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Comparison of the Effects of Basal and Conventional Dental Implants on Salivary Levels of IL-1α, IL-1β, and TNFα.

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ABSTRACT

Background and Objective: Dental implants represent an innovative and effective therapeutic alternative for the replacement of missing teeth within the dental arch. The long-term success or failure of implant therapy is fundamentally determined by the establishment and maintenance of osseointegration-the direct structural and functional connection between the implant surface and the surrounding bone tissue. Osseointegration may extend over a period of up to 6 months, during which it remains susceptible to immune system modulation and may be associated with the release of pro-inflammatory cytokines, including IL-1α, IL-1β, and TNFα. The present study aimed to compare the impact of basal versus conventional dental implants on salivary levels of IL-1α, IL-1β, and TNFα.

Methods: This cross-sectional investigation was performed on 65 subjects, who were assigned to two groups: a conventional implant group (n=45) and a basal implant group (n=20). Unstimulated whole saliva samples (3 mL) were obtained from each participant two hours following the last meal. All samples were immediately in a deep freezer until analysis. Cytokine concentrations were quantified using a Sandwich ELISA, and the results were subsequently compared between the two groups.

Findings: Of the 90 enrolled participants, 47 (52.2%) were female and 43 (47.8%) were male. In the conventional implant group, the mean salivary levels of IL-1α and IL-1β were 0.439±0.02 and 1.049±0.02 ng/mL, respectively. In the basal implant group, corresponding values were 0.442±0.05 and 1.39±0.02 ng/mL. For both markers, the mean TNFα level was 1.070±0.01 ng/mL in the conventional implant group and 1.214±0.04 ng/mL in the basal implant group (p=0.0007).

Conclusion: The present findings indicate that dental implants provoke an inflammatory response, as evidenced by the release of pro-inflammatory cytokines (IL-1α, IL-1β, and TNFα), which may potentially modulate the rate of osseointegration. Nevertheless, there was no statistically significant difference in the immunological response to these cytokines between the two implant types evaluated in this study.

Keywords: *Dental Implants, Immune Response, Cytokines, Saliva, Osseointegration*.

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Introduction

Dental implants represent an innovative and well-established approach for the replacement of missing teeth, and have been successfully employed by oral surgeons for decades. Dental implants are described as "a graft that lays down closely related to or deep within alveolar bone." Implants are used to replace a single tooth as well as partially or completely edentulous arches. They are typically used to restore missing teeth in clinics. Although there have been a great deal of materials, procedures, and implant designs, implant failure during treatment remains a major concern for both dentists and patients (1-3). Implants exhibiting clinical mobility, progressive bone loss, implant fracture, or bone loss extending to critical anatomic structures are generally considered to have a hopeless prognosis. Furthermore, implants that are unsuitable for prosthetic restoration are also classified as failures. Implant fracture is one of several contributing factors to implant failure, along with peri-implantitis and failed osseointegration. Mechanical factors such as surgical trauma, micro-movement, overloading, patient medical history, smoking, poor implant design, improper patient selection, staff negligence, poor oral hygiene with bacterial plaque accumulation, incorrect prosthetic restoration, debris accumulation, and bone preparation without coolant irrigation have also been implicated (4, 5).

Integration of dental implants with both soft and hard tissues is essential for their long-term success. Therefore, one of the fundamental challenges in implant dentistry is achieving osseointegration (4). Osseointegration has been defined as "a process in which rigid fixation of alloplastic materials is obtained and maintained within the alveolar bone during functional loading" (6). Osteogenesis at the implant interface plays a critical role in osseointegration. This dynamic process involves complex inflammation-related events, including angiogenesis, neurogenesis, and bone apposition and resorption (7). To restore homeostasis in response to immune reactions and inflammation, well-orchestrated biochemical processes are required, ultimately facilitating implant osseointegration (8). An important component of the immune response is cytokines, which are soluble molecules produced by various immunocompetent cells and serve as mediators of intercellular communication (9).

TNF-α triggers inflammation by activating a cascade of vital mediators. Mediators linked to IL-1β and TNF-α promote the production of proteases, prostaglandins, and bone resorption in several cell types, including fibroblasts and osteoblasts (10). High concentrations of TNF-α have been detected in areas affected by periodontitis and peri-implantitis. These conditions demonstrate that excessive TNF-α secretion is a significant clinical concern in both acute and chronic inflammatory diseases (10). TNF-α induces its effects through two mechanisms: directly by stimulating bone marrow-derived osteoclast precursors, and indirectly via modulation of the osteoprotegerin (OPG)/RANKL pathway.

Pro-inflammatory cytokines, including IL-1β, have been implicated in a wide range of biological processes, such as inflammation, connective tissue metabolism, immune modulation, osteoclastogenesis, and activation of mature osteoclasts resulting in bone resorption (11, 12). The positive correlation between gingival inflammation and IL-1β levels in peri-implant tissues enables early detection of peri-implant mucositis before its progression to peri-implantitis. IL-1β initiates the inflammatory response within this microenvironment by directly modulating the immune response to infectious stimuli and may also play a protective role in bacterial biofilm formation (11, 13). Moreover, IL-1β regulates prostaglandin E2 synthesis, which is believed to be a key factor in promoting hard tissue degradation (12, 14).

The detection of these markers in oral saliva may serve as a valuable non-invasive diagnostic biomarker for oral and periodontal diseases (15, 16).

The present study aimed to evaluate the association between salivary levels of IL-1α, IL-1β, and TNF-α in patients with dental implants, and to compare these biomarker levels between two implant types.

Methods

This case study was conducted on 90 subjects. It aims to compare the levels of IL-1α, IL-1β, and TNF-α between subjects with conventional versus basal dental implants. This research was carried out at the Microbiology Department, College of Medicine, University of Baghdad, Iraq, as part of the researcher's master's degree requirements. The study was conducted over a six-month period, from the initiation of sample collection on July 20, 2023, to the final data analysis on January 17, 2024.

The present investigation received ethical approval from the Institutional Review Board of the Department of Microbiology, College of Medicine, University of Baghdad, on July 17, 2023, and from the Research Ethics Committee of the College of Medicine, University of Baghdad, on August 4, 2024 (approval No. 0239).

Two types of dental implants were included in this study, both of which were placed in the subjects by oral or maxillofacial surgeons specializing in dental implantology: the conventional two-piece dental implant system and the basal single-piece dental implant system.

Study participants and sampling: A total of 65 patients were included in this study as the study group (patients with one or more dental implants). This group comprised 38 females (age range 33-58 years) and 27 males (age range 23-75 years). Of these, 45 patients received conventional dental implants, while 20 received basal type implants. Informed verbal consent was obtained from all participants before sample collection.

A 3 mL sample of unstimulated saliva was collected from each participant 2 hours after meal consumption and stored in a deep freezer. A screening questionnaire was administered to all patients to identify and exclude those who did not meet the eligibility criteria. Following collection, each saliva sample was placed in a test tube and stored in a cool box at -4°C, secured in a dedicated rack to minimize agitation. At the end of each daily collection session, the samples were transported to the laboratory freezer for storage. Upon completion of sample collection and prior to the assay, the frozen samples were thawed at room temperature for 3 hours.

Inclusion criteria: Dental implants were placed by specialists using either the conventional or basal implant method. The procedure was performed at least one month before sample collection, with patients receiving one or multiple implants. Patients were required to have no chronic diseases and were not taking systemic medications (e.g., steroids) that could suppress the immune system.

Exclusion criteria: Patients were excluded if they had viral or bacterial infections, benign or malignant tumors, tooth extraction within the month preceding sample collection, chronic diseases, or use of systemic immunosuppressive medications.

Test principle: Enzyme-linked immunosorbent assay (ELISA) was conducted on the collected samples in accordance with the manufacturer's protocol.

The Statistical Analysis System (SAS 2018) program was applied to reveal the impact of various groups and biomarkers included in our study. A statistical advisor was sought out to complete the statistical results of the study. The t-test was employed for comparing the means of cytokines (IL-1α, IL-1β, and TNF-α) included in the study, while the Chi-square test was employed for comparing the percentages (0.05 and 0.01 probability levels). Additionally, correlation coefficients between biomarkers were calculated. Graphs were generated using Microsoft Excel 2018.

Results

Of the 90 participants, 47 were female and 43 were male. The mean levels of IL-1α and IL-1β in the conventional implant group were 0.439±0.02 and 1.049±0.02 ng/mL, respectively, while in the basal implant group they were 0.442±0.05 and 1.39±0.02 ng/mL, respectively. The mean TNF-α level was 1.070±0.01 ng/mL in the conventional group and 1.214±0.04 ng/mL in the basal group (p=0.0007).

Demographic and general characteristics of the study groups: The study cohort consisted of 65 participants, of whom 38 (58.5%) were female (age range: 33-58 years) and 27 (41.5%) were male (age range: 23-75 years). Implant placement was performed using either the conventional technique in 45 patients (69.2%) or the basal implant system in 20 patients (30.8%).

Analysis of IL-1α, IL-1β and TNFα levels in patient groups based on sex: Statistical analysis was conducted to compare three immunological parameters according to sex. Mean salivary cytokine levels for female and male participants are presented in Tables 1 and 2, respectively. As shown in Table 1, no statistically significant differences were observed between genders within the patient group.

Table 1. The effect of sex on IL-1A, IL-1B, and TNF levels in study groups

Group	Mean±SE		
	IL-1α (ng/ml)	IL-1β (ng/ml)	TNFα (ng/ml)
Female	0.352±0.02	1.039±0.02	1.061±0.02
Male	0.402±0.03	1.052±0.02	1.065±0.04
p-value	0.0934	0.676	0.916

Analysis of the cytokine levels (IL-1α, IL-1β and TNFα) in the two groups of dental implants included in the study (conventional and basal dental implant types): The table (2) shows a comparison between the conventional and basal groups in the levels of cytokines (IL-1α, IL-1β and TNFα). Substantial differences were observed between the two groups. No significant difference was observed in the concentrations of IL-1α and IL-1β between the two groups. However, a significant difference was observed at a level of p≤0.01 in both groups for the parameter TNF-α.

Table 2. Analysis of the cytokine levels (IL-1α, IL-1β and TNFα) in the two implant groups

Group	Mean±SE		
	IL-1α (ng/ml)	IL-1β (ng/ml)	TNFα (ng/ml)
Conventional	0.439±0.02	1.049±0.02	1.070±0.01
Basal	0.442±0.05	1.039±0.02	1.214±0.04
p-value	0.859	0.771	0.0007

Discussion

Dental implants are used to replace missing teeth by drilling into the bone of either jaw (17), while cytokines are inflammatory mediators in the immune system responsible for the body's reaction to foreign bodies (18). This study aims to investigate the relationship between these mediators (IL-1α, IL-1β, and TNF-α) and dental implants as foreign bodies. Cytokine levels were compared between the two types of implants included in the study (45 conventional and 20 basal). No significant differences were observed in IL-1α and IL-1β levels, but a significant difference was found in TNF-α levels, consistent with other studies (19, 20). This difference in TNF-α levels might be attributed to the surgical procedure required for implant

placement. Basal implants necessitate greater bone removal to reach the basal bone, thereby increasing the implant surface area exposed as a foreign body and requiring a more extensive bone regeneration process compared to conventional implants, which involve a more conservative bone removal. The lack of significant difference in IL-1α and IL-1β levels between the two types may be due to a similar immunological response, as both implant types elicit comparable serum levels and are processed through the same pro-inflammatory pathway (21).

No significant differences were observed in salivary cytokine levels (IL-1α, IL-1β, and TNF-α) between males and females in either implant group. Although sex hormones such as estrogen and progesterone may contribute to gender-based differences in immune responses, the findings suggest that the salivary levels of the cytokines measured in this study are not directly influenced by sex hormones, accounting for the lack of significant differences (22, 23). The results indicate that dental implants can trigger an inflammatory response characterized by the release of IL-1α, IL-1β, and TNF-α, which may influence the rate of osseointegration. No significant differences in the immunological response to these cytokines were observed between the two implant types.

The levels of IL-1α found in the collected saliva in both male and female subjects showed no significant difference between the two types of dental implants. Regarding the levels of IL-1β found in the collected saliva, there was an increase shown in the subjects with dental implants, with no significant difference between the two types of dental implants. Regarding the levels of TNF-α found in the collected saliva, there was an increase in the subjects with dental implants, with no significant difference between males and females, and a significant difference between the two types of dental implants.

Conflict of interests: The authors declare that there is no conflict of interest regarding this study with any other institution or publication. No financial support was received from any source for this manuscript.

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