



Review Article

Periodontitis and macular degeneration: A systematic review

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ABSTRACT

Periodontitis is a chronic inflammatory disease of supporting structures of teeth. Macular degeneration which is a common cause of blindness in older population is found to be associated with periodontitis. This systematic review summarizes the findings concerning the relation between periodontitis and macular degeneration.

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1. Introduction

Periodontitis is a chronic inflammatory disease of supporting structures of teeth characterised by loss of alveolar bone, tooth mobility, and may result in tooth loss. It commonly found in middle age population. Without any clinical intervention and oral hygiene measures, it continues to increase in severity. In the past, it had been associated with various systemic diseases such as diabetes, cardiovascular diseases, and respiratory diseases.^{1,2}

Furthermore, a correlation has been established between periodontitis and diabetes and other systemic diseases.³ Researchers have found that the microorganisms that causes periodontal disease enter into the systemic circulation and causes inflammation in other organs in the body.⁴ In the last few decades, macular degeneration which is a common cause of blindness in older population is found to be associated with periodontitis. The cause of this disease, age-

related macular degeneration (AMD) is unknown, however, several risk factors such as old

age, hypertension, high cholesterol, have been identified as risk factors. Some suggests genetic and environmental factors together have a role in the development of AMD.⁵ This review summarizes the findings concerning the relation between periodontitis and macular degeneration.

2. Materials and Methods

2.1. Study design

MEDLINE, PubMed, PubMed Central and ScienceDirect databases were searched for various studies in English from 2000 onwards. The examination included MeSH key words as follow: “periodontitis”, “periodontal disease”, “macular degeneration”, “age related macular degeneration”. The search also included a combination of the MeSH key words as follow:

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“periodontitis” or “macular degeneration” AND “periodontal disease” or “diseases of eye” AND “age-related macular degeneration” OR “retinal disease” OR “ocular disease”.

2.2. Inclusion criteria

The inclusion criteria of the review process consisted of the following:

1. Clinical studies that observed relationship of periodontitis and age-related macular degeneration. This included observational studies, cohort study, cross-sectional studies based on data from the national surveys or active recruitment of participants. The methods may include all the age groups, gender, race, medical status, socioeconomic status.
2. Studies that discuss the mechanism of correlation between periodontitis and age-related macular degeneration.

2.3. Exclusion criteria

Those studies which did not meet the criteria included in inclusion criteria were excluded from the study.

2.4. Search strategy

Full text articles as well as abstracts on MEDLINE, PubMed, PubMed Central databases were taken for this review. All the relevant information related to the topic was extracted from these resources. The keywords were carefully taken into consideration while searching articles in all the databases.

3. Discussion

3.1. Age related macular degeneration

This disease is one of the serious illnesses of eye and one of the leading cause of blindness in people all over the world. There is degeneration of photoreceptor cells, retinal pigment epithelial cells, and choroidal endothelial cells (CECs). The exact cause is unknown. Several causes have been proposed so far. A study by Chirco et al⁶ identified the structural and molecular changes in the choroid with increasing age that can cause the disease. Photoreceptor cells, RPE cells, Bruch’s membrane (BrM), and choriocapillaris are different layers of the outer retina or choroid in the eye. These layers are dependent on each other in order to function properly. Associated risk factors of this disease are age, ethnic origin, smoking, and it has a genetic predisposition.⁷ It is most likely to occur over the age of 60 and the risk continues to increase dramatically with age. In addition, La et al⁸ found high prevalence in men, and in patients with diabetes and high blood pressure. The prevalence in patients aged 40-49 years was found to be 6%, however in patients 50 years and

above, it was 0.6%. There are two primary forms of disease: dry and wet. The dry form is atrophic and non-exudative, whereas the wet form is neovascular and exudative.⁹ There have been studies which introduced therapies to halt or reverse symptoms of disease, but their usefulness to treat the disease has not established yet.^{10,11}

Clinical studies showing correlation between periodontitis and AMD Sun et al¹² investigated the association between the periodontitis and also age-related macular generation. A cohort study was conducted based on data collected from the National Health Insurance Research Database National Health Insurance Research Database. They had two cohorts including one with periodontitis and another with no periodontitis with 41,661 participants in each cohort. They found out that patients who had periodontitis showed an increased incidence for both dry AMD and wet AMD. The results indicated that there could be a greater risk of developing AMD with periodontitis than those without periodontitis.

In the cross-sectional study by Shin et al,¹³ a total of 13,072 participants were enrolled with age 40 years or above. Photographs of retinal fundus were taken and community periodontal index (CPI) was extracted from the Korean National Health and Nutrition Examination Survey (KNHANES). Participants were divided into a middle age group that included adults with age ≤62 years and an old age group consisted of adults with age >62 years. In the results, it was concluded that participants with severe PD in the middle age group had 1.61 times more chances to have AMD (Odds Ratio 1.61, 95% Confidence interval 1.02-2.54). Thus concluding severe PD was independently associated with AMD in adults of age 62 years or younger.

Wagley et al¹⁴ carried out secondary analysis of data obtained in the National Health and Nutrition Examination Survey III (NHANES III). Using the photographs of eye fundus collected during the survey, they evaluated patients with AMD above 60 years of age and patients with AMD at age 60 years or below. After adjusting confounding factors using logistic regression model, the results were interpreted. They suggested that periodontitis increased the risk of AMD in patients 60 years or below with odds ratio = 1.96, 95% confidence interval = 1.22-3.14 and p value = 0.006. Nevertheless, this association was not seen in patients above 60 years of age.

Karesvuo et al¹⁵ conducted a population-based cross sectional study with a study sample of 1751 men at and above 30 years. Men with a self-reported medical history of AMD were included in the study. A clinical oral exam, radiographic interpretation, and laboratory analysis were used to detect periodontal diseases in the study group. Data was collected and statistical methods were used. Logistic regression model was used to adjust confounding factors namely age, smoking, diabetes, alveolar bone loss and interpretation of results. They concluded that alveolar bone

Table 1: Clinical studies showing correlation between periodontitis and AMD

Source	No. of Participants /age/ race	Methods	Conclusion
Sun et al, 2019	83322 patients/< 60 yr and ≥ 60 yr/Asian	Cohort study, National Health Insurance Research Database, with a 13-year follow-up	
Shin et al, 2017	13072 patients/> 40 yr/Asian	Cross-sectional study, Korean NHANES, divided into 2 groups: ≤ 62 yr, > 62 yr, Diagnosis of AMD: Ocular Fundus photographs Thus Diagnosis of PD:CP Index score 3 and 4	Only severe PD was Independently associated with AMD in adults of age 62 years or younger
Wagley et al, 2015	5887 patients/> 40 yr/white and non white	Cross-sectional study, US NHANES III, divided into 2 groups: ≤ 60 yr, > 60 yr Diagnosis of AMD: Ocular fundus photographs Diagnosis of PD: > 10% of sites with > 3 mm of CAL	Periodontitis randomly increased the risk of AMD in patients 60 years or below. This association was not seen in patients above 60 years of age
Karesvuo et al, 2013	1751 patients/≥ 30 yr/white	Cross-sectional study, national population-based Health survey Dental and Periodontalcheckups Self-reported AMD	Alveolar bone loss had an association with AMD in males
Brzowska & Puchalska-Niedbał et al In 2012	56 patients/45–90 yr/white	Cross-sectional study showed Dental and periodontal checkups + radiography	All the patients with AMD in the study group had some inflammatory lesion present in the oral cavity. The most common lesions were periodontal lesions.

loss had an association with AMD in males. In a study by Brzowska et al¹⁶, 56 patients with dry/wet AMD were chosen for the study. In these patients, teeth with necrosis, root canal treated, tooth amputated, pathological pocket formation, loss of epithelial attachment, tooth mobility were noted. The results of the study showed all the patients with AMD in the study group had some inflammatory lesion present in the oral cavity. The most common lesions were periodontal lesions. Authors believed them as the most dangerous ones in the development of AMD. They also suggest further studies required to confirm the association between periodontal health and AMD.

Proposed mechanism of correlation between periodontitis and AMD None of the studies has mentioned the mechanisms of this correlation except two studies. Pockpa et al proposed various ways which may be helpful to understand the relation of periodontitis with age-related macular degeneration. According to the authors, two diseases share common characteristics which explain their relationship. These characteristics are innate immune response with similar risk factors, and thus changing of eye choroid thickness. They highlighted these features as the hypotheses of the mechanism of the correlation.¹⁷ Chiu et al¹⁸ investigated whether the infection with *Porphyromonas gingivalis* (*P. gingivalis*) is associated with the occurrence of AMD. A case-control study was carried out which used data from the Third National Health and Nutrition Examination Survey (NHANES III) and

related serum *P. gingivalis* immunoglobulin G (IgG) to the presence of early AMD (n=201 cases) in patients of age 60 years or more. *P. gingivalis* also plays a vital role in the dysbiotic oral microbiota. They hypothesised that AMD shares risk factors and etiology with the *P. gingivalis*-related diseases such as diabetes, cardiovascular disease, and Alzheimer's disease. The study results showed a significant association between

P. gingivitis in periodontal microbiota and AMD. According to the authors, oral microbiota play an important role in causing retinal diseases.

4. Conclusion

The review studied the correlation between periodontitis and age-related macular degeneration. Several studies have shown that periodontitis in the oral cavity can be linked with the macular degeneration in patients below the age of 60 years. However, more number of studies will provide insight into the pathogenesis of this relationship. Therefore, studies in this area are scarce and more scientific evidences are certainly needed to establish a relationship. Overall, periodontal diseases may contribute to the development of age-related macular degeneration.

5. Ethical Policy and institutional ethical board

All studies included in this systematic review were approved from the respective institutional ethical committee boards

and hence can be relied upon to study the association between the two diseases.

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7. Conflict of Interest

The authors declare they have no conflict of interest.

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