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Comparison of peri-implant clinical and radiographic inflammatory parameters and whole salivary destructive inflammatory cytokine profile among obese and non-obese men

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ABSTRACT

The aim of the present cross-sectional retrospective study was to compare the peri-implant clinical and radiographic inflammatory parameters and whole salivary destructive inflammatory cytokine profile among obese and non-obese men. Thirty-five obese and 37 non-obese men were included. Information regarding age, obesity, systemic health status, and habits was collected using a questionnaire. Clinical examination to evaluate peri-implant parameters and radiographic examination to assess marginal bone loss were conducted. Levels of interleukin (IL)-6 and IL-1β in collected un-stimulated whole saliva were measured using enzyme-linked immunosorbent assay. Data was statistically analyzed using Kruskal Wallis test. The mean scores of peri-implant bleeding on probing ($P < 0.05$) and peri-implant probing depth ($P < 0.05$) were significantly higher among obese compared with non-obese individuals. The mean marginal bone loss was also statistically significantly higher among individuals in the test-group compared with the control-group ($P < 0.05$). Whole salivary IL-1β ($P < 0.001$) and IL-6 ($P < 0.001$) levels were significantly higher among individuals in the test-group compared with the control-group. Clinical and radiographic peri-implant inflammatory parameters were worse, and whole salivary IL-6 and IL-1β were higher in obese than non-obese subjects. Obese patients are at greater risk of peri-implant inflammation than non-obese healthy subjects. It is highly recommended that clinicians should educate obese patients seeking implant treatment regarding the association between obesity and peri-implant inflammation. In addition, obese patients with osseointegrated implants must follow strict oral hygiene regimen to prevent inflammation and maintain optimum peri-implant tissue health.

1. Introduction

Peri-implant diseases (peri-implant mucositis and peri-implantitis) and periodontitis are inflammatory conditions that jeopardize the soft tissues and alveolar bone around implants and teeth, respectively [1,2]. If left untreated, these inflammatory conditions may lead to suppuration, loss of supporting alveolar bone and ultimately implant failure and tooth loss, correspondingly [1]. Besides local risk-factors such as poor oral hygiene status, tobacco smoking and previous history of periodontitis [3,4]; systemic conditions that have been associated with the etiology of periimplant diseases and periodontitis include poorly-controlled diabetes mellitus, acquired immune deficiency syndrome and osteoporosis [5–7]. Obesity (accumulation of superfluous amounts of fat in the body, to a degree that may debilitate health [8,9]) is also a significant risk-factor of periodontitis. According to World Health Organization criteria [8], individuals with body mass index (BMI) over 30 kg/m^2 are categorized as "obese". Around 300 million individuals are estimated to be obese globally [10]. According to Atabay et al. [11], obesity may enhance periodontal destruction by elevating oxidative stress in periodontal tissues. *In-vitro* results by Huang et al. [12] demonstrated that obesity compromises the efficiency of the innate periodontal immune response by decreasing infiltration and activation of macrophages thereby further aggravating periodontal inflammation. However, it is pertinent to mention that there are no studies in indexed literature that have

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assessed the influence of obesity on peri-implant soft and hard tissue status.

Unstimulated whole saliva is a complex oral fluid that can be collected non-invasively. Under oral inflammatory conditions, such as periodontitis and peri-implant diseases, unstimulated whole saliva expresses raised levels of destructive inflammatory cytokines which makes unstimulated whole saliva a useful investigative tool for the evaluation of oral inflammatory conditions [13–17]. However, there are no studies that have compared the destructive inflammatory cytokine profile in unstimulated whole saliva of obese and non-obese individuals (controls). Since obesity is a significant risk factor for periodontitis, it is hypothesized that (a) peri-implant soft tissue inflammation and marginal bone loss are significantly higher among obese compared with non-obese individuals; and (b) levels of destructive inflammatory cytokines (interleukin [IL]-6 and IL-1beta) are significantly higher in the unstimulated whole saliva of obese compared with controls.

The aim of the present cross-sectional retrospective study was to compare the peri-implant clinical and radiographic inflammatory parameters and whole salivary destructive inflammatory cytokine profile among obese and non-obese individuals.

2. Materials and methods

2.1. Ethical guidelines

The College of Dentistry Research Centre (CDRC), King Saud University, approved the study protocol for this study. All volunteering individuals were requested to sign a consent form and were informed that reserved the right to retired from the research project at any stage of the investigation.

2.2. Study design

The present study had a cross-sectional retrospective design in which, data was gathered from a defined cohort (obese and non-obese individuals) with functioning dental implants.

2.3. Eligibility criteria

The inclusion criteria were as follows: (a) patients with obesity (patients with BMI of $\geqslant$30 kg/m^2 (test-group) [8]); (b) non-obese individuals (patients with BMI ranging from 18.5 to 24.9 kg/m^2) (control-group); and (c) patients with dental implants in function since at least 12 months. The exclusion criteria were as follows: (a) individuals that self-reported systemic diseases other than obesity (for example acquired immune deficiency syndrome, cardiovascular disorders, diabetes mellitus, hepatitis, and renal disorders); (b) lactation and pregnancy; (c) used of antibiotics, steroids and/or non-steroidal anti-inflammatory drugs within the past 3 months; (d) tobacco smoking, smokeless tobacco use and habitual alcohol consumption; (e) patients on bisphosphonates therapy; and (f) patients that received non-surgical periodontal therapy (scaling and root planning) within the past 3 months.

2.4. Participants

Obese and non-obese individuals having restored and functional implant treatment, which has been in service for at least 12 months were included. Obesity was defined as body mass index (BMI) of $\geqslant$30 kg/m^2 [8]. Individuals with BMI ranging from 18.5 to 24.9 kg/m^2 were defined as controls. All patients were assessed at the dental clinics at the College of Dentistry, King Saud University, Riyadh, Saudi Arabia.

2.5. Questionnaire

Data regarding age, gender, duration of obesity, family history of obesity, daily oral hygiene maintenance, last visit to an oral healthcare provider and implant therapy jaw location, functional duration, number of implants placed, and loading protocol (immediate or delayed loading), were collected using a questionnaire.

2.6. Collection unstimulated whole saliva samples

All unstimulated whole saliva samples were collected at early morning hours (between 7:00 and 9:00 am) by a trained and calibrated investigator (FV). The overall score for the intra-examiner reliability was 0.88. Briefly, the participants were comfortably seated on a dental chair and were requested to allow saliva to accumulate in the mouth for 5 continuous minutes. At the end of this time duration the participants were requested to expectorate into a gauged measuring cylinder. During the process saliva accumulation in the mouth the participants were advised to avoid swallowing and moving their tongue and lips. Unstimulated whole salivary flow rate was determined by dividing the total amount of saliva collected in the measuring cylinder by 5. Unstimulated whole salivary flow rate was expressed in milliliters per minute (ml/min) [18–20]. All salivary samples were assessed within 3 months of collection.

2.7. Assessment of destructive inflammatory cytokine (IL-6 & IL-1β) levels in unstimulated whole saliva

Levels of IL-6 and IL-1β in unstimulated whole saliva samples were investigated using enzyme-linked immunosorbent assay (ELISA). All laboratory based investigations were performed by a trained and calibrated examiner (MAK). The kappa score for intra-examiner reliability was 0.88. In summary, unstimulated whole saliva samples were diluted (1:100) in phosphate-buffered saline and the 96-well plates were coated in duplicate with specific protein antibodies. The 96-well plates were kept at room temperature for 60 min and then washed 3 times. A conjugate solution was added to the plates, following which they were re-incubated for 120 min. Fifty ml of stop solution was added to terminate color formation. The sensitivity of ELISA was 99% and 98.6% for whole salivary IL-6 and IL-1β levels, respectively.

2.8. Evaluation of clinical and radiographic parameters peri-implant inflammation

Clinical examinations were carried out by one trained and calibrated investigator (TA). The overall *kappa* for intra-examiner reliability was 0.92. Among obese individuals and controls, peri-implant bleeding on probing [21] and peri-implant probing depth [22] were measured at six sites per implant (mesiobuccal, midbuccal, distobuccal, distolingual/palatal, midlingual/palatal and mesiolingual/palatal). Peri-implant probing depth was measured to the nearest millimeter using a graded periodontal probe (Hu-Friedy, Chicago, IL, USA) [23].

Intra-oral digital bitewing radiographs were taken for each implant by a trained and calibrated examiner (FAS). The overall *kappa* for the intra-examiner reliability was 0.88. The radiographic technique was standardized by using a film holder as a guiding tool for X-ray beams (Belmont ACURAY 071A Intra Oral X-ray System, Hudson, FL, USA). Marginal bone loss was defined as the linear distance from the implant-abutment junction to the most coronal part of the alveolar crest [24]. Marginal bone loss was recorded in millimeters using a software program (Scion Image, Scion Corp., Fredrick, Maryland, USA).