

Is there an association with Periodontitis and Obstructive Sleep Apnea? – Systematic Review

Vanessa Rocha Rodrigues¹, Susana Falarido Ramos²

- 1- Dentist, Post-graduation in Periodontology and Implants, PhD Student in Periodontology.
- 2- DDS, MSc, PhD, Accreditation Dental Sleep Medicine Level by EADSM, International Certificant by ABDSM, Scientific Committee Member AADSM, Vice-President EADSM

Study Objectives | Investigate whether there is an association between periodontitis and obstructive sleep apnea (OSA).

Methods | An electronic search was performed on PubMed, Lilacs and Cochrane without any time or language restrictions and it was undertaken until, January 31, 2021. Using the following keywords: (“obstructive *sleep apnea*” and “*periodontitis*”; “*treatment of periodontitis*” and “obstructive *sleep apnea*”). Only studies that used laboratory-based polysomnography to evaluate the OSA were included. For the diagnostic of Periodontitis, only studies that used evaluation of pocket depth and clinical attachment loss were included. This review was registered with the identification number CRD42021236096, in the PROSPERO International Prospective Register of Systematic Reviews hosted by the National Institute for Health Research, University of York, Centre for Reviews and Dissemination.

Results | The search strategy resulted in 6 papers. Only case-control and cross-sectional studies were included. The studies ^(2,8,9,11,2) included, evaluated the association between periodontitis and OSA and one study ⁽¹⁰⁾ assessed the concentrations of a number of salivary cytokines in OSA syndrome and non-OSA syndrome subjects. The reported prevalence of periodontitis ranged between 17.5 and 77–96,4% in patients with OSA

Conclusion | Most of the included studies support the hypothesis that exist an association between Periodontitis and OSA, however more intervention studies are needed.

Clinical Implications | OSA may be a potential risk factor for periodontal disease, however randomized controlled clinical trial with longer follow-up times are needed.

Keywords: “*obstructive sleep apnea*” and “*periodontitis*” and “*periodontal treatment*”

Abbreviations

OSA - Obstructive sleep apnea.

AHI - Apnea-Hypopnea Index.

PICO -Patient, intervention, comparison, outcome question.

NOS- Newcastle-Ottawa Scale.

GI- Gingival index.

BOP – Bleeding on Probing.

PD- Probing depth.

CAL- Clinical attachment level.

GR- Gingival Recession.

PI- Plaque index.

OSA- Obstructive sleep apnea.

CP-Chronic Periodontitis,

IL-6 – interleukin 6.

TNF- α - Tumor necrosis factors alpha.

RANK- activator of nuclear factor receptor kappa-B ligand.

GCF- Gingival crevicular fluid.

IL-1 β - Interleukin 1 beta.

CRP- C-reactive protein.

Introduction

Periodontitis is a multifactorial infection that results in connective tissue destruction, alveolar bone resorption and eventually tooth loss. ⁽¹⁾ Periodontal disease is one of the most prevalent chronic inflammatory diseases worldwide. The association between periodontitis and systemic diseases has been studied over several years. The association has been made mainly with diabetes mellitus, cardiovascular diseases, rheumatoid arthritis ⁽²⁾

In recent years, attention has grown between periodontitis and obstructive sleep apnea (OSA). Given that, these two diseases, have similar risk factors, such as age, gender and smoking. ⁽²⁾ Furthermore, the inflammatory mediators play a role in both diseases. These two conditions are associated with similar systemic inflammatory responses and involve common inflammatory mediators such as interleukin-1B, interleukin-6, tumor necrosis factor-alpha, C-reactive protein. ⁽³⁾

OSA comprises episodes of partial or complete occlusion of the upper airways during sleep and causes cessation of breathing and resulting in hypoxia, hypercapnia, sleep fragmentation. ⁽³⁾

OSA has also been linked to several systemic conditions including, cardiovascular disease ^(4,5) stroke ⁽⁶⁾, endocrine diseases (such as diabetes) and hypertension. ⁽⁷⁾

The severity of OSA is based on the Apnea-hypopnea index (AHI). The apnea-hypopnea index, which is the total number of apnea and hypopnea episodes that occur during sleep divided by the hours of sleep, is a summary measure used for sleep-disordered breathing. “In adults, an AHI of less than 5 events per hour is considered normal. Mild OSA is defined as an AHI \geq 5-15 per hour, moderate OSA $>$ 15-30 events per hour and severe OSA as $>$ 30 events per hour”. ⁽⁸⁾

The purpose of this review was to evaluate the association between periodontal disease and obstructive sleep apnea (OSA).

Materials and Methods

Study registration

The review was registered with the identification number CRD42021236096, in the PROSPERO International Prospective Register of Systematic Reviews hosted by the National Institute for Health Research, University of York, Centre for Reviews and Dissemination.

Research and study selection

An electronic search without time or language restrictions was undertaken between January 31, 2021 in the following database: PubMed, Lilacs and Cochrane *using the following* keywords and Mesh terms: (“Obstructive Sleep Apnea” and *Periodontitis*”; and “*Treatment of Periodontitis*”).

Design of the included studies, eligibility criteria and Patient, intervention, comparison, outcome (PICO) question

The methodology used to carry out this article was based on the study published by Al-Jewair *et al.*, 2015. However, in this systematic review only cross-sectional and case-control studies were included and for the diagnostic of OSA only articles that used polysomnography were included. For the diagnostic of periodontitis only the studies that include evaluation of probing pocket depth and clinical attachment level were included.

This systematic review utilized the Meta-analyses of observational studies in epidemiology (Moose guidelines) statement and checklist.

Risk of bias in individual and across studies

For the assessment of non-randomized studies, the Newcastle-Ottawa Scale (NOS) was used to assess the risk of bias, by two authors (VR) and (SFR).

The Newcastle-Ottawa Scale (NOS) is a tool used to assess the quality of non-randomized studies included in a systematic review and/or meta-analyses and evaluates three elements. A score with a range of 0-9 was allocated to each study, and those with a score of 6 or more were considered to be high-quality studies.

For the three case-control studies included ^(2,9,10) two of them ^(2,9) were categorized with low risk of bias (scored 8-9). The study ⁽¹⁰⁾ was categorized at medium risk of bias. For the three cross-sectional studies included ^(8,11,12) two of them ^(8,12) were categorized with high risk of bias (scored ≤ 5). The study ⁽⁸⁾ was categorized low risk of bias (scored 8-9).

Results

Literature search

The study selection process is summarized in Fig. 1. An electronic search was performed on PubMed, Lilacs and Cochrane without any time or language restrictions and it was undertaken until, January 31, 2021. Records were also, identified through other sources (such as professional organization websites, cited or citing references). Using the following keywords: (“obstructive *sleep apnea*” and “*periodontitis*”; “*treatment of periodontitis*” and “obstructive *sleep apnea*”). Only studies that used laboratory-based polysomnography to evaluate the OSA were included. For the diagnostic of Periodontitis, only studies that used evaluation of pocket depth and clinical attachment loss were included. The search strategy resulted in 6 papers. All data were extracted by two reviewers (*VR and SFR*), independently and in duplicate operating with data extraction forms.

All the data collected were loaded to Review Manager software and checked. The following problems were taken:

- a. Type of study, year of publication, population, age and gender that were included
- b. Diagnostic of periodontitis and OSA
- c. Results
- d. Risk of bias

After reading the title or abstract, 96 articles were excluded (inter-reader agreement $k = 0.944 \pm 0.056$ for kappa calculation the following site was used <https://www.graphpad.com/quickcalcs/kappa1.cfm>). Any disagreement was resolved by discussion.

All the authors of the included studies were contacted and asked if they have more information or unpublished material. None of the authors have replied.

Articles between selected records and full-text articles were excluded by study title and abstract, because they don't meet the objectives of the systematic review and they were not control or cohort studies.

The full-text reports of the remaining 10 articles led to the exclusion of 4 since they did not meet the inclusion criteria, the diagnostic for OSA were self-reported of the Berlin's questionnaire (Bq), the Epworth's sleepiness

scale (ESS) ^(13,14) and the STOP-Bang questionnaire ^(14,15) were applied to determine the risk for OSAS. The study ⁽¹⁶⁾ was excluded because one year later the author published a similar article ⁽¹⁰⁾.

Study design and follow-up

Of the selected studies, all were Cross-sectional and Case-control studies.

Discussion

The aim of this review was to investigate the association between periodontal disease and OSA.

Five of the Six studies ^(2,8,9,11 e 12) included, evaluated the association between periodontal disease and OSA and one study ⁽¹⁰⁾ assessed the concentrations of a number of salivary cytokines in OSA syndrome and non-OA syndrome subjects (see Table 1)

The reported prevalence of periodontitis ranged between 17.5 and 77–96,4% in patients with OSA ^(2,8,9,11 e 12)

Gunaratnam *et al.*, in 2009 ⁽¹²⁾ reported a 77 % prevalence of periodontitis in OSA patients. The prevalence of periodontitis in a group of patients with OSA is greater than the national average.

Besides that, in the studies ^(9,11,12) the prevalence of periodontitis was higher in the OSA group (96.4%) than in the controls (75%) ($p < 0.001$)

Five studies found significant relationship between periodontitis and OSA ^(2,8,9,11 e 12). On the contrary, one cross-sectional studies ⁽⁸⁾ failed to show significant differences in the clinical attachment level between the OSA groups.

The study realized by Seo *et al.*, ⁽¹¹⁾ revealed that there is a significant association between OSA and periodontitis. The authors state that OSA may be a risk factor for periodontitis and the treatment can prevent the progression of periodontitis. They concluded that Periodontitis was more frequent in patients with OAS than in individuals without OAS (17.5%).

Another study ⁽⁹⁾ included, after adjusting the socioeconomic factors, concluded that patients with OSA had 1.75 (95% CI = 1.67–1.88; $p < 0.001$) times more likely than controls (individuals without OSA) to have Periodontitis. (33.8% versus 22.6%, $p < 0.001$).

Furthermore, all the clinical periodontal parameters, including index of plaque and gingival index, bleeding on probing, probing pocket depth and clinical attachment loss, were significantly higher in the OSA group than in the controls. ^(9, 11, 12)

Conversely, other study evaluating the association between periodontal disease severity and OSA severity found no association between OSA and periodontitis. ⁽⁸⁾ The only parameter with a significant associated was the plaque index ⁽⁸⁾

Other studied include ⁽¹⁰⁾ we were able to detect greater numbers of periodontally relevant pathogenic microorganisms in patients with the most severe OSA. The differences in microbial ecology, which might influence onset and/or progression of periodontitis, may be explained by a low-grade inflammation associated with OSA together with intermittent decrease in oxygenation. The drying of the oral cavity may also prevent self-cleaning ability of the oral mucosa and result in increased bacterial colonization. ^(16 e17)

The findings in this systematic review need to be interpreted with caution because the quality of the evidence was low in many studies. The assessment of periodontal disease and definitions used differed among the studies which may have resulted in over or underestimation of the disease prevalence. Also the AHI index for OSA ascertainment varied among the studies. More randomized controlled clinical trial with longer follow-up times are needed, to give clear recommendations on this association.

Conclusions

The evidence on the association of periodontal disease and OSA are insufficient. Most of the included studies support the hypothesis that exist an association between Periodontitis and OSA, however more intervention studies are needed to confirm a cause-effect relationship between periodontitis and OSA.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

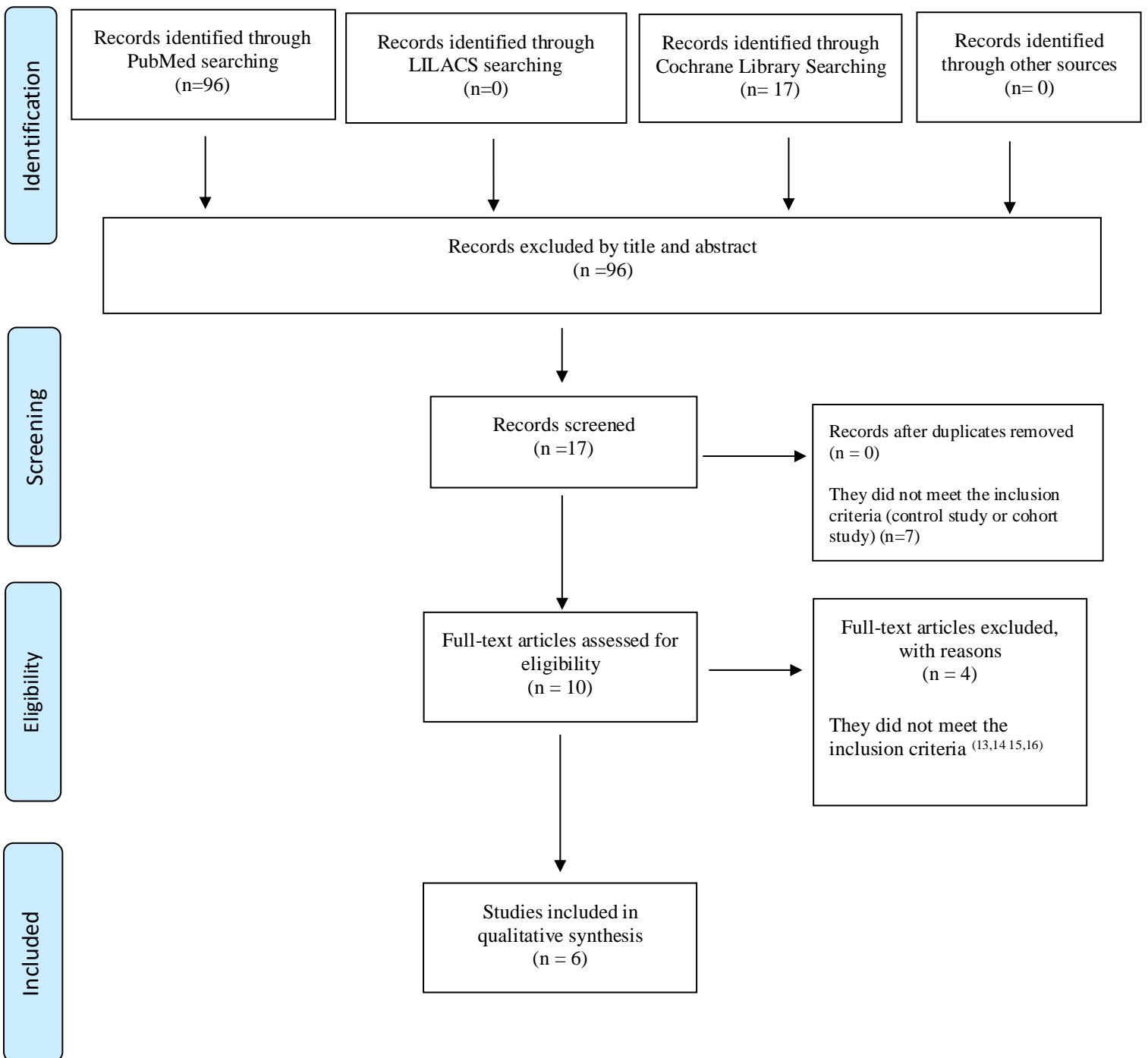
Table 1 - Evidence-based table for studies of association between periodontal disease and OSA

Author	Aim	Study/ Sample	Evaluated Parameters	Diagnosis or risk for OSA	Results	Conclusion
Loke <i>et al.</i> , 2015	Investigated whether OSA has any association with periodontitis	-Cross-sectional -A total of 100 patients were included	PD, GR CAL, BOP and PI	Polysomnography	Moderate to severe periodontitis was verified in 73% Between the AHI groups, no significant differences were found in the prevalence of periodontitis. After adjusting for age, they found a significant association between the AHI severity categories and % of sites with plaque,	The author didn't find significantly associated. Only found a significant associated with the % of plaque
Seo <i>et al.</i> , 2012	Evaluate the prevalence of periodontitis in patients with OSA.	-Cross-sectional -Total of 687 participants	PD, GR, CAL, BOP, GI and PI	Polysomnography	According to the results 17.5% of the participants had periodontitis.	The authors found a significant relationship between OSA and Periodontitis
Keller <i>et al.</i> , 2012	Assess the association between OSA and periodontitis	-Population based case-control -Study population: 29,284 sampled	PD, BOP, radiographic and tooth mobility	Polysomnography	There was a significant difference in the prevalence of periodontitis between cases and controls (33.8% versus 22.6%, $p < 0.001$).	The authors found a association between OSA and periodontitis
Gunaratnam <i>et al.</i> , 2009	Assess the association between OSA and periodontitis	-Cross-sectional -Study population: 66 (54 men and 12 women)	PD, GR, CAL, BOP, GI and PI	Polysomnography	The prevalence of periodontitis ranged between 77–79%,	OSA is associated with periodontitis.
Gamsiz-Isik <i>et al.</i> , 2016	Evaluate if periodontitis is more prevalence in patients with OSA when compared with de controls	-Case-control -Study population: 163 individuals: 83 individuals (18 females; 65 males) with OSA and 80 non-OSA individuals (23 females; 57 males) as controls.	PD, CAL, BOP, GI and PI	Polysomnography	Periodontitis in the OSA group was detected in 96.4% and was significantly higher than in the control group 75%, ($p < 0.001$).	Higher prevalence of periodontitis and higher levels of GCF, IL-1 β and serum CRP in OSA patients.
Nizam <i>et al.</i> , 2015	Evaluate the association between OSA and periodontitis through salivary, biomarkers, and subgingival bacteria.	-A preliminary case-control study -Study population: 52 patients were grouped according to the severity of OSA: 13 participants served as controls, 17 patients had mild-	PD, CAL, BOP Serum, saliva, and subgingival plaque samples were collected	Polysomnography	The different cytokines were detected with higher concentration in the OSA groups, but there was not statistically significant.	OSA appeared to correlate with increasing periodontal disease severity.

		to-moderate OSA, and 22 severe OSA.	Salivary, serum concentrations of (IL-6, TNF- α and RANKL)			
--	--	-------------------------------------	---	--	--	--

Legend – GI- Gingival index, BOP – Bleeding on Probing, PD- Probing depth, CAL- Clinical attachment level, GR- Gingival Recession, PI- Plaque index, OSA- Obstructive sleep apnea; CP-Chronic Periodontitis, OSA - obstructive sleep apnea; AHI- apnea hypopnea index; IL-6 – interleukin 6; TNF- α - Tumor Necrosis Factors Alpha; RANK- activator of nuclear factor receptor kappa-B ligand, GCF- Gingival crevicular fluid IL-1 β - Interleukin 1 beta, CRP- C-reactive protein.

Figure 1



Bibliography

1. Drisko C. Nonsurgical periodontal therapy. *Periodontol.* 2000. 2002; *Vol. 25, Jan 25 (1):* 77–88. <http://doi.org/10.1034/j.1600-0757.2001.22250106.x>
2. Gamsiz-Isik H, Kiyani E, Bingol Z, Baser U, Ademoglu E, Yalcin F. Does Obstructive Sleep Apnea Increase the Risk for Periodontal Disease? A Case-control Study. *Journal of Periodontology.* 2016; DOI: 10.1902/jop.2016.160365.
3. Al-Jewair T, Al-Jasser R, Almas K. Periodontitis and obstructive sleep apnea's bidirectional relationship: a systematic review and meta-analysis. *Sleep Breath* 2015;
4. Moee T, Rabben T, Wiklund U, Franklin KA, Eriksson P. Sleep-disordered breathing in women: occurrence and association with coronary artery disease. *Am J Med.*1996;101:251–256
5. Moee T, Rabben T, Wiklund U, Franklin KA, Eriksson P. Sleep-disordered breathing in men with coronary artery disease. *Chest.*1996;109:659–663
6. Capampangan DJ, Wellik KE, Parish JM, Aguilar MI, Snyder CR, Wingerchuk D, Demaerschalk BM. Is obstructive sleep apnea an independent risk factor for stroke? A critically appraised topic. *Neurologist.* 2010; 16:269 273
7. Mahmood K, Akhter N, Eldeirawi K, Onal E, Christman JW, Carley DW, Herdegen JJ. Prevalence of type 2 diabetes in patients with obstructive sleep apnea in a multi-ethnic sample. *J Clin Sleep Med.*2009; 5:215–221
8. Loke W, Girvan T, Ingmundson P, Verrett R, Schoolfield J, Mealey BL. Investigating the association between obstructive sleep apnea (OSA) and periodontitis. *J Periodontol.*2014; 9:1–15
9. Keller JJ, Wu CS, Chen YH, Lin HC. Association between obstructive sleep apnea and chronic periodontitis: a population-based study. *J Clin Periodontol.*2013; 40:111–117
10. Nizam N, Basoglu OK, Tasbakan MS, Nalbantsoy A, Buduneli N. Is there an association between obstructive sleep apnea syndrome and periodontal inflammation? *Clin Oral Invest.* 2015; DOI 10.1007/s00784-015-1544-y
11. Seo WH, Cho ER, Thomas RJ, An SY, Ryu JJ, Kim H, Shin C. The association between periodontitis and obstructive sleep apnea: a preliminary study. *J Periodontal Res.*2013; 48:500–506
12. Gunaratnam K, Taylor B, Curtis B, Cistulli P. Obstructive sleep apnoea and periodontitis: a novel association? *Sleep Breath.* 2009;13:233–239
13. Sales-Peres SH, Groppo FC, Rojas LV, de C Sales-Peres M, Sales-Peres A. A periodontal status in morbidly obese patients with and without obstructive sleep apnea syndrome risk: a cross-sectional study. *J Periodontol.* 2016;87(7):772–782.
14. Sanders *et al.*, Periodontitis and Sleep Disordered Breathing in the Hispanic Community Health Study/Study of Latinos. *SLEEP.* 2015; *Vol. 38, No. 8, 2015.*
15. Ahmad NE, Sanders AE, Sheats R, Brame JL, Essick GK. Obstructive sleep apnea in association with periodontitis: a case-control study. *J Dent Hyg.* 2013;87(4):188–199.

16. Nizam N, Basoglu O, Tasbakan M, Nalbantsoy A, Buduneli N. Salivary cytokines and the association between obstructive sleep apnea syndrome and periodontal disease. *J Periodontol.* 2014; Jul;85(7):251-8.
17. Alexander AG. Habitual mouthbreathing and its effect on gingival health. *Parodontologie.* 1970; 24:49-55