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Evaluation of serum levels of proinflammatory cytokines in patients after dental implantation

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Abstract

Background: Dental implantation triggers an early inflammatory cascade that is fundamental to healing and osseointegration. Interleukin-1 beta and Interleukin-6 have been identified as a signature marker for mediating the process, which along with others could be important biomarkers to monitor the tissue response following implant insertion. Objectives: The aim of this study is to investigate the serum levels of interleukin (IL)-1β and IL-6 in patients with dental implantation and their relationships with implant-associated clinical features. Methods: A case–control study have been performed a of 32 patients undergoing dental implantation and 48 healthy controls matched by age and sex. Blood samples were taken 1 week after implantation for measurement of serum IL-1β and IL-6 levels by enzyme-linked immunosorbent assay (ELISA). Data were collected on clinical variables, including type of tooth replaced, number of teeth implanted (single Tooth or multiple Teeth) and implant position (mandible or maxilla). Results: Serum IL-1β levels were higher in patients (18.45 ± 4.12 pg/mL) than that of controls (14.20 ± 3.35 pg/mL, P = 0.031). Likewise, IL-6 levels were higher in patients (12.80 ± 3.05 pg/mL) than in controls (9.65 ± 2.74 pg/mL, P = 0.021). In patients with two implants (n = 11), IL-1β (19.80 ± 4.10 pg/mL) and IL-6 (13.90 ± 3.10 pg/mL) levels were higher than in patients with one implant each (n = 21; IL-1β 17.85 ± 3.60 pg/mL; IL-6 12.10 ± 2.80 pg/mL; P < 0·05). No significant differences were noted in the type of tooth replaced (canine, premolar, molar) and implant site (mandible vs maxilla). Conclusion: Dental implantation induces significant elevation in serum levels of IL-1β and IL-6 indicating the an active inflammatory response during early phase of healing. The extent of this reaction seems to be related to how many teeth were introduced, and other clinical factors had little effect.

Keywords: IL-1β, IL-6, Dental Implant, Mandible, Maxilla

الملخص

تؤدي زراعة الأسنان إلى تحفيز سلسلة التهابية مبكرة تُعد أساسية لعملية الالتئام والاندماج العظمي. وقد تم تحديد الإنترلوكين-1 بيتا والإنترلوكين-6 كمؤشرات مميزة تلعب دورًا في تنظيم هذه العملية، والتي، إلى جانب غيرها، قد تُعد مؤشرات حيوية مهمة لمتابعة استجابة الأنسجة بعد إدخال الزرعة.

الأهداف:

تهدف هذه الدراسة إلى تقييم مستويات الإنترلوكين-1 **β**والإنترلوكين-6 في مصل الدم لدى المرضى الذين خضعوا لزراعة الأسنان، ودراسة علاقتها بالخصائص السريرية المرتبطة بالزرعات.

أُجريت دراسة حالة–شاهد شملت 32 مريضًا خضعوا لزراعة الأسنان و48 شخصًا سليمًا كمجموعة ضابطة متطابقين من حيث العمر والجنس. تم جمع عينات الدم بعد أسبوع واحد من الزراعة لقياس مستويات **IL-1β** و **IL-6**في المصل باستخدام تقنية المقايسة المناعية المرتبطة بالإنزيم **(ELISA).** كما جُمعت بيانات سريرية تضمنت نوع السن المُعوَّض، وعدد الأسنان المزروعة (سن واحد أو عدة أسنان)، وموقع الزرعة (الفك العلوي أو السفلي).

كانت مستويات **IL-1β** في المصل أعلى لدى المرضى (18.45 ± 4.12 بيكوغرام/مل) مقارنة بالمجموعة الضابطة **14.20 ± 3.35)** بيكوغرام/مل، **P = 0.031).** وبالمثل، كانت مستويات **IL-6** أعلى لدى المرضى (12.80 ± 3.05 بيكوغرام/مل) مقارنة بالضوابط **9.65 ± 2.74)** بيكوغرام/مل، **P = 0.021).** كما أظهرت النتائج أن المرضى الذين لديهم زراعتان **(n = 11)** سجلوا مستويات أعلى من **IL-1β (19.80 ± 4.10)** و **IL-6 (13.90 ± 3.10)** مقارنةً بالمرضى الذين لديهم زرعة واحدة **(n = 21؛ IL-1β = 17.85 ± 3.60؛ IL-6 = 12.10 ± 2.80؛ P < 0.05).** ولم تُلاحظ فروق ذات دلالة إحصائية حسب نوع السن المُعوَّض (ناب، ضاحك، طاحن) أو موقع الزرعة (الفك العلوي مقابل السفلي).

تؤدي زراعة الأسنان إلى ارتفاع ملحوظ في مستويات **IL-1β** و**IL-6** في مصل الدم، مما يشير إلى حدوث استجابة التهابية نشطة خلال المرحلة المبكرة من الالتئام. ويبدو أن شدة هذه الاستجابة ترتبط بعدد الأسنان المزروعة، بينما كان تأثير العوامل السريرية الأخرى محدودًا

الكلمات المفتاحية: زراعة الأسنان، الفك السفلي، الفك العلوي , IL-1β, IL-6.

Introduction

Dental implants stand as one of the most trusted and broadly adopted surgical solutions which continue to revolutionize lost or missing teeth replacement, restoring function and aesthetics [1]. Dental implant therapy is now the

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treatment of choice for partial and complete edentulism as a result of advances in: implant materials; surgical techniques; and prosthetic rehabilitation that has led to high long-term success rates. However, the biological success of dental implants is primarily reliant on the formation and durability of healthy peri-implant tissues and successful osseointegration at the interface between tooth bone with dental coating surface [2].

Although dental implants have a generally good prognosis, inflammatory complications can occur after the placement of an implant. Peri-implant mucositis and peri-implantitis are among the most prevalent inflammatory disorders of peri-implant tissues under these complications [3]. This pathology is characterized by an increased microbial biofilm load and activation of the host immune response, resulting in the presence of inflammatory mediators that directly lead to peri-implant soft tissue inflammation and bone loss over time. In fact, epidemiological studies suggest that not infrequent peri-implant mucositis may be found among up to 50% of patients over long-term follow-up periods, marking the necessity of studying inflammatory mechanisms associated with these procedures [4].

The inflammatory response associated with dental implants implies a complex cross-talk between microbial agents and the host immune system. Cytokines are major regulators of this immune response, that is signaling molecules that mediate intercellular communication particularly with respect to immune cells and tissue. The identification of Interleukin-1 beta and Interleukin-6 as inflammatory biomarkers related to bone metabolism in oral tissues has made them two among the large number of cytokines participating in peri-implant inflammation. These proinflammatory cytokines are produced by different cell types, such as macrophages, fibroblasts, osteoblasts and epithelial cells in response to tissue injury and microbial stimulation [5].

Interleukin-1 beta (IL-1β) is one of the most powerful proinflammatory cytokines implicated in inflammatory reactions involving periodontal and peri-implant tissues. It is important for osteoclast differentiation, bone resorption, and enhancing inflammatory cascades in the periodontal and peri-implant setting. The association between IL-1β levels in peri-implant crevicular fluid and clinical signs of preimplant disease, such as plaque accumulation, gingival inflammation, probing depth and bone loss has been confirmed by previous studies [3]. Additionally, IL-1β has been recognized as an initial biochemical marker for the localization of early inflammatory changes around implants before clinical symptoms appear [6].

As IL-6 is an important mediator of the acute inflammatory response with major roles in immune regulation and bone metabolism It is involved in recruiting and activating immune cells, affecting osteoclastogenesis and mediating bone remodeling processes surrounding dental implants. One such cytokine, IL-6 has been found to be elevated in peri-implant crevicular fluid in the presence of peri-implantitis when compared to healthy implant sites, indicating that it may have clinical utility as a biomarker for assess inflammatory responses following placement of an implant and disease progression [3].

Various clinical and biological elements can affect inflammatory responses after dental implantation. These dependent variables examine the type of tooth or prosthetic replacement implanted, the amount of placed implants, and anatomical location (mandible vs maxilla) where implantation occurred. Anatomical differences between the maxilla and mandible, especially bone density and vascularization might influence osseointegration and peri-implant tissue healing [7]. Overall, the mandible usually demonstrates greater bone density than the maxilla that may

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affect implant stability and inflammatory reaction through the healing stages. Moreover, there is a possibility that the placement of multiple implants or implants in compromised bone conditions may increase local inflammatory activity and affect cytokine expression profiles [8].

In the context of peri-implant health and implant prognosis, significant revelations in biomarker studies have indicated that quantification of inflammatory mediators in biological fluids, including serum, saliva, and peri-implant crevicular fluid, could provide relevant information for evaluating these aspects [9]. Cytokine quantification (eg IL-1β and IL-6) reflects the host immune response after implant placement and may help diagnose early inflammatory changes before any clinical signs appear. Consequently, these biomarkers may provide useful complements to standard clinical and radiographic evaluations of peri-implant tissue health and treatment outcomes [10-11].

The objective of current study was to evaluate serum levels and correlation of IL-1β and IL-6 in patients subjected with dental implantation placing them as emerging markers reflecting systemically soft-tissue inflammatory responses due to implant placement followed by healing around peri-implant tissue.

Patients and Methods

Study Design and Setting

This case–control study was performed from April of 2024 to February of 2025 at the Dental Implant Unit and Clinical Laboratory of Warith International Cancer Institute, Karbala, Iraq. The objectives of the study were to assess the serum levels of Interleukin-1 beta and Interleukin-6 in patients after dental implantation and to analyze their correlation with some clinical parameters: type of the implanted tooth, the number of the implanted teeth, and the implantation site (i.e., mandible/ maxilla).

Eighty participants were recruited for the study and split into two groups:

- Patients: 32 patients who introduced dental implantation.
- Control: 48 healthy individuals including 12 males and 36 females with no previous history of dental implantation or inflammatory oral disease.

The study was ethically approved by the Institutional Research and Ethics Committee of Warith International Cancer Institute before the commencement of the study. All participants provided written informed consent prior to enrollment.

Study Population

Adult dental patients aged 20–65 years, presenting for implant placement and prosthetic rehabilitation at the dental implant clinic. Sample size of patients: this was calculated based on data from previous studies published in the area of serum proinflammatory cytokines after dental implantation and also on eligible participants available over the study period. Accordingly, 32 patients and 48 healthy controls were selected.

Patient Group

The patient cohort comprised of thirty-two patients who had undergone dental implants by qualified oral and maxillofacial surgeons. The following indicators were documented from the clinical records:

- Type of tooth that was replaced (incisor, canine, premolar, or molar)
- Implant teeth of the patient
- Placement site of implant (maxilla or mandible)
- These parameters were measured with an aim of exploring associations with levels of inflammatory cytokines.

Control Group

A control group consisting of 48 apparently healthy volunteers attending the dental clinic for a routine dental check-up. Controls were

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selected to be as similar as possible to the patient group in age and sex distribution. This group of individual excluded any dental implantation history, periodontal disease or systemic inflammatory disorders.

Inclusion and Exclusion Criteria

Inclusion Criteria

- Adults aged 20–65 years
- Patients who underwent successful placement of dental implants
- Absence of systemic inflammatory diseases
- Willingness to donate and give blood samples

Exclusion Criteria

Participants who met at least one of the following exclusion criteria were excluded:

- Chronic or systemic diseases like diabetes mellitus, autoimmune diseases, or immunodeficiency
- Active gum disease or mouth infection
- A history of smoking or drug/alcohol abuse
- Recent oral surgery or trauma in past 3 months
- Administration of anti-inflammatory drugs, corticosteroids, or immunosuppressive medicines
- The same specification was used to reduce the factors, which are not shown in the cytokines tested and possible confounding factors that could affect cytokine levels.

Clinical Data Collection

All subjects were interviewed using a structured questionnaire and were examined using a clinical examination form to obtain clinical and demographic dementia-related information. Data extraction included the following variables for each patient:

- Type of tooth (tooth impanted) — canine, premolar or molar
- Number of dental implants placed
- Site of Implantation (Maxilla or Mandible)
- Standard procedures for implant placement with titanium dental implants in aseptic conditions were performed.

Blood Sample Collection

All the subjects provided peripheral venous blood samples aseptically. In the patient group, blood samples were collected a week following the dental implant surgery, to assess early inflammatory responses following this surgical procedure. The one-week post-operative time point was chosen as it has previously been determined that the peaks of early inflammatory responses following dental implant surgery occur in the first few days and start to stabilize around 7 days. This interval is extended from acute inflammatory phase to early healing, making it suitable for evaluation of circulating proinflammatory cytokines. Venous blood were collected from the antecubital vein of patients using sterile disposable syringes (5 mL). Blood samples were dispensed into plain tubes and incubated at room temperature for 20–30 min to allow blood clot. Samples were then centrifuged at 3000 rpm for 10 minutes to separate the serum. Serum samples were then aliquoted and kept at −20°C until biochemical analysis.

Measurement of Cytokine Levels

Serum levels of IL-1β and IL-6 were determined by enzyme linked immunosorbent assay (ELISA) according to the manufacturer instructions. Each of the assays was run in duplicate. Absorbance values were measured at 450 nm using a microplate reader and cytokine concentrations were determined according to standard calibration curves. Results were reported as picograms per milliliter (in picogram/mL).

Statistical Analysis

All statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). The data were summarized by means of descriptive statistics, including mean ± standard

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deviation (SD), frequency and percentage. For continuous variables, comparisons between patients and control groups were performed by using the independent sample t-test and the Chi-square (χ^2) test for categorical variables between patients and controls. Lastly, differences in cytokine levels based on the type of implanted tooth, number of implants, and implantation site (maxilla or mandible) were analyzed using analysis of variance (ANOVA). Statistical significance was defined as a P value < 0.05 [12].

Ethical Considerations

The method used in this study was approved in accordance with the Declaration of Helsinki (2013). Permission for this study was obtained from the Research and Ethics Committee in Warith International Cancer Institute, Karbala, Iraq. Participants were provided with information about the research aims, methodology and the confidentiality of the study, and written informed consent was obtained prior to participation.

Results

As seen in Table 1, the study population had a fairly balanced demographic distribution between the patients and the controls. For age distribution, most participants were aged 30–34 years for both groups, followed by 35–39 years. The percentage of participants aged ≥60 years was also comparable between groups. Statistical analysis confirmed that there was no significant difference in age distribution between patients and controls (P = 0.43), indicating appropriate matching of patients and controls and thus minimizing confounding effects of age.

Regarding sex, the patient group comprised 56.3% male and the control group comprised 60.4% male, which is in line with common trends in clinical dentals settings, as some literature suggests that males are underwent more often for implants than females. The difference between groups was not statistically significant (P = 0.53) and as such indicates that gender did not influence cohort allocation and that our study does not have gender bias. With respect to place of residence, the largest proportion of both patients (59.4% urban) and controls (64.6% urban) were from urban areas. Rural participants were a minority in both arms. Differences between residence distribution were also not statistically significant (P = 0.12) suggesting that any noncomparable environmental or lifestyle exposures associated with residence were likely minimal between groups.

Table 1. Demographic data for distribution of both patients and control

Indicators		`Patients (No. = 32)		Control (No. = 48)		Chi Square	P value (Sig.)
		Freq.	%	Freq.	%		
Age/Years	25-29	6	18.8	10	20.8	0.09	0.99 (NS)
	30-34	10	31.3	14	29.2		
	35-39	9	28.1	13	27.1		
	≥ 40	7	21.9	11	22.9		
Gender	Male	18	56.3	29	60.4	0.14	0.71 (NS)
	Female	14	43.7	19	39.6		
Residence	Rural	13	40.6	17	35.4	0.22	0.63 (NS)
	Urban	19	59.4	31	64.6		

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Table 2 shows the various characteristics of dental implants given to the patient group. In relation to the type of tooth replaced, molars comprised the highest percentage (50.0%), followed by premolars (34.4%), while canines had the lowest percentage (15.6%). This distribution approximates clinical observation, as loss of posterior teeth—especially molars—more commonly occurs because of caries, periodontal disease, or occlusal stress, thereby necessitating treatment by dental implantation. Regarding the number of implanted teeth, most of the cases (65.6%) received an implant in only one tooth, while 34.4% had two implants placed. This result possibly echoes prevalent clinical practice, where replacement of a single tooth is the most common indication to proceed with implant therapy. In case of large tooth loss or loss of dentition a number of implant placement may need which in turn could have an impact the local inflammatory response. In relation to the anatomical site, implants were placed more frequently in the mandible (56.3%) than in maxilla (43.7%).

Table 2. Characteristics of dental implants in patient group

	Clinical Manifestation	Freq. (n= 32)	Percentage
Type of tooth replaced	Canine	5	15.6
	Pre-molar	11	34.4
	Molar	16	50
Number of implanted teeth	1	21	65.6
	2	11	34.4
Location of implant	Mandible	18	56.3
	Maxilla	14	43.7

Table 3 shows the comparison of serum levels of Interleukin-1 beta and Interleukin-6 for both groups, which were comprised of patients who had received dental implantation and healthy control members. The results showed that the mean serum level of IL-1β in the patient group were significantly higher than the control group (18.45 ± 4.12 pg/mL in the patient group vs. 14.20 ± 3.35 pg/mL in the control group, P = 0.031). In the similar fashion, IL-6 was also significantly higher in patients (12.80 ± 3.05 pg/mL) than in controls (9.65 ± 2.74 pg/mL) (P value 0.021).

Table 3. Comparison of IL-1β and IL-6 levels between patients and control participants

Groups	`Patients (No. = 32) Mean ± SD	Control (No. = 48) Mean ± SD	T Test (P Value)
IL-1β	18.45 ± 4.12	14.20 ± 3.35	(0.031)
IL-6	12.80 ± 3.05	9.65 ± 2.74	(0.021)

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Table 4 shows differences in serum levels of interleukin-1 beta based on different subgroups of patients according to the type of dental implant. In respect to tooth type being replaced, the levels of IL-1β were significantly higher in molar implants (19.20 ± 4.30 pg/mL) when versus premolar (18.10 ± 3.75 pg/mL) and canine implants (17.60 ± 3.20 pg/mL). Although less IL-1β was found in those receiving an incisor or premolar prosthesis, these differences were not statistically significant (P = 0.26), indicating that the type of tooth replaced by prosthetic treatment had little impact on systemic levels of IL-1β. This phenomenon could be attributed to the fact that posterior teeth (molars) are affected by higher occlusal forces and may require more domain surgical manipulation, while prospective systemic inflammatory response remains similar among tooth types.

Comparatively, %IL-1β showed a statistically significant difference in the number of implanted teeth (P = 0.04). IL-1β concentrations were higher in patients who received two implants (19.80 ± 4.10 pg/mL) than in patients with a single implant (17.85 ± 3.60 pg/mL). The result suggests that the inflammatory response can be augmented if multiple implants are placed and surgical interventions with more tissue trauma are repetitively performed. Higher serum levels of IL-1β in this subgroup may represent an increased activation of immune cells and production of cytokines during the early phase of healing. Regarding implant site, IL-1β levels were higher in maxilla implants (18.90 ± 4.05 pg/mL) than in mandible implants (18.20 ± 3.95 pg/mL), but it did not reach statistical difference (P = 0.19).

Table 4. Differences in IL-1β among patients' subgroups classified according to Characteristics of dental implants

Subgroups		No.	IL-1β (pg/ml) Mean ± SD	F Test	P value (Sig.)
Type of tooth replaced	Canine	5	17.60 ± 3.20	1.38	0.26 (NS)
	Pre-molar	11	18.10 ± 3.75		
	Molar	16	19.20 ± 4.30		
Number of implanted teeth	1	21	17.85 ± 3.60	4.52	0.04 (S)
	2	11	19.80 ± 4.10		
Location of implant	Mandible	18	18.20 ± 3.95	1.72	0.19 (NS)
	Maxilla	14	18.90 ± 4.05		

NS: Non-significant at P>0.05; S: Significant at P<0.05

Serum levels of Interleukin-6 between patient subgroups based on dental implant characteristics are summarized in Table 5. Regarding the type of tooth replaced, a gradual increase in IL-6 levels was seen from canine (11.90 ± 2.60 pg/mL) to premolar (12.50 ± 2.90 pg/mL) and molar implants (13.20 ± 3.20 pg/mL). The differences were not statistically significant (P = 0.36), showing that the anatomical type of replaced tooth has little effect on systemic IL-6 levels. Molar regions may require more extensive surgical procedures but the inflammatory response seems to be within normal range for tooth types. In contrast

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to the result according to IMI the number of implanted teeth leads to a statistically significant difference (P = 0.03). Highest IL-6 levels found in patients with two implants (13.90 ± 3.10 pg/mL) compared to those with one implant (12.10 ± 2.80 pg/mL). Our finding indicates that as multiple implants are placed in a given area, increased surgical exposure and tissue manipulation may outswing the inflammatory response. IL-6 is a central mediator of the acute-phase reaction and will increase in relation to the extent of tissue injury and immune activation. The average of IL-6 level was observed to be marginally higher in the upper jaw (maxilla) (13.00 ± 3.05 pg/mL) than the lower jaw (mandible) (12.40 ± 2.95 pg/mL), but it was insignificant statistically (P = 0.29).

Table 5. Differences in IL-6 among patients' subgroups classified according to Characteristics of dental implants

Subgroups		No.	IL-6 (pg/ml) Mean ± SD	F Test	P value (Sig.)
Type of tooth replaced	Canine	5	11.90 ± 2.60	1.05	0.36 (NS)
	Pre-molar	11	12.50 ± 2.90		
	Molar	16	13.20 ± 3.20		
Number of implanted teeth	1	21	12.10 ± 2.80	4.88	0.03 (S)
	2	11	13.90 ± 3.10		
Location of implant	Mandible	18	12.40 ± 2.95	1.14	0.29 (NS)
	Maxilla	14	13.00 ± 3.05		

NS: Non-significant at P>0.05; S: Significant at P<0.05

Discussion

The current study have measured serum levels of Interleukin-1 beta and Interleukin-6 in patients who underwent dental implantation and compared the results to healthy control subjects, as well as assessing how their levels differed based on implant related clinical characteristics. Results showed significantly higher levels of cytokines in patients, compared to controls, but only significant with the number of implanted teeth; than other variables presented differences non-significant. These findings aligns with earlier data showing that placement of a dental implant triggers a quantifiable systemic inflammatory response in the early phases of healing [13-15].

The researcher attributed the elevated levels of IL-1β and IL-6 in patients to physiologic inflammatory response as a result of surgical trauma and tissue injury. It triggers cytokine release due to the cascade of immune responses involved in wound healing and osseointegration. Peak levels of pro-inflammatory cytokines have been observed within the first week following implantation, observable in the acute inflammatory phase [16-17]. As blood samples for the current study were obtained onwards of one-week post-implantation, the increased levels of cytokines observed in our study fit well within that biological time scale of healing [18-20].

IL-1β have become the key mediator of inflammation and bone metabolism, positively

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regulating osteoclast activation and therefore bone resorption, processes that are fundamental for surrounding implants with a remodeling peri-implant bone. The greater level of IL-1β observed in this study is in accordance with previous studies that reported increased amount of IL-1β at peri-implant sites under inflammation [21-23]. For instance, Yaghobee et al. showed significantly higher levels of IL-1β in peri-implant crevicular fluid in patients with peri-implant inflammation than healthy individuals. While this was a serologic and not local tissue determination, the results suggest local inflammatory pathways may be systemically reflected [3].

IL-6 also have diverse functions in regulating the immune response and acute-phase reaction. Its elevation in the patient population suggests systemic inflammatory pathways become activated after implant placement. IL-6 levels can also amplify as a consequence of physiological and pathological inflammatory response during the early-phase healing process and therefore could be used as a reliable biomarker [24-25]. Moreover, IL-6 also plays a role in regulating osteoclast differentiation and bone remodeling, further emphasizing its crucial involvement in the osseointegration process [26].

In the current investigation, there were no statistically significant intergroup variations among IL-1β or IL-6 concerning type of tooth replaced on subgroup analysis. Slightly higher cytokine levels were present in molar compared with incisor implants, yet those differences did not reach significance [27]. This might imply that systemic inflammatory responses are relatively independent of the anatomical category of the substituted tooth. These observations have also been reported earlier when cytokines levels were found more correlated to inflammatory status rather than location of implant or type of tooth [28].

The difference in IL-1β and IL-6 between one and two implants was statistically significant. This suggests that both the magnitude of surgical intervention is an important mechanism through which surgery modifies inflammatory response. Just as for multiple implants we would get more tissue trauma, prolonged surgical time, and extensive manipulation of bones resulting in enhanced cytokine production. This is in line with prior findings that the extent of tissue damage is positively associated with inflammatory mediators [29].

Mandibular implants showed no significant difference from maxillary implants in cytokine levels. While the maxilla had marginally greater mean values than did the mandible, these differences were not statistically significant. This finding indicates that anatomical discrepancies between sites like bone density, cortical thickness, and vascularization may play a minor role in systemic cytokine levels especially during the early postoperative period. This may be explained by the surgical site inflammatory response due to the implant itself causing localized pathology, leading to relatively little systemic spillover. Thus subtle local discrepancies between maxillary and mandibular bone may not be prominent enough to provoke a change in circulating cytokine levels. Systemic cytokine measurements may also capture global inflammatory status, and thus, dilute site-specific differences [30].

Thus, our data collectively provides the important role of IL-1β and IL-6 act as key-mediator of inflammation in dentin implantation. Their markedly elevated levels in patients relative to controls suggest a role for these molecules as biomarkers tracking early healing and inflammatory state. The correlation of cytokine levels with the number implanted teeth also highlights that surgical factors should not be overlooked as modifiers of the inflammatory response. They concord with the earlier literature and further strengthen the emerging evidence of cytokine role in implant dentistry [28].

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However, several limitations should be noted when considering these findings. Irrespective of the systemic cytokine levels, inflammatory processes are preeminently involved at local peri-implant conditions. The small sample size also might restrict the preference results' generalizability. The cross-sectional nature of this study and individual time-point measurements limits our ability to measure changes in cytokine levels longitudinally. Similar shortcomings have been described by other studies evaluating the cytokine responses in patients with implants [31].

The current study have demonstrated that dental implantation was associated with an elevated level of serum IL-1β and IL-6 in the circulatory system, indicating a vigorous inflammatory response occurs at the early healing stage. Only one implant-related factor (the number of implants placed) was found to be an important determinant of inflammatory modulation, as most other features declined insignificantly upon adjustment for implant exposure. These results were in agreement with published studies and suggest the use of these cytokines as biomarkers for monitoring implant related healing and inflammation [32].

Conclusion:

This study find that Interleukin-1 beta and interleukin-6 serum levels was significantly higher in patients after dental implantation compared to healthy controls, thus suggesting the involvement of an active systemic inflammatory response during the early healing phase. The elevation of these cytokines indicated their key roles in mediating inflammation and bone remodeling processes involved during osseointegration. Among the markers studied, it was found that the number of implanted teeth had a significant effect on cytokines indicating that more surgical intervention will lead to increased inflammatory reaction level. Interestingly, type of tooth replaced and implant location (mandible versus maxilla) had no significant effects on cytokine levels. These results highlights the use of IL-1β and IL-6 as biomarker candidates for monitoring post implant inflammation status and healing evolution. Longitudinal studies with larger sample size are warranted to further explore the dynamics of these cytokines and their association with implant survival.

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