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Dentistry Section

Comparison of Salivary Cortisol Levels among Patients with Temporomandibular Disorder with and without Depression and Healthy Controls: A Cross-sectional Study

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ABSTRACT

Introduction: Temporomandibular Disorders (TMDs) are musculoskeletal conditions often linked to psychological stress. Cortisol, a key stress biomarker, may play a role in the pathophysiology of TMD. The present study compares salivary cortisol levels in young adults with TMD, with and without depression, and in healthy controls to explore the psychological and physiological interplay in these conditions. Identifying distinct cortisol patterns across these groups could aid in understanding the role of stress-related endocrine function in TMD.

Aim: To test salivary cortisol levels in young adults diagnosed with TMD, both with and without depression, and to compare these results with an age-matched control group without TMD and depression.

Materials and Methods: The present cross-sectional observational study was conducted at Vishnu Dental College, Bhimavaram, between January and May 2024. The present study included individuals aged 18-28 years of both genders who experienced pain in the Temporomandibular Joint (TMJ) region for a minimum of three months, in accordance with the Research Diagnostic Criteria for TMD (RDC/TMD). A total of 45 patients were divided into three groups: TMD with depression (n=15), TMD without depression (n=15), and a control group (n=15). Patients were evaluated for TMD based on the RDC/TMD criteria. Psychological status was assessed using the RDC/TMD Axis 2 self-report for all participants, including those with TMD and the control group without TMD. Post awakening salivary samples were collected between 7 and 8 a.m., and salivary cortisol levels were measured using an Enzyme-Linked Immunosorbent Assay (ELISA) kit. Data analysis was performed using a paired t-test, and Pearson correlation was used to examine the relationship between morning and evening cortisol levels. An Analysis of Variance (ANOVA) test was conducted to compare cortisol levels across groups, with a p-value <0.001 considered significant.

Results: A strong, significant correlation was found between morning and evening salivary cortisol levels in all groups (TMD with depression: r=0.99; TMD without depression: r=0.989; controls: r=0.725; p<0.001). Morning cortisol was highest in TMD patients with depression (55.7 ng/mL), followed by those without depression (19.63 ng/mL) and controls (12.66 ng/mL). Evening levels followed a similar pattern. Females showed significantly higher cortisol levels than males, especially in the TMD without depression and control groups (p<0.001). In TMD with depression, females had higher levels, though this was not statistically significant.

Conclusion: Assessing salivary cortisol levels may provide insight into psychological factors that contribute to the development of TMD. Salivary cortisol could serve as a valuable indicator in detecting psychological elements potentially linked to TMDs.

Keywords: Anxiety disorders, Biological markers, Hydrocortisone, Immunoassay, Stress

INTRODUCTION

The TMDs encompass a wide range of musculoskeletal and neuromuscular conditions that affect the TMJ, the masticatory muscles, and related structures. Patients with TMDs often experience jaw pain, restricted or painful movement, and joint sounds such as clicking or popping. The aetiology of TMD is complex, involving various factors such as anatomical or occlusal abnormalities, genetic predisposition, and environmental influences [1,2]. In recent years, psychological factors, including stress, depression, and anxiety, have been found to predispose individuals to TMD symptoms [3,4]. Conversely, some studies highlight the complexity of TMD aetiology, emphasising that psychological factors may have little or no role in the aetiopathogenesis of TMD [5,6].

Psychological stress is thought to influence the development and progression of TMD through its impact on the autonomic nervous system and the Hypothalamic-Pituitary-Adrenal (HPA) axis. This system regulates the body's response to stress and is responsible for the production of cortisol, a glucocorticoid hormone that plays a vital role in maintaining homoeostasis and regulating inflammation, metabolism, and immune responses [7,8]. In stressful situations, cortisol levels rise, helping the body manage stress. However, chronic stress can lead to prolonged elevations in cortisol, potentially resulting in detrimental health effects [9,10]. Such effects can induce muscle tension, alter pain perception, and delay recovery [11], all of which contribute to the intensification of TMD symptoms.

Salivary cortisol has gained attention as a valuable and non-invasive biomarker for assessing the body's response to stress. It provides an accurate measure of free, bioactive cortisol, reflecting the activity of the HPA axis [12]. Unlike blood samples, salivary samples are easier to collect and less likely to cause stress during collection, making them ideal for evaluating cortisol levels in stress-related conditions such as TMD [13,14]. Cortisol levels in saliva are particularly informative for understanding stress responses, which are critical in conditions where psychological factors are implicated [15,16].

Several studies have highlighted the link between elevated cortisol levels and the worsening of TMD symptoms, particularly in patients experiencing psychological conditions such as anxiety and depression [17,18]. Furthermore, the coexistence of TMD and mental health disorders presents a challenge in clinical settings, necessitating a multidisciplinary approach to treatment that incorporates both physical and psychological interventions [19].

Despite the growing body of research supporting the connection between psychological stress and TMD, the exact relationship between cortisol levels and TMD remains insufficiently explored. Most existing studies either focus solely on the presence of psychological symptoms in TMD patients or assess cortisol levels without differentiating between patients with and without psychological co-morbidities [20]. There remains a lack of comparative studies evaluating salivary cortisol patterns in TMD patients stratified by psychological status, particularly distinguishing those with depression from those without and from healthy controls. This gap limits understanding of how psychological factors modulate physiological stress responses in TMD pathophysiology.

Therefore, the present study aimed to bridge that gap by comparatively analysing salivary cortisol levels across these distinct groups to better elucidate the psychobiological interplay in TMD.

Understanding how stress-induced fluctuations in salivary cortisol impact the pathophysiology of TMD could help clinicians develop more effective, individualised treatment strategies. The present study aimed to assess salivary cortisol as a potential biomarker in TMD patients, particularly those with underlying psychological conditions. The null hypothesis states that there is no significant difference in salivary cortisol levels (morning and evening) among TMD patients with depression, TMD patients without depression, and healthy controls. In contrast, the alternate hypothesis suggests that there is a significant difference in salivary cortisol levels (morning and evening) among these groups, further elucidating the role of stress in these disorders.

The correlation statistics of morning and evening salivary cortisol within each group were analysed to assess the presence or alteration of diurnal rhythm across the study population. A comparison of morning and evening cortisol levels among the three groups was conducted to determine intergroup differences and evaluate whether conditions such as stress, depression, or TMD influenced circadian secretion patterns. Additionally, salivary cortisol levels were compared between genders to examine the possible modifying effect of sex-related hormonal and physiological differences on the stress response. Together, these analyses aimed to identify both within-group and between-group variations, thereby offering a comprehensive picture of salivary cortisol behaviour in the study population.

MATERIALS AND METHODS

The present cross-sectional observational study was conducted at Vishnu Dental College, Bhimavaram, between January and May 2024. Ethical approval was obtained from the institutional ethical committee, as documented in letter no. IECVDC/24/PG01/OMR/IVV/60, and written informed consent was obtained from all participants. Not a single patient declined to participate in the study.

Sample size calculation: Based on a pilot study, sample size calculation was conducted using a one-way ANOVA (fixed effects, omnibus test) to determine the minimum number of participants required to detect a medium-to-large effect size (f=0.4867) with adequate statistical power. The analysis was performed with a significance level (α) of 0.05, a desired power of 0.80, and three comparison groups. The results indicated that a total sample size of 45 participants (15 per group) would be sufficient to achieve the required power. The analysis yielded a noncentrality parameter (λ) of 10.659, a critical F-value of 3.220, with numerator and denominator degrees of freedom being 2 and 42, respectively. The actual power achieved with this sample size was 0.812, confirming that the study is adequately powered to detect the specified effect size [21].

Inclusion and Exclusion criteria: Participants with any systemic disease or concurrent medication that could elevate salivary or blood cortisol levels were considered exclusion criteria for all groups. This includes conditions like hyperpituitarism (overactive pituitary gland), both benign and malignant pituitary tumours (such as adenomas), adrenal tumours, Cushing syndrome, and prolonged use of high-dose corticosteroids for treating asthma, arthritis, or certain cancers. Pregnancy was also an exclusion factor. For the TMD group, including those both with and without depression, the inclusion criterion required individuals to have experienced pain in the TMJ region for a minimum of three months, in accordance with the RDC/TMD criteria.

Study Procedure

The study involved a total of 45 participants, ranging in age from 18 to 28 years; of them, 23 were males and 22 were females. Among these participants, 15 were diagnosed with TMDs and showed signs of depression, another 15 had TMDs but no depression, and the remaining 15, serving as the control group, had neither TMDs nor depression. Patients were evaluated for TMD based on the RDC/TMD criteria.

RDC/TMD Criteria [21,22]

a. AXIS-1 (Physical Conditions)

Group 1- with myofascial pain

- Group 1a- with limited opening
- Group 1b- without limited opening

Group 2- with disc displacement

- Group 2a- with reduction
- Group 2b- without reduction and with limited mouth opening
- Group 2c- without reduction and without limited opening

Group 3- with arthralgia or arthritis

b. AXIS-2 (Psychological Factors)

All participants completed the RDC/TMD Axis II self-report assessments, which included the Graded Chronic Pain Scale (GCPS) and depression screening tools, as recommended by the RDC/TMD guidelines. The GCPS is a validated 7-item tool that assesses chronic pain severity and its impact over six months. It is both valid and reliable, with excellent internal consistency demonstrated by Cronbach's alpha values of 0.71 for pain intensity and 0.54 for disability, along with test-retest reliability of 0.80. The GCPS includes three questions on pain intensity (current, worst, and average) and four on pain-related disability (activity interference and days of limitation). Scores are used to calculate a pain intensity index and disability score, classifying patients into one of four grades (I-IV), ranging from low pain and disability to high pain with severe limitations. The GCPS is widely used in TMD and chronic pain assessments [23], while depression levels were evaluated using the standardised SCL-90 questionnaire.

The SCL-90-R depression subscale is part of the Symptom Checklist-90-Revised (SCL-90-R): A widely used self-report instrument developed to assess psychological distress and psychopathology across various domains. It comprises 13 items, each rated on a 5-point Likert scale (0-4), designed to assess depressive symptoms such as low energy, hopelessness, suicidal thoughts, and emotional distress over the past week. The total score is calculated as the mean of all 13 item scores, with higher scores indicating greater severity. In terms of interpretation, a mean score ≥1.00 suggests clinically relevant depression, with scores of 1.00-1.49 indicating mild, 1.50-1.99 indicating moderate, and ≥2.00 indicating severe depressive symptoms. The subscale demonstrates excellent internal consistency (Cronbach's alpha: 0.85), good test-retest reliability (~0.86), and strong construct validity, correlating well with other standard depression measures [24]. These questionnaires were used to subjectively evaluate the severity of chronic pain and the presence of depressive symptoms in each individual.

Control group participants were randomly selected, and only individuals without a history of systemic diseases and classified as depression-negative based on the questionnaire were included.

Participants were provided with plain plastic tubes for collecting saliva samples at home, in a single day, once between 7:00 AM and 8:00 AM upon waking and again between 8:00 PM and 10:00 PM, in line with the circadian rhythm of cortisol [21]. They were instructed to avoid eating and drinking for one hour prior to collection, although drinking water was permitted. Participants were also asked not to smoke, exercise, or brush their teeth before providing samples.

The morning saliva samples were delivered to the laboratory immediately, while the evening samples were refrigerated at about 2-8°C overnight and submitted the next day. Upon arrival, the saliva samples were centrifuged, and the clear supernatant was used for analysis. Cortisol levels were measured using commercially available reagent kits, specifically a cortisol saliva ELISA kit from Bioassay Technology Laboratory (BT LAB), as ELISA is a reliable and widely validated method for measuring salivary cortisol levels, offering high sensitivity, specificity, and reproducibility when standard protocols are followed. All analyses were conducted at the Pharmacology Laboratory.

STATISTICAL ANALYSIS

Statistical analysis was conducted using the Statistical Package for the Social Sciences (SPSS) software (version 23.0). For each group, the mean, median, range, and Standard Deviation (SD) were calculated. A paired t-test was applied to assess the difference in ratios between the TMD group and the control group, while Pearson correlation was used to examine the relationship between morning and evening cortisol levels. ANOVA was employed to compare the salivary cortisol levels among TMD patients without depression, TMD patients with depression, and the control group. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The present study included three groups: Control, TMD with Depression, and TMD without Depression, each comprising 15 participants. The mean age of participants in the Control group was 21.8±0.641 years, in the TMD with Depression group it was 21.7±0.538 years, and in the TMD without Depression group it was 22.8±0.567 years. Each group consisted of eight males (53.3%) and seven females (46.6%), except for the Control group, which had seven males (46.6%) and eight females (53.3%). The age and gender distribution were comparable across the groups [Table/Fig-1].

Group	Mean age (±SD)	Males n (%)	Females n (%)
Control	21.8±0.641	7 (46.6%)	8 (53.3%)
TMD with depression	21.7±0.538	8 (53.3%)	7 (46.6%)
TMD without depression	22.8±0.567	8 (53.3%)	7 (46.6%)

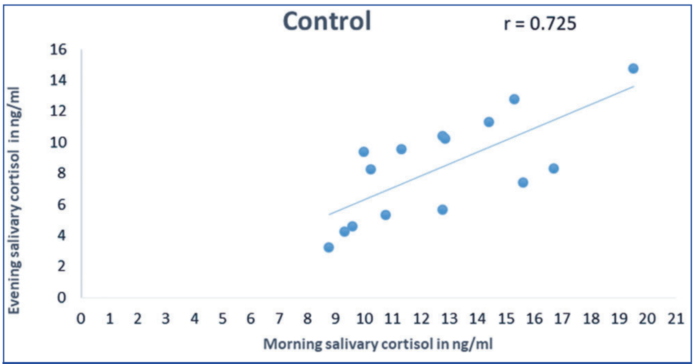
[Table/Fig-1]: Demographic distribution of study participants.
Data are presented as mean±SD for age and number (percentage) for gender.

Pearson correlation analysis was conducted to examine the relationship between morning and evening salivary cortisol levels. The results indicated a strong correlation, with correlation coefficients of 0.99 for TMD patients with depression, 0.989 for those without depression, and 0.725 for the Control group. All groups demonstrated a highly significant correlation, with a p-value of less than 0.001, except for the Control group which showed a significant correlation with a p-value of 0.002 [Table/Fig-2-5]. These findings suggest that salivary cortisol levels are consistently higher in the morning compared to the evening, with the highest mean value observed in TMD patients with depression in the morning group [Table/Fig-6].

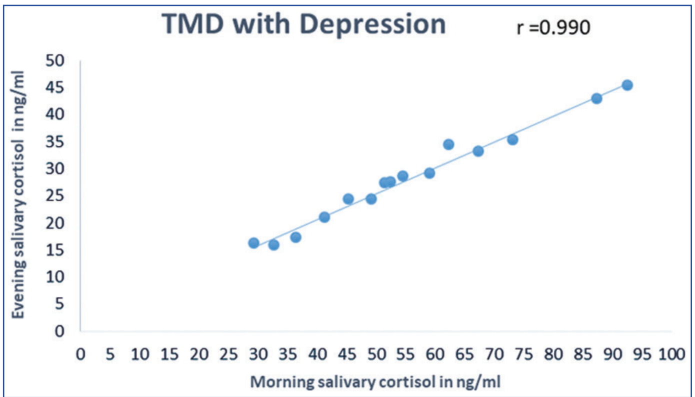
A paired sample t-test was used to compare morning and evening salivary cortisol levels within each group. All comparisons were statistically significant with p<0.001 [Table/Fig-7]. The ANOVA test indicated that the mean morning salivary cortisol levels were significantly higher in TMD patients with depression compared to those without depression and the Control group, with mean values

Parameters		N	Correlation (r)	p-value
Control	Morning saliva and evening saliva	15	0.725	0.002*
TMD with depression	Morning saliva and evening saliva	15	0.990	0.001**
TMD without depression	Morning saliva and evening saliva	15	0.989	0.001**

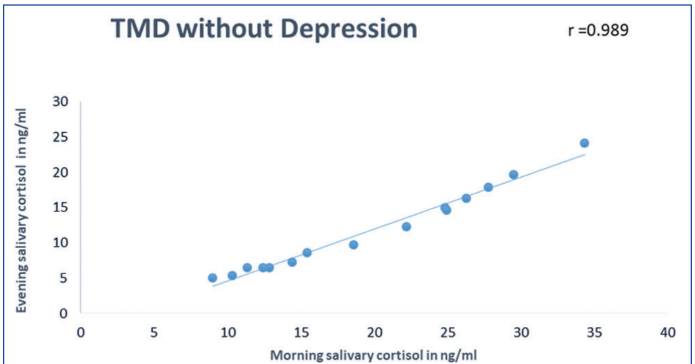
[Table/Fig-2]: Correlation between morning and evening salivary cortisol levels.
The Pearson correlation test was applied to assess the association between morning and evening salivary cortisol levels. N: Number of subjects in each group, *p <0.05 indicates statistical significance; **p<0.001 indicates high statistical significance, TMD: Temporomandibular disorder



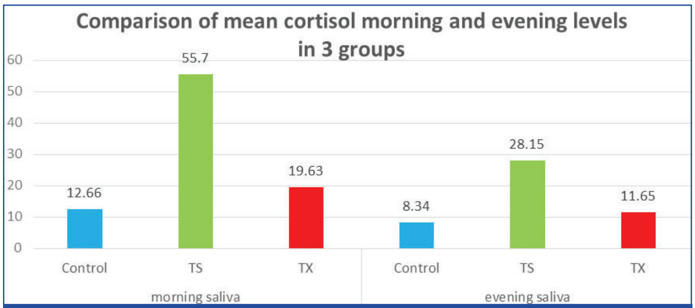
[Table/Fig-3]: Scatter plot showing the correlation between morning and evening salivary cortisol levels in the control group.
Each point represents an individual participant. A positive linear relationship was observed (Pearson correlation coefficient r=0.725, p<0.002), indicating a statistically significant association. A trend line (regression line) has been added to visualise the correlation. r: Pearson's correlation coefficient



[Table/Fig-4]: Scatter plot illustrating the correlation between morning and evening salivary cortisol levels in the TMD with depression group.
A strong positive linear relationship was observed (Pearson correlation coefficient r=0.990, p<0.001) indicating a statistically significant association. Each point represents an individual participant, and the trend line reflects the regression line. TMD: Temporomandibular disorder, r: Pearson's correlation coefficient, p: Probability value (significance level)



[Table/Fig-5]: Scatter plot showing the correlation between morning and evening salivary cortisol levels in the TMD without depression group.
A strong positive linear association was observed (Pearson correlation coefficient r=0.989, p<0.001) indicating a statistically significant association. Each point represents an individual participant, and the trend line represents the fitted regression line. TMD: Temporomandibular disorder, r: Pearson's correlation coefficient, p: Probability value (significance level)



[Table/Fig-6]: Mean cortisol levels in the morning and evening across the groups.
Means of morning salivary cortisol level in TMD patients without depression, TMD patients with depression, and with the control group. TS: TMDs with depression, TX- TMDs without depression

of 55.7, 19.63, and 12.66, respectively. Similarly, when comparing the evening salivary cortisol levels across the groups, TMD patients with depression exhibited significantly elevated levels compared to TMD patients without depression and the Control group, with mean values of 28.15, 11.65, and 8.34, respectively [Table/Fig-8].

A Student's t-test assessed salivary cortisol levels in males and females across the three groups, revealing significantly higher values for females. In TMD patients without depression, females had significantly higher morning and evening cortisol levels than males (p<0.001). In TMD patients with depression, females also showed higher morning (p=0.097) and evening levels (p=0.092) than males. In the Control group, females had a significantly higher evening cortisol level (p<0.001), though morning differences were not statistically significant. Overall, females demonstrated higher average salivary cortisol levels, particularly in TMD patients with depression in the morning [Table/Fig-9].

DISCUSSION

The TMDs are multifactorial conditions, with contributing factors that include physiological, behavioural, psychological, and environmental elements [25]. In dental research, particular attention has been given to dental occlusion and parafunctional activities as key aetiological factors in epidemiological studies [26]. This study focused on a cohort of young adults aged 18 to 28 years, with an

Parameters		Mean (ng/mL)	N	SD	Std. error mean	T value	p-value
Control	Morning saliva	12.6684	15	3.12305	0.80637	6.972	<0.001**
	Evening saliva	8.3478	15	3.32404	0.85826		
TMD with Depression	Morning saliva	55.7096	15	18.57522	4.79610	10.901	<0.001**
	Evening saliva	28.1513	15	8.95526	2.31224		
TMD without Depression	Morning saliva	19.6397	15	8.02566	2.07222	13.488	<0.001**
	Evening saliva	11.6507	15	5.96683	1.54063		

[Table/Fig-7]: Salivary cortisol statistics related to the morning and evening times.
A paired sample t-test was used to compare morning and evening salivary cortisol levels within each group. All comparisons were statistically significant (p <0.001). TMD: Temporomandibular disorder; N: Number of participants, SD: Standard deviation; Std. Error Mean: Standard error of the mean; ng/mL: Nanograms per millilitre, T value: t-test value, *p<0.05 = significant; **p<0.001 = highly significant

Parameters		N	Mean	SD	Std. error	95% Confidence interval for mean		F value	p-value
						Lower Bound	Upper Bound		
Morning saliva	Control	15	12.6684	3.12305	.80637	10.9389	14.3979	57.291	<0.001**
	TMD with Depression	15	55.7096	18.57522	4.79610	45.4230	65.9962		
	TMD without Depression	15	19.6397	8.02566	2.07222	15.1952	24.0842		
	Total	45	29.3392	22.29950	3.32421	22.6397	36.0388		
Evening saliva	Control	15	8.3478	3.32404	.85826	6.5071	10.1886	39.930	<0.001**
	TMD with Depression	15	28.1513	8.95526	2.31224	23.1920	33.1105		
	TMD without Depression	15	11.6507	5.96683	1.54063	8.3464	14.9551		
	Total	45	16.0500	10.82153	1.61318	12.7988	19.3011		

[Table/Fig-8]: Compare mean salivary cortisol levels (morning and evening) among the three study groups.
One-way ANOVA was applied to compare mean salivary cortisol levels (morning and evening) among the three study groups. The analysis revealed statistically significant differences across all groups (p<0.001). TMD: Temporomandibular disorder, N: Number of participants, SD: Standard deviation; Std. Error: Standard Error of the Mean, CI: Confidence Interval, F-value: Test statistic from ANOVA, ng/mL: Nanograms per milliliter, *p<0.05 = significant; **p<0.001 = highly significant.

Parameters		Gender	N	Mean	SD	Std. Error Mean	T value	p-value
Control	Morning saliva	Male	7	11.9396	3.18800	1.20495	-0.836	0.419
		Female	8	13.3061	3.13043	1.10677		
	Evening saliva	Male	7	5.5213	1.79939	0.68011	5.230	<0.001**
		Female	8	10.8211	2.08402	0.73681		
TMD with depression	Morning saliva	Male	8	47.6524	9.94891	3.51747	1.829	0.097
		Female	7	64.9179	22.45284	8.48638		
	Evening saliva	Male	8	24.5012	6.22255	2.20000	-1.822	0.092
		Female	7	32.3227	10.19251	3.85241		
TMD without depression	Morning saliva	Male	8	13.0576	3.06238	1.08271	-7.653	<0.001**
		Female	7	27.1621	3.94580	1.49137		
	evening saliva	Male	8	6.8862	1.57872	0.55816	-6.804	<0.001**
		Female	7	17.0959	3.91241	1.47875		

[Table/Fig-9]: Comparison of salivary cortisol levels between males and females within each group and time point (morning and evening).
Independent samples t-test was used to compare salivary cortisol levels between males and females within each group and time point (morning and evening). Statistically significant differences were observed in evening saliva levels in the control and TMD without depression groups (p=0.000). TMD: Temporomandibular disorder, N: Number of participants, SD: Standard deviation; Std. Error Mean: Standard Error of the Mean, ng/mL: Nanograms per milliliter, *p<0.05 = significant; **p<0.001 = highly significant.

overall mean age ranging from 21.7 to 22.8 years among the groups. This is consistent with findings by LeResche L (1997), who noted that TMD is predominantly observed in young and middle-aged adults, with a prevalence approximately twice as high in women compared to men [27]. This prevalence pattern underscores the importance of investigating biological and psychosocial factors that may predispose women to TMD more than men [28].

Physical factors, such as erupting third molars, could cause occlusal interferences while trying to accommodate in the jaw. Psychological factors, such as pursuing careers, establishing coursework, and peer pressure, particularly in this age group, appear to play significant roles in the onset and maintenance of TMD [29]. Psychometric assessments and endocrine measurements can provide valuable insights into these psychological influences. The variations observed between different diagnostic categories of TMD may have critical implications for understanding and managing the condition [30].

Growing evidence implicates the HPA axis in the pathophysiology of TMD [31]. The HPA axis is the primary endocrine response system to stress in humans. Upon activation, the hypothalamus releases Corticotropin-Releasing Hormone (CRH), leading to the secretion of Adrenocorticotropic Hormone (ACTH) from the pituitary gland, which in turn stimulates cortisol release from the adrenal cortex [32]. Interestingly, facial pain may trigger a stronger HPA-axis response compared to pain located elsewhere in the body, suggesting a unique interplay between psychological stress and physical symptoms in TMD patients [33].

In the present study, we found that cortisol levels were significantly higher in the morning compared to the evening across all three groups-TMD patients with depression, TMD patients without depression, and the control groups-with a p-value <0.001. This aligns with findings from Wilhelm et al., who reported a distinct morning peak in cortisol levels that serves as an indicator of adrenocortical activity [34]. Furthermore, TMD patients with depression exhibited higher cortisol levels both in the morning and evening compared to those without depression and the control group, with a p<0.001. These results resonate with Jones DA et al., (1997), who demonstrated that TMD patients showed a heightened cortisol response to psychological stress compared to controls [35].

In the analysis of gender differences, we found that female TMD patients without depression had significantly higher morning and evening cortisol levels than their male counterparts (p<0.001). Similarly, female TMD patients with depression exhibited significantly elevated morning (p=0.097) and evening cortisol levels (p=0.092) compared to males. Notably, when comparing female TMD patients with and without depression, those with depression showed significantly higher cortisol levels, reinforcing the impact of depressive symptoms on physiological stress responses [36]. This aligns with findings by Berger M et al., who argued that the relationship between depression and TMD is more complex than previously theorised, as biological processes can translate psychological distress into pain sensations [37]. These findings reject the null hypothesis.

In managing TMD, treatment strategies often focus on alleviating pain and dysfunction. Interventions such as analgesics, anti-inflammatory medications, psychological counselling, intraoral appliances, and even arthrocentesis have been employed to address the underlying aetiological factors [38]. Additionally, integrating psychological interventions, stress management, and habit modification may prove effective in reducing pain and tension in TMD patients, particularly those with co-occurring depressive symptoms [39]. This study underscores the multifaceted nature of TMD, emphasising the significant interplay between psychological and physiological factors.

Limitation(s)

The potential influence of confounding factors such as systemic musculoskeletal disorders (e.g., fibromyalgia), psychological conditions (e.g., anxiety, depression), neurological disorders, recent trauma, and dental pathologies may mimic or impact the clinical presentation of TMD. Although efforts were made to consider and address these factors based on RDC/TMD criteria, their complete exclusion may not have been possible, potentially affecting diagnostic accuracy. Additionally, significant variability in salivary cortisol levels reported across the literature may stem from population-specific differences, individual physiological variability, and lifestyle-related factors-particularly among students. Variables such as irregular sleep patterns and academic stress have influenced cortisol levels in the present study, thus serving as additional potential confounders.

CONCLUSION(S)

The present study emphasises the multifactorial nature of TMD, highlighting the strong link between psychological and physiological factors. Elevated salivary cortisol levels in TMD patients, especially those with depression, suggest a dysregulated stress response that may worsen the condition. Notable gender differences indicate that females may be more susceptible to stress-related effects on TMD. These findings stress the need for holistic management approaches that address both physical and psychological aspects of TMD. Future longitudinal studies are essential to clarify causal relationships and assess the effectiveness of integrated treatment strategies.

REFERENCES

[1] De Leeuw R, Klasser GD; American Academy of Orofacial Pain. Orofacial Pain: Guidelines for Assessment, Diagnosis, and Management. 6th edn. USA: Quintessence Publishing. 2018. Available from: https://api.pageplace.de/preview/DT0400.9780867159301_A38521160/preview-9780867159301_A38521160.pdf.

[2] Peck CC, Goulet JP, Lobbezoo F, Schiffman EL, Alstergren P, Anderson GC, et al. Expanding the taxonomy of the diagnostic criteria for temporomandibular disorders. J Oral Rehabil. 2014;41(1):02-03.

[3] List T, Axelsson S. Management of TMD: Evidence from systematic reviews and meta-analyses. J Oral Rehabil. 2010;37(6):430-51.

[4] Manfredini D, Winocur E, Guarda-Nardini L, Paesani D, Lobbezoo F. Epidemiology of bruxism in adults: A systematic review of the literature. J Orofac Pain. 2013;27(2):99-110.

[5] Minervini G, Franco R, Marrapodi MM, Fiorillo L, Cervino G, Cicciù M. Prevalence of temporomandibular disorders in children and adolescents evaluated with diagnostic criteria for temporomandibular disorders: A systematic review with meta-analysis. Journal of Oral Rehabilitation, 2023;50(6):522-30.

[6] Sharma S, Gupta DS, Pal US, Jurel SK. Etiological factors of temporomandibular joint disorders. National journal of maxillofacial surgery. 2011;2(2):116-19.

[7] Slade GD, Fillingim RB, Sanders AE, Bair E, Greenspan JD, Ohrbach R, et al. Summary of findings from the OPPERA prospective cohort study of incidence of first-onset temporomandibular disorder: Implications and future directions. J Pain. 2013;14(12):T116-24.

[8] Gameiro GH, da Silva Andrade A, Nouer DF, Ferraz de Arruda Veiga MC. How may stressful experiences contribute to the development of temporomandibular disorders? Clin Oral Investig. 2006;10(4):261-68.

[9] Hellhammer DH, Wüst S, Kudielka BM. Salivary cortisol as a biomarker in stress research. Psychoneuroendocrinology. 2009;34(2):163-71.

[10] Ohrbach R, Dworkin SF. The evolution of TMD diagnosis: Past, present, future. J Dent Res. 2016;95(10):1093-101.

[11] Carlson NR. Physiology of Behaviour. Pearson Higher Education; 2013.

[12] Kirschbaum C, Hellhammer DH. Salivary cortisol in psychobiological research: An overview. Neuropsychobiology. 1989;22(3):150-69.

[13] Vreeburg SA, Hoogendijk WJ, van Pelt J, DeRijk RH, Verhagen JC, van Dyck R, et al. Major depressive disorder and hypothalamic-pituitary-adrenal axis activity: Results from a large cohort study. Arch Gen Psychiatry. 2009;66(6):617-26.

[14] Adam EK, Kumari M. Assessing salivary cortisol in large-scale, epidemiological research. Psychoneuroendocrinology. 2009;34(10):1423-36.

[15] LeResche L, Dworkin SF. The role of stress in inflammatory disease, including periodontal disease: Review of concepts and current findings. Periodontology 2000. 2002;30(1):91-103.

[16] Slavich GM, Irwin MR. From stress to inflammation and major depressive disorder: A social signal transduction theory of depression. Psychological Bulletin. 2014;140(3):774-815.

[17] AlSahman L, AlBagieh H, AlSahman R. Is there a relationship between salivary cortisol and temporomandibular disorder: A systematic review. Diagnostics. 2024;14(13):1435.

[18] Wänman A. Longitudinal course of symptoms of craniomandibular disorders in men and women: A 10-year follow-up study of an epidemiologic sample. Acta Odontol Scand. 1996;54(6):337-42.

[19] Gereau RW 4th, Sluka KA, Maixner W, Savage SR, Price TJ, Murinson BB, et al. A pain research agenda for the 21st century. J Pain. 2014;15(12):1203-14.

[20] Cheon CY, Park HJ, Ryu JW, Ahn JM. Comparative analysis of salivary cortisol in young adult patients with temporomandibular disorders. J Oral Med Pain. 2022;47(4):183-88.

[21] Goyal G, Gupta D, Pallagatti S. Salivary cortisol could be a promising tool in the diagnosis of temporomandibular disorders associated with psychological factors. J Indian Acad Oral Med Radiol. 2020;32(4):354-59.

[22] Dworkin SF, Sherman J, Mancl L, Ohrbach R, LeResche L, Truelove E. Reliability, validity, and clinical utility of the research diagnostic criteria for Temporomandibular Disorders Axis II Scale: Depression, non specific physical symptom and graded chronic pain. J Orofac Pain. 2002;16(3):207-20.

[23] Von Korff M, Ormel J, Keefe FJ, Dworkin SF. Grading the severity of chronic pain. Pain. 1992;50(2):133-49. Doi: 10.1016/0304-3959(92)90154-4.

[24] Tomioka M, Shimura M, Hidaka M, Kubo C. The reliability and validity of a Japanese version of symptom checklist 90 revised. Bio PsychoSocial Medicine. 2008;2(1):19.

[25] Okeson JP. Treatment of Temporomandibular Joint Disorders. In: Management of Temporomandibular Disorders and Occlusion. 5th Edition, St. Louis: Mosby; 2003. P. 413-35.

[26] Mackie A, Lyons K. The role of occlusion in temporomandibular disorders-A review of the literature. N Z Dent J. 2008;104(2):54-59.

[27] LeResche L. Epidemiology of temporomandibular disorders: Implications for the investigation of etiologic factors. Crit Rev Oral Biol Med. 1997;8(3):291-305.

[28] Ryan J, Akhter R, Hassan N, Hilton G, Wickham J, Ibaragi S. Epidemiology of temporomandibular disorder in the general population: A systematic review. Adv Dent Oral Health. 2019;10(3):555787.

[29] Rollman GB, Gillespie JM. The role of psychosocial factors in temporomandibular disorders. Curr Rev Pain. 2000;4(1):71-81.

[30] Huttunen J, Qvintus V, Suominen AL, Sipilä K. Role of psychosocial factors on treatment outcome of temporomandibular disorders. Acta Odontol Scand. 2019;77(2):119-25.

[31] Lambert CA, Sanders A, Wilder RS, Slade GD, Van Uum S, Russell E, et al. Chronic HPA axis response to stress in temporomandibular disorder. J Dent Hyg. 2014;88(suppl 1):05-12.

[32] Sotiropoulos I, Cerqueira JJ, Catania C, Takashima A, Sousa N, Almeida OF. Stress and glucocorticoid footprints in the brain-the path from depression to Alzheimer's disease. Neurosci Biobehav Rev. 2008;32(6):1161-73.

[33] Lee YH, Chon S, Auh Q, Verhoeff MC, Lobbezoo F. Clinical, psychological, and haematological factors predicting sleep bruxism in patients with temporomandibular disorders. Sci Rep. 2025;15(1):19148.

[34] Wilhelm I, Born J, Kudielka BM, Schlotz W, Wüst S. Is the cortisol awakening rise a response to awakening?. Psychoneuroendocrinology. 2007;32(4):358-66.

[35] Jones DA, Rollman GB, Brooke RI. The cortisol response to psychological stress in temporomandibular dysfunction. Pain. 1997;72(1-2):171-82.

[36] Jo KB, Lee YJ, Lee IG, Lee SC, Park JY, Ahn RS. Association of pain intensity, pain-related disability, and depression with hypothalamus-pituitary-adrenal axis function in female patients with chronic temporomandibular disorders. Psychoneuroendocrinology. 2016;69:106-15.

[37] Berger M, Oleszek-Listopad J, Marczak M, Szymanska J. Psychological aspects of temporomandibular disorders-literature review. Curr Issues Pharm Med Sci. 2015;28(1):55-59.

[38] Matheson EM, Fermo JD, Blackwelder RS. Temporomandibular disorders: Rapid evidence review. Am Fam Physician. 2023;107(1):52-58.

[39] Orlando B, Manfredini D, Salvetti G, Bosco M. Evaluation of the effectiveness of biobehavioural therapy in the treatment of temporomandibular disorders: A literature review. Behav Med. 2007;33(3):101-18.

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