Investigation of the relationship between psychosocial stress and temporomandibular disorder in adults by measuring salivary cortisol concentration: A case-control study

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INTRODUCTION

Temporomandibular disorders (TMDs) are a collective term used to describe a group of related disorders involving the temporomandibular joints (TMJs), masticatory muscles and occlusion with common symptoms such as pain, restricted movement, muscle or joint tenderness and intermittent joint sounds.[1]

Although the pain is generally the defining characteristic of TMD, patients often suffer from marked degrees of stress in daily life.[2]

The etiology of TMDs is considered to be multifactorial, but the relative importance of individual etiological factors is still controversial. TMD patients exhibit a
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variety of psychosocial and behavioral characteristics including increased somatization, stress, anxiety and depression. Muscle-related disorders have increased severity of pain and suffer from enhanced psychological distress.[3] The importance of psychosocial factors in the etiology of TMDs has led to the hypothesis that these disorders may be a part of a wider group of somatoform disorders.[4] Since (TMD) is a somatic manifestation of stress, previous studies suggested a role of the hypothalamic-pituitary-adrenal (HPA) axis in TMD. Additional cortisol release was reported in TMD patients who exhibited abnormalities of response to stress.[5]

The HPA axis is essential for an organism’s response to physiological and psychological stress. Activation of the HPA axis leads to the release of the cortisol hormone that impacts on physiological systems throughout the organism.[6]

Stress is a state of physiological or psychological strain caused by different stimuli; physical, mental or emotional; internal or external that tends to disturb the function of an organism and which the organism naturally desires to avoid. Socioeconomic factors, type of occupation, daily schedule, competitive workloads and emotional disturbances have led to increased stress levels in the modern lifestyle.[7]

Psychological stress has a direct effect on the HPA cortex axis.[8,9] It is hypothesized that prolonged activation of this axis can be detrimental to organisms’ health and may provide a link between mental stress and physical illness.[10‑12]

Cortisol is a hormone secreted when the body faces a physical or a psychological stressor. Cortisol is considered as a physiological marker of stress. When a stressor is perceived, the HPA axis is activated and the end product of which is the secretion of cortisol from the adrenal glands.[13]

The measurement of cortisol in saliva provides a reliable tool for investigations of the HPA axis activity. As with plasma cortisol, the concentration of cortisol in the saliva is a reliable marker of stress. The major advantages of salivary cortisol are that its sampling technique is noninvasive, and it can be performed in nonstressful conditions and without laboratory surroundings.[14]

The need for the study: Some previous studies have shown a positive correlation between high cortisol concentration and TMD.[5,13,16] On the contrary, other studies have reported a negative correlation.[17] There is no study that investigated the relationship between stress and TMD in Syrian population. Therefore, the objective of this study was to evaluate the correlation between stress and TMD in the Syrian society.

MATERIALS AND METHODS

Study population
The present study was conducted at the Faculty of Dentistry and Medicine, Damascus University, Damascus, Syria from December 2012 to February 2014. 120 subjects, both males and females, 60 TMD patients and 60 controls were included in the study.

Inclusion criteria
- Subjects in the age range of 19–44
- Regular sleep habits
- Complete dental arches (erupted third molars were not required)
- The inclusion criterion for TMD patients was present clinical symptoms.

Exclusion criteria
- Systemic illness affecting joints
- Use of steroidal, oral contraceptives, or antipsychotic drugs
- Trauma at face or jaw
- Cushing syndrome
- Addison disease
- Pregnancy
- Alcohol consumption
- Smoking
- Orthodontic treatment
- Gingivitis and periodontitis
- Removable prostheses
- TMD patients with severe pain.

Methodology
A case-control study was carried out after an approval was obtained from the Local Ethics Committee prior to the commencement of the study, and informed patient consent was received from all study participants.

The sample consisted of 120 individuals aged 19–44 with an average age 29.11. The sample included two groups; the first group consisted of 60 TMD patients, and the control group consisted of 60 healthy subjects. TMD case status was determined using Research Diagnostic Criteria for TMD (RDC/TMD);[18] in which the diagnosis of TMD was divided into the following groups:
- Muscle disorders: (a) myofascial pain; (b) myofascial pain with limited opening (<40 mm).
- Disc displacements: (a) disc displacement with reduction; (b) disc displacement without reduction with limited opening; (c) disc displacement without reduction without limited opening.
- Other common joint disorders: (a) arthralgia; (b) osteoarthritis of TMJ; (c) osteoarthrosis of TMJ.
The patient medical history was recorded, and the physical examination was carried out (by the same examiner) by a chair side examination [Figure 1]. The following steps were conducted “as in the method mentioned by (RDC/TMD).”[18]

- Recording opening pattern and vertical range of motion of the mandible
- Recording TMJ sounds on palpation for vertical range of motion, lateral excursions and protrusion
- Recording pain or tenderness on muscle and joint palpation: Temporalis, masseter, and digastic muscles were palpated Extraorally, whereas lateral pterygoid area and tendon of temporalis were palpated intraorally. Joint palpation sites that were palpated: Lateral pole of the condyle and posterior attachment (bilaminar zone) of the joint which was palpated intrameatally. The participants completed two questionnaires: The first was the 10-item perceived stress scale (PSS)[19] using a reference interval of the past 6 months. The second was the 31-item depression and distress questionnaire Axis II RDC/TMD.[18] Every participant was instructed to collect three samples in equal volumes of saliva at awakening, 30 min and 60 min after awakening. The three samples were pooled to create one sample that physically averages the fluctuations over that time period. The strategies for collecting salivary cortisol were followed,[20] and saliva samples were stored at −20°C. For the quantitative determination of cortisol concentration in saliva, an enzyme-link immunosorbent assay (ELISA) was used. The samples were analyzed using cortisol saliva ELISA kit (DiaMetra, Italy) [Figure 2]. The instructions of manufacturing company were followed [Figure 3] step by step as the following: thawing the salivary samples, centrifuging for 15 min at 3000 rpm, pipetting the samples and the standards, adding the diluted conjugate, incubating at 37°C for 1 h, washing 2 times with distilled water, adding the TMB substrate, incubating at (22–28°C) for 15 min in the dark, adding the stop solution, and reading the absorbance at 450 nm by microplates reader. Data were analyzed using statistical package for social sciences (SPSS 17). Descriptive statistics for variables (cortisol concentration, scores of PSS 10, and scores of distress) of the study groups (patients, controls) and independent t-test were used [Table 1]. To study the difference in cortisol levels between the groups of TMD, one-way ANOVA test was used [Table 2].

**RESULTS**

Temporomandibular disorder cases perceived higher stress than controls ($P = 0.000$) and higher levels of depression and distress ($P = 0.000$). Significant differences in salivary cortisol concentration have been observed between TMD cases and controls ($P = 0.000$). RDC/TMD history questionnaire and clinical assessment data were used to derive Axis I, so this study showed that Group I muscle disorders were the most common and found in 56.7% of patients, Group II (disc displacement) disorders were found in 26.7% and Group III disorders (arthralgia/arthrosis/arthritis) were revealed in 16.7%. The study also showed females were more likely to suffer from TMD than males (females 70% and males 30%). There was no statistically significant difference between the TMD groups at cortisol concentration ($P = 0.845$).
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Table 1: Descriptive statistics of variables (cortisol concentration, scores of PSS 10, and scores of distress) of study groups (patients, controls)

|                  | Study groups | n | Mean  | SD   | SEM  |
|------------------|--------------|----|-------|------|------|
| Cortisol         | Patients     | 60 | 21.77583 | 13.68786 | 1.767098 |
| concentration    | Controls     | 60 | 7.13093  | 4.280831 | 0.552653  |
| Scores of PSS 10 | Patients     | 60 | 23.98    | 5.287  | 0.683  |
| Controls         | 60          | 17.80 | 4.977 | 0.643 |
| Scores of distress | Patients | 60 | 41.80 | 9.330 | 1.024 |
| Controls         | 60          | 28.37 | 7.702 | 0.994 |

SD: Standard deviation, SEM: Standard error of mean, PSS: Perceived Stress Scale

Table 2: One-way ANOVA test

| Cortisol concentration | Sum of squares | df  | Mean square | F     | Significant |
|------------------------|---------------|-----|-------------|-------|-------------|
| Between groups         | 65.140        | 2   | 32.570      | 0.169 | 0.845       |
| Within groups          | 10988.993     | 57  | 192.789     |       |             |
| Total                   | 11054.134     | 59  |             |       |             |

df: Degree of freedom, ANOVA: Analysis Of Variance

DISCUSSION

Salivary cortisol response to psychological stress and its relationship to temporomandibular dysfunction were examined in 60 TMD sufferers and 60 control participants. The participants completed two questionnaires: the 10-item PSS and the 31-item depression and distress questionnaire Axis II (RDC/TMD). The results of this case-control study revealed significant differences between patient and control groups at the three parameters of psychosocial stress ($P < 0.05$). These results are in correlation with the study done by Rai and Kaur;[16] they reported high levels of salivary cortisol and salivary melatonin in the TMD group, while the study of Jones et al.[21] proposed a dual relationship between TMD symptoms and stress response. The data of that study revealed that the TMD group was heterogeneous; and it was composed of a group whose response to stress was hypersecreted cortisol, and another group whose cortisol response was not significantly different from the control group.

Another study reported that salivary cortisol levels on waking did not differ between patients and controls.[22] Doepel, Soderling et al.[23] conducted a study to explore treatment-induced changes in salivary cortisol, IgA, and flow rate values in TMD patients suffering from myofascial pain and they concluded that there were no treatment-induced changes in saliva parameters despite successful appliance therapy. However, Celic, et al.[24] demonstrated increased levels of depression and somatization in TMD patients. These differences in results between studies may be due to differences in study design, population and socioeconomic factors. Increased occurrence of this disorder was noted in women (70%). This result is in agreement with the study done by Casanova et al. who concluded that women are an associated factor with TMD.[25] Another study recorded that more women suffer from TMD than men.[26] This result may be due to the fact that women seek consultation and treatment more than men, or due to hormonal differences.

There was no statistically significant difference between the groups of TMD at cortisol concentration ($P = 0.845$). This result is not in agreement with the study done by Pankhurst, which reported that muscle-related disorders have enhanced psychological stress.[3]

This research found that Group I muscle disorders were the most common and existed in 56.7% of patients, and this result is in correlation with the study that assessed the distribution of temporomandibular disorders sub-types, psychological distress and psychosocial dysfunction in southern Chinese people seeking treatment for TMD.[27]

This study concluded that psychosocial stress plays an important role in etiopathogenesis of TMD. Women are at increased risk of TMD when compared to men. Sub-types TMD patients approximately have the same level of stress. Muscle disorders were the most common.

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