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**Review Article** 

## Relationship between Periodontal Disease and Sleep Apnoea: Current Literature & Review

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#### ABSTRACT

Obstructive Sleep Apnoea (OSA) is a sleep-related respiratory condition that involves a temporary cessation of breathing or complete halt in airflow despite an ongoing effort to breathe. Undiagnosed OSA is closely associated with serious health problems, including hypertension, diabetes and cardiac related disorders. Periodontitis is characterized by local bacterial infection within tooth supporting structures leading to destruction of periodontium. It is a previously unrecognized but highly prevalent and clinically relevant disease associated with OSA. It also adversely impacts cardiovascular health by increasing the production of cytokines, promoting atherosclerosis, which is also highly associated with OSA.

**Keywords:** sleep apnoea, periodontitis, cytokines

#### **INTRODUCTION**

Obstructive sleep apnoea (OSA) is a highly prevalent disorder affecting between 10–50% of middle-aged men. <sup>[1]</sup> OSA is characterized by recurrent upper airway obstruction associated with cyclic changes in oxyhemoglobin saturation, intermittent arousals from sleep and alterations in intrathoracic pressure. These alterations oxidative induce stress, sympathetic activation, and metabolic dysregulation.<sup>[2]</sup> OSA is currently diagnosed with an overnight sleep diagnostic test known as a poly-somnogram (PSG), which remains the gold standard of diagnosis. <sup>[3]</sup> The standard definition of an apnoeic event includes a minimum 10-second interval between breaths, with a neurologic arousal, a blood oxygen desaturation of 3% to 4% or greater, or both arousal and desaturation. <sup>[4-6]</sup>

Prolonged SF is also implicated in vascular changes similar to the enhanced

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and cardiovascular morbidities associated with OSA. <sup>[7,8]</sup> In children experiencing OSA. elevated systemic levels of lipopolysaccharide (LPS)-binding protein, a surrogate marker of underlying low-grade LPS endotoxemia from the gut, <sup>[9]</sup> were independently associated with BMI and with measures of OSA severity, as well as with established measures of insulin resistance. The apnoea-hypopnoea index (AHI) is used to determine the presence of obstructive sleep apnoea (OSA). An AHI score of 5 is indicative of the presence of OSA, a common disorder characterized by repeated obstructions of breathing during sleep and known to be prevalent in 24-38% of middle aged men in western countries (10-<sup>12)</sup> and in 42% of middle-aged men in Korea. <sup>[13]</sup>

Periodontal disease is a chronic inflammatory disease and its prevalence

increases with age. Risk factors for periodontal disease are age, smoking, obesity and various other socioeconomic factors. Recently it has been proved that periodontal diseases have relationship with various systemic diseases like diabetes, coronary disease, osteoporosis and low birth weight deliveries. Obstructive sleep apnoea is another one of these conditions associated with an inflammatory response. <sup>[14]</sup>

#### Relationship between Sleep Apnoea and Pro-inflammatory Cytokines

Recently, periodontitis has received increasing attention because it may have systemic including infective effects. endocarditis, disease. coronary heart diabetes mellitus, respiratory diseases, osteonecrosis and even malignancy. [15-19] Interleukin (IL)-1b and IL-33 are associated with both acute and chronic inflammation. <sup>[20]</sup> Increased levels of IL-1b were detected in saliva, gingival tissue, and gingival crevicular fluid (GCF) of patients with periodontitis.<sup>[21-23]</sup> The prominent biologic effect of IL-33 is the induction of T-helper 2 cytokines, <sup>[24]</sup> and it also possesses antiinflammatory activity.<sup>[25]</sup>

Pro-inflammatory cytokines are also up-regulated in patients with Obstructive Sleep Apnoea (OSA). <sup>[26-28]</sup> In particular, significant elevations in serum levels of tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), interleukin 1 $\beta$  (IL-1 $\beta$ ), and interleukin 6 (IL-6) have been seen in patients with obstructive sleep apnoea. <sup>[29-33]</sup> The recent meta-analysis (MA) showed that there is an increase in levels of inflammatory markers in subjects with OSA including CRP, TNF  $\alpha$ , IL-6, IL-8, ICAM, VCAM and Selectins. This effect is positively influenced by severity of OSA. <sup>[34]</sup>

# Recent evidences highlighting the relationship between Obstructive Sleep Apnoea and Periodontitis

A preliminary study conducted by Seo WH et al. showed significant association between OSA and periodontal disease. The results showed that 17.5% of the participants had periodontitis, 46.6% had OSA and 60.0% who were diagnosed with periodontitis had OSA. Authors identified old age, male gender, current smoking status and mouth breathing during sleep as risk factors for periodontitis. OSA was positively associated with periodontitis in subjects with 55 years of age, but not in subjects < 55 years of age. <sup>[35]</sup>

Keller et al looked at associations between obstructive sleep apnoea and chronic periodontitis in a population-based case control study. They included 7673 subjects with OSA as cases and randomly selected 21,963 subjects without a history of OSA as controls and performed conditional logistic regression analyses to explore the association between OSA and having been previously diagnosed with CP. The authors significant difference found in the prevalence of prior chronic periodontitis between cases and controls. They concluded there is associated between OSA and periodontitis.<sup>[36]</sup>

A Small Exploratory study conducted in Australia by Gunaratnam, et al reported a significant positive relationship between polysomnography–derived apnoea hypopnoea index with less than 5 events/hour and periodontitis.<sup>[37]</sup>

A case–control study conducted by Ahmad NE et al found a positive significant association between moderate or severe periodontitis. They further concluded that the patients with moderate to severe periodontitis were 4.1 times more likely to be at risk for obstructive sleep apnoea than the control patients with gingivitis or slight periodontitis (p=0.007). <sup>[38]</sup>

Latorre et al conducted a recent study to identify the association between periodontal disease and OSA in adults with different comorbidities. One hundred and ninety-nine individuals (107 women and 92 men) underwent polysomnography with a mean age of 49.9 years were recruited. They reported а significant link between Periodontitis and mild OSA and this association was more frequent in women with hypertensive cardiomyopathy. In addition, periodontitis was associated with severe OSA in men who showed any of two comorbidities such as hypertension or hypertensive cardiomyopathy.<sup>[39]</sup>

Hikmet Gamsiz Isik et al compared periodontitis prevalence between controls and patients with OSA by assessing clinical periodontal parameters and gingival crevicular fluid (GCF) levels of interleukin (IL-1 $\beta$ ), tumor necrosis factor (TNF- $\alpha$ ), and high- sensitive C-reactive protein (hs -CRP); serum hs - CRP was also sampled. They concluded higher prevalence of periodontitis and higher levels of GCF IL -1 $\beta$  and serum hs - CRP in patients with OSA. <sup>[40]</sup>

On the contrary cross sectional study conducted by Loke W et al concluded that Obstructive Sleep Apnoea (OSA) was not significantly associated with the prevalence of moderate/severe periodontitis and the periodontal parameters examined, except percentage plaque.<sup>[41]</sup>

### CONCLUSION

There appears to be some evidence indicating higher levels of markers of systemic inflammation in patients with Periodontitis is associated with Obstructive Sleep Apnoea. Still this association is in very preliminary stage and further studies are needed to explore the role of these markers on the progression of Obstructive Sleep Apnoea both from the research and clinical perspective.

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