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Association between Salivary Cortisol Levels and Temporomandibular Joint Disorders: A prospective Clinical Cohort Study

Al-Buriahy Khaldon. T. S. A[1], Al-Ghllabi Kamal. T. A.[2]*, Al-Zamzami Sarah A.A[1], Abdulmajeed Omar A. S. A[1], Farhan Asma. H[1], Al-Amery Khlood S[1], Abdo Sarah. H[1], Alezzi Hani. A[1], Al-Hammadi Ahmed A[1], Al-Dobaiby Safwan H.A[1]

[1] *Dentistry Department, Faculty of Medicine and Health Sciences, University of Science and Technology, Taiz City branch, Yemen.*
[2] *Dentistry Department, Faculty of Medicine and Health Sciences, Taiz University, Yemen.*

ABSTRACT

Background: Temporomandibular disorders (TMD) represent a spectrum of conditions affecting the jaw joint and associated musculature, often manifesting as chronic pain and functional impairment. Recent investigations have implicated stress-related physiological markers, particularly salivary cortisol, as potential contributors to TMD development and progression.
Objective: This study sought to examine the correlation between heightened salivary cortisol concentrations and TMD presentation, while concurrently evaluating demographic patterns and treatment outcomes among affected individuals.
Methods: The investigation employed a prospective clinical design at Al-Awlaki Laboratory in Sana'a, Yemen, enrolling 20 patients with confirmed myofascial TMD diagnoses. Standardized morning saliva collections (8:30-10:00 AM) facilitated cortisol quantification via electrochemiluminescence immunoassay, complemented by comprehensive clinical evaluations to exclude confounding conditions. A multimodal therapeutic approach incorporating behavioral interventions, physical therapy, and dental appliances was implemented, with specialist referrals as clinically indicated.
Results: Analysis revealed consistently elevated cortisol levels across all participants (mean 22.3 ng/mL), with no significant gender-based variations observed. All participants presented with hallmark symptoms, cephalgia, and muscular tension—accompanied by measurable psychological distress markers. Post-intervention assessments documented substantial clinical improvements, with a 70% reduction in pain and normalized cortisol profiles achieved uniformly across the cohort.
Conclusion: These findings substantiate the psychophysiological dimension of TMD pathology, demonstrating both the biomarker's diagnostic relevance and the therapeutic value of stress-modulating strategies. The results advocate for integrated biopsychosocial management approaches while underscoring the necessity for expanded longitudinal studies to further elucidate these relationships.

Keywords: hypothalamic-pituitary-adrenal axis, orofacial pain, psychoneuroimmunology, biomarker analysis, musculoskeletal disorders.

**** Corresponding author address:*** *kamalalghllabi@gmail.com*

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INTRODUCTION

Temporomandibular disorders (TMDs) represent a common cluster of musculoskeletal conditions affecting the temporomandibular joint and surrounding masticatory muscles, typically characterized by painful symptoms, limited mandibular mobility, and audible joint phenomena [1]. The development of TMDs involves a complex interplay of biomechanical disturbances, psychological influences, and neuroendocrine responses [2]. Particularly noteworthy is stress as a key pathogenic element, where hypothalamic-pituitary-adrenal (HPA) axis dysfunction and consequent cortisol elevation mediate chronic pain pathways and muscular abnormalities [3]. Salivary cortisol measurement provides a non-invasive method for evaluating stress-related physiological changes [4]. Elevated concentrations are consistently observed in TMD sufferers, suggesting chronic stress exacerbates symptoms [5]. Cortisol-mediated mechanisms promote muscular overactivity, inflammatory processes, and heightened pain perception in the temporomandibular complex [6]. This relationship is complicated by frequent psychological comorbidities (e.g., anxiety, depression) that correlate with abnormal cortisol secretion [7]. While evidence points to a cortisol-TMD association, significant knowledge gaps persist regarding non-Western populations [8]. This investigation examines this relationship within a Yemeni demographic while assessing the therapeutic potential of stress-reduction strategies through integrated clinical, biochemical, and psychological assessments.

METHODOLOGY

Study Design and Setting

This study employed a prospective clinical cohort study design to investigate the association between salivary cortisol levels and temporomandibular disorders (TMDs).

Study Area

The research was conducted at Al-Awlaki Laboratory in Sana'a, Yemen, adhering to standardized clinical and biochemical protocols.

Participant Selection and Sample Size

A total of 20 participants (10 males, 10 females; age range: 20–45 years) diagnosed with myofascial-type TMD were recruited based on the following criteria:

Inclusion Criteria

- Chronic TMJ pain (≥3 months) with associated symptoms (headaches, muscle tightness, and jaw clicking).
- Clinical signs of masticatory muscle tenderness (masseter, temporalis) and restricted jaw movement.
- No prior surgical interventions for TMD.
- No systemic inflammatory or endocrine disorders (e.g., Cushing's syndrome, rheumatoid arthritis).

Exclusion Criteria

- Recent corticosteroid use (within 3 months).
- Severe dental malocclusion or untreated oral pathologies.
- Pregnancy or lactation (due to hormonal influences on cortisol).

Clinical and Laboratory Procedures

Clinical Examination

Each participant underwent a comprehensive clinical assessment encompassing both physical and psychological components. The evaluation included palpation of the masticatory muscles—specifically the masseter and temporalis—as well as the cervical muscles to assess tenderness and identify potential myofascial pain. Jaw mobility was examined by measuring maximum mouth opening and lateral excursions to evaluate functional limitations of mandibular movement. Auscultation of the temporomandibular joint (TMJ) was performed to detect the presence of joint sounds such as clicking or crepitus, indicative of internal derangements or degenerative alterations. In addition, psychological distress was assessed through self-reported measures addressing anxiety, insomnia, and bruxism, providing insight into the psychosocial factors potentially influencing temporomandibular dysfunction.

Imaging and Baseline Tests

- Panoramic radiography (OPG) to rule out bony abnormalities.

- Routine blood tests (CBC, thyroid function, CRP, ESR) to exclude systemic inflammation or metabolic disorders.

Saliva Collection and Cortisol Measurement

Saliva Collection Protocol

- Samples were collected between 8:30 AM and 10:00 AM to account for diurnal cortisol variation (Hellhammer et al., 2009).
- Participants were instructed to refrain from eating, drinking, or brushing teeth 30 minutes before collection.
- Unstimulated saliva was collected via passive drool, following brief gum chewing to standardize flow rate (to standardize flow rate).
- Approximately 10 mL of saliva was collected per participant and immediately stored at -20°C to prevent degradation.

Sample Processing

- Frozen samples were thawed at 37°C and centrifuged at 8,000 rpm for 10 min to remove debris.
- The supernatant was aliquoted into microtubes for cortisol analysis.

Cortisol Quantification

- Electrochemiluminescence Immunoassay (ECLIA, Roche Diagnostics) was used for high-sensitivity cortisol measurement.
- The Cortisol Saliva ELISA Kit (DRG International) was employed for cross-validation.
- Intra- and inter-assay coefficients of variation (CV) were maintained at <5% for reliability.

Intervention and Follow-Up

Participants received a multimodal treatment protocol:

1. Stress management (cognitive-behavioral techniques, relaxation therapy).
2. Physiotherapy (TMJ mobilization, cervical muscle exercises).
3. Occlusal splint therapy (soft night guard for bruxism).
4. NSAIDs (as needed) for acute pain relief.
5. Referrals to endocrinology (for cortisol dysregulation) and psychology (for anxiety/depression).

Follow-Up Evaluations

- Clinical reassessment at 4 and 8 weeks post-intervention.
- Repeat salivary cortisol testing to monitor normalization.
- Subjective pain improvement recorded via visual analog scale (VAS).

Data Analysis

Data analysis was performed using IBM SPSS Statistics version 26 (IBM Corp., Armonk, NY, USA). Descriptive statistics, including mean and standard deviation (mean ± SD), were used to summarize cortisol levels and participants' age distribution. Paired t-tests were conducted to compare pre- and post-treatment cortisol levels, while Chi-square tests were applied to assess differences based on gender. Additionally, the Pearson correlation coefficient was employed to examine the relationship between cortisol levels and symptom severity.

Ethical Considerations

- The study followed Helsinki Declaration guidelines.
- Confidentiality was maintained via de-identified data coding. This study was approved by Medical Research Ethics Committee (MEC/AD0118).

RESULTS

Demographic and Clinical Characteristics

The study included 20 participants (10 males, 10 females) with a mean age of 34.2 ± 7.8 years (range: 20-45 years). Table 1 presents the demographic distribution of participants.

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Table 1: Demographic Characteristics of Study Participants

Variable	Male (n=10)	Female (n=10)	Total (n=20)
Age (years)	33.4 ± 8.1	35.0 ± 7.6	**34.2 ± 7.8**
Age Groups:			
20-30 years	3 (30%)	3 (30%)	**6 (30%)**
31-45 years	7 (70%)	7 (70%)	**14 (70%)**
Symptom Duration	8.2 ± 3.1	9.0 ± 2.8	**8.6 ± 2.9**

Salivary Cortisol Levels

All participants exhibited elevated morning salivary cortisol levels at baseline (mean: 22.3 ± 1.5 ng/mL). Gender-based analysis showed no statistically significant difference (p=0.32).

Table 2: Salivary Cortisol Levels (ng/mL) by Gender and Age Group

Group	n	Mean ± SD	Range	p-value
Total	20	22.3 ± 1.5	19.4-24.7	-
Gender				**0.32**
Male	10	22.0 ± 1.6	19.4-24.3	
Female	10	22.6 ± 1.4	20.3-24.7	
Age Group				**0.18**
20-30 years	6	21.7 ± 1.3	19.4-22.5	
31-45 years	14	22.6 ± 1.5	20.5-24.7	

Independent samples t-test

Clinical Symptom Severity

All participants (100%) presented with:

- TMJ pain (VAS: 7.2 ± 1.1)
- Morning muscle tightness (100%)
- Audible joint clicking (85%)
- Restricted mouth opening (<35 mm in 90%)

Table 3: Baseline Clinical Features

Clinical Feature	Prevalence (n=20)	Mean ± SD / Percentage
TMJ pain (VAS 0-10)	20 (100%)	**7.2 ± 1.1**
Muscle tenderness	20 (100%)	-
Limited mouth opening	18 (90%)	**31.4 ± 3.2 mm**
Joint clicking	17 (85%)	-
Psychological distress	20 (100%)	-

Treatment Outcomes

Post-intervention results showed significant improvements (p<0.01).

Table 4: Pre- vs. Post-Treatment Outcomes

Parameter	Baseline	8-Week Follow-Up	Improvement	p-value
Cortisol (ng/mL)	22.3 ± 1.5	14.1 ± 2.3	36.8% ↓	**<0.001**
TMJ pain (VAS)	7.2 ± 1.1	2.1 ± 1.4	70.8% ↓	**<0.001**
Mouth opening (mm)	31.4 ± 3.2	39.8 ± 2.9	26.8% ↑	**<0.001**
Headache frequency	6.5 ± 1.8/week	1.9 ± 1.2/week	70.8% ↓	**<0.001**

Paired samples t-test

Correlation Analysis

A strong positive correlation was found between baseline cortisol levels and initial VAS pain scores (r=0.72, p<0.01). Cortisol reduction and pain improvement (r=0.68, p<0.01).

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Subgroup Analysis

No significant differences were observed in treatment response by gender (p=0.45), and age group (p=0.28).

DISCUSSION

This study substantiates the association between elevated salivary cortisol levels and temporomandibular disorders, reinforcing HPA axis dysregulation in TMD pathophysiology. The current findings align with systematic reviews concluding TMD patients exhibit significantly higher cortisol levels than healthy controls [9], particularly in stress-related subtypes. Recent evidence shows TMD patients with disc displacement exhibit cortisol levels nearly 8-fold higher than controls [10], supporting our observations. These results corroborate biopsychosocial models identifying stress-induced HPA activation as a contributor to TMD chronicity [2]. Contrasting evidence exists, including null findings in pediatric populations despite elevated anxiety [11], suggesting age-related biomarker variations. Methodological factors may explain discrepancies, as cortisol differences are sometimes only significant in males with acute symptoms [12]. The heterogeneity is further exemplified by cortisol's specific linkage to parafunctional habits like bruxism [13]. The current observed post-treatment cortisol normalization aligns with clinical trials demonstrating occlusal splints reduce cortisol by 36.8% [14].

Future research must standardize sampling protocols (e.g., diurnal measurements) and control for confounders like hormonal variations to clarify these associations.

CONCLUSION

This study confirms a strong association between elevated salivary cortisol levels and myofascial-type TMD, underscoring stress as a significant contributor to TMD pathophysiology. The uniform improvement across all participants following stress-management interventions underscores the importance of addressing psychological factors in TMD treatment.

Recommendations

Future studies should adopt standardized biomarker protocols, including uniform saliva collection times and validated assays, to enhance data comparability. Subtype-specific and longitudinal designs are recommended to clarify cortisol dynamics and their role in distinct TMD subtypes. Incorporating multimodal stress assessments—combining biochemical markers such as α-amylase and IL-6 with validated psychological tools like the Perceived Stress Scale (PSS)—would provide a more comprehensive understanding of stress mechanisms. Larger, diverse samples with appropriate control groups are essential to improve the validity and generalizability of findings.

Conflict of Interest

The authors declare that there is no conflict of interest.

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