

## Biochemical Changes Related with Temporomandibular Joint Disorders and Inflammatory Arthritis

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### ABSTRACT

This study aimed to determine vitamin D, calcium, total alkaline phosphatase activity, and interleukin-1 in sera of temporomandibular joints disorder patients suffer from rheumatoid arthritis. The present study conducted 45 temporomandibular disorder patients with rheumatoid arthritis. While remaining 45 apparently healthy subjects were selected as controls. There was a significant decrease in vitamin D in temporomandibular disorder patients as compared to the controls, ( $P=0.001$ ). While a significant increase in serum total alkaline phosphatase activity and interleukin-1 in temporomandibular disorder patients as compared to the controls, ( $P=0.01$ ). There was a decrease in serum calcium levels in temporomandibular disorder patients as compared to the controls, but it was not significant. There was a significant negative correlation between serum vitamin D activity with total alkaline phosphatase activity and interleukin-1 in temporomandibular disorder patients, ( $P=0.001$ ). This study demonstrated that serum vitamin D levels were significantly lower in temporomandibular disorder patients with RA. Also, there was a significant increase in serum total alkaline phosphatase as bone marker and interleukin-1 in temporomandibular disorder patients which provide a more reliable and complete profile of inflammatory contributors to temporomandibular disorder.

**Keywords:** Temporomandibular joint, Temporomandibular joint disorder ; Rheumatoid arthritis, Interleukin-1

### INTRODUCTION

Temporomandibular joint and muscle disorders are a group of situations that cause pain and dysfunction in the jaw joint and the muscles that control jaw movement <sup>1</sup>.

Patients with Temporomandibular joint disorder (TMD) most commonly existent with imperfect mandibular motion, TMJ sounds, and pain<sup>2</sup>. The pain is often restricted to the jaw, muscles of mastication, and TMJ sounds. Common related symptoms as tinnitus, ear pain and stuffiness,

neck pain, dizziness, and headache. Sometimes, the case is acute and symptoms are mild and self-limiting. In other patients, a chronic TMD develops, with persistent pain and physical, psychological, behavioral, and psychosocial symptoms parallel to those of patients with chronic pain syndromes in other parts of the body <sup>3</sup>, e.g. chronic headache, chronic regional pain syndrome, arthritis, low back pain, and fibromyalgia, totally needing a diagnostic and dealing method <sup>4</sup>.

The occurrence of TMJ involvement in inflammatory arthritis is frequently undervalued,



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and practice in treatment among rheumatologists is incomplete. Three situations have an affinity toward the TMJ: psoriatic arthritis (PA), ankylosing spondylitis (AS), and rheumatoid arthritis (RA). The prevalence is the highest in RA, followed by PA <sup>5</sup>.

Patients with RA are at risk of TMJ involvement, and 67-71% patients will have at least one symptom. Typical and clinical outcomes include stiffness, joint pain, sounds, and limitation of movement <sup>6</sup>. Patients with RA tend to have more recurrent and severe signs, symptoms, and radiographic alterations when compared to PA and AS patients<sup>7</sup>.

Disease-modifying anti-rheumatic drugs can diminish joint injury by suppressing inflammation in all of the inflammatory arthritis, and the target of the rheumatologist should be to complete remission if possible <sup>8</sup>.

In fact, RA is an autoimmune disease with a high multifaceted physiopathology. The major initiating incident could be the triggering of antigen-dependent T cells leading to an essentially Th1 type immune response. The consequent effects are various, counting the activation and the proliferation

of endothelial and synovial cells, recruitment and activation of pro-inflammatory cells, secretion of cytokines like interleukin-1 (IL-1), proteases by macrophages and fibroblast-like synovial cells, and production of autoantibodies <sup>9</sup>.

Thus, association between vitamin D and RA has been broadly deliberated, and the data persist debated. Certain studies demonstrate that RA patients have lesser concentrations of vitamin D <sup>10,11</sup>.

Calcium (Ca<sup>+2</sup>) is the main content in bones and joints and intracellular, free Ca<sup>+2</sup> has an imperative role in muscle contraction and Ca<sup>+2</sup> deficiency, as a medical situation, also has numerous of the same symptoms and characteristics <sup>12</sup>. The concentration of Ca<sup>+2</sup> in serum is usually reserved in a very limited range so as to prevent the disorder of some physiological roles, such as muscle contraction <sup>13</sup>. Bone is a mineral reservoir for Ca<sup>+2</sup> and phosphorus. Over 99% of total Ca<sup>+2</sup> in human body is kept in bone and teeth. Calcium plays significant roles in the formation process of new bone and conservation of existing bone by cooperating with other factors such as phosphorus, vitamin D and Ca<sup>+2</sup>-binding proteins <sup>14</sup>.

**Table 1: Signs and symptoms in TMD patients**

Signs and Symptoms	TMD Patients (n,%)
Headaches	40 (88.90 %)
Pain in the temple area	30 (66.70 %)
Pain in and around the TMJ	45 (100 %)
Back pain and stiffness in the neck	28 (62.22 %)
Limited movement and opening of the jaw	36 (80 %)
Earaches	21 (46.70 %)
Dizziness	18 (40 %)

**Table 2: Anthropometric characteristics of the studied groups**

Parameter	TMD with RA(n= 45)	Control (n= 45)	P value
Age (years)	12.60± 50.58	8.50±43.02	0.001
Male/ Female	15/30	22/23	-
SBP (mmHg)	138.40 ± 2.65	123.18 ± 1.12	0.001
DBP (mmHg)	83.50 ± 2.26	74.60 ±1.94	0.01

The objective of this study was to determine vitamin D, Ca<sup>2+</sup>, total ALP activity, and IL-1 in sera of TMD patients suffer from RA.

**MATERIALS AND METHODS**

The present study was performed in the Medical City Hospital during the period from January 2017 until the end of July 2017. It was conducted on 45 TMD patients 15 males (33.33%) and 30 females (66.66%). The ages ranging from (47-70) years with mean age (58.50) years. While remaining 45 apparently healthy subjects were selected as controls. The differential diagnosis of TMD included: periodontal disease and caries.

**Laboratory Tests**

Routine investigations including ESR were recorded.

Serum vitamin D, total ALP activity, Ca<sup>2+</sup> were measured using a chemical analyzer in the medical laboratories. Cytokines levels were determined in sera via a sandwich immunoassay kit provided by Human IL-1.

**Radiographic Examination**

Rheumatologists evaluated the joints most commonly affected in the RA. The TMJ images

were performed at the Oral Radiology Department/ College of Dentistry-University of Baghdad.

**Statistical Analysis**

Descriptive statistics were presented as mean (±SD). Correlation coefficient was used to assess the relationships between vitamin D and other variables studied.

**RESULTS**

Signs and symptoms in TMD patients illustrate in table (1). Pain in and around the TMJ, headaches, and limited movement represent the higher ratios in TMD patients (greater than 80 %).

Anthropometric characteristics of the studied groups are in table (2). There was a significant increases in age, systolic- and diastolic blood pressure (SBP, DBP) in TMD patients as compared to the controls.

Table (3) shows the laboratory characteristics of the studied groups. There was a significant decrease in vitamin D in TMD patients as paralleled to the controls, (P= 0.001). While a significant increase in serum total ALP activity and IL-1 in TMD patients as paralleled to the controls, (P= 0.01).

**Table 3: Laboratory characteristics of the studied groups**

Parameter	TMD with RA(n= 45)	Control(n= 45)	P value
Vitamin D (IU/ml)	30.40 ± 13.50	55.24 ± 32.28	0.001
Ca <sup>2+</sup> (mg/dl)	6.20 ± 0.65	11.5 ± 0.55	0.52
Total ALP (U/L)	133.42 ± 26.50	124.0 ± 18.90	0.01
IL-1 (Ág/ml)	12.55 ± 8.22	4.0 ± 1.35	0.01

**Table 4: Correlations between serum vitamin D and other parameters in TMD group**

Vitamin D (IU/ml)	Correlation coefficient (r)
Ca <sup>2+</sup> (mg/dl)	0.23
Total ALP (U/L)	-0.95**
IL-1 (Ág/ml)	-0.90**

\*\* P = 0.001

There was a reduction in serum Ca<sup>2+</sup> levels in TMD patients as paralleled to the controls, but it was not significant.

Correlations coefficient between serum vitamin D and other parameters in TMD group in table (4) showed that there was a significant negative correlation between serum vitamin D activity with

total ALP activity and IL-1 in TMD patients, ( $P=0.001$ ).

## DISCUSSION

Temporomandibular disorders are a collective cause of craniofacial pain, it is imperative for the health care supplier to find a comprehensive history, complete physical investigation, and find suitable investigative methods to eliminate other potentially serious disorders<sup>15</sup>.

The most collective symptom recounted by patients with TMD is unilateral facial pain. Severe pain usually generated by movements of the mandible and may be existing regular or occasionally<sup>16</sup>.

Vitamin D is required to control  $Ca^{+2}$  absorption and homeostasis. Low levels of vitamin D have been concerned in a numeral of chronic diseases including RA<sup>17</sup>. Moreover, it is complicated in IL-2 inhibition, antibody production, and in lymphocyte proliferation, and, thus, is reflected a regulator of the immune system crucial in the development and function of both T-regulatory cells and dendritic cells<sup>18</sup>.

This is the first study investigating the associations between vitamin D and TMD. However, consistent evidence recommends that higher intakes of  $Ca^{+2}$ , dairy-foods and vitamin D are inversely connected with caries and periodontitis<sup>19</sup>. Dietary  $Ca^{+2}$  absorption is critical for  $Ca^{+2}$  availability for bone mineralization and vitamin D status is a significant parameter influencing intestinal  $Ca^{+2}$  absorption<sup>20</sup>.

Current data, therefore, suggests that well vitamin D intakes facilitate beneficial effects of higher  $Ca^{+2}$  intakes, probably by improvement of  $Ca^{+2}$  absorption.

Calcium and vitamin D is required to improve and conserve healthy bones and teeth. Sufficient  $Ca^{+2}$  intake is essential for all peoples and particularly for RA patients which are vulnerable to steroid-induced and disease related osteoporosis. In RA, vertebral bone density has been found to be 5-15% less than aged matched controls<sup>21</sup>. Furthermore, corticosteroids, used

in the management of RA, impair intestinal  $Ca^{+2}$  absorption<sup>22</sup>.

Experimental evidence suggests that vitamin D effects the process by which immune cells acquire signaling molecules that permit them to transfer to normal extra lymphoid tissue sites, in addition to sites of inflammation<sup>23</sup>. Additionally, it is celebrated that biologically active form of vitamin D  $1,25-(OH)_2D_3$  inhibits  $IFN-\gamma$  secretion and negatively controls IL12 production by down regulating NF- $\kappa$ B<sup>24</sup>.

In this study, patients ALP activity is higher relative to control, which is in agreement with the study of Kumar *et al.*,<sup>25</sup>.

According to the present data, ALP showed a strong negative correlation with vitamin D.

The role of ALP is implicated in osteoid formation and mineralization and expression of its isoform is in osteoblasts, leucocytes, breast, liver, kidney, and brain. The bone construction markers are measured in serum and about 1/2 of ALP in serum comes from bone. Increased activity may be due to inflammatory cytokines as interleukin-1 (IL-1) which has been associated with the acute phase reactants levels<sup>26</sup>. The role of T-cells is well recognized in the pathogenesis of RA. Increased ALP activity may be due to its leakage from injured or killed cells. Alkaline phosphatase has been implicated as marker in RA patients. It can offer diagnostic evidence by measurements of isoform of ALP activity derived from bone or liver<sup>27</sup>.

Interleukin-1 is one of the most predominant and first cytokines produced as a response to excessive loading of the TMJ<sup>28</sup>. Ahmed *et al.*, investigated the association of IL-1 and TMD in RA patients and found a relationship between IL-1 and RA<sup>29</sup>.

## CONCLUSIONS

This study demonstrated that serum vitamin D levels were significantly lower in TMD patients with RA. Vitamin D insufficiency is predominant in patients with RA compared to healthy subjects. Calcium and vitamin D levels correlate inversely with

RA activity and related with vulnerability to RA and RA activity in TMD patients. Additionally, IL-1 provide a more reliable and complete profile of inflammatory contributors to TMD.

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