e-ISSN: 2637-0611

Available online at
https://myjms.mohe.gov.my/index.php/corals

Compendium of Oral Science 11(2) 2024, 57 – 70

Compendium of Oral Science

Clinical Manifestation of Academic Stress in Temporomandibular Joints Disorders (TMDs) among Undergraduate Dental Students of Universiti Teknologi MARA, Malaysia

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ARTICLE INFO

Article history:
Received 12 September 2023
Revised 22 December 2024
Accepted 25 February 2024
Online first
Published 1st September 2024

Keywords:
temporomandibular disorders
academic stress
dental students
clinical manifestation

DOI:
10.24191/cos.v11i2.27504

ABSTRACT

Objectives: Numerous studies have indicated that academic stress is associated with detrimental impacts on mental well-being among undergraduate students. Here, we examined the clinical manifestations of the temporomandibular disorder (TMD) of perceived academic stress among dental students in Universiti Teknologi MARA. **Methods:** 27 TMD-diagnosed students with perceived academic stress were examined for the clinical manifestations of temporomandibular disorder. Research Diagnostic Criteria for temporomandibular disorders (RDC/TMD) a widely acceptable international TMD diagnostic tool was applied for this examination. RDC/TMD contains axis I and II. Statistical analysis was performed using the Fisher exact test using SPSS 20.0. The significance level was set at $P \leq 0.05$. **Result:** Regardless of the year of study, out of the 27 TMD-diagnosed students, 19 students (9.4%) had disk displacements with reduction, 8 students (3.9%) had TMJ arthralgia (n=7) and arthrosis (n=1), and 3 TMD patients (1.5%) presented myofascial pain (n=2) with limited jaw opening (n=1). **Conclusion:** Moderate to severe academic-related stressors may have contributed to the pathophysiological complications of TMD. Further research is needed to understand the pathophysiological mechanism of academic stressors in TMD development and progression.

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INTRODUCTION

Temporomandibular disorders (TMDs) refer to musculoskeletal dysfunctions involving the orofacial region affecting the temporomandibular joint (TMJ) and masticatory muscles. The etiology of TMD is believed to be multifactorial and complex. Reports documented that symptoms caused by TMD are usually chronic and difficult to manage thereby affecting the quality of life. Most importantly, undergraduate students aged between 21 and 25 years with TMD demonstrated significantly higher scales of depression/anxiety (Paulino et al., 2018); (Staniszewski et al., 2018); (Sojka, et al., 2019); Ahuja, et al., 2018).Temporomandibular disorders commonly present as myofascial pain (myofascial pain syndrome), disc displacements, and arthralgia, arthritis, and arthrosis (Chan, et al., 2022).

The pathophysiology of temporomandibular disorders is unknown (Wheeler, et al.,1998). Among the multifactorial contributing factors: predisposing factors are considered to increase the risk of developing a condition, initiating factors are thought to be responsible for the onset or incidence of the condition, and perpetuating factors may contribute to the persistence of the TMD condition in focus (DeBoever et al., Our previous study showed that academic stress was significantly higher in the clinical manifestation of TMD compared to social stress (Mazuan, et al., 2024).

Our body's homeostasis is constantly threatened or perceived by adverse forces termed stressors. The stress response is perceived and mediated by a greatly interconnected central effector of the stress system located in the central nervous system and peripheral organs. A stress response, created by a real or perceived threat (stressor) is associated with behavioral and somatic disorders. Optimal responsiveness of the stress system is crucial for maintaining overall well-being through adaptive physiological and behavioral responses (Chrousos, 2009) (Daviu, et al., 2019). The exact pathophysiology of academic stress remains unclear which makes it challenging for precise therapeutic interventions. This study aimed to investigate the clinical manifestations of temporomandibular disorder (TMD) among a group of diagnosed TMD patients, who were students (n=27), experiencing perceived academic stress.

Students encounter various real-life experiences during their academic journey, leading to common academic stress triggered by internal and external emotional struggles, which can adversely affect their mental well-being (Barbayannis, et al., 2022). Stress is affected by an individual's beliefs and attitudes (Kumar et al., 2009), resulting in either positive or negative consequences (Rajab et al., 2011); (Sanders, et al., 2002).

METHODOLOGY

Participants

This is the continuation of our previous study (Mazuan, et al., 2024), the "Dental Environment Stress (DES) questionnaire was used to determine the stress level of dental students (n=202) in UiTM (Z.H. Al-Sowygh et al) which comprised 202 undergraduate dental students from the first to fifth years enrolled in the Bachelor of Dental Surgery (BDS) program in UiTM Shah Alam, Selangor. The previous study demonstrated that. Ethical approval for performing this study was obtained from the UiTM ethics committee (reference number 600-FPG (PT.1/5)).

Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) is a tool that is a widely accepted internationally dual-axis diagnostic procedure for the diagnosis of Temporomandibular disorder (Dworkin, et al.,1992). The RDC/TMD contains two different parts, axis I and axis II. Axis I involves the clinical TMD conditions for one or more of the following diagnosis groups: muscle disorders (group I); disk displacement (group II); and arthralgia, osteoarthritis, and osteoarthritis (group III). Axis II involves

https://doi.org/10.24191/cos.v11i2.27504

pain-related disability and psychological status. Both axis was performed according to the guidelines available.

The diagnosis of TMD was divided into groups which are: Ia, myofascial pain; Ib, myofascial pain with a limited opening; IIa, disk displacement with reduction; IIb, disk displacement without reduction with a limited opening; IIc, disk displacement without reduction without limited opening; IIIa, arthralgia; IIIb, osteoarthritis; and IIIc, osteoarthrosis (Dworkin, et al.,1992).

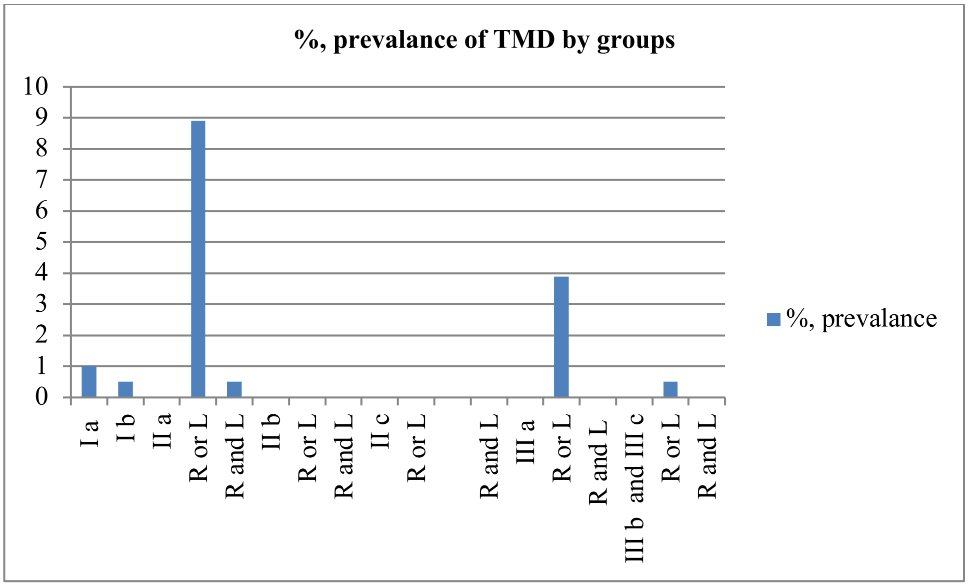
Statistical analysis

Statistical analysis was performed using Fisher-exact test using SPSS 20.0 to associate TMD development to stress with a significance level set at $P \leq 0.05$.

RESULT

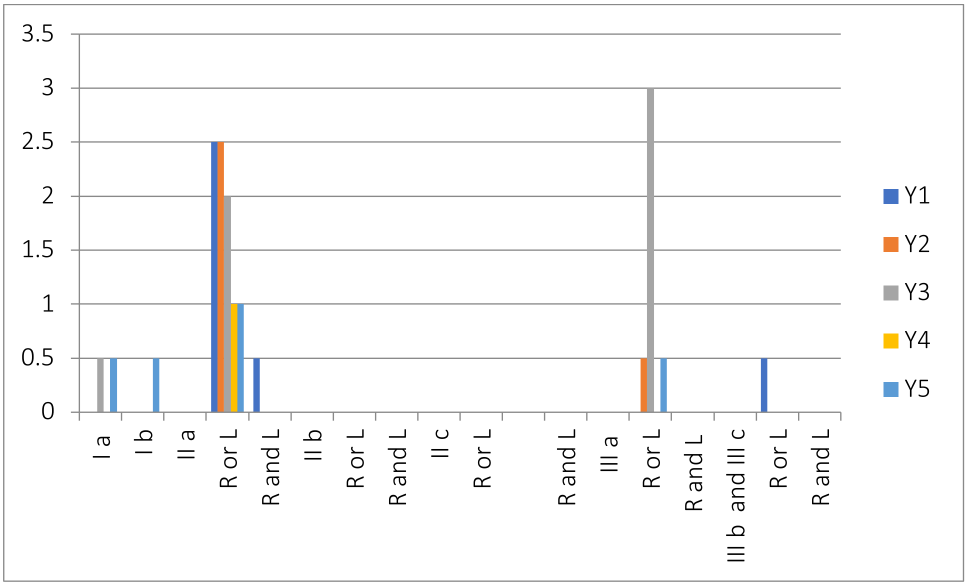
Out of 203 students examined for the clinical manifestation of TMD, 27 students (13.3%) were diagnosed with TMD. It is noteworthy to mention that our previous report demonstrated that academic stress was higher compared to social stress irrespectively TMD or non-TMD according to overall class (Nik, et al., 2024).

Regardless of the year of study, group I disorder was diagnosed in 3 patients (1.5%), which comprised Ia for 2 patients (1.0%), and Ib for 1 patient (0.5). Group IIa disorders (disk displacements with reduction) were the most diagnosed group comprised of 19 students (9.4%). For group III disorders, only type IIIa (arthralgia) and IIIc (artherosis) were diagnosed. 8 students (3.9%) were diagnosed with type IIIa (arthralgia), while only one student came out with type IIIc (0.5%) (Graph 1 and Graph 2).



Graph 1. Prevalence of students in diagnosis of RDC/TMD; R, right joint; L, left joint; Ia, myofascial pain; Ib, myofascial pain with limited opening; IIa, disk displacement with reduction; IIb, disk displacement without reduction with limited opening; IIc, disk displacement without reduction without limited opening; IIIa, arthralgia; IIIb, osteoarthritis; IIIc, osteoarthrosis.

https://doi.org/10.24191/cos.v11i2.27504



Graph 2. The prevalence of Temporomandibular Disorders by groups regarding the year of studies.

DISCUSSION

Regardless of the year of study, group I disorder was diagnosed in 3 patients (1.5%), which comprised Ia for 2 patients (1.0%), and Ib for 1 patient (0.5). Group IIa disorders (disk displacements with reduction) were the most diagnosed group comprised of 19 students (9.4%). For group III disorders, only type IIIa (arthralgia) and IIIc (artherosis) were diagnosed. 8 students (3.9%) were diagnosed with type IIIa, while only one student came out with type IIIc (0.5%) (Graph 1 and Graph 2).

Among 27 TMD patients, disk displacements with reduction were the most prevalent (n=19) TMD manifestation followed by arthralgia and artherosis (n=8) (Graph 1 and Graph 2).

The temporomandibular joint(TMJ) is a synovial joint between the mandible's condylar head and the temporal bone's mandibular fossa. This joint is separated by an articular disc that forms two synovial cavities The temporomandibular joint(TMJ) consists of muscles of mastication and ligaments that stabilize the TMJ. The main sensory innervation is from the masseteric branches of the mandibular nerve (V3), and the auriculotemporal branch of the trigeminal nerve. Some of the cell bodies of primary afferent sensory neurons of the trigeminal nerve, lie within the brain, in the mesencephalic trigeminal nucleus mostly glutamatergic in nature, convey the proprioceptive information of masticatory muscles and play a key role in oral–motor movements (e.g., masticatory jaw reflex) by projecting to the trigeminal motor nucleus. The main role of proprioceptive neural supply is to provide sensory feedback from orofacial tissues to trigeminal motor neurons (Lazarov, et al., 2007). More importantly, mesencephalic proprioceptive input neurocircuitry is a central relay region for coordinating orofacial movements, including chewing and swallowing (Lazarov, 2002; Fortin et al., 2021).

Proprioceptive fibres from The mesencephalic nucleus innervate the hard palate, teeth, periodontium, temporomandibular joint (TMJ) capsule, and the extraocular and masticatory muscles' Golgi tendon organs and muscle spindles (Joo, et al., 2014).

https://doi.org/10.24191/cos.v11i2.27504

Among 27 TMD patients, disk displacements with reduction were the most prevalent (n=19) TMD manifestation followed by arthralgia and artherosis (n=8). General Health Questionnaire (GHQ) and quality of life were assessed using the World Health Organization Quality Of Life-Brief Version (WHOQOL-BREF) in patients with TMD and demonstrated that the item "death wish" (GHQ) was related to severe muscle-related TMD. An association was observed between disc displacement with reduction and social domain (WHOQOL-BREF) (Resende, et al., 2013; Oliveira, et al., 2013)

Stressors can evoke various pathophysiological complications in our body depending on the severity of the stressors, its effects range from alterations in homeostasis to death (Yaribeygi et al., 2017). Previous studies documented that academic stressors may disrupt optimal homeostasis regulation (Ekpenyong, et al., 2013).

A recent report hypothesized and demonstrated a central mechanism underlying the neuro-signaling system between psychological stressors and TMD. Psychological stressors activate glutamatergic excitatory projections from the mesencephalic trigeminal nucleus (a key nucleus for masticatory proprioception and orosensory–motor control) to the trigeminal motor nucleus. Thus leading to the overactivity of oral–motor movements. Further, this study revealed significantly increased expression of acetylcholinesterase (AChE) and creatine kinase muscle-type (CK-MM) in masticatory muscle (Zhao, et al., 2022). AChE is mainly expressed in the neuromuscular junctions of muscles (Silman and Sussman, 2008) and noxious stimulation decreases junctional AChE activity. AChE is believed to be a protein marker of motor activation. (Pregelj, et al., 2007) (Bonansea, et al., 2016).

Mastication releases the enzyme neprilysin involved in the clearance of Aβ peptide. Impaired mastication and muscle reduced the axonal transportation of neprilysin to the mesencephalic nucleus the protective mechanism against the deposition of Aβ thus triggering general neuroinflammation (Kondo, et al., 2019); (Kobayashi, et al., 2019). Another recent report suggested that TMD caused compensatory muscle behaviors with modifications of the masticatory muscles and their altered function. Moreover, an asymmetrical and low synergetic pattern of masticatory muscle contractions was observed compared to those without TMD patients (Pelai, et al., 2023).

A variety of postsynaptic receptors are expressed in mesencephalic trigeminal neurons, including neurotrophins and growth factors. The neurochemical plasticity of mesencephalic neurons in the proprioceptive system might be modulated presynaptically through various mechanisms of the divergent neural inputs they receive (Lazarov, et al., 2007). It is noteworthy that, mesencephalic trigeminal nucleus projects to hypothalamic nuclei, prefrontal cortex, the thalamus, the limbic system, the Locus Coeruleus, the reticular parvocellular area, the mesencephalic reticular formation, the dorsal raphe nucleus (serotoninergic), laterodorsal tegmental nucleus (cholinergic). Further, mesencephalic pseudounipolar cells expressed GABA receptors (Hayar, et al., 1997) contribute to the activation of the ascending reticular activating system (ARAS) by releasing neurotransmitters including noradrenaline, dopamine, serotonin, acetylcholine, and glutamate (Giovanni, et al., 2021). Importantly, The central nucleus of the amygdala project to the mesencephalic neurons (Lazarov, et al., 2011) responsible for stress and anxiety.

Therefore, we cautiously indicate that academic stress-induced TMD might link to a more diverse thus impacting the pathophysiology processes of the homeostatic mechanisms of health, where future studies using the “Academic stress-TMD model” (Nik, et al., 2024). The trigeminal nerve is a huge and diverse somatosensory system that contains approximately 180,000 nerve fibers. in its periphery system, fibers from diverse origins are synaptically linked by sympathetic, parasympathetic, and gustatory nerve fibers (Lazarov, et al., 2002). About 5%–12% of the general population suffers from TMD. More importantly, WHO recognized TMD as the third most common dental disease. Academic stress is thought to be a major causative factor for depressive symptoms, academic stress that contributes to depressive symptoms directly or indirectly accounts for 62% (American Society of Temporomandibular Joint Surgeons 2023);. Further, the World Health Organization warranted that “depression is one of the leading causes of disability

https://doi.org/10.24191/cos.v11i2.27504

worldwide and is projected to significantly contribute to the overall global burden of disease by 2030" (James, et al., 2018); (Mathers et al., 2002) ; (Zhang et al., 2018). Therefore, to reveal the pathophysiological circuitries underlying the clinical disorders observed in our study, future studies will be necessary to unravel a more complete picture of the "academic stress-human TMD model" with the application of modern technology e.g., pluripotent stem cell (iPSC) technology, epigenomic (competing endogenous RNAs (ceRNAs)), will provide valuable insights for understanding of above clinical manifestation of academic stress in TMD. Mechanistic research using innovative methods will facilitate the development of comprehensive therapeutic approaches for academic stress, such as predictive, diagnostic and therapeutic biomarkers (Shrivastava, et al., 2021).

The report showed a significantly upregulated HPA axis with higher cortisol and the sum of glucocorticoids (cortisol and cortisone) levels in the TMD group (Staniszewski, et al., 2018). Higher cortisol levels impact genetic and epigenetic mechanisms, thus modulating transcriptional rate, ultimately leading to changes in the cell's specific protein content (Kaplan, et al., 1992) (Rahman, et al., 2022). It is noteworthy to mention that, epigenetic conditions are potentially reversible. Antidepressants, psychotherapy and nonverbal emotion communication training on brain function and structure can be used in patients to change the epigenetic marks of relevant genes linked to the stress response (Perroud, et al., 2018; Yehuda, et al., 2018). In this regard, the report documented that epigenetics modifications observed by psychotherapy in peripheral tissues (DNA extracted from peripheral blood) are associated with recovery and improvement of relevant tissues as the brain possesses neuroplasticity. Neuroplasticity of the trigeminal somatosensory circuitry allows it to be regulated by its peripheral presynaptic neuromodulators (e.g., noxious proprioception, dental injury) and their excitatory actions on neurons in these pathways or central alterations (e.g. attention, stress). More importantly, the central nervous system's neuroplasticity allows for long-lasting changes in neuronal connections in response to its physical and social environment, leading to structural, physiological, and behavioral adaptations based on experiences. More importantly, studies documented epigenetic mechanisms (DNA methylation, histone modification, and microRNA) in chondrocyte of TMD patients. It is noteworthy to mention that, as an epigenetic factor stress causes various epigenetic changes and induces long-term phenotypic adaptations that contribute to neuropsychiatric disorders (Rahman et al., 2022); (Buschdorf, et al., 2015).

Recently, research on academic stress and depression among students has gained increasing attention. The World Health Organization indicated that "depression is one of the leading causes of disability worldwide and is projected to significantly contribute to the overall global burden of disease by 2030 (James et al., 2018); (Mathers et al., 2002); (Zhang et al., 2018).

It is difficult to explain how academic stress causes TMJ disorders (such as disk displacements with reduction, arthralgia, arthrosis) at a pathophysiological level Graph 1 and Graph 2). However, the above reports provide clear evidence and contribute to our understanding of the relationship between psychological academic stress and the development of TMD. To understand the psychobiology of academic stress, further investigations are essential, particularly regarding the neurochemical plasticity of the trigeminal mesencephalic proprioceptive system, including the circuitry involved in presynaptic and post-synaptic neuromodulation. "Academic stress-human TMD model" could play an important role in enhancing our understanding of the molecular, cellular, and circuit mechanisms underlying the dynamic process of academic stress (Lazarov et al., 2007).

This study had certain limitations. Future studies should consider including more variables, such as students from various faculties, and account for inter-study differences, such as specific tissues with types of stressors. Additionally, studies should aim for a larger sample size with equal male and female participants and use comprehensive tools to assess psychosocial and behavioral factors. In our study, we did not utilize the updated dual-axis Diagnostic Criteria to diagnose temporomandibular disorders (DC/TMD) (Schiffman, et al., 2014; Sójka, et el., 2016). The discovery of new biomarkers (Shrivastava, et al., 2021) of academic stress pathways would provide valuable insights into understanding the mechanism

https://doi.org/10.24191/cos.v11i2.27504

(e.g., noncoding miRNA, single-cell RNA sequencing) (Chao, et al., 2013) ; (Lee, et al., 2023). Thus, more sophisticated and comprehensive studies need to be conducted such as proprioceptive physiotherapy of the trigeminal mesencephalic system (Aman, et al., 2015); (Lazarov, et al., 2007) somatic experiencing therapy (Payne, et al., 2015), religious psychotherapy (Bachtiar, et al., 2023), acupuncture (Park, et al., 2023) are crucial to elucidate the integrated mechanisms and to develop predictive, preventive, and therapeutic methods that can be integrated with the intervention of academic stress in TMD pathophysiology.

CONCLUSION

The results of this study clinically demonstrated that students experiencing academic stressors developed temporomandibular joint disorders. We cautiously indicate the "academic stress-related TMD clinical manifestations" phenomenon observed in our study may offer significant opportunities for scientific advancement in understanding the pathophysiology of academic stress. Our results suggest that academic stress represents an important challenge and underlying pathophysiological circuitry in developing TMD may provide insight into the mechanism of academic stress for early prevention, diagnosis, and integrated treatment strategies (Aman, et al., 2015); (Lazarov, et al., 2007).

ACKNOWLEDGEMENTS/FUNDING

The authors would like to acknowledge the support of Faculty of Dentistry, Universiti Teknologi Mara (UiTM) Sungai Buloh Campus, Selangor, Malaysia for providing the support on this research.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflicts of interest related to the contents of this article.

AUTHORS' CONTRIBUTIONS

Nik Mohd Mazuan Nik Mohd Rosdy - Conceptualization, data analysis, review and editing of the manuscript. Co-supervisor of this ERP project.

Farlyana Alia Azizan - Involved as a student in this Elective Research Project (ERP). Faculty of Dentistry, Universiti Teknologi MARA (UiTM) Sg Buloh Campus, Malaysia.

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Khairil Anuar Md. Isa - Performed the Statistical analysis of this project.

Jamil Ahsan Kazi - Conceptualized the central research idea, developed the theoretical framework, conducted data analysis, and drafted and revised the manuscript, and approved the article submission. Main supervisor of this ERP project.

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https://doi.org/10.24191/cos.v11i2.27504