

## Evaluation of Serum Creatine Kinase Level in Hypothyroidism Patients Regarding their Periodontal Condition

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### Abstract

**Introduction** Periodontal disease is a chronic inflammatory destructive condition; its target is supporting structures that may lead to the loss of teeth. Hypothyroidism is a condition in which the thyroid gland does not produce and release enough thyroid hormones into the bloodstream which may affect the entire body's metabolism. Many biomarkers like creatine kinase (CK) have been proposed for early detection of both periodontal disease and hypothyroidism. **Objectives** The study aimed to assess and make a comparison for the level of serum CK and the status of the periodontium. **Materials and Methods** The 100 participants who chose to be in the study were aged 25-55 years old. They divided into three groups: 50 hypothyroidisms suffering from periodontitis (stage 2 and 3 periodontitis with grade B), 30 patients have periodontitis (stage II and III periodontitis with grade B) that have good general health and no thyroid dysfunction, and 20 participants exhibiting healthy gum condition (clinically healthy periodontium and systemically). The samples of blood were gathered from the subjects for an automated blood analyzer to evaluate the level of CK after the clinical periodontal examination had been completed. **Results** The result proved that there were highly significant differences among the study and control groups in the clinical periodontal (CAL, BOP score 1, GI, PLI, and PPD). The highest mean values of CK appear in periodontitis (stage II and III grade B) with hypothyroidism (245.32) while the lowest value of the mean of CK shows in the control group (42.13). The correlation of CK with clinical periodontal parameters approximately in three groups revealed a weak positive correlation. **Conclusion** Evaluating the level of CK in the blood is considered a good biological indicator for anticipating the development of periodontal disease in subjects suffering from thyroid dysfunction, and this gives a good idea about the effect of systemic disease on the periodontal tissues.

**Keywords: Hypothyroidism; periodontal disease; creatine kinase (CK).**

## Introduction

Many recent studies explore the relationship between systemic diseases and the health of the oral cavity by linking oral diseases with major non-oral disorders (Bui et al, 2019; Irhayyim et al, 2018), we can use the oral cavity as a mirror for many systemic diseases because it is easily accessible, and non-invasive test can be done in it (Farah et al, 2018; Irhayyim, 2020). Periodontal disease is a common inflammatory disorder of the periodontal tissues developed due to changes in the microbial balance in the oral cavity and may lead to tooth loss. Although the main etiological factor is a dental biofilm the response of the immunity of the host is responsible for most of the tissue destruction that takes place (Azodo & Ojehanon, 2016; Havle et al, 2017). Hypothyroidism is a common disorder that occurs due to the thyroid gland not producing a sufficient amount of thyroid hormones that meet the metabolic demand of the body (de Montmollin et al, 2020). Laboratory testing is very essential for the accurate diagnosis of hypothyroidism. Evaluation of the level of thyroid-stimulating hormone, (TSH) in serum is the best diagnostic test. Any elevation in TSH and lowering in the level of the thyroxin hormones (T4) and triiodothyronine (T3) below the reference range can be considered a signal of primary hypothyroidism (Burch, 2019; Szczepanek-Parulska et al, 2017). Hajer A. Aldulaijan et al, 2020 found that there is a significant relation between hypothyroidism and periodontitis where patients with thyroid underfunction have an increase in susceptibility to loss of bone that leads to periodontitis (Aldulaijan et al, 2020). CK is an enzyme that mainly exists or is found in the muscle of skeletal type, brain and cardiac muscle. This enzyme is released to blood bloodstream when this tissue injury exists. The level of this enzyme is elevated when the muscle is exposed to injury, disease or inflammation (myositis) (Alshail et al, 2016). The increased activity of CK can be used as a marker for gingival inflammation and in the measurement of other diseases related to oral-dental disease (Aldulaijan et al, 2020), also the

level of this enzyme is elevated in patients with hypothyroidism because of the damage of skeletal muscle that often associated hypothyreosis cause an elevation in the value of this enzyme (Gul & Phil, 2019). Because the traditional methods for diagnosis of periodontal diseases are deficient in detecting the progression and regression which take place in the site of the disease previously and newly developing, the biochemical changes that occur in the biological fluids and tissues can consider advanced methods for the diagnosis and detection of the host response to periodontal diseases and thyroid disease and measurement the effectiveness of therapy by evaluating the level of these biomarkers (Alshail et al, 2016). This study aimed to monitor the potential relationship between thyroid dysfunction and periodontal disease. The study goal is to define if there is a correlation between the level of serum CK (a marker of thyroid dysfunction) and the status of periodontal health. This is achieved by evaluating the clinical periodontal parameters and comparing the level of serum CK to these parameters. The study seeks to add to the existing body of knowledge by exploring a possible connection between two commonly seen medical conditions and determining if there is a causal relationship between them.

## Materials and Methods

This study is a cross-sectional study, 100 randomly selected subjects, aged 25-55 years old. The present study recruited specimens from the periodontology department at the Teaching Hospital of Collage of Dentistry, University of Tikrit, as well as from clinics and laboratories of Salah Al-Din Hospital in Tikrit over six months, spanning from January to June of 2022. The endocrinologist based on clinical signs and the lab examination, by evaluating the serum level of TSH, T4, and T3 diagnosed all the subjects with hypothyroidism. Subjects were involved in the study divided into three groups: 50 hypothyroidism with periodontitis (stage II and III periodontitis grade B) according to the 2017 classification (Papapanou et al, 2018), 30 patients

have periodontitis (stage II and III periodontitis with grade B) that have good general health and no thyroid dysfunction and the control group which consist from 20 subjects with clinically healthy periodontium and good medical health. All the participants in the study were subjected to serum evaluation for the CKc level. The subject's acceptance was documented by signing specially designed informed consent, and the information of each participant was collected by using special a questionnaire case sheet to record dental and medical histories. We confirm that this research, which involves participants of human subjects, adheres to the Helsinki Declaration of 1975, as updated in 2013. Furthermore, it has received approval from the appropriate institutional Ethics Committee (Association, 2013). All the teeth involved in the measurement except wisdom teeth, while the exclusion criteria of the study included smokers people, alcoholism, pregnant and lactating women, patients with other systemic diseases like diabetes, immunosuppressive disorders, blood diseases, patients who receive an antibiotic or anti-inflammatory medication or other drugs known to effect on the periodontium or used within the last 3 month. Periodontal health status was examined and measured for all the participants according to specific periodontal parameters, which include plaque index (Löe & Silness, 1964), gingival index (Löe, 1967), bleeding on probing (Newman et al, 2020), probing pocket depth (Newman et al, 2020) and clinical attachment level (Periodontitis, 2015). Stage II and III periodontitis patients in both groups were diagnosed according to the criteria made by the 2017 World Workshop Classification system for periodontal and peri-implant disease and condition (Papapanou et al, 2018) which developed to meet advanced knowledge derived from both clinical and biological research, that had emerged since 1999 International Classification for Periodontal Diseases. Blood samples (5ml) were collected from all the subjects from the vein in the antecubital area for the measurement of CK levels, after that the blood was transferred into Ethylene diamine tetraacetic acid (EDTA)

in special tubes. After sampling, at 2500 rpm at 4° C the tubes were centrifuged for 10 minutes. Plasma samples were obtained with stored at -40° C, and all samples were assessed within 1 month from the optimal collection. the level of CK was evaluated in serum with reference interval 0-100 UIL. The spectrophotometric method used in CK activity determination using a (Biosystem S.A. Costa Brava 30, 08030 Barcelona (Spain) (Schumann et al, 2002, 2010).

### Statistical Analysis

The statistical analysis was conducted utilizing the SPSS V. 26 software program that was used to analyze my result. The study conducted a descriptive statistical analysis utilizing various measures such as mean, mean percentage, standard deviation (SD), Mann-Whitney U test, and Simple person's correlation coefficients (r). In statistical analysis, the utilization of significance levels (S) was employed whereby non-significant (NS) was indicated when  $P > 0.05$ , highly significant (HS) was indicated when  $P \leq 0.01$ , and when  $0.05 \geq P \geq 0.01$ .

### Results

Tables summarized the characteristics of the study and control subjects. The result in Table (1) reveals high mean values of age parameters in periodontitis (stages 2 and 3) with hypothyroidism (40). The control group shows the lowest mean values (26), While the statistical analysis (mean and SD) of the clinical periodontal parameters appears in Table (2) where there are the study groups exhibited statistically significant differences (periodontitis stage II and III with grade B with hypothyroidism) and (periodontitis stage II and III with grade B without hypothyroidism) in PLI, GI, BOP score 1, PPD and CAL. The result in Table (3) revealed the statistically highly significant differences in (CK) among the study and control groups. The highest mean values of CK appear in periodontitis (stage II and III with grade B) in the hypothyroidism group (245.32) and the lowest mean values of CK in the control group (42.13). Table (4) shows an almost non-

significant weak positive correlation of CK with clinical periodontal parameters (PLI, GI, BOP score1, PPD, and CAL).

**Table (1): Descriptive statistics about the age parameters of both the study groups and the control group.**

Groups	No.	Mean	SD±
Periodontitis (stage II III grade B) with hypothyroidism	50	40	0.24
Periodontitis (stage II and III grade B) without hypothyroidism	30	34	0.36
Control group	20	26	0.54

No.=number, SD=standard deviation.

**Table (2): Statistical analysis to evaluate clinical periodontal parameters across various study groups.**

Groups	PLI		GI		BOP score 1		PPD		CAL	
	Mean	SD±	Mean	SD±	Mean%	SD±	Mean	SD±	Mean	SD±
Periodontitis (stage II III grade B) with hypothyroidism	2.42	0.192	2.52	0.032	23.35	0.019	5.32	1.49	5.42	1.13
Periodontitis (stage II and III grade B) without hypothyroidism	1.57	0.064	1.49	0.042	17.46	0.024	4.12	0.31	4.47	1.07
Control group	0.21	0.022	-	-	-	-	-	-	-	-
Mann-Whitney U test	20.86		33.18		42.14		38.92		32.25	
P-value	0.000		0.000		0.000		0.000		0.000	
Sig.	HS		HS		HS		HS		HS	

PLI=plaque index, GI=gingival index, BOP=bleeding on the probing, CAL=clinical attachment loss, PPD=probing pocket depth, Sig.=significant, SD=standard deviation, HS=highly significant, P-value=probability

**Table (3): Statistical analysis of CK (U/L) in study and control groups.**

Groups	CK	
	Mean	SD±
Periodontitis (stage II III grade B) with hypothyroidism	245.32	70.59
Periodontitis (stage II and III Grade B) without hypothyroidism	76.60	9.539
Control group	42.13	2.672
Mann-Whitney U test	56.17	
P-value	0.000	
Sig.	HS	

CK=creatin kinase

**Table (4): Correlation between CK (U/L) level with clinical periodontal parameters in study and control groups.**

GROUPS	PLI			GI			BOP score1			PPD			CAL		
	r	p	Sig.	r	p	Sig.	r	p	Sig.	r	p	Sig.	r	p	Sig.
Periodontitis (stage II III grade B) with hypothyroidism	0.081	0.544	NS	0.382	0.337	NS	0.143	0.289	NS	0.002	0.971	NS	0.132	0.161	NS
Periodontitis (stage II and III grade B) without hypothyroidism	0.001	0.748	NS	0.118	0.466	NS	0.135	0.217	NS	0.046	0.810	NS	0.108	0.370	NS
Control group	0.297	0.201	NS	-	-	-	-	-	-	-	-	-	-	-	-

P=probability, r= Simple person's correlation coefficient.

## Discussion

The result revealed that the high values of the mean age parameter manifest in the periodontitis group (stage II and III) with hypothyroidism. This may be due to the incidence of periodontitis and hypothyroidism associated with old age, overly aggressive brushing and flossing is one of the common side effects of ageing, in addition, the incidence of systemic diseases increase with ageing that may lead to many etiological factors such as dry mouth, restricted dexterity, the effect

of many medications on the health of the gum, delay of healing after any simple inflammation, all of these lead to increase loss of bone and loss of attachment and finally lead to severe periodontitis (Genco & Sanz, 2020; Huang & Dong, 2022). The thyroid disorders especially the incidence of hypothyroidism increase with elderly people, this is due to the endocrine organs, such as the thyroid gland, subject to important functional changes and subclinical disturbances of the thyroid function during ageing. One of these disorders in the gland includes an increase in the level of thyrotropin (TSH) and normal free thyroxine (FT4) (Gesing, 2015; Rozing et al, 2010). Clinical periodontal parameters values (PLI, GI, PPD, BOP score1, and CAL) increase in (periodontitis stage II and III with grade B with hypothyroidism) more than (periodontitis stage II and III with grade B without hypothyroidism) because there are many mechanisms which make the hypothyroidism patients more susceptible to periodontitis than a healthy one. Thyroid dysfunction causes a liberated number of cytokines that initiate amplified inflammatory response in combination with the effect of endotoxin released from plaque biofilm which leads to a concentration of local inflammatory mediators such as prostaglandin, cytokines, matrix metalloproteinase (MMP), and other proteinases which have a destructive effect that leads to bone and periodontal breakdown (Monea et al, 2014). Any defect or regularity of thyroid hormone can affect the body's bone metabolism and bone formation slowed with an increase of bone resorption (direct effect on joint action between osteoblast and osteoclast) (Aldulajjan et al, 2020). This irregularity also decreases the proliferative process of wound healing by suppressing type-IV collagen and hydroxyproline leading to a delay in wound healing and finally harming the alveolar bone and periodontal breakdown (Yussif et al, 2017). In addition to the aforementioned direct effects of hypothyroidism on gum health and surrounding tissues, there is also an observed negative and indirect effect of medication used to compensate

for hormonal deficiencies, such as levothyroxine. However, the impact of these medications on the gums is indirect and primarily occurs through their influence on the health and function of salivary glands. These medications lead to a reduction in saliva secretion in the mouth, resulting in dry mouth and increased formation of dental caries. Consequently, it can be concluded that both controlled and uncontrolled hypothyroidism affect oral tissues (Hauge et al, 2021; Muralidharan et al, 2013). Also, we can show in our study the level of CK which revealed that the high value of the mean shown in periodontitis stage II and III with grade B with hypothyroidism group, and this result agrees with (Basma and Maha, 2016) that found the high value of the mean of CK in chronic periodontitis group and strong positive correlation with clinical periodontal parameters, this is due to that CK is an intracellular enzyme involved in any metabolic procedure that takes place in our body and liberates from the dead cell of periodontal tissues as a result of inflammation so can be used as a good salivary biomarker for the manifestation of gingival inflammation (Omer, 2015). The relation between CK and hypothyroidism in the study show also elevated levels of this enzyme in thyroid dysfunction (Hemavathi & Hanumanthaiah, 2016; Prakash et al, 2007; Reena et al, 2019).

## Conclusions

It can be concluded that the current study and result revealed the serum level of CK biomarker serves as a well-individualized biological biomarker indicator for assessing the possible development of periodontal diseases in subjects suffering from hypothyroidism. Furthermore, it proves to be a useful marker for evaluating the periodontal destruction.

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