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Research Article

Impact of Different Treatment Modalities on Vitamin D3 and Oxidative Stress Markers in Serum and Saliva of Iraqi Patients with Behçet's Disease

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Abstract:

Background: It is believed that vitamin D is a major environmental factor that can affect the occurrence of many inflammatory and autoimmune disorders, such as Behcet's disease.

Objectives: To evaluate the impacts of medical treatment and body mass index on vitamin D3 and certain oxidative stress markers (Glutathione, Nitric Oxide) in Iraqi patients afflicted by Behcet disease. Additionally, it sought to explore any potential correlations between such markers and Vitamin D3 with the severity of Behcet disease, and the diagnostic potential of saliva in measuring such markers.

Methods: This is a case-control study conducted at Merjan Teaching Hospital in Babylon, Iraq. between December 2023 and March 2024. Forty-five patients suffering from Behcet disease, and meeting international criteria, were divided into three groups: 15 on azathioprine treatment, 15 newly diagnosed untreated cases, and 15 on anti-TNF-α (Infliximab) biological therapy. A control group of 15 subjects matched for age and sex was included. Serum and salivary 25-hydroxy vitamin D levels were measured using an enzyme-linked immunosorbent assay. Spectrophotometric methods were used to assess levels of reduced Glutathione and Nitric Oxide in serum and saliva across the groups. Statistical Package for the Social Sciences software, version 26, was used to analyze data. A significance level of $P \leq 0.05$ has been established as statistically significant.

Results: Vitamin D3 level was significantly lower in newly diagnosed Behcet disease patients as well as those on Infliximab therapy compared with controls. The greatest serum Glutathione level was found in cases of Infliximab treatment compared with other groups. Serum Nitric Oxide showed an inverse correlation with a highly significant difference in disease severity.

Conclusion: Newly diagnosed Behcet disease cases and those on Infliximab therapy were linked to vitamin D deficiency. A positive correlation between serum and salivary D3 was established. Salivary Nitric Oxide increased during Behcet disease. Since serum Nitric Oxide levels fall as the disease progresses, it could evaluate the severity of Behcet disease.

Keywords: Behçet's disease; Glutathione; Nitric Oxide; Oxidative Stress; Vitamin D3.

Introduction

Behçet's Disease (BD) represents a chronic and rare inflammatory disorder that could affect several other areas of the body by causing inflammation of the blood vessels. In addition, it is characterized by a range of skin lesions, ocular problems, and recurrent, painful genital as well as oral ulcers (1, 2). Uncertainty surrounds the precise etiology of the disease. Various biological processes are thought to be influenced by the secosteroid hormone vitamin D. Growing research suggests that vitamin D could control both inflammatory and immune responses (3). As mentioned earlier, there is a substantial association between vitamin D insufficiency and various diseases, including BD (4). Endothelial cell dysfunction and vasculitis are the hallmarks of BD. Nitric oxide (NO), referred to as an endothelium-derived relaxing factor, can also be defined as a free oxygen radical that endothelial cells synthesize in response to immunologic, infectious, and inflammatory stimuli (5). Increased NO concentrations are linked to disease activity in BD patients (6). Evidence supporting NO's function throughout BD has been mounting lately.

Pro-inflammatory cytokines, as well as inflammation, stimulate the expression of the vascular endothelial growth factor (VEGF), which in turn, increases the expression of NO synthase in endothelial cells, resulting in the generation of a significant quantity of NO and the mobilization of leukocytes (7). It is widely acknowledged that reactive oxygen species (ROS) produced by neutrophils might be connected to BD pathogenesis despite the disease's unclear etiology. On the other hand, it was reported that patients with BD have reduced levels of endogenous free radical-scavenging enzymes, which include catalase, superoxide dismutase, and glutathione peroxidase (8). Accordingly, oxidative stress is thought to be caused by antioxidant enzyme depletion

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and altered oxidant/antioxidant balance (9). Vitamin D regulates the immune system and has an endocrine influence on immune system cells, which causes anti-inflammatory responses (10). Furthermore, it possesses the potential to treat neoplasms, psoriasis, and autoimmune diseases (11). It is still unclear how vitamin D functions in autoimmune diseases on a basic level. Glutathione (GSH) regulates redox homeostasis precisely, making it one of the most significant defenses against oxidative stress. The regulation of cell survival, growth, and death depend on GSH, which is also involved in numerous metabolic activities (12).

It is envisaged that saliva will become a biological sample that represents the status of health because it contains a variety of biological substances, such as enzymes and vitamins (13). The quantities of certain markers in serum and saliva have been found to be comparable in many studies, and some of those markers could be quantified as laboratory tests for diagnosis (14). The method most frequently employed for the assessment of blood indicators is the collection of venous blood samples. Nonetheless, there is a chance of contamination throughout the venous blood sample collection and transit processes. Furthermore, salivary sample collection is a noninvasive method that patients often accept (15). Our study aimed to demonstrate the association of oxidative stress with the pathogenesis of BD and the antioxidant capacity of Vitamin D3, and relate them with possible factors that could have an impact on them.

Patients and Methods

Study design and participants

This case-control study was conducted from December 2023 to March 2024, in which 60 Iraqi volunteers were recruited. Following the International Criteria for Behcet's Disease (ICBD) (16), 45 patients were diagnosed with BD. For the ICBD, genital aphthosis, ocular lesions, and oral aphthosis are each assigned 2 points, whereas skin lesions, vascular manifestations, and central nervous system involvement are each assigned 1 point, respectively. 1 point for the pathergy test when used. A patient is classified as having BD if scoring ≥4 points. Of these, 29 were males and 16 were females with a mean disease duration of 3.97 ± 0.5 years and a mean age of 34.93 ± 3.4 years. The individuals have been enlisted from the Rheumatology Department at Merjan Hospital/Al-Hilla, Babil, Iraq. Three groups of patients were formed: 15 were newly diagnosed, 15 were receiving biological anti-TNF-α treatment (Infliximab) monotherapy with a mean treatment duration of 4.06 years, and 15 were receiving Azathioprine monotherapy with a mean treatment duration of 1.08 years. Additionally, 15 age- and sex-matched, healthy-looking subjects served as a control group for comparison. Professional rheumatologists obtained a detailed medical history and conducted a comprehensive physical examination. With a study power of 80% and a significance level of α = 0.05, the sample size (n = 15) for each group was determined.

Exclusion criteria

Pregnancy, antioxidants and vitamin D supplementation within three months prior to the study, as well as no history of (or overlap with) other autoimmune diseases, parathyroid disorders, thyroid disorders, diabetes mellitus, fibromyalgia, cigarette smoking, neoplasia, liver disease, chronic renal failure and patients on steroids or other types of treatment which not included in the inclusion criteria. From every subject, 3 mL of blood and saliva were collected. With the use of the Human (25-OH-D) enzyme-linked immunosorbent assay (ELISA) test, 25-Hydroxy vitamin D (25-OH-D) has been quantified. Reduced glutathione (GSH) and nitric oxide (NO) levels in serum and saliva were measured and compared between healthy persons and those with BD using spectrophotometric techniques. Vitamin D levels below 20 ng/mL were considered to be in "deficiency." Vitamin D "insufficiency" has been defined as vitamin D levels greater than 20 ng/mL and lower than 30 ng/mL. Vitamin D levels above 30 ng/mL were considered sufficient (17).

BD's clinical severity score -was determined by summation of one point for minor symptoms(-like oral aphthous, arthralgia, genital ulcers, besides common skin lesions like papulopustular lesions, folliculitis, , and erythema nodosum), two points for the moderate symptoms (-as arthritis, gastrointestinal involvement, and legs venous thrombosis and anterior uveitis), plus three scores for severe indexes of the disease (posterior/panuveitis , as well as bowel perforation, arterial thrombosis, and neuro-Behçet's). Patients were divided into three groups based on the score of disease severity: mild group (score < 4 points), moderate group (scoring between 4 and 6 points), and severe group (score ≥ 7 points) (18).

The participant's height was measured by metal measure in a standing position without shoes; weight was taken by an electronic scale, and then the BMI was calculated by using Equation (1) according to WHO, 2000 guidelines:

$$BM = \frac{weight(kg)}{[height\ (m)]^2} \quad (1)$$

The participants gave their informed consent so that the study could be carried out with ethical approval from the Ethical Committee, College of Dentistry, University of Baghdad (No. 877; 3/12/2023).

Statistical Package for the Social Sciences software, version 26.0 (SPSS Inc. Chicago, Illinois, USA) was used to analyze data. Continuous variables were expressed (mean and standard error). One-way analysis of variance (ANOVA) was applied to compare the means of the four groups. Duncan's Multiple Range test was used to determine critical values for comparisons between means. Pearson's correlation coefficient (r) was used to determine the correlations between factors under study. A $P \leq 0.05$ significance level was deemed as being statistically significant.

Results

Body mass index (BMI): As shown in Table 1, there was a nonsignificant difference (p = 0.359) in BMI among the studied group, although the biological group had a higher BMI than the other groups.

Table 1: Mean BMI (Kg/m^2) of study groups

Group	Control (N=15)	Newly diagnosed BD cases (N=15)	BD cases with Infliximab treatment (N=15)	BD cases with azathioprine treatment (N=15)	*p* value
	Mean ± S.E				
Mean of BMI	24.69 ± 3.3	24.36 ± 5.0	27.38 ± 2.1	24.98 ± 2.7	0.359 N.S

N: number, S.E: standard error, N.S: non-significant.

Vitamin D3

Table 2 showed that the (mean ± S.E) of serum vitamin D3 level was highest in BD patients in the Azathioprine group (20.9±1.7 ng/mL), while it was the lowest in the Infliximab group (12.9±3.3 ng/mL). The (mean ± S.E) levels of saliva vitamin D3 level was highest in the control group (21.5 ± 3.1 ng/mL), while it was the lowest in BD patients in the Azathioprine group (11.6 ± 2.2 ng/mL).

Table 2: Variations in vitamin D3 concentration (ng/mL) in serum and saliva of study groups

Group	Serum D3	Saliva D3
	Mean ± S.E	
Control	18.0 ± 2.3 b	21.5 ± 3.1 c
Newly diagnosed untreated	14.1 ± 1.9 a	16.5 ± 2.4 b
Infliximab	12.9 ± 3.3 a	12.9 ± 1.6 a
Azathioprine	20.9 ± 1.7 b	11.6 ± 2.2 a

S.E: standard error.
Different letters indicate significant difference at P ≤ 0.05 (Duncan's Multiple Range test); (a) statistically different from (b), (b) statistically different from (c) …. etc.

Nitric oxide (NO)

As shown in Table 3, the (mean ± S.E.) of serum NO level in the newly diagnosed group (45.5 ± 6.1 µm/mL) was significantly lower (P ≤ 0.05) than Infliximab (54.9 ± 4.4), Azathioprine (69.6 ± 5.7 µm/mL) and control (69.7 ± 5.3 µm/mL) groups.
It has been shown that the (mean ± S.E) of saliva level of NO in patients with BD in the Infliximab group (288.5 ± 9.9 µm/mL) was significantly higher than that of the other groups.

Table 3: Variations in NO concentration (µm/mL) in serum and saliva of study groups

Groups	Serum NO	Saliva NO
	Mean ± S.E	
Control	69.7 ± 5.3 c	233.2 ± 10.7 a
Newly diagnosed untreated	45.5 ± 6.1 a	259.3 ± 11.3 b
Infliximab	54.9 ± 4.4 b	288.5 ± 9.9 c
Azathioprine	69.6 ± 5.7 c	220.0 ± 8.2 a

S.E: standard error.
Different letters indicate significant differences at P ≤ 0.05 (Duncan's Multiple Range test); a) statistically different from (b), (b) statistically different from (c) …. etc.

Reduced glutathione (GSH): The results showed that the (mean ± S.E) of serum GSH in the Infliximab group (84.4 ± 3.4 µg/L) was statistically higher than the other groups ($P \leq 0.05$), and we did not find any significant differences in the (mean ± S.E.) of saliva GSH between the four groups as shown in Table 4.

Table 4: Variations in GSH concentration (µg/L) in serum and saliva of study groups

Groups	Serum GSH	Saliva GSH
	Mean ± S.E	
Control	20.5 ± 4.6 a	11.7 ± 1.8 a
Newly diagnosed untreated	14.1 ± 2.0 a	13.4 ± 1.3 a
Infliximab	84.4 ± 3.4 b	10.0 ± 2.2 a
Azathioprine	19.1 ± 2.2 a	9.6 ± 1.7 a

S.E: standard error.
Different letters indicate significant difference at P ≤ 0.05 (Duncan's Multiple Range test); (a) statistically different from (b), (b) statistically different from (c) …. etc.

Severity of Behcet's disease

Severity levels of BD are placed in three categories; these are moderate, mild, and severe. In 9 patients (20%), the disease severity was considered to be mild. In another group of patients, 22 (48.8%) had a moderately severe disease, and 14 (31.1%) of the patients had a severe level of the disease. On comparing vitamin D3, NO, and GSH levels in the three groups with regard to disease severity, there was significant variation in serum NO and GSH levels (P=0.001 and 0.013, respectively). The same findings were reported in saliva; vitamin D3, NO levels (P = 0.041 and 0.024, respectively) in the three groups. No statistically significant difference was found in serum D3 and salivary GSH levels with regard to the disease severity, as shown in Table 5.

Table 5: Comparison of D3, NO, and GSH levels in relation to the severity of the disease score

Variable	Sample	Mild (N = 9)	Moderate (N = 22)	Severe (N = 14)	***P*** value
		Mean ± S.E			
Vit. D3 (ng/mL)	Serum	15.45 ± 2.2	16.63 ± 2.5	19.41 ± 3.3	0.915 N.S
	Saliva	9.03 ± 1.2	18.21 ± 1.7	15.47 ± 4.1	0.041*
NO (µm/mL)	Serum	104.16 ± 8.9	59.19 ± 5.3	46.36 ± 5.7	0.001**
	Saliva	227.89 ± 6.7	293.32 ± 11.7	196.25 ± 11.8	0.024*
GSH (µg/L)	Serum	19.03 ± 3.4	61.41 ± 3.8	22.54 ± 3.6	0.013*
	Saliva	7.29 ± 1.4	10.88 ± 1.7	12.08±1.6	0.314 N.S

** Significant difference at P<0.05,*
*** Highly significant difference at P < 0.001, N: number, S.E: standard error, N.S: nonsignificant.*

Discussion

To the best of our knowledge, till now, this is the first study to investigate the impact of different treatment modalities on vitamin D3 and certain oxidative stress markers (NO, GSH) in the serum and saliva of Iraqi patients concerned with Behçet's disease.
This study revealed that the newly diagnosed BD patients had much lower serum as well as salivary levels of vitamin D than the healthy controls. These

conclusions coincide with those of other researchers, indicating vitamin D deficiency throughout the duration of BD, which highlights the amplified risk of autoimmune disease inception with vitamin D deficiency (19). Additionally, a reduction in levels of vitamin D has been observed in healthy controls and patients on TNF-α blocker (Infliximab) therapy. One concept to explain this finding is that the inhibition of TNF-α inflammatory pathways has a negative feedback influence on the liver, skin, and kidney enzymatic machinery involved in vitamin D synthesis (20). Likewise, the majority of participants in the control group had either inadequate or insufficient vitamin D, which is another intriguing finding from this study. Besides, this finding agrees with the study that recognized a deficiency of vitamin D in the healthy population (21). Lifestyle choices such as being indoors all the time, having a preexisting vitamin D deficiency, air pollution (22), Islamic garments, and potential sunscreen use ultimately lead to insufficient UV irradiation in terms of both quality and quantity (23). The above-mentioned causes could perhaps account for the high prevalence of vitamin D deficiency in the Iraqi population.

The present study revealed a significant increase in salivary NO during BD compared with healthy controls, and this agreed with another study, which had similar findings, and this could highlight the involvement of NO in cytotoxic tissue damage and ulceration (24).

In comparison with other groups, patients receiving TNF-α blocker (Infliximab) medication showed a notable rise in serum GSH, which could be explained by the finding of the study that demonstrated higher levels of TNF-α in the serum of patients with Behcet's Disease, focusing on the critical involvement of TNF-α in BD pathogenesis (25). Since the production of ROS (which can harm essential cellular components, including lipids, proteins, and DNA, and cause cell injury) is one of the potential processes behind the toxicity induced by TNF (26), TNF-α inhibitors were created and used successfully in the treatment of autoimmune diseases, including BD, rheumatoid arthritis, and Crohn's Disease (25, 27). Thus, by blocking TNF's activity, ROS will be reduced, cellular antioxidants will not be depleted, and the harmful effects of free radicals will be lessened with the resultant existence of sufficient GSH in the circulation (26).

GSH is a crucial defense against oxidative stress and harmful substances (28). Hepatic GSH depletion, which could happen during the first stage of azathioprine metabolism, puts the body at risk for oxidative stress, which might result in damage to proteins as well as nucleic acids directly, or lead to lipid peroxidation. Azathioprine toxicity to hepatocytes is caused by GSH depletion, which causes mitochondrial damage, severe ATP depletion, and necrosis-induced cell death. This might account for the drop in GSH levels observed in patients receiving Azathioprine medication. This result was in agreement with the conclusion of another study (29). The fact that our bodies nowadays have a lot to deal with stress, lack of sleep, environmental pollutants, poor diet, high sugar consumption, food intolerances, and the list goes on, illuminates why the GSH levels were diminished, in addition to, when an autoimmune disease is included, the body's susceptibility to stress and inflammation increases significantly with the consequential decrease of antioxidants.

In this study, no significant correlations were found between BMI and the levels of serum and salivary vitamin D3, NO, and GSH in all study groups

In line with a study conducted in Tabriz (30), which reported a positive correlation between serum and saliva levels of vitamin D in patients who have recurrent aphthous stomatitis, there has been a positive as well as significant correlation between salivary and serum levels of vitamin D in the current study. Moreover, the salivary 25 (O.H.) D assay was approved by Sari et al. (13) as a noninvasive substitute for the serum 25 (O.H.) D assay.

The existing study showed an inverse relationship between serum NO and the severity of BD, which in agreement with the study that had been conducted in Turkey (31), which proposed a putative dysfunction in the endothelial cells, a major nitric oxide producer, and demonstrated that patients who have active disease presented lower levels of serum NO compared with those in remission. Fadini et al. (32) found a gradual decline in the circulation of endothelial progenitor cells in patients who have BD, which might indicate a mechanism for vascular damage, and this is further reinforced our study results. Moreover, the current study have displayed a positive correlation between serum GSH and duration of exposure to sun, which could be clarified for instance, when 7-dehydrocholesterol in the skin is exposed to sunshine, it absorbs ultraviolet B rays, which transforms into provitamin D3, which then isomerizes to form vitamin D3 (33). Given the fact that vitamin D serves as a potent antioxidant by participation in the metabolism of GSH by stimulating the synthesis of GSH, vitamin D has strong anti-inflammatory and antioxidant characteristics (34). The blood's level of reactive oxygen species is dropped with the use of GSH. These findings support the hypothesis that vitamin D may upregulate GSH formation (35). Also, this confirms the suggestion that vitamin D may control serum GSH levels by influencing the amounts and functions of the enzymes responsible for GSH production, which are glutathione reductase (GR) and Glutamate-cysteine ligase catalytic (GCLC) (36).

As stated by (37) , increased NO generation may be responsible for the overall inflammatory BD process. This finding is in agreement with the current study that established a positive correlation between disease duration and serum NO levels. This can be further clarified by that TNF-α, one of the main cytokines that is known to be involved in BD pathophysiology, may contribute to the generation of NO in these patients and subsequent inflammatory response (38). The negative correlation between salivary vitamin D3 and CRP in this study may reflect the anti-inflammatory property of vitamin D3. Since CRP, a

non-specific marker of systemic inflammation, is known to be synthesized by vascular endothelium, vitamin D3 could have the ability to lower inflammation in the body, which is in congruence with (39). Consequently, a positive correlation exists between CRP and BMI. As it is accepted that CRP is a helpful biochemical marker of inflammation and plays a substantial part in the inflammatory process, and since obese subjects typically have higher numbers of abdominal visceral adipocytes, which are thought to produce about 25% of systemic Interleukin-6 *in vivo*. Thus, cytokines, which include Interleukin-6, Interleukin-1-β, and TNF-α, may also stimulate CRP as stated by (40).

Limitations

This study has several limitations. First, the method of whole saliva collection used may not accurately reflect the primary source containing the highest or lowest concentrations of the biomarkers. Second, the study did not measure calcium and parathyroid hormone levels, which are known to influence vitamin D levels. Third, potential bias could have arisen during participant interviews due to the respondents' honesty, memory recall, and possible under- or over-estimation of their exact sun exposure duration. Moreover, seasonal variations in sun exposure were not accounted for. Finally, the study did not evaluate the impact of periodontal diseases such as periodontitis and gingivitis on the biomarkers, particularly nitric oxide (NO), despite these conditions acting as influences and potentially elevating NO levels.

Conclusions

Newly diagnosed BD cases and those undergoing anti-TNF therapy were linked to vitamin D deficiency. It was discovered that there was a positive correlation between serum and salivary D3 levels. However, no significant correlation was found between the severity of BD and vitamin D3 as well as glutathione levels. BMI did not exert a meaningful effect on serum and salivary vitamin D3, NO, or GSH levels. Since serum NO levels fall as the disease progresses, it was possible to evaluate the severity of BD. Although saliva samples could be used instead of blood samples, blood samples are still the most reliable.

We suggest studying the genetic polymorphism of vitamin D receptors in the Iraqi population, and the effect of other types of treatment of BD on oral findings, and on saliva and serum oxidative stress markers and antioxidants.

Authors' declaration

We confirm that all the Figures and Tables in the manuscript belong to the current study. Besides, the Figures and images, which do not belong to the current study, have been given permission for re-publication attached to the manuscript. Authors sign on ethical consideration's Approval-Ethical Clearance: The project was approved by the local ethical committee in the College of Dentistry, University of Baghdad according to the code number (877723) on (3/ 12/ 2023).

Conflict of Interest: None

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Authors' contributions

Study conception & design: (Qabas A. Mohammed & Ban AL-Drobie). Literature search: (Qabas A. Mohammed). Data acquisition: (Qabas A. Mohammed). Data analysis & interpretation: (Qabas A. Mohammed & Ban AL-Drobie). Manuscript preparation: (Qabas A. Mohammed & Ban AL-Drobie). Manuscript editing & review: (Hayder A. Hasan).

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Appendix: (Supplement File)

تأثير مختلف العلاجات الطبية على فيتامين D3 و مؤشرات الإجهاد التأكسدي في اللعاب والمصل لدى المرضى العراقيين المصابين بمرض بهجت

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خلفية البحث:
خلفية: يُعتقد أن فيتامين د هو عامل بيئي رئيسي يمكن أن يؤثر على احتمالية الإصابة بالعديد من الاضطرابات الالتهابية والمناعة الذاتية، مثل مرض بهجت.
الاهداف: تقييم تأثير العلاج الطبي ومؤشر كتلة الجسم على فيتامين D3 وبعض مؤشرات الإجهاد التأكسدي (الجلوتاثيون، أكسيد النيتريك) لدى المرضى العراقيين المصابين بمرض بهجت بالإضافة إلى ذلك، استكشاف أي ارتباطات محتملة بين هذه المؤشرات وفيتامين **D3** وشدة مرض بهجت، وإمكانية استخدام اللعاب قياس هذه المؤشرات.
طرق العمل: هذه الدراسة اجريت في مستشفى مرجان التعليمي في محافظة بابل بين ديسمبر 2023 ومارس 2024, تم تقسيم خمسة وأربعين مريضًا بمرض بهجت، والذين يستوفون المعايير الدولية، إلى ثلاث مجموعات: 15 مريضًا يتلقون علاج الأزاثيوبرين، 15 حالة تم تشخيصها حديثًا ولم تتلق علاجًا، و15 مريضًا يتلقون العلاج بمضادات TNF-α. تم تضمين مجموعة ضابطة مكونة من 15 فردًا متوافقين مع المرضى في العمر والجنس. تم قياس مستويات فيتامين D في المصل واللعاب باستخدام اختبار المقايسة المناعية الانزيمية . تم استخدام طرق قياس الطيف لتقييم مستويات الجلوتاثيون المخفض وأكسيد النيتريك في المصل واللعاب بين المجموعات. تم استخدام برنامج الحزمة الأحصائية للعلوم الاجتماعية,الاصدار 26 لتحليل البيانات.تم تحديد مستوى الدلالة عند على انه ذو دلالة احصائية.
النتائج: كانت مستويات فيتامين D3 منخفضة بشكل ملحوظ لدى المرضى الذين تم تشخيصهم حديثًا بمرض بهجت وأولئك الذين يتلقون علاجًا بمضادات TNF-α مقارنة مع المجموعة الضابطة . كانت اعلى نسبة بخصوص الكلوتاثايون في المصل في الحالات التي تتلقى علاج ال Infliximab مقارنة مع الكروبات الاخرى .أظهر أكسيد النيتريك في المصل ارتباطًا عكسيًا مع فرق ذو دلالة عالية فيما يتعلق بشدة المرض.
الاستنتاجات: ارتبطت حالات مرض بهجت التي تم تشخيصها حديثًا وأولئك الذين يتلقون علاجًا بمضادات TNF-α بنقص فيتامين D. كان هناك ارتباط إيجابي بين مستويات فيتامين D3 في المصل واللعاب. ارتفع مستوى أكسيد النيتريك في اللعاب أثناء مرض بهجت. وبما أن مستويات أكسيد النيتريك في المصل تنخفض مع تقدم المرض، فقد يمكن استخدامها كمؤشر لقياس شدة مرض بهجت.
الكلمات المفتاحية: مرض بهجت؛ الأدوية البيولوجية؛الكلوتاثايون؛أكسيد النيتريك؛الاجهاد التأكسدي؛اللعاب؛مصل؛ فيتامين D3 ..