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study, Reviewing the article before submission scientifically besides spelling and grammar. ***OZTURK N:*** Constructing the hypothesis or idea of research and/or article, Planning methodology to reach the Conclusions, Organizing, supervising the course of progress and taking the responsibility of the research/studyTaking responsibility in necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study, Reviewing the article before submission scientifically besides spelling and grammar. ***YORUK O:*** Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments. ***TURKERI ON:*** Taking responsibility in logical interpretation and conclusion of the results. ***BAKAN N:*** Taking responsibility in logical interpretation and conclusion of the results.

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**Gereç ve Yöntemler:** 2015 yılı Mart-Eylül ayları arasında yapılan prospektif çalışmaya 25 hasta ve 25 sağlıklı kontrol dahil edilmiştir. Araştırma örnekleminde hasta grubuna kronik tonsillit, horlama ve ağızdan nefes alma şikayeti ile adenotonsiller hipertrofi tanısı alan ve adenotonsillektomi planlanan çocuklar dahil edilmiştir. Serum ve idrar örneği hasta grubundan ameliyat öncesi ve sonrası iki kez, kontrol grubundan bir kez alındı. Tüm numunelerin 8-hidroksi-2-deoksiguanozin düzeyleri EIA yöntem, protein karbonil düzeyleri ELISA yöntem ve malondialdehit düzeyleri manuel spektrofotometrik yöntem kullanılarak belirlenmiştir.

**Bulgular:** Çalışmada adenotonsiller hipertrofisi olan çocukların serum malondialdehit düzeylerinin kontrol grubuna göre anlamlı olarak yüksek olduğu (p=0.003) ve diğer parametreler açısından fark olmadığı (p>0.050) bulunmuştur. Ameliyattan sonra değerlendirilen her üç parametrenin de öncekine göre anlamlı düzeyde azaldığı tespit edilmiştir (p<0.050). Operasyon öncesi malondialdehit ile 8-hidroksi-2-deoksiguanozin değerleri arasında istatistiksel olarak anlamlı ve zayıf bir korelasyon olduğu belirlenmiştir (p=0.003, r=0.566).

**Sonuç:** Pediatrik popülasyonda yaygın görülen hipertrofik adenotonsiller birçok klinik duruma neden olarak çocukların sağlığını ve yaşam kalitesini olumsuz etkilemektedir. Bulgularımız doğrultusunda obstrüktif ATH'li çocuklarda serum ve idrar MDA düzeyleri ile doku PCO düzeylerinin oksidatif hasarın değerlendirilmesinde yararlı belirteçler olduğunu ve hastalığın etyopatogenezini aydınlatmaya yardımcı olabileceğini söyleyebiliriz. ATH sağlık üzerindeki olumsuz etkileri sebebiyle hastalığın klinik, biyokimyasal ve histopatolojik çalışmalarının daha geniş bir örneklem grubunda incelenmesi önerilmektedir.

**Anahtar Sözcükler:** Adenotonsiller hipertrofi, 8-hidroksi-2-deoksiguanozin, Malondialdehit, protein karbonil

## INTRODUCTION

Adenoid and tonsillar tissue, which is a component of Waldeyer's ring, has strategic importance due to its anatomical location (1). These tissues, which play a role in mucosal immunity, provide stimulation of immunity against microorganisms and antigens that enter the body through respiration and digestion (2,3). Recurrent and chronic infections of the adenoids and tonsils result in hypertrophy of the lymphoid tissues. Adenotonsillar hypertrophy (ATH) is the enlargement of tonsils and adenoids and often causes partial or complete obstruction of the upper airways as a result of narrowing of the nasopharynx and oropharynx (4). Although the pathophysiology of obstructive ATH has not been fully elucidated, it has been suggested that recurrent episodes of hypoxia/reoxygenation and decreased blood oxygen saturation and increased reactive oxygen species (ROS) with changes in cell metabolism may be effective in the formation of the disease (5). Oxidative stress is defined as the increase in reactive oxygen species (ROS) and ROS can damage DNA's, lipids and proteins by various mechanisms (6,7). Levels of 8-hydroxy-2-deoxyguanosine (8-OHdG), malondialdehyde (MDA) protein carbonyl (PCO) levels are widely used as oxidative stress markers (8,9). We aimed in this study to investigate the relationship between oxidative stress and ATH in children by using 8-OHdG, PCO and MDA levels in plasma and urine samples and PCO and MDA levels in adenoid/tonsillar tissues.

## PATIENTS and METHODS

The study was approved by Atatürk University, Faculty of Medicine, Non-Invasive Clinical Research Ethics Committee (19.02.2015/B.30.2ATA.0.01.00/28). The study group consisted of 25 patients with the diagnosis of ATH who subsequently underwent surgical treatment. In the study sample, children who were diagnosed with adenotonsillar hypertrophy due to chronic tonsillitis, snoring and mouth breathing and who were planned for adenotonsillectomy were included in the patient group. Control group included 25 healthy volunteers with the same demographic characteristics. Blood and urine samples were taken from the patients twice, preoperatively and during the 6th month follow-up visits after surgery. To measure 8-OHdG, PCO and MDA levels, single samples of peripheral venous blood (2 mL) and urine (3 mL) were collected from both children with ATH and children without obstructive ATH and maintained at –80°C until analysis. At the same time, the adenoid / tonsillar tissues of patients who underwent adenotonsillectomy were collected in a sterile manner and stored until the study day –80°C.

### Statistical Analysis

The suitability of the parameters to the normal distribution was evaluated with the Kolmogrov-Smirnov test. Paired t-test was used in dependent samples to compare the pre- and postoperative values of children with ATH. Independent samples t-test (independent samples t-test or student t-test) was used to compare the values of the patient and control groups. Correlation between parameters was evaluated by pearson correlation analysis. Results are given as mean ± standard deviation (SD). For the significant difference between the groups, p <0.050 was used. Statistical analysis was performed using the SPSS 20.0 program. (SPSS, Chicago, IL, United States)

## RESULTS

The demographic characteristics of the patients (study group) and controls are given in Table I.

**Table I: Demographic characteristics of participants.**

| Parameters | Patient group | Control group | p |
|---|---|---|---|
| Age (years) | 8.24 ± 2.48 | 9.20 ± 2.43 | 0.174 |
| Height (cm) | 135.16 ± 19.38 | 126.76 ± 20.78 | 0.146 |
| Weight (kg) | 29.88 ± 8.11 | 26.20 ± 4.85 | 0.058 |

**Table II: Pre-operative serum levels of biomarkers in control group and patients.**

| Parameters | Patient group (n =25) | Control group (n =25) | p |
|---|---|---|---|
| 8-OHdG (ng /mL) | 45.84±24.17 | 41.06±27.50 | 0.518 |
| MDA (µM) | 3.52±1.16 | 2.49±1.20 | 0.003* |
| PCO (nmol / mL) | 17.35±4.00 | 14.32±3.25 | 0.423 |

*: *Statistically significant p value.*

**Table III: Urinary levels of biomarkers in patients with adenotonsillar hypertrophy and control group.**

| Parameters | Patient group (n=25) | Control group (n=25) | p |
|---|---|---|---|
| 8-OHdG(ng /mL) | 318.57 ± 649.19 | 186.65 ± 168.66 | 0.330 |
| MDA (µM) | 4.34 ± 1.10 | 1.33 ± 0.87 | 0.001* |

***: *Statistically significant p value.*

**Table IV: Pre and postoperative serum levels of biomarkers in patients with adenotonsillar hypertrophy.**

| Parameters | Preoperative (n=25) | Postoperative (n=25) | p |
|---|---|---|---|
| 8-OHdG(ng /mL) | 45.84 ± 24.17 | 26.23 ± 19.54 | 0.002* |
| MDA (µM) | 3.52 ± 1.16 | 1.88 ± 0.86 | 0.001* |
| PCO (nmol / mL) | 17.3 ± 4.00 | 15.04 ± 2.98 | 0.001* |

***: *Statistically significant p value.*

**Table V: MDA, PCO levels of adenoid and tonsillar tissues.**

| Parameters | Adenoid Tissue (n= 11) | Tonsillary Tissue (n = 20) | p |
|---|---|---|---|
| MDA (µM) | 8.95 ± 1.23 | 8.62 ± 1.71 | 0.580 |
| PCO(nmol/ mL) | 115.10 ± 58.53 | 67.67 ± 37.21 | 0.021 * |

***: *Statistically significant p value.*

The mean ± standard deviation and p values of serum 8-OHdG, MDA, PCO of the patients and controls are given in table II.

Serum MDA levels of patients were significantly higher than the control group, and there was no difference in terms of other parameters. (Table II).

Urinary MDA levels of patients with ATH were statistically significantly higher (p <0.050) than the control group, and the 8-OHdG levels were not different between the two groups (p <0.050, Table III).

Postoperative 8-OHdG, MDA and PCO levels of the study group were significantly lower than the preoperative values. (p <0.050, Table IV).

There was no significant difference between MDA values of the adenoid and tonsillar tissues removed after surgery, but PCO values were higher in adenoid tissue than the tonsillar tissue (Table V).

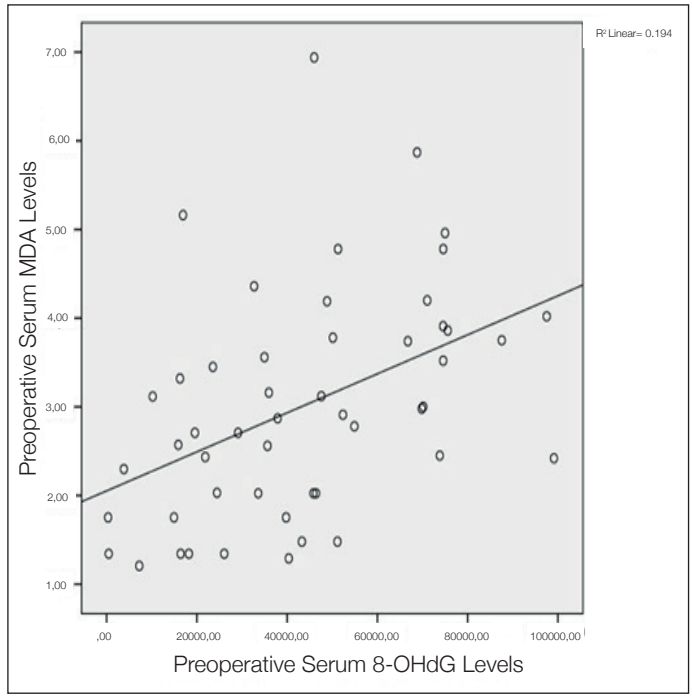


**Figure 1:** Scatter / Dot Graph Between Pre-Operation MDA and 8-OHdG Values.

There was a weak statistically significant correlation between preoperative MDA and 8-OHdG values at correlation analysis. (p = 0.003, r = 0.566, Figure 1).

## DISCUSSION

Acute tonsillitis, adenoiditis and ATH attacks are common in preschool and school-age children and can affect school performance and sleep quality (10). Hypertrophic tonsils and adenoids can cause various degrees of upper respiratory tract obstruction and recurrent respiratory tract infections. In the treatment of these diseases, adenoidectomy and tonsillectomy are frequently applied (11). Oxidative stress is caused by excessive ROS formation as a result of cellular metabolic reactions or exogenous conditions and inability of the antioxidant system to neutralise these excessive ROS (5). ROS causes toxicity by damaging biomolecules in the cell and plays an important role in the pathophysiology of many diseases (5,6,8). It is not exactly clear how ATH causes oxidative stress, but it is assumed that oxidative stress is secondary to hypoxia/ reoxygenation periods in ATH (5). The studies reporting that there is a significant relationship between oxidative stress and obstructive ATH support this information (5,7). Doğruer et al.(12) found excessive ROS production in individuals with obstructive ATH while Abuhandan et al. (5) and Ekinci et al. (13) reported that total oxidant status and oxidative stress index levels were significantly higher in children with ATH. In our study, we investigated the levels of 8-OHdG, MDA and PCO, which are indicators of oxidative stress in adenoid and tonsillar tissues

and body fluids (blood, urine) of children with ATH. One of the important results obtained in the study is that the preoperative serum 8-OHdG, PCO and MDA levels of the patient group were significantly higher than the postoperative period.

8-OHdG levels rise as a result of damage to DNA by ROS during various biochemical reactions (6,14). 8-OHdG is the most frequently studied oxidative stress parameter as a DNA damage indicator (15,16). Under normal circumstances, 8-OHdG is excreted in the urine during DNA repair (17). In our study, we determined that serum 8-OHdG levels decreased significantly after ATH surgery. The decrease in 8-OHdG levels compared to the preoperative period suggests that oxidative stress may play a role in the etiopathogenesis of ATH. Yörük et al. (18) found that serum 8-OHdG and MDA levels in children with adenotonsillar hypertrophy were higher than in the control group. In the same study, they reported that urinary 8-OHdG levels were higher in children with obstructive adenotonsillar hypertrophy compared to the control group. They suggested that the use of 8-OHdG levels in the evaluation of oxidative damage in children with obstructive adenotonsillar hypertrophy may be a useful marker.

Another important finding was that serum MDA levels were higher in children with ATH than in controls. There are similar studies stating that MDA levels decrease after tonsillectomy in children with chronic tonsillitis, acute otitis media and ATH (18-20). Cethana et al. (21) in their study, it was determined that children with chronic tonsillitis had low antioxidant capacity and their superoxide dismutase levels increased relatively after tonsillectomy. In the same study, it was reported that serum MDA levels of the patient group decreased compared to the preoperative period, but could not reach the levels of the control group (21).

In our study, MDA and PCO levels of adenoid/tonsillar tissues were also determined to investigate the role of free radicals in the pathogenesis of ATH. It was determined that adenoid tissue PCO levels of ATH patients were higher than tonsil tissue levels. When the relevant literature is examined, it is the first study in which PCO levels were determined in adenoid/tonsillar tissue samples of children with adenotonsillar hypertrophy and it is important in terms of its results. Repeated exposure of adenoid and tonsillar tissues with pathogenic microorganisms causes intense episodes of hypoxia/reoxygenation and this situation disrupts the balance of ROS production and antioxidant defense. The presence of deep-going mucosal folds larger than the palatine tonsils in the unencapsulated adenoid tissue suggests that this tissue may be more affected by oxidative stress caused by recurrent upper respiratory tract infections (22). Again, our result, the high PCO levels in adenoid tissue, may be due to the fact that the half-life of PCO is longer than that of lipid peroxidation products (23). ROS that increase as a result of oxidative stress cause oxidative modifications on proteins and thus lead to structural and functional changes of proteins (24). PCO is the most widely used marker of protein oxidation and is widely used in the evaluation of oxidative damage (25,26). In our study, it was determined that PCO levels decreased after surgical intervention. In line with these findings, we can say that children with adenotonsillar hypertrophy are under oxidative stress and the increase in oxidative stress may play an important role in the pathogenesis of the disease.

## CONCLUSION

The most common cause of upper airway obstruction, which is common in the paediatric population, is the loss of hypertrophic tonsillar muscle tone, as well as many clinical conditions such as difficulty in breathing, mouth breathing, speech and feeding disorders, recurrent respiratory tract infections, and otitis media (27,28). This situation negatively affects the health and quality of life of children (29). In line with our findings, we can say that serum and urine MDA levels and tissue PCO levels are useful markers in the evaluation of oxidative damage in children with obstructive ATH and may help to elucidate the etiopathogenesis of the disease. Considering the additional health problems that ATH may cause, it is recommended to be considered as an important health problem and to examine clinical, biochemical and histopathological studies in a larger sample group.

## REFERENCES

1. Gray LP. The T's and A's problem—Assessment and reassessment. J Laryngol Otol 1977;1: 11-32.
2. Verma SP, Stoddard T, Gonzalez-Gomez I, Koempel JA. Histologic analysis of pediatric tonsil and adenoid specimens: is it really necessary? Int J Pediatr Otorhinolaryngol 2009; 73.4: 547-50.
3. Arambula A, Brown JR, Neff L. Anatomy and physiology of the palatine tonsils, adenoids, and lingual tonsils. World J Otorhinolaryngol Head Neck Surg 2021;3: 155-60.
4. Li H, Ji CY, Zong XN, Zhang YQ. Height and weight standardized growth charts for Chinese children and adolescents aged 0 to 18 years. Zhonghua Er Ke Za Zhi 2009;7: 487-92.
5. Abuhandan M, Bozkuş F, Demir N, Eren E, Koca B, Guler OK, Selek S. The preoperative and postoperative oxidative status of children with chronic adenotonsillar hypertrophy. Clin Ter 2013;3: e163-7.
6. Özcan O, Erdal H, Çakırca G, Yönden Z. Oxidative stress and its impacts on intracellular lipids, proteins and DNA. J Clin Exp Invest 2015;3: 331-6.
7. Yılmaz T, Koçan EG, Besler HT. The role of oxidants and antioxidants in chronic tonsillitis and adenoid hypertrophy in children. Int J Pediatr Otorhinolaryngol 2004;8: 1053-8.
8. Cho JH, Suh JD, Kim YW, Hong SC, Kim IT, Kim JK. Reduction in oxidative stress biomarkers after adenotonsillectomy. Int J Pediatr Otorhinolaryngol 2015;9: 1408-11.
9. Eken A. Rat kan ve doku örneklerinde oksidatif stres parametreleri. J Clin Anal Med 2017; 69-73.
10. Kang KT, Chou CH, Weng WC, Lee PL, Hsu WC. Associations between adenotonsillar hypertrophy, age, and obesity in children with obstructive sleep apnea. PloS one 2013;10: e78666.

11. Tagaya M, Nakata S, Yasuma F, Miyazaki S, Sasaki F, Morinaga M, et al. Relationship between adenoid size and severity of obstructive sleep apnea in preschool children. Int J Pediatr Otorhinolaryngol 2012;12:1827-30.
12. Doğruer ZN, Ünal M, Eskandari G, Pata YS, Akbaş Y, Çevik T, et al. Malondialdehyde and antioxidant enzymes in children with obstructive adenotonsillar hypertrophy. Clin Biochem 2004;8: 718-21.
13. Ekinci A, Dağıstan H, Aksoy A, Ekinci H. Comparison of Preoperative and Postoperative Antioxidant Levels in Patients with Adenotonsillar Hypertrophy. Allergy 2020;2: 34-8.
14. Breen AP, Murphy JA. Reactions of oxyl radicals with DNA. Adv Redox Res 1995;6: 1033-77.
15. Helbock HJ, Beckman KB, Ames BN. 8-Hydroxydeoxyguanosine and 8-hydroxyguanine as biomarkers of oxidative DNA damage. Methods Enzymol 1999;300:156-66.
16. Gonzalez-Hunt CP, Wadhwa M, Sanders LH. DNA damage by oxidative stress: Measurement strategies for two genomes. Curr Opin Toxicol 2018;7:87-94.
17. Özbilgic T, Suslu AE, Aykan HH, Pehlivanoglu B, Onal D, Kasikci M, et al. The impact of the Adenotonsillectomy on cardiac functions and oxidative stress. Int J Pediatr Otorhinolaryngol 2022; 111039.
18. Yoruk O, Alp H, Yuksel S, Bakan E. DNA damage in children with obstructive adenotonsillar hypertrophy. J Craniofac Surg 2014; 6: 2156-9.
19. Cemek M, Dede S, Bayiroğlu F, Çaksen H, Cemek F, Yuca K. Oxidant and antioxidant levels in children with acute otitis media and tonsillitis: a comparative study. Int J Pediatr Otorhinolaryngol 2005;6: 823-7.
20. Kaygusuz N, İlhan T, Karlıdağ E, Keleş Ş, Yalçın HÇ. Adenoid Hipertrofisinde Serbest Oksijen Radikallerinin Rolü. Turk Arch Otorhinolaryngol 2003; 41:146- 50.
21. Chethana R, Devan PP, Sushmitha K. The Role of Oxidants and Antioxidants in Chronic Tonsillitis. Indian J Otolaryngol Head Neck Surg 2020; 1-6.
22. Cvetković T, Vlahović P, Todorović M, Stanković M. Investigation of oxidative stress in patients with chronic tonsillitis. Auris Nasus Larynx 2009; 36: 340-4.
23. Levine RL. Carbonyl modified proteins in cellular regulation, aging, and disease. Adv Redox Res 2002;9:790-6.
24. Reznick AZ, Packer L. Oxidative damage to proteins: spectrophotometric method for carbonyl assay. In: Methods in enzymology. Academic press 1994;357-63.
25. Levine RL, Garland D, Oliver CN, Amici A, Climent I, Lenz AG, et al. Determination of carbonyl content in oxidatively modified proteins. In: Methods in enzymology. Academic Press 1990;464-78.
26. Dalle-Donne I, Rossi R, Giustarini D, Milzani A, Colombo, R. Protein carbonyl groups as biomarkers of oxidative stress. Clin Chim Acta 2003;2: 23-38.
27. Horiuchi F, Oka Y, Komori K, Tokui Y, Matsumoto T, Kawabe K, et al. Effects of adenotonsillectomy on neurocognitive function in pediatric obstructive sleep apnea syndrome. Neurocase 2014; 2014.
28. Aksu H, Günel C, Özgür BG, Toka A, Başak S. Effects of adenoidectomy/adenotonsillectomy on ADHD symptoms and behavioral problems in children. Int J Pediatr Otorhinolaryngol 2015; 7: 1030-3.
29. Kang KT, Chou CH, Weng WC, Lee PL, Hsu WC. Associations between adenotonsillar hypertrophy, age, and obesity in children with obstructive sleep apnea. PloS one 2013; 8.10: e78666.