

Atenção Interdisciplinar em Saúde

**Samuel Miranda Mattos
Kellen Alves Freire
(Organizadores)**

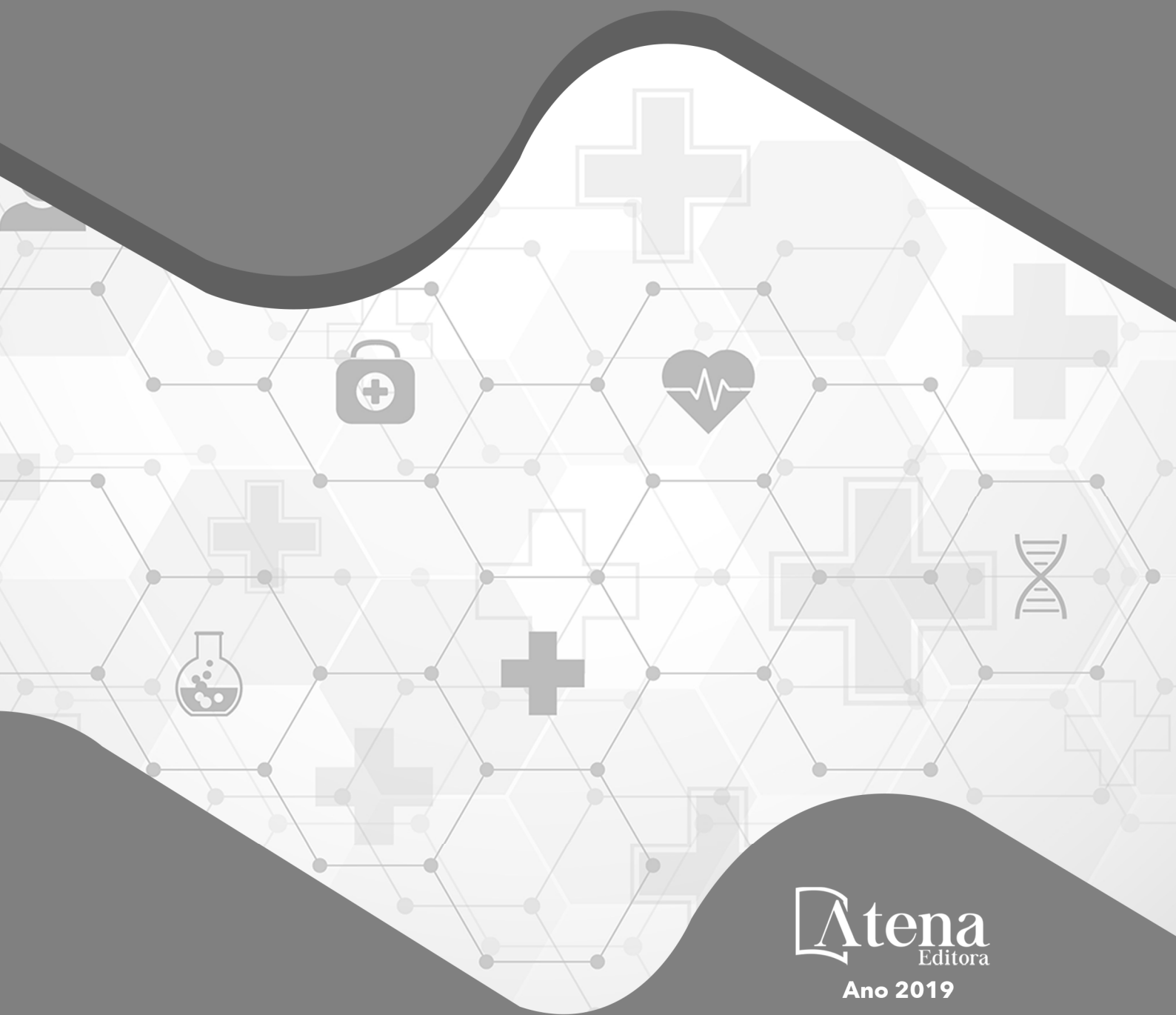


Atena
Editora

Ano 2019

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Editora Chefe: Profª Drª Antonella Carvalho de Oliveira
Diagramação: Lorena Prestes
Edição de Arte: Lorena Prestes
Revisão: Os Autores



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Dados Internacionais de Catalogação na Publicação (CIP) (eDOC BRASIL, Belo Horizonte/MG)	
A864	Atenção interdisciplinar em saúde 1 [recurso eletrônico] / Organizadores Samuel Miranda Mattos, Kellen Alves Freire. – Ponta Grossa, PR: Atena Editora, 2019. – (Atenção Interdisciplinar em Saúde; v. 1) Formato: PDF Requisitos de sistema: Adobe Acrobat Reader Modo de acesso: World Wide Web Inclui bibliografia ISBN 978-85-7247-761-1 DOI 10.22533/at.ed.611191311 1. Administração dos serviços de saúde. 2. Hospitais – Administração. I. Mattos, Samuel Miranda. II. Freire, Kellen Alves. III. Série. CDD 362.11068
Elaborado por Maurício Amormino Júnior – CRB6/2422	

Atena Editora
Ponta Grossa – Paraná - Brasil
www.atenaeditora.com.br
contato@atenaeditora.com.br

Atena
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Ano 2019

APRESENTAÇÃO

Constata-se que a interdisciplinaridade profissional reflete diretamente no avanço e melhoria de atendimento na população. Dentro do campo interdisciplinar, encontramos o setor saúde, este que é composto por diversos profissionais que trabalham arduamente para a melhoria dos serviços de saúde, contribuindo na prática clínica e científica.

Acredita-se que registrar e divulgar o modo de trabalho, o conhecimento científico e relatar experiências são estratégias para o aprimoramento do avanço da humanidade.

Sendo assim, nesta coletânea “*Atenção Interdisciplinar em Saúde*”, o leitor terá a oportunidade de encontrar trabalhos de pesquisa de caráter nacional e internacionais sobre saúde, produzidos em língua portuguesa, inglesa e espanhola, divididos em quatro volumes.

Destaca-se que o volume I e II tem-se predominantemente pesquisas de revisão de bibliográfica, literatura, integrativa, sistemática e estudo de caso. Já o volume III e IV, encontra-se pesquisas com diferentes desenhos de estudo. Todos os artigos trazem uma ampla visão de diferentes assuntos que transversalizam a saúde.

Acredita-se que o leitor após a leitura desta coletânea estará preparado para lidar com a diversidade de barreiras técnicos/científico no setor saúde. Por fim, convido ao leitor a realizar uma excelente leitura e uma reflexão sobre as temáticas apresentadas, AbraSUS!

Samuel Miranda Mattos

Kellen Alves Freire

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ASSOCIATION BETWEEN CHRONIC PERIODONTITIS AND SERUM ALBUMIN: LITERATURE REVIEW

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ABSTRACT: Aim: To review the literature about the relationship between chronic periodontitis and serum albumin. Methods: The study was performed in January and June 2016 and the following databases were used: Pubmed, Google Scholar and LILACS including articles published from 2000 onwards. The following keywords were used: Chronic Periodontitis, Serum Albumin and Hypoalbuminemia.

Meta-analyses and clinical trials with a large sample size were preferred. Results: A total of 891 articles were available in the databases (PubMed 25, Google Scholar 331 and LILACS 535). Forty-two articles were included in the review after eliminate double references and using the inclusion criteria. Conclusions: This review has shown inverse relationship between serum albumin concentration and periodontal disease in adults and elderly groups, not being this a clear association of cause and effect. It is suggested, thus, prospective studies and large sample size clinical trials to clarify pending issues from this association.

KEYWORDS: Chronic Periodontitis, Inflammatory mediators, Body Mass Index, Hypoalbuminemia.

ASSOCIAÇÃO ENTRE PERIODONTITE CRÔNICA E ALBUMINA SÉRICA: REVISÃO DE LITERATURA

RESUMO: Objetivo: Realizar uma revisão de literatura sobre a relação entre Periodontite crônica e albumina sérica. Métodos: O estudo foi realizado no período entre Janeiro e Junho de 2016 utilizando as seguintes bases de dados: Pubmed, Google Acadêmico e LILACS incluindo artigos desde 2000 até o presente ano. As seguintes palavras-chave foram utilizadas: Periodontite crônica, albumina sérica

e hipoalbuminemia. Estudos de meta-análise e clínicos com grande tamanho amostral foram evidenciados. Resultados: Um total de 891 artigos foram avaliados nas bases de dados (PubMed 25, Google Scholar 331 and LILACS 535). Quarenta e dois artigos foram incluídos nessa revisão após eliminar referências concomitantemente citadas e usando os critérios de inclusão. Conclusões: A presente revisão mostrou relação inversa entre concentração sérica de albumina e doença periodontal em grupos de adultos e idosos, não sendo uma associação clara de causa e efeito. Sugere-se, portanto, estudos prospectivos e ensaios clínicos de grande porte para esclarecer questões pendentes desta associação

PALAVRAS-CHAVE: Periodontite Crônica, Albumina Sérica, Índice de Massa Corporal, Hipoalbuminemia.

1 | INTRODUCTION

Periodontal disease (PD) still remains worldwide as one of the most prevalent and complex pathologies concerning the nature of its etiology, classification of different forms, treatment and maintenance (KINANE et al., 2017). It affects 20% to 50% of the world population, which represents the major cause of tooth loss (NAZIR, 2017). PD is considered a public health issue that affects heterogeneously different regions of the world, however, with indications that the least developed countries present greater prevalence of the disease (FRENCKEN et al., 2017). It preferably affects adult individuals, nonetheless capable of affecting children as well (BOTERO et al., 2015). The most common periodontal diseases can be grouped into two distinct groups: Gingivitis and Periodontitis (TROMBELLI et al., 2018; PAPAPANOU et al., 2018).

Periodontitis is defined as an inflammatory condition of the gingival tissues, characterized by loss of connection of the periodontal ligament and the bone support of the tooth (KINANE et al., 2017). Additionally, the bacteria trigger inflammatory responses from the host causing those clinical effects. The individual characteristics that diminish the efficiency of host response can include medical factors such as malnutrition, which always impairs the innate and adaptive host defenses including phagocytic function, cell-mediated immunity, complement system, secreting antibody, and production and the function of cytokines (TAYLOR et al., 2006).

The expression risk factor refers to any personal behavior or lifestyle, an exposure environment or an innate or inherent characteristic, which, according to epidemiological evidence, increases the possibility of disease. To this, such factor must meet two criteria: being biologically plausible as the causal agent of the disease and identified in longitudinal studies (KOSHI, 2012).

Risk factors are biologically related to the manifestation of the disease, however, do not necessarily imply a cause and effect relationship, that is, just because an individual has a certain risk factor it does not necessarily mean they will develop the disease (KOSHI, 2012). The relationship between periodontal disease and systemic

diseases has been assessed for more than 20 years of well-conducted studies that suggest CPD playing a modulating role in systemic diseases such as cardiovascular (VEDIN et al., 2014), diabetes (LICCARDO et al., 2019), adverse pregnancy outcomes (OPACIC et al., 2019), rheumatoid arthritis (ACHARYA et al., 2019), chronic kidney disease (VILELA et al., 2011; LERTPIMONCHAI et al., 2019), anemia (CARVALHO et al., 2014) and hypoalbuminemia (PATIL et al., 2015).

Alterations in vascular permeability, such as those that occur in the duration of an inflammatory process, in PD for example, result in loss of albumin from the intra to the extravascular space resulting in a rapid fall in serum levels (HILL, 1985). From the foregoing, it seems of fundamental importance to assess the relationship between chronic periodontitis and concentrations of serum albumin, these being associated to malnutrition.

2 | METHODS

This is a literature review focused on scientific production contained in english and non-english languages journals, both in print and online to the field of periodontal medicine, starting from 2000 to 2016, but with inclusion of some previous publications cited in the references considered important for the understanding of the subject. The following means were used: Pubmed, Google Scholar and LILACS (Latin American Literature in Health Sciences) through these keywords: Chronic Periodontitis, Serum Albumin and Hypoalbuminemia.

The present study considered as content of the analysis the datas contained in the discussion and in particular the conclusions of the articles selected for the research, excluding articles about severe periodontal diseases. The datas inferred were analyzed in order to point out the relationship between Chronic Periodontitis and serum albumin.

3 | RESULTS OF SELECTION

The search resulted in 891 articles in databases after inform the following descriptors: Chronic Periodontitis and Serum Albumin (757), Chronic Periodontitis and hypoalbuminemia (134). After exclusion of the concurrent references was selected 42 articles, as well as, 1 manual and 1 guide about serum albumin and nutrition to present review, following cited standards.

4 | LITERATURE REVIEW

4.1 Considerations on Serum Albumin

The physiological properties of albumin were first recognized in 1837 by Ancell

(1840) and, since then, its complexity has been revealed. However, its physiological role is still not fully acknowledged in relation to the PD, being studied by some researchers (KAYSEN, 2002; PATIL et al., 2015).

Serum albumin is the most abundant plasmatic protein, comprising a total of 50% from the total human serum proteins. One of the important functions of albumin is its role in the maintenance of the circulating plasma volume, due to its relatively low molecular weight and its high concentration. It is responsible for 80% of the colloid osmotic pressure, but under conditions of extremely low albumin concentrations, only a slight edema is surprisingly observed, suggesting that this role can be played by other plasma proteins (DOWEIKO et al., 1991).

Serum albumin is a major binding protein for various substances in plasma, being synthesized only by the liver as pre-proalbumin that has an N-terminal peptide that is removed prior to the formation of the protein being released from the rough endoplasmic reticulum. The product, pro albumin, by its turn, is cleaved in the Golgi vesicles to produce the secreted albumin (ZUNSZAIN et al., 2003).

About 12% to 20% of hepatic synthesis capacity is made available for the synthesis of this protein, producing 150mg to 250mg of albumin per kilogram of body weight daily in healthy individuals (ANCELL, 1840; CARVALHO et al., 2014), which consumes 6% of the daily nitrogen intake (ZUNSZAIN et al., 2003).

Albumin synthesis is not influenced by serum levels, but it depends on a complex interaction between colloid osmotic pressure in the hepatic extracellular fluid, serum levels of hormones well-known to stimulate this synthesis (corticosteroids, anabolic steroids and thyroxine), presence of pro-inflammatory cytokines that inhibit this synthesis, and nutritional status, including the availability of energy, protein and micronutrients (WHICHER and SPENCE, 1987).

The concentration of albumin in the intravascular fluid is the result of the balance between synthesis and catabolism. These processes are complex and independent, although they occur simultaneously. Normal serum albumin concentrations are between 3.5 g / dL and 5.0 g / dL (HILL, 1985). However, the chosen method to carry out their dosages can have direct influence on the result, and therefore on the clinical analysis from this data (KOLTE et al., 2010).

The most widely used method is the colorimetric, by the fact it can be applied to all major analytical systems. In this method, two techniques stand out: bromocresol red and bromocresol green. Extensive works have shown that both techniques have poor accuracy, so that the albumin concentrations may be underestimated when using bromocresol red or overestimated when using bromocresol green (HILL, 1985).

In clinical practice, the frequently used method is bromocresol green. The origin of the low specificity of bromocresol green has been studied and the results have shown that, at least in samples with high concentrations of α 1-globulin, α 2-globulin and β -globulin fractions, this overestimation is due to the fact that the bromocresol green technique allows a reaction to occur with these proteins, that end up being interpreted

as albumin molecules (WEBSTER, 1974). Immunochemical methods are potentially the most accurate methods for measuring serum albumin. It has been shown that the immunoturbidimetric technique applied for the measurement of albumin is very precise and sensitive and, therefore, must be the method of choice for the measurement of serum albumin (SPENCER and PRICE, 1979).

Serum albumin concentrations are influenced by several factors, including: changes in the distribution of body fluids, hydration status, body losses, synthesis and catabolism rates. Under normal conditions, the albumin is lost through the vessel walls to the extravascular compartment, but most of it returns to the intravascular compartment via lymphatic system (WHICHER and SPENCE, 1987).

In the duration of an inflammatory process, such as in chronic periodontitis, there is release of inflammatory cytokines (IL-1, IL-6 and TNF- α) (SCHALK et al., 2004) and changes occur in vascular permeability, which result in the decrease of serum albumin levels. Besides, in clinical situations characterized by disorders in body plasma volume, such as acute dehydration, pregnancy, congestive heart failure, hepatic failure and kidney failure, albumin concentrations show up altered, therefore, for proper interpretation of these values, these conditions should be considered (WHICHER and SPENCE, 1987).

Wahid et al. (2013) found significant association between gingival index and serum albumin levels. The precise mechanism of this relation is not yet understood, but it was hypothesized that not only the nutritional aspect but also the inflammatory markers may influence the serum albumin concentration and the periodontal disease condition.

It has been suggested that the harmed dentition status, as tooth loss due to periodontal infection can affect individuals, causing food restriction, being able to compromise the nutritional status and welfare. In terms of association between serum albumin and oral disease it has been recently reported that the number of untreated teeth is a factor strongly associated with the concentration of serum albumin in the elderly (NAZIR, 2017).

Therefore, there is evidence that the severity of PD may be indicated and monitored by serum albumin levels. However, the studies conducted to assess the relationship between the state of the periodontal disease and the albumin concentration in serum did not show this association clearly (AMITHA et al., 2012).

4.2 Serum albumin versus BMI

Nutritional status reflects the extent to which physiological nutrient needs are being reached to maintain the proper composition and functions of the organism, resulting in the balance between intake and nutrient requirements. Changes in nutritional status contribute to increased morbimortality. Thus, malnutrition predisposes a range of serious complications, including tendency to infection, wound healing deficiency,

respiratory failure, heart failure, decreased glomerular filtration rate, decreased gastric juice production and protein synthesis at a hepatic level with abnormal metabolites production (BRASIL, 2000; ACUÑA and CRUZ, 2004).

Protein-caloric malnutrition has multiple causes and albumin is the most commonly used biochemical marker because of its ease of measurement and its association with clinical events in chronic inflammatory diseases (KELLER, 2019). Several studies have shown a strong correlation between low levels of albumin and increased risk of morbimortality (STEFANELLI et al., 2010).

A periodic evaluation of nutritional status should be performed in patients who have chronic diseases. Serum albumin is a practical marker for assessing the general health of an individual, since it demonstrates the severity of the underlying disease and even mortality (SHIBATA et al., 1991).

Stenvinkel et al. (2000) investigated in 83 patients who were in pre-dialysis (outpatient treatment) a possible association between nutritional status, inflammation and lipid metabolism, noting that in malnourished patients, albumin levels were significantly lower ($p < 0.01$) than in well-nourished patients, with no statistical difference in relation to total cholesterol, HDL and LDL between the groups. For patients with decreased albumin levels and higher RPC levels there was higher prevalence of cardiovascular disease.

Malnutrition can also be a means of monitoring the serum albumin concentration (DON and KAYSEN, 2004). Albumin in the presence of an inflammation shows decrease of serum concentration, decreasing its rate of synthesis and the same occurs in the presence of malnutrition (ENWONWU et al., 2002).

Insufficient food intake causes a 50% reduction in hepatic synthesis of albumin in the very first 24 hours and it persists if this situation lasts (ROTHSCHILD et al., 1972). It seems that the effect of poor food intake has a greater impact on the synthesis of albumin than on the synthesis of other proteins produced by the liver (JEPSEN and KUCHEL, 2006).

It is imperative to study the relationship between periodontal disease and serum albumin concentrations which are related to BMI and reflects on the overall health status of an individual, who may be at a higher risk of developing conditions or systemic inflammatory disorders (STENVINKEL et al., 2006).

4. 3 Hypoalbuminemia and Chronic Periodontitis: a plausible relationship

Clinical studies with scientific basis of recent decades have led to a better understanding and appreciation of the complexity and pathogenesis of periodontal disease (SOCRANSKY et al., 1998). It has in its essence bacterial etiology, specifically, periodontal pathogens associated to the destruction of the periodontal tissues. However, these pathogens, themselves, do not cause periodontal disease (LOE, 1993).

Hypoalbuminemia or low serum albumin concentration may be caused by various conditions such as cirrhosis of the liver, nephrotic syndrome, burns, haemodilution, increased vascular permeability or decreased lymphatic clearance, acute disease states (WAHID et al., 2013) and malnutrition (KOLTE et al., 2010).

Protein reduction results in hypoproteinemia with large pathological indications including muscle atrophy, weakness, weight loss, anemia, leukopenia, edema, decreased resistance to infections, slow wound healing, lymphoid decreasing and reduced ability of forming certain hormones and enzymes. The reduction of serum proteins has shown in experimental studies with animals damage to the periodontium, periodontal ligament degeneration, osteoporosis in the alveolar bone, impaired cementum deposition, slow wound healing and tongue atrophy (KOLTE et al., 2010; SARAVANAN et al., 2012).

These observations reveal alveolar bone loss resulting from the inhibition of normal bone formation activity, rather than being caused by the introduction of destructive factors. Protein deficiency also highlights the destructive effects of dental biofilm and occlusal trauma in periodontal tissues, but the beginning of gingival inflammation and its severity depends on the dental biofilm (VEDIN et al., 2014).

In the study by Patil et al. (2015) a significant association between periodontal disease and serum albumin concentration was found in adult groups and systemically healthy elderly, non-smokers, not pregnant or lactating women, showing an inverse relationship between serum albumin concentration and PD, in accordance to a cross-sectional (OGAWA et al., 2006) study that showed a consistent association between the occurrence of periodontal disease and hypoalbuminemia, associating that the number of untreated teeth was a significant factor for this low serum albumin concentration in individuals residing in senior living community. Another cross-sectional (MOJON et al., 1999) study with 85-year-old elderly individuals low serum albumin concentration was found in patients who had chronic periodontitis, agreeing that there is an association between oral health, in particular, control of periodontal disease and serum albumin levels.

Kolte et al. (2010) conducted a study with individuals who aged between 40 and 70 years old finding a statistically significant association of serum albumin levels between clinically healthy individuals and patients with chronic periodontitis, showing an inverse relationship between periodontal disease and serum albumin concentrations (below 4,6 g/dl), these being exclusively affected by the inflammatory component of chronic periodontitis, indicating strong evidence of association between the state of oral health, periodontal disease and concentrations serum albumin.

In the elderly, impaired teeth status and nutritional life style along with the possibility of compromised systemic health, may reflect on the serum albumin concentration values. Although this is a possibility, it is difficult to infer whether serum albumin concentrations are affected by inflammatory components of chronic periodontitis or compromised by nutritional status, due to the individual's general

health status (SPENCER and PRICE, 1979; KOLTE et al., 2010).

The reduction in serum albumin concentration has a positive relationship with alveolar bone loss which suggests the fact that patients with chronic periodontitis have low serum albumin concentration when compared to individuals with healthy periodontium (MOJON et al., 1999; KOLTE et al., 2010; AMITHA et al., 2012). These results were found in studies by Amitha et. al. (2012) in 60 individuals aged between 30 and 40 years old divided into two groups: periodontally healthy and with chronic periodontitis.

Okamura et al. (2007) reported a decrease in vital activity and gradual increase in the mortality rate with the reduction in serum albumin levels in individuals aged between 60 and 74 years old, showing that albumin levels below 4.0 g / dL indicate higher mortality rate. Shibata et al. (STEFANELLI et al., 2010) reported the significantly lower 10-year survival rate for patients with low serum albumin and emphasizes that the status of the periodontal disease has a significant influence not only in serum albumin, but also on the overall health all aspects. However, studies (FRENCKEN et al., 2017; TAYLOR et al., 2006; VEDIN et al., 2014; PATIL et al., 2015; KOLTE et al., 2010; STEFANELLI et al., 2010; OGAWA et al., 2006) that show the inverse relationship between serum albumin and chronic periodontitis do not confirm the clear association of cause and effect between serum albumin levels and periodontal disease.

5 | CONCLUSION

This review showed an inverse relationship between serum albumin concentration and periodontal disease in groups of adults and seniors, not being a clear association of cause and effect. It is suggested, thus, prospective studies and large sample size clinical trials involving periodontally healthy adult individuals and those with chronic periodontitis without any systemic diseases, which may be the initial step to clarify pending issues from this association.

6 | AUTHORS' CONTRIBUTIONS

Walder Jansen de Mello Lobão: Drafting of the manuscript; critical revision of the manuscript for important intellectual content. José Eduardo Batista: critical revision of the manuscript for important intellectual content. Adriana de Fátima Vasconcelos Pereira: critical revision of the manuscript for important intellectual content. Antonio Luiz Amaral Pereira: orientation and critical revision of the manuscript for important intellectual content.

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Agência Brasileira do ISBN

ISBN 978-85-7247-761-1



9 788572 477611