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(RESEARCH ARTICLE)

Involvement of Osteonectin and Matrix metaloproteinas-8 in pathogenesis of Periimplantitis

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Abstract

Periimplantitis is a condition that can be described by inflammation of the soft tissues and bone loss around the implant. It is a disorder that causes inflammation and increases the synthesis and activation of cytokines. The aim of the present study was to investigate salivary osteonectin and matrix metaloproteinas 8 (MMP8) levels in periimplant health and periimplantitis, to determin the correlation between osteonectin and MMP8 in periimplantitis patients. Methods Forty-five patients with peri-implantitis, and 44 individuals with peri-implant health as a control group have participated in the research. Modified sulcus bleeding index(MSBI), modified plaque index (MPI), and probing depth (PD)were among the actual indicators that were noted. The saliva samples collected then osteonectin and MMP8 levels were analyzed by ELISA. Results, there were significant differences in salivary osteonectin and MMP8 levels of periimplantitis compared to periimplant healthy controls groups. Periodontal clinical parameters were significantly correlated with salivary osteonectin and MMP8 levels in periimplantitis groups. There was significant correlation of osteonectin with MMP8. Conclusions periimplantitis patients were showed that increased saliva levels of osteonectin and MMP8. The elevated level of osteonectin supports their participation in bone resorption via altering control of bone remodeling, as shown in periimplantitis. MMP8 has the potential function in periodontal tissue deterioration and can be used to assess the progressing of periimplant disorders. Therefor these significant findings of the two biomarkers may have a potential role in pathogenesis of periimplantitis.

Keywords: Periimplantitis; Osteonectin; Periimplant healthy; MMP8

1 Introduction

Periimplantitis (PI) is a pathologic illness which impacts the tissues around implant dentistry. It is distinguished by osteolysis due to inflammation, that is the diagnostic characteristic of the condition [1]. It causes periimplant bone tissue to become inflamed and destroyed, resulting in implant failure and loss [2]. The process of inflammation influences both the soft and hard tissues around an osseointegrated implant and is linked to purulence, pocket formation, periimplant epithelial seal disintegration and loss of bone progressively [3,4]. The development of periimplantitis has been related to a number of variables, such as smoking, trauma from occlusal, micro gaps, infection from bacteria, and traumatic implant surgery[5].

Even though the area around the implant has unique architectural and histological features, the etiology of periodontitis and periimplantitis was investigated., with analogous immune cell exudates and bacterial-type colonization[6,7,8]. It was thought to have started as a dysbiotic microbiota caused by an overpopulation of pathogens in biofilms. The hard and soft tissues around dental implants have inflammatory reactions as a result of this microbial buildup and related

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virulence factors [9]. The mucosa surrounding the implant is first impacted by these inflammatory lesions, but when the illness worsens or becomes chronic, they spread into the bone, causing periimplantitis and eventual loss of bones [10].

Osteonectin, a non-collagenous matrix protein generated by osteoblasts, is essential for controlling bone remodeling and preserving bone quantity and quality because it starts mineralization and encourages the creation of mineral crystals[11,12]. It plays a part in tissue remodeling through cell-matrix interaction. Osteonectin is secreted by osteoblasts, fibroblasts, and endothelial cells. Because osteonectin is present in active osteoblasts, this component of bone has been used as a marker for bone development [13,14]. However, in peri-implantitis, its role is unknown.

The matrix metalloproteinases (MMPs) family has five distinct categories and has been recognized for its ability to deteriorate almost every basement membranes and outer matrix of cells components in biological repairing and pathological demolition of tissues[15]. Furthermore, prior investigations have linked irreparable periimplant damage of tissues thru overexpression MMPs [16,17]. MMP8 is mostly produced by neutrophils, however other type of cells can also express it[18]. An important contributor to the development of periodontal disease, it is a molecule has a strong propensity starting the inflammation degradation of connective tissue collagens. In periimplantitis, MMP8 has been linked to the same detrimental characteristic[19].

However, until date no study evaluating salivary osteonectin values at diverse periimplant conditions and no study correlated between osteonectin with MMP8 levels in periimplantitis. The current study's objectives were to investigate salivary osteonectin and MMP8 levels in periimplant healthy and periimplantitis, to determine the correlation between osteonectin and MMP8 in peri-implantitis patients for exploring the potential role in pathogenesis of peri-implantitis.

2 Materials and Methods

2.1 Study Design

A case-control study was carried out in karabla, Iraq, from October 2023 to September 2024. The Declaration of Helsinki's guidelines on experiments involving human subjects were followed in the conduct of the study. The study received ethical approval from the University of Al-Ameed's College of Dentistry Ethics Committee (reference number: 126). An informed written consent form was signed by the participants at the University of Al-Ameed's College of Dentistry.

Eighty-nine participants, either periimplant health participants or patients with a diagnosis of periimplantitis according to the 2017 Workshop on the categorization of conditions and diseases around implants (periimplant PD greater 5 mm, flow of blood upon probing with indications of bone resorption)[20]; of them males and females, aged between 3o and 55 years.

The participants divided into two study groups,44 individuals in periimplant healthy group, Perimplants were detected thru sets of implants was identified by the lack of BOP and the lack of radiographic bone loss other than typical remodeling. Periimplantitis group included 45 patients, perimplants identified via BOP with a minimum of just one implant region, PD less than five 5 mm, and radiographically discernible loss of bone greater 2 right out of the implant base following preliminary transformation [21]. When there was just 2 mm of destruction of bone and no bleeding, it wasn't regarded as periimplantitis [21].

The inclusion criteria regarded as osseointegrated implant patients with a follow-up duration of at least five months from implantation, identification a periimplant PD greater five millimeters, and a bone loss of at least fifty percent, at least three implant with in patient mouth. The study excluded volunteers who were hesitant to participate, children, teenagers, patients with autoimmune illnesses, pregnant or breastfeeding women, those who smoked, those with systemic conditions including diabetic or osteoporosis, and those who had received radiation treatment.

2.2 Clinical examination

For each implant, six sites were measured for probing depth (PD) using a plastic periodontal probe. Two metrics were noted: the modified plaque index (MPI)[22] and the modified sulcus bleeding index (MSBI)[22]. Each implant's periapical radiograph was obtained. The participant's periodontal condition was also determined by recording their PD, CAL, flow of blood on prob [23], and biofilm indictor [24].

2.3 Salivary samples collection and analysis

All patients had their unstimulated saliva samples taken before to clinical examination; they were instructed to abstain off food and liquids for no less than 1 hour before the saliva sample gathering. Moreover, the drool was drained from the lower lip into a plastic cup over the course of five minutes whereas they were sitting upright with their heads bowed. Next, 500 µl of the collected saliva was drawn into a plastic Eppendorf tube using a micropipette to remove the entire amount from the disposable cup. Following collection, samples were centrifuged for 20 minutes at 3000 rpm in order to separate the salivary supernatants from the cellular debris. The salivary fluid was centrifuged, removed from the cellular debris, then aspirated once more, stored at -20°C 'til the day of assessment using ELISA kits. The conventional curves contained in each test were used to calculate the amounts of human osteonectin and MMP8 after salivary samples were added to the wells of microtiter plates.

2.4 Statistical Analysis

A descriptive analysis the records were conducted in order to establish the average and its corresponding standard deviation. The obtained data were entered into a Microsoft Office Excel spreadsheet. The Shapiro-Wilk test was used to assess the distribution of the data. For a parametric t-test was employed in a standard dissemination. The IBM SPSS Statistics statistical software (version 23.0, Norman) utilized the information of examination. The criterion for significantly variances set by p 0.05.

3 Results

The mean of age of periimplantitis group was (45.6 ± 1.1), while the control group was (47.2 ± 1.8), with non-significant differences Table 1. Additionally, gender distribution Table1 also showed non-significant differences among the groups. Male to female ratios were 20/25 in the healthy group and 23/21 in the people had periimplantitis group. The gender and age variations were insignificant among both groups that participated. In comparison to the periimplant health group, clinical information of the sampling locations showed that the periimplantitis group had substantially higher MPI and MSBI scores for both indicators. As anticipated, the periimplantitis group's PD value was substantially greater than that of the periimplant health group. The periimplantitis group and the periimplant health group had significantly different MPI, MSBI, and PD.

Furthermore, in contrast to the periimplant health group (0.23 ± 0.14 ng/ml, and 37.66 ± 0.08 pg/ml resp), Table 2 demonstrates a significant rise in the mean heights of osteonectin and MMP8, in the periimplantitis group (3.02 ± 0.04 ng/ml, and 183.04 ± 0.6 pg for resp).

According to Table 3's correlation coefficient (r), this investigation found highly significant relationships among diagnostic indicators (MPI, MSBI, PD) and salivary concentrations of osteonectin and MMP8. Interestingly, osteonectin and MMP8 concentrations were significantly correlated (r = 0.823, p= 0.03) Table 4.

Table 1 Demographic characteristic and periimplant conditions indicators of the study groups

Parameters	Periimplant healthy group (control)	Periimplantitis group	p-value
Age	45.6 ± 1.1	47.2 ± 1.8	0.068 NS
Sex Male Female	23 (55.0%) 21 (45.0%)	20 (33.8%) 25 (66.2%)	0.980 NS
MPI	0.000 ± 0.000	3 ± 0.21	0.01
MSBI	0.000 ± 0.000	3 ± 0.22	0.02
PD	2.9 ± 0.4	9.13 ± 0.12	0.04

p ≤ 0.05, significant.

Table 2 Osteonectin and MMP8 concentrations in saliva of the study groups

Parameters	Periimplant healthy group	Periimplantitis group	p-value
Osteonectin (ng/ml)	0.23 ± 0.14	3.02 ±0.04	0.000
MMP8 (pg/ml)	37.66 ± 0.08	183.04 ± 0.6	0.000

$p \leq 0.05$, significant

Table 3 Correlation among biomarkers and periimplant conditions indicators

Osteonectin			MMP8	
Parameters	r	p-value	r	p-value
MPI	0.432	0.02	0.592	0.02
MSBI	0.781	0.01	0.733	0.03
PD	0.357	0.03	0.784	0.01

r: correlation coefficient

Table 4 Correlation between Osteonectin and MMP8

		Osteonectin
MMP8	r	p-value
	0.823	0.03

statistically significant at $p \leq 0.05$

4 Discussion

Peri-implantitis is a degenerative illness characterized by the occurrence of inflammatory osteolysis around dental implants[25]. The findings of this investigation revealed the salivary osteonectin levels were significantly elevated in peri-implantitis group compared to peri-implant healthy. Osteonectin proteins are associated to bone remodeling[14], and osteolysis occurred with prolonged inflammation of the soft tissues with alter regulation of bone formation [26,27]. In peri-implantitis, the inflammatory milieu contains higher osteonectin levels, which contribute to the pathogenesis of the disease.

However, the present study outcomes revealed significant variance of healthy periimplants and peri-implantitis. On the other hand, GCF osteonectin values did not differ significantly of periodontal disese and healthies participants, according to Baeza et al. [28]. likewise, although salivary osteonectin protein is involved in the metabolizing of bones, Taylor [29] explained that the outcomes are contradictory. Regarding peri-implantitis, In the research by Cakal et al. [30], osteonectin values in the peri-implant crevicular fluid groups of periimplant conditions were not substantially distinct. In Flores et al. study[27], the findings clarified the decline of osteonectin forming, based on aberrant matrix of bones, caused by an inability to regulate peri-implant remodeling of bones in the more severe stages of the disorder.

Matrix metaloproteinas 8 is a proteolytic enzyme. The development of diseases across the body has been connected to abnormal MMP8 expression, which has also been associated to inflammation [31]. MMP8 concentrations were observed to be considerably higher in periimplantitis patients than in periimplant health in the current investigation, suggesting a possible association of MMP8 and periimplantitis. According to these findings, MMP8 was the sole collagenase linked to extensive peri-implantitis during prolonged bone loss[32].

Mostly, major inflammatory cells and resident connective tissue cells typically release MMPs in response to stimuli during pathologic tissue destruction or remodeling during osseointegration of implant inserted and periimplant conditions [18,33].

The periimplantitis diagnosis usually entails assessing bone loss, bleeding, pocket depth, and inflammation surrounding dental implants. Even if these techniques are dependable and practical [34]. The significantly correlated of osteonectin, MMP8 with clinical parameters. Dissimilar with Cakal et al.[30] study that observed probing depths were not correlated with osteonectin levels in periimplantitis. When the illness is at its worst phase, decreased forming of osteonectin at tissue from the bones around an implant during inflammation may connect to periimplant failing bone remodeling [27]. According to the meta-analysis, people had peri-implantitis had significantly higher MMP8 values than people had health. periimplants. The present study evaluates whether the osteonectin, MMP8 level in saliva has a connection to peri-implantitis.

The meaningfully correlated of osteonectin with MMP8. There was alter regulatory osteonectin function of the forming bones at periimplantitis. This may be connected the inadequate control development of bones and the subsequent late-phase periimplant condition reduction in bone. Increased MMP8 levels have been repeatedly associated with periimplantitis, which happened as a result of inflammatory activation during the pathologic tissue deterioration process. Therefor these significant findings of the two biomarkers may have potential role in pathogenesis of periimplantitis.

This is the first study evaluating salivary osteonectin heights in diverse periimplant illnesses. Moreover, correlation of osteonectin with MMP8 in periimplantitis has been established.

The present study has some limitations. First, limiting the number of samples. Second, the expressions of molecules, microbiological and histopathological aspects are not examining in this study. Future study should look into regenerative treatments and targeted immunomodulators, as well as the impact of oral hygiene on risk factors for diseases.

5 Conclusion

Periimplantitis is a complicated dental condition where microbial infection and immune responses, particularly bone remodeling proteins and proteolytic enzymes. Periimplant tissue degeneration is a sign of periimplantitis. causes a rise in osteonectin and MMP8 levels. The elevated biomarker levels in peri-implantitis compared peri-implant health to provide significant insights into the process of osseointegration in peri-implant health, hence contributing valuable information about the course of diseases. There was alter regulatory osteonectin function of the forming bones at periimplantitis. This may be connected the inadequate control development of bones and the subsequent late-phase periimplant condition reduction in bone level. Increased MMP8 levels have been repeatedly associated with peri-implantitis, which happened as a result of inflammatory activation during the pathologic tissue deterioration process. Therefor these significant findings of the two biomarkers may have potential role in pathogenesis of peri-implantitis. Certain salivary indicators were shown to be effective in discriminating between healthy and unhealthy peri-implant conditions. As well, alterations in developing of bone and MMP8 have demonstrated the potential to serve as biomarkers for condition advancement. Early identification and evaluation of periodontal tissue and bone loss is critical for preventing future significant peri-implant bone loss.

Compliance with ethical standards

Disclosure of conflict of interest

If two or more authors have contributed in the manuscript, the conflict of interest statement must be inserted here.

Statement of informed consent

No conflict of interst to be disclosed.

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