Review Article

ASSOCIATION OF OBESITY AND RESISTIN LEVELS IN PERIODONTAL DISEASE

ABSTRACT

Objectives: The aim of this systematic review is to evaluate the association between obesity and resistin levels in periodontal disease.

Methods: Search strategy included relevant articles from December 2010 to April 2021 using relevant key indexing terms such as PUBMED, Google scholar. Data were retrieved from 10 articles that were included in this review (2 cross sectional, 2 prospective, 6 case control studies). The total number of sample size taken ranged between 10 and 116 participants consisting both female and male individuals with a mean age between 20 and 65 years. The interrelation between obesity and resistin levels in periodontal disease were included in this systematic review.

Results: Following screening through the electronic search out, a total of 45 articles were retrieved of which based on the inclusion criteria 10 studies were included in the review. Due to a lack of data, no meta-analysis was conducted but results from the studies indicated that there is an association between resistin levels in periodontitis patients with obesity.

Conclusion: Individuals with obesity in chronic periodontitis patients had increased resistin levels when compared to healthy individuals in GCF, serum and saliva. Further investigation is required in order to support their relationship.

Keywords: Obesity, resistin, adipokines, periodontal disease.

INTRODUCTION

Obesity is among the most underappreciated issues of public health, afflicting together rich and developing nations. Its global prevalence is a source of concern due to its potential influence on mortality, morbidity, and health-care costs.[1] Obesity and overweight are defined as excessive accumulation of fat that may impair health. An adult is considered to be overweight if its body mass index (BMI= kg/m2), is ≥ 25 and obese if it's BMI is ≥30. A high BMI has been discovered to be a significant risk factor for a variety of diseases, including diabetes, cardiovascular disease, cancer, and periodontitis.[2]Overweight and obesity affect nearly 1.9 billion persons, with 650 million of them being obese. It is said to be the cause of 2.8 million deaths per year.[3.]

Periodontal disease is considered to be an inflammatory and infectious illness of the supporting structures of the tooth that develops as a result of pathogen-host relationship. After the host immune system has been activated, tissue damage occurs as a result of release of proinflammatory mediators, cytokines, and metalloproteinases. It is among

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The link between periodontitis and obesity is regarded to be the most recent area of research in periodontal medicine, but the elementary molecular mechanisms are unknown. This interrelation was initially documented in animals by Perlstein & Bissada in 1977, then in humans by Saito et al in 1998. Nonetheless, adipose tissue produces

proinflammatory cytokines and hormones known as adipocytokines, which cause oxidative stress and inflammatory processes, resulting in a pathophysiology that is comparable in both diseases.[4]

Adipokines with anti-inflammatory [e.g. adiponectin, interleukin (IL)-10, IL-4, IL-13] or pro-inflammatory {e.g. resistin, leptin, tumour necrosis factor [TNF-α], and interleukin (IL)-6} activity are secreted by the adipose tissue in a physiologically balanced manner. Adipose-associated immune cells and adipocytes increases the pro-inflammatory protein expression while decreasing anti-inflammatory adipokine expression as obesity progresses. As a result, a low-grade inflammatory condition develops over time.[5]

Resistin is a secretory protein having a mature sequence of 108 amino acids and a molecular weight of 12.5 kDa. Resistin is a protein that is present in macrophages, neutrophils, and lymphocytes that regulates a variety of biological processes, including inflammation. Through the nuclear factor NF-κB pathway, the function of resistin in the inflammatory pathway has been speculated.[6] The proinflammatory property of resistin include the secretion of tumour necrosis factor (TNF-) and interleukin (IL)-6 which impacts the anti-inflammatory actions of adiponectin.

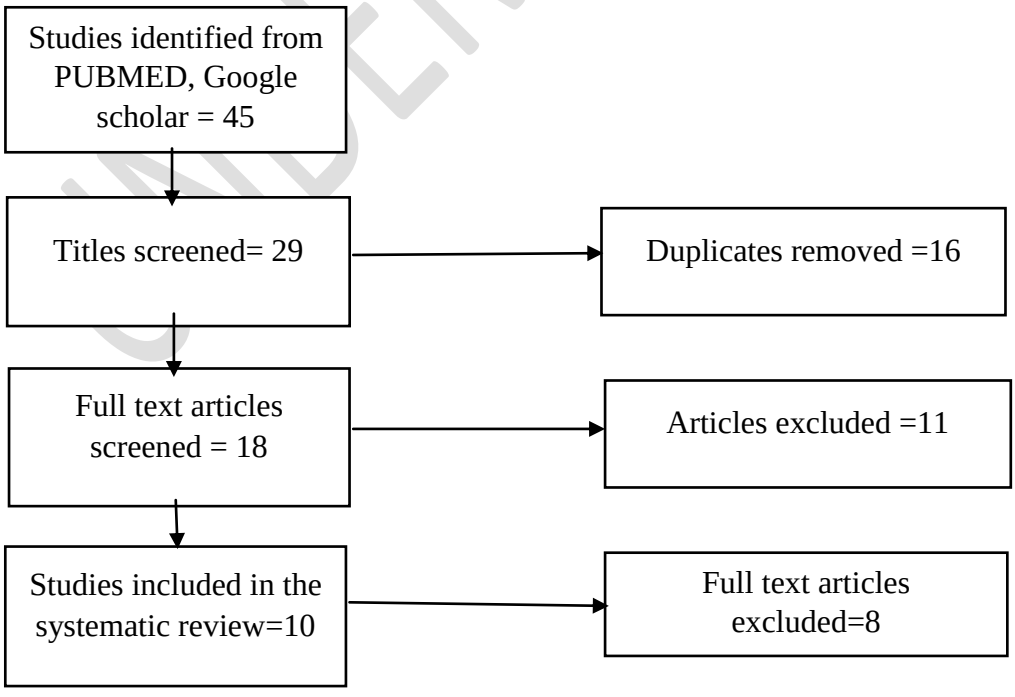
In the light of the above facts, this systematic review aimed to evaluate the association between obesity and resistin levels in periodontal disease.

METHODS

Search Strategy and Study Selection

A literature search was conducted for relevant articles that has been published between the year December 2010 to April 2021 in English language using relevant MesH terms such as (“Adipokines”, OR “Adipocytokines”, OR “Biomarkers”, OR “Resistin”) AND (“Saliva”, OR “Gingival crevicular fluid”, OR “Serum”) AND(“Obesity”, OR “Obese”, OR “Overweight”, OR “Body Mass Index”, OR” Waist circumference”, OR “Waist-hip ratio”) AND (“Periodontal diseases”, OR “Periodontitis”, OR “ Chronic Periodontitis”)through online database such as PUBMED, Google scholar. Out of 45 articles, 10 articles were selected based on the inclusion criteria through this electronic search as shown in Figure 1.

Figure 1-Consort diagram for study selection in this systematic review



INCLUSION **C**RITERIA**-**

1. Primary articles that compares resistin levels in GCF, saliva or serum in individuals with and without obesity (BMI: > 25kg/m^2- < 40kg/m^2)

2. Mean age criteria was between 20-65 years

2. Studies conducted between the years December 2010 to April 2021

3. Cross-sectional studies, retrospective studies, observational studies

4. Articles that were published in English

EXCLUSION **C**RITERIA**-**

1. Studies without control group

2. Animal studies

3. Literature review

4. Studies with any habit

DATA ANALYSIS

For each article, a list of grounds for inclusion was created. The total number of patients, type of study, methods of assessing resistin levels with and without obesity in periodontal disease and main results were all gathered. Evidence tables and written evidence summaries were used to undertake qualitative synthesis. To reduce heterogeneity, studies were summarised showing general characteristics of the included studies as described in Table 1. No meta-analysis was performed due to limited data and significant heterogeneity among the studies. For each study, the risk of bias was determined. In this review, the Consort standards were followed in the selection and exclusion of studies.

Table 1- Showing general characteristics of the included studies

Author and year	**Type of study**	**Sample size**	**Method of evaluation**		**Results**
			Periodontitis	**Type of Assay**	
Tahir KM et al 2020 BMC Oral Health [6]	Prospective study	Group1:OBCP-18 Group2:NBCP-30	Gingival Bleeding Index (GBI),Plaque Index (PI), Clinical Attachment	Enzyme-linked immunosorbent assay (ELISA)	No significant difference was found in serum resistin level and mean counts for P.

			Loss (CAL) and Probing Pocket Depth (PPD)		gingivalis, P. intermedia and T. forsythia between obese and normal weight groups following NSPT.
Mahmood TJ et al 2020 Sulaimani Dent J [7]	Case control	Group1:NBHP-10 Group2:NBCP-25 Group3:OBHP-26 Group4:OBCP-25	Bleeding Index (BI), Plaque Index (PI), Probing Pocket Depth (PPD) and Clinical Attachment Loss (CAL)	Enzyme-linked immunosorbent assay (ELISA)	Significant correlations were not found among clinical periodontal parameters and BMI and the resistin levels in the four groups tested in this study.
Li Z et al 2018 Int J Clin Exp Pathol [8]	Cross sectional	Group1:NBHP-50 Group2:OBCP-116	Bleeding on probing (BOP), probing depth (PD), and clinical attachment loss (CAL)	Enzyme-linked immunosorbent assay (ELISA)	Both the OB group and the OBCP group exhibited considerably greater serum levels of visfatin, leptin, and resistin than the normal control group, and significantly lower serum levels of APN than the normal control group, according to adipocytokine assays.
Suresh S et al 2018 J Indian Soc Periodontol [9]	Case control	Group1:OBCP-30 Group2:NBCP-30	Pocket probing depth (PPD),Gingival index (GI), Plaque index(PI), and clinical attachment level (CAL)	Enzyme-linked immunosorbent assay (ELISA)	Obese patients with chronic periodontitis had higher levels of plasma ROM, serum, and GCF resistin than normal-weight patients with

					chronic periodontitis.
Al-Hamoudi N et al 2018 J Invest Clin Dent [10]	Prospective Clinical Trial	Group1:OBCP-35 NBCP-35 Group2:OBHP-34 NBHP-33	Pocket probing depth (PD) and bleeding on probing (BOP)	Enzyme-linked immunosorbent assay (ELISA)	Obese patients with CP have significantly greater periodontal inflammatory markers as well as total salivary IL-6 and resistin levels than non-obese patients with CP; and SRP lowers BOP, PD, and IL-6 and resistin levels in whole saliva in both obese and non-obese CP individuals
Suresh S et al 2016 JCDR [11]	Case control	Group1:OBCP-25 Group2:OBHP-25 Group3:NBCP-25 Group4:NBHP-15	Gingival Index (GI), Plaque Index (PI) and Clinical Attachment Level (CAL)	Enzyme-linked immunosorbent assay (ELISA)	When compared to nonobese participants with healthy periodontium, obese subjects with periodontitis have higher GCF resistin levels.
Varghese T et al 2016 J Contemp Dent Prac [12]	Case control	Group1:OBCP-100 Group2:NBCP-100	Clinical Attachment Level (CAL), Plaque Index (PI), Gingival Index (GI) and Pocket probing depth(PP)	Enzyme-linked immunosorbent assay (ELISA) Spectrophotometer	Significant reductions in plasma oxygen reactive metabolite and GCF resistin levels were seen in obese participants following NSPT. In obese patients with chronic periodontitis, they

					were also found to be substantially linked with clinical periodontal parameters.
Goncalves T E et al 2015 J Clinical Periodontol [5]	Case control	Group1:OBCP-20 Group2:NBCP-20	Probing depth (PD) and clinical attachment level (CAL)	Enzyme-linked immunosorbent assay (ELISA)	Obese patients had a more overall pro-inflammatory adipokine profile at the periodontal level than non-obese patients, particularly in respect to resistin and TNF-a levels.
Patel SP et al 2014 J Indian Soc Periodontol [13]	Case control	Group1:NBHP-30 Group2:NBCP-30 Group3:OBCP-30	Probing pocket depth (PPD), Gingival index (GI), clinical attachment level (CAL) and radiographic evidence of bone loss.	Enzyme-linked immunosorbent assay (ELISA)	Resistin levels were found in all of the samples in each group. Group 3 had the greatest mean resistin concentrations in GCF and serum, while Group 1 had the lowest mean resistin concentrations.
Zimmermann GS et al 2013 J Periodontol [14]	Cross sectional	Group1:NBHP-20 Group2:NBCP-20 Group3:OBHP-18 Group4:OBCP-20	Bleeding on probing (BOP), marginal bleeding (MB), Probing depth (PD) and clinical attachment level (CAL)	Enzyme-linked immunosorbent assay (ELISA)	Periodontitis increases serum resistin levels in both groups, implying that periodontal inflammation may influence systemic levels of this proinflammatory marker irrespective of obesity.

OBCP: Obese with chronic periodontitis, NBCP: Non obese with chronic periodontitis, NBHP: Non obese with healthy periodontium, OBHP: Obese with healthy periodontium,

RESULTS

Study Selection

A total of 45 originally generated publications, out of which a total of 29 articles were accepted for title review. After the title review, 11 studies were excluded as they did not have the control group, or studies evaluating the resistin levels with and without obesity in periodontal disease or association of any systemic disease and the animal studies. A total of 10 studies were then included in the present systematic review that accomplished the inclusion criteria. All articles included in this systematic review was published in English language between the years 2010-2021.

Out of 10 articles that were included in this review enlisted 2 cross sectional, 2 prospective, 6 case control studies. The total number of sample size taken from the studies ranged between 10 and 116 participants consisting both female and male individuals with a mean age between 20 and 65 years.

One study collected GCF and two studies collected serum while for other five studies both GCF and serum samples were collected. Two studies collected saliva for the evaluation of resistin levels .All the studies used enzyme linked immunosorbent assay (ELISA) for the detection of resistin levels except one study that used both ELISA and spectrophotometer. Of the 10 studies, Tahir KM et al [6] and Mahmood T J et al [7] showed no significant difference in resistin levels between clinical periodontal parameters and BMI. While studies by Li z et al [8], Suresh S et al [9], Al Hamoudi N et al [10], Suresh et al [11], Varghese T et al [12], Goncalves TE et al [5], Patel SP et al [13], Zimmermann GS et al [14] in comparison to the healthy control group, found a favourable correlation between resistin levels in obesity with chronic periodontitis.

DISCUSSION

Obesity as defined by the World Health Organization is a disease in which fat accumulates in the body to such an extent that it has a negative impact on health.[10] Periodontal disease, on the other hand, is one of the most frequent chronic disorders initiated by periodontal bacteria colonisation and an excessive inflammatory response, which results in loss of tooth-supporting tissues. The onset and progression of periodontal disease has shown to be affected by obesity.[11]Although the link between periodontal diseases and obesity, as well as the fundamental biologic mechanisms are still being debated and it has been reported many pro-inflammatory cytokines are secreted by adipose tissues, and they are linked to inflammatory processes in both inflammatory diseases, implying a shared pathophysiological pathway.[10] Obesity is intimately linked to adipose tissue. Adipose tissue which is capable of secreting a variety of bioactive chemicals, including resistin, visfatin, leptin and adiponectin, where resistin enhances the synthesis of adhesion molecules and other pro-inflammatory biomarkers in peripheral blood mononuclear cells and macrophages, and it also inhibits adiponectin's anti-inflammatory actions on endothelial cells.[5] Studies have found higher resistin levels in serum, GCF and saliva samples of patients with periodontitis as compared to healthy individuals, indicating that it has pro-inflammatory effects. Suresh N et al [11] in the study concluded that when compared between nonobese participants with healthy periodontium, obese subjects with periodontitis had higher levels resistin in GCF. Another study by Patel S P et al [13] stated that periodontal inflammation raised resistin levels, suggesting that it may play an inflammatory function in periodontitis. Various other studies also stated that following non-surgical periodontal therapy (NSPT) had a considerable influence on plaque index and gingival bleeding index in

periodontitis patients regardless of weight status. However, the effect of NSPT on serum resistin and periodontal pathogens was non-significant in patients with periodontitis.[5,6] Additionally in a study by Mahmood TJ [7] no significant positive relationships were found between the levels of salivary resistin levels and clinical periodontal and obesity characteristics. But in a study by Al-Hamoudi N et al [10] it stated that obese patients with chronic periodontitis have significantly greater periodontal inflammatory markers as well as total salivary IL-6 and resistin levels than those of non-obese chronic periodontitis patients. The link between diabetes and periodontitis is an example of systemic disease predisposing to oral infection, which then exacerbates systemic disease after the infection is established. Resistin levels that are elevated in diabetes mellitus emphasise its impact on a person's glycaemic condition. There is a growing scope for finding the most specific and sensitive biomarker, with resistin being one such newly recognised marker. With advancements in technologies for early detection, intervention, and prompt treatment of diseases, there is a growing scope for finding the most specific and sensitive biomarker.[15]

Thus this systematic review on the basis of the evidences from the previous studies emphasized on how obesity may influence resistin levels in the systemic and periodontal tissues in a pro-inflammatory manner. Despite the fact that the majority of the research included in the study found a favourable connection between the resistin levels when compared to obesity from normal healthy individuals in periodontal disease more research is needed, with a focus on the mechanisms that underpin them.

LIMITATIONS

More studies should have been included for establishing a relation between resistin and periodontal disease and thus due to lack of data and considerable heterogeneity among the trials no meta-analysis could have been performed. Further research employing particular resistin could help to clarify the role of resistin in inflammatory illnesses like periodontitis.

CONCLUSION

On the basis of the evidences from the studies that have been included in this review concluded that periodontitis patients with obesity have higher resistin levels than healthy people. Thus resistin can possibly be utilised as a surrogate marker to identify those at risk of developing periodontitis.

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