Prevalence and characteristics of referred pain in patients diagnosed with temporomandibular disorders according to the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) in Sharjah, United Arab Emirates [version 2; peer review: 1 approved, 1 approved with reservations]

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Abstract
Background: Referred pain often complicates and delays the diagnosis of temporomandibular disorders (TMD). Elaborating the prevalence and characteristics of TMD-associated referred pain as well as the distribution of referred pain in different TMD classes will significantly improve the diagnostic process. The objectives of the present study were to assess the prevalence and to evaluate the characteristics of referred pain associated with TMD diagnosed according to the DC/TMD.

Methods: A total of 252 patients were evaluated using the DC/TMD Axes-I and –II assessment tools. Different modalities were used to treat the diagnosed TMD. Referred pain was diagnosed when the location of the perceived pain in response to palpation extended beyond the boundary of the structure that was examined. For pain locations that were perceived as deep, patients were asked to locate the surface of the area of pain. The result of the assessment was identified as positive if the patient described his perceived pain during the clinical examination as being familiar pain that was experienced in the same location in the last 30 days.

Results: TMD-associated referred pain was recorded in 153 patients (60.7%). The most common referred pain location was the temporal area (45.2%), followed by the ear (42.1%). The referred pain was recorded in disc displacement with reduction with intermittent locking and myofascial pain with referral in all patients (100%). The proportion of patients with referred pain was significantly different between the different TMD diagnostic subgroups (P < 0.001). The recorded

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Any reports and responses or comments on the article can be found at the end of the article.
percentage of improvement in the referred pain following the treatment was 50.41% after 3 months and 56.65% after 6 months.

Conclusions: Referred pain is a prominent feature of TMD. The prevalence of referred pain associated with TMD was 60.7%. A strong strength association between the different diagnostic subgroups and the presence of referred pain existed.

Keywords
Temporomandibular disorders, Temporomandibular joint, Referred pain, Orofacial pain, Diagnostic Criteria for Temporomandibular Disorders
Introduction

Temporomandibular disorders are a combination of muscular, skeletal, and neuromuscular pathologic conditions that influence the temporomandibular joint (TMJ), the muscles of mastication, and the related tissues. The common symptoms of TMD are headache (occipital area, temporal area, and forehead), pain during chewing food, pain on opening or closing the jaws, TMJ pain, pain in the back of the neck, joint sounds, deviation upon opening the mouth, and limitation of mouth opening. The pain associated with TMD is often a concatenation of diverse entangled pain sources. Microtrauma due to bruxism, joint laxity, and functional overloading are reported as the main causes of TMD, whereas TMD have been described as the most prevalent cause of non-odontogenic orofacial pain. The reported prevalence of TMD was contradicting among studies, mainly due to the different evaluation techniques, diagnostic criteria and different TMD taxonomy used in different studies. Patients tend to ignore their TMD symptoms which can lead to more advanced forms of these disorders. The prevalence of incidentally discovered TMD was 10.8% in one study, among whom osteoarthritis was diagnosed in 11.69%.

The diagnosis of TMD is challenging even to the most experienced practitioner mainly due to the concurrence of symptoms among different disorders. TMD diagnosis is usually achieved through history, physical examination and different imaging modalities. The Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) is a reliable instrument for TMD diagnosis, and it incorporates two axes; Axis-I involves the clinical and the radiographical diagnostic criteria, whereas Axis-II focuses on the evaluation of the psychosocial status and pain-related disabilities. An updated diagnostic protocol that relied on strong evidence was published in 2014 to enhance the sensitivity and specificity of the original RDC/TMD. The modified protocol was identified as the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD), and included new Axis-I assessment algorithms, and new Axis-II evaluation methods. The Axis-I assessment algorithms are combinations of different assessment tools like pain screeners, symptom questionnaires, clinical examination criteria using specific examiner’s commands and radiographic criteria. The results of the assessment tools are used to interpret a decision tree that leads to the diagnosis of a specific TMD class. The DC/TMD instruments proposed new nomenclature for different TMD classes, as it expanded to evolve new instruments on evaluating pain perspective, psychological standing and psychosocial behavior.

TMD referred pain has been described as a familiar pain that spreads to an anatomically distant location away from the boundaries of the muscle or joint being examined. Familiar pain is the pain that can be reproduced in response to clinical provocation and has been experienced by the patient in the same anatomical location for 30 days prior to the clinical setting. It is often challenging to the patient to identify the location of referred pain that spreads to deeper structures. Referred pain often complicates the diagnosis of TMD, as pain appears to originate from areas outside the anatomical boundaries of the joint and the associated muscles. In one study that compared the prevalences of comorbid headache, back, neck and joint pains in patients diagnosed with TMD in the United States, it has been reported that 0.77% of the studied population reported no comorbid pain, whereas 53% reported severe headache and migraine, 54% reported neck pain, 64% reported back pain and 62% reported joint pain. The close relationship between TMD, headache and neck pain was confirmed in another study that suggested that headache intensifies TMD pain. The information about the TMD referred pain is still however limited in the literature. Elaborating the prevalence and characteristics of referred pain associated with TMD will benefit the patients’ community as well as the medical professionals by facilitating the complex diagnostic process of these disorders.

The aim of this study was to assess the prevalence of referred pain associated with TMD diagnosed according to the DC/TMD in Sharjah, United Arab Emirates, to evaluate the characteristics of TMD referred pain, and investigate the correlations between the distribution of referred pain and the different TMD classes.
Methods
The study was performed at the College of Dental Medicine, University of Sharjah, United Arab Emirates, between February 2020 to June 2021. Ethical approval was granted by the Institutional Review Board at the University of Sharjah (REC-20-11-02-01-S). The ethical principles for medical research involving human subjects as mentioned in the Declaration of Helsinki were applied in this study. Sample size was calculated based on the formula $n = \left(\frac{z}{d}\right)^2 \frac{p(1-p)}{d^2}$, where $z$ = level of confidence according to the standard normal distribution, $p$ = estimated proportion of the population and $d$ = tolerated margin of error. Comprehensive TMJ clinical examination was performed for all patients during their preliminary screening procedures. All patients who were initially diagnosed as having signs and symptom of TMD were enlightened about the objectives of the study and were asked to sign consent forms before participation.

All subjects aged 18 to 60 years with signs and symptoms of TMD that were diagnosed during the initial examination were invited to participate in this study. The inclusion criteria involved all the signs and symptoms of TMD as clicking or crepitus sounds, TMJ pain, deviation in the path of mouth opening, catching sensation on opening or closure, limitation in mouth opening, headaches, ear pain and tenderness in the muscles of mastication. Patients were excluded from the study if they have been previously treated from TMD or if they had any systemic disease or used any medications that interfered with the perception of pain. Pregnant women were not enrolled in the study to prevent any detrimental effects from radiation. Patients were further evaluated using the DC/TMD validated assessment tools that included questionnaires, clinical examination, and radiographic examination. Helkimos clinical dysfunction index (Di) was utilized to identify patients with severe dysfunction symptoms (group Di III) and refer them for cone beam computed tomography (CBCT) examination. The diagnosis of disc displacement was endorsed by the use of magnetic resonance imaging.

DC/TMD questionnaires
The Axis-I assessment instruments used to evaluate all patients were the TMD Pain Screener, Symptom Questionnaire, and Demographic Questionnaire.

DC/TMD Axis I evaluation
Axis I-based clinical and radiographic examinations and structured diagnosis were carried out and included palpating the muscles of mastication and cervical muscles to diagnose the sites of tenderness or sustained contraction, auscultating, and palpating the joints during mandibular motion, observing the pattern of opening, and measuring the maximal mouth opening (pain free opening, maximum unassisted and assisted openings). Lateral excursions and the range of mandibular protrusion were also recorded. Pain level was assessed using the 10-point visual analogue scale (VAS) (0 indicating no pain and 10 indicating the most severe pain). The TMJ clinical evaluation was carried out by an oral and maxillofacial surgeon, who had over 15 years specialization in the management of TMDs. This examiner was blinded to the outcome of the initial screening procedure (performed by a general dental practitioner) as well as to any related outcomes that were evaluated in all questionnaires. Calibration of the examiners based on the DC/TMD protocol was accomplished before the start of the study by asking each examiner to assess the same 20 subjects independently. The results were then analyzed, and any disagreements were resolved through group discussion. Inter-rater reliability was measured using the intraclass correlation coefficients (ICCs). Radiographic evaluation was done by using CBCT for any suspected degenerative joint diseases, whereas MRI was conducted to evaluate suspected internal derangement. All CBCT assessments were performed using GALILEOS 3-D X-ray systems (SIRONA Dental Systems, York, PA), whereas MRI examinations were performed using a 1.5 Tesla machine (CHORUS 1.5 T, ISOL Technology, Gyeonggi-do, South Korea) with a TMJ surface coil. The joints were evaluated observing any disc displacement with any indication of recapture. MRI and CBCT records were analyzed twice, with a 1-week interval, by a specialist in oral radiology with 32 years of experience. The radiologist was blinded to the clinical evaluation outcomes. Intra-rater reliability was measured using the intraclass correlation coefficients (ICCs). TMD were then diagnosed and classified according to the DC/TMD Axis I criteria.

DC/TMD Axis II evaluation
Pain drawings, Graded Chronic Pain Scale (GCPG), disability score, muscle tenderness score and Jaw Functional Limitations Scale were used as assessment tools for DC/TMD Axis II evaluation. A diagram was given for the patients to illustrate and shade the area of pain and referred pain. GCPG was measured with a time frame of 30 days and classified by using the 10-point VAS. The disability scale assessed the pain related dysfunction while opening the mouth, while eating and after waking up, and was graded as no disability = 0 points, mild disability = 1 point, moderate disability = 2 points and severe disability = 3 points. The muscle tenderness assessments was graded as no tenderness = 0 points, mild tenderness = 1 point, moderate tenderness = 2 points and severe tenderness = 3 points. Functional Limitations Scale was measured by asking the patients if they develop any limitation during chewing hard food, wide opening, eating, yawning and talking. Back pain, neck pain, ear pain, dizziness and trouble sleeping were also evaluated. All patients were asked about their oral behavior in regard to clenching or grinding teeth while sleeping or when awake.
Treatment modalities for different TMD classes

Conservative therapy

Conservative therapy involved the use of stabilizing occlusal splints, soft diet, hot fomentation, limitation of mouth opening and non-steroidal anti-inflammatory drugs when needed. All patients were reevaluated postoperatively at 1, 3, and 6 months later to decide if any further treatment was required.

Prolotherapy

Prolotherapy was used for the treatment of patients with subluxation. The auriculo-temporal nerve was anaesthetized then 10% dextrose solution was injected at four locations. The first injection point was employed for the upper joint compartment, and the pericapsular tissues where the needle was inserted 10 mm anterior to the tragus and 2 mm below the canthal-tragus line. The needle was then directed anteromedially and 0.8 ml of the solution was injected intraarticularly. The needle was then withdrawn and 0.4 ml solution was injected into the pericapsular tissues. The second injection point was marked 2 mm below the canthal-tragus line and 1 cm in front of the mid-tragus and the needle was inserted at a depth of 3 mm from the skin surface targeting the superior capsular attachment and 0.4 mL of solution was deposited. Then the inferior capsular attachment was injected at the third injection point; 1 cm below the first one, and 0.4 mL of solution was applied. The forth injection point was placed anterior to the tragus and the needle was inserted to a depth of 20 mm to reach the posterior disc attachment and 0.4 mL of the solution was then applied.20

Arthrocentesis

The skin was prepared with povidone iodine then local anesthetic solution was injected to block the auriculo-temporal nerve. For the double-needle arthrocentesis technique; the location for the first needle puncture point was decided by marking the canthal-tragus line and marking the puncture point at either 10 mm or 7 mm anterior to the tragus depending on the canthal-tragus distance, and 2 mm under the canthal-tragus line. The second needle was inserted at a point 10 mm anterior to the first point and 10 mm under the line.21 The condyle was located and distracted downward and forward to widen the joint compartment and two 18-gage needles were inserted into each entry point. Single-needle arthrocentesis was done using a Y-shaped double-port cannula (Shepard cannula, Normed, Tuttingen, Germany). The location for insertion was identical to the first needle in the double-needle technique. The joints were irrigated with 300 mL normal saline followed by the articular injection of 1 mL of low-molecular-weight Hyaluronic Acid (HA) (Hyalgan®; Fidia, Abano Terme, Italy). TMJ physical exercise regimen started after the procedure and continued for one month. Splint therapy was provided, and all patients were reevaluated at 1 week, 1 month, 3 months, and 6 months.

Botulinum toxin (Botox) injection

Patients diagnosed with local myalgia and local myalgia with referral were treated by the injection of OnabotulinumtoxinA (BOTOX®, Allergan Inc., Dublin, Ireland) combined with conservative treatment. Trigger points in the masseter muscle were injected by a maximum of 35 units, whereas the trigger points in the temporalis muscle were injected by a maximum of 25 units. The patients were recalled for follow up after one week and then at 1 month, 3 months and 6 months. The injections were repeated after 3 months if needed.

Evaluation of referred pain associated with TMD

Referred pain was confirmed as being positive or negative using a bilateral manual palpation technique. Palpation was done at the following sites; temporalis muscle, masseter muscle, lateral pole of the TMJ, around lateral pole of the TMJ, posterior mandible, submandibular area, lateral pterygoid muscle area and tendon of the temporalis. The patients were asked to bite slightly and relax to ensure palpation of the correct muscle site. The result of the assessment was identified as positive if the site of the perceived pain in response to palpation had extended past the outline of the structure that was examined. For pain locations that were perceived as deep, patients were asked to locate the surface of the area of pain. In addition, the result of the assessment was identified as positive only if the patient described his perceived pain during the clinical examination as being familiar pain that was experienced in the same location in the last 30 days before the examination. The correlations between the presence of referred pain and the TMJ pain level, duration of TMJ pain, maximal mouth opening, muscle tenderness and disability scores were assessed. The evaluation of referred pain was repeated following the treatment in each follow up session. The location of referred pain was recorded for each patient as well as the pain characteristics that were described as dull, sharp and throbbing and heterogeneous pain (mixed intermittent dull and sharp throbbing).
Statistical analysis
Statistical analysis was performed using SPSS (version 20). Quantitative variables were described by the Mean, Standard Deviation (SD), Range (Minimum-Maximum), Standard Error (SE), and 95% confidence interval of the mean. Shapiro-Wilk test of normality was used to test the normality hypothesis of quantitative variables for further choice of appropriate parametric and non-parametric tests. Paired sample t-test was used for comparing pain levels at two-time points. Mann-Whitney U test was used for comparing mouth opening and duration between two groups. Qualitative categorical variables were described by proportions and Percentages. The $\chi^2$ test of independence was used to determine the association between the 2 categorical variables. Various measures of correlation were applied as appropriate including; Cramer’s V measure of association, Point-biserial correlation coefficient, Rank biserial correlation coefficient and Phi correlation coefficient. Pareto Analysis was applied followed by the application of a z-test of 2 proportions to detect any statistically significant differences between the proportions of two groups. Reliability was measured using the Bland-Altman analysis. The significance level was set at $P < 0.05$. Two-Tailed tests were assumed throughout the analysis for all statistical tests.

Results
In the present study, 252 patients (137 male and 115 female) with a mean age of 34.19 ± 10.85 were enrolled. Patients were mainly Asian (53.2%), followed by Whites (39.7%) and Others (7.1%). TMD were diagnosed in the left TMJ in 180 patients (71.4%), whereas the right TMJ was involved in 167 patients (66.3%). TMJ pain on one side was reported in 141 patients (56.0%), whereas bilateral TMJ pain was reported in 103 patients (40.9%). Anterior disc displacement with reduction was the most prevalent diagnosis (40.5%), followed by local myalgia (13.9%), anterior disc displacement without reduction with limited mouth opening (13.5%), myofascial pain with referral (11.5%), osteoarthritis (8.3%), hypermobility (6.0%), anterior disc displacement without reduction without limited mouth opening (5.2%) and disc displacement with reduction with intermittent locking (1.2%). Muscle tenderness was recorded on the masseter muscle in 76 patients (30.2%), in the temporalis muscle in 62 patients (24.6%) and in the lateral pterygoid muscle in 23 patients (9.1%). Excellent inter-rater and intra-rater reliability was achieved for the clinical and radiographic diagnosis respectively (ICC = 0.95-0.96). Axis II evaluation showed that 83.7% of patients had moderate to severe GCPG that interfered with their ability to work and with social activities, whereas 71.8% of patients had severe limitation according to the Jaw Functional Limitations Scale.
Referred pain was recorded in 153 patients (60.7%). The highest prevalence of referred pain was seen in the temporal area (45.2%), followed by the ear (42.1%), neck (19.0%) and forehead (17.5%) (Figure 1). The prevalence of referred pain felt at more than one location in the same patient was 46.43% (117 patients). Referred pain has been recorded at only one location in 36 patients (14.3%), two locations in 70 patients (27.8%) and three locations in 27 patients (10.7%). The highest prevalence of referred pain reported at two locations was at temporal and ear (32.9%), followed by temporal and forehead (12.7%) then ear and neck (11.5%). The most frequent pain characteristic reported in the current study was dull type pain in 107 patients (42.5%), followed by sharp and throbbing pain in 91 patients (36.1%) and the heterogeneous pain in 6 patients (2.4%).

The referred pain was recorded in disc displacement with reduction with intermittent locking and myofascial pain with referral in all patients (100%), in osteoarthritis in 19 patients (90.48%) and in hypermobility in 11 patients (73.33%) (Figure 2). The proportion of patients with referred pain was significantly different between the different DC/TMD diagnostic subgroups (P < 0.001). The Cramer’s V measure of association showed a strong strength association between the different diagnostic subgroups and the presence of referred pain (P < 0.001). Referred pain was recorded in anterior disc displacement with reduction in the temporal area in 35 patients (36.8%) and in the ear in 30 patients (31.6%). In anterior disc displacement without reduction with limited mouth opening, referred pain was recorded in the temporal in 20 patients (36.4%) and in the ear in 20 patients (36.4%). In myofascial pain with referral, referred pain was recorded in the temporal in 18 patients (29.0%) and in the ear in 18 patients (29.0%) (Table 1 and Figure 3). The correlation between the different TMD classes and the referred pain locations was not significant (P > 0.05). The Cramer’s V measure of association showed a weak association between the different TMD classes and the referred pain locations (P > 0.05). The TMJ pain level recorded in patients with referred pain (5.29 ± 2.65) was significantly higher compared to the pain level recorded in patients without referred pain (4.12 ± 2.74) (P < 0.001). The Point-biserial correlation coefficient showed a weak strength association between the presence of referred pain and the TMJ pain level (P < 0.001). The TMJ pain duration in patients with referred pain (28.71 ± 39.10) was significantly higher than in patients without referred pain (21.66 ± 29.27) (P < 0.05). The Point-biserial Correlation Coefficient showed a very weak strength association between the presence of referred pain and the duration of TMJ pain (P > 0.05). The mouth opening in patients with referred pain (30.46 ± 9.56) was significantly lower than the mouth opening in patients without referred pain (41.24 ± 8.04) (P < 0.05). The Point-biserial Correlation Coefficient showed a weak strength association between the mouth opening and the presence of referred pain (P < 0.05). The disability score in patients with referred pain was significantly higher than in patients without referred pain (P < 0.001). The Rank biserial correlation coefficient showed a moderate strength association between the presence of referred pain and the disability score.
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Referred pain locations</th>
<th>Pain character</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Temporal</td>
<td>Ear</td>
</tr>
<tr>
<td>Anterior disc displacement with reduction with intermittent locking</td>
<td>2(25.0%)</td>
<td>3(37.5%)</td>
</tr>
<tr>
<td>Myofascial pain with referral</td>
<td>18(29.0%)</td>
<td>18(29.0%)</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>19(34.5%)</td>
<td>19(34.5%)</td>
</tr>
<tr>
<td>Hypermobility</td>
<td>6(26.1%)</td>
<td>6(26.1%)</td>
</tr>
<tr>
<td>Anterior disc displacement without reduction without limited mouth opening</td>
<td>5(29.4%)</td>
<td>5(29.4%)</td>
</tr>
<tr>
<td>Anterior disc displacement without reduction with limited mouth opening</td>
<td>20(36.4%)</td>
<td>20(36.4%)</td>
</tr>
<tr>
<td>Anterior disc displacement with reduction</td>
<td>35(36.8%)</td>
<td>30(31.6%)</td>
</tr>
<tr>
<td>Total</td>
<td>105(33.33%)</td>
<td>101(32.1%)</td>
</tr>
</tbody>
</table>
The correlation between the masseter muscle and temporalis muscle tenderness and the presence of referred pain was significant ($P < 0.001$).

In anterior disc displacement with reduction, dull referred pain was reported in 41 patients (40.2%), sharp and throbbing referred pain was reported in 24 patients (23.5%) and heterogeneous referred pain was reported in 2 patients (1%). In anterior disc displacement with reduction with intermittent locking, dull referred pain was reported in 2 patients (66.7%) and sharp and throbbing referred pain was reported in 1 patient (33.3%) (Table 1). The Cramer’s V Measure of Association showed a moderate strength association between pain character and different DC/TMD diagnoses ($P < 0.001$).

In the present study, 198 patients (78.6%) received the required treatment for their TMD. Following treatment, 83 patients (62.4%) reported improvement of their referred pain (Figure 4). The referred pain level significantly decreased following treatment at 3 months ($P < 0.001$), and at 6 months ($P < 0.001$).
Discussion
The referred pain often complicates the diagnosis of TMD and may lead to progression to advanced forms of the disorders before the proper diagnosis is reached. Referred pain is mainly due to the visceral and somatic senses that have been carried to the brain through the same neurons, accordingly patients are not capable to localize the origin of the pain. The convergence projection theory stated that the sensory information travel to the central nervous system (CNS) through nerves that converge to neurons. The number of neurons is less than the number of nerves so the information from multiple nerves has to converge to a less number of neurons to be carried to the CNS. The convergence appears at the level of the neurons that transmit impulses from deep structures like teeth pulp, joints, and muscles rather than from superficial structures. The neurons that originate from the TMJ and the masseter muscle appear mainly to converge in the trigeminal subnucleus caudalis. This theory elucidates the difficulty in localizing the pain which originates from the TMJ and the associated muscles and leads to referred pain away from the pain origin site.22 The central sensitization theory also explains the referred pain mechanism through the continuous painful stimulus that can lead to the activation of distinct receptors that expand the sensitivity of neurons, thus widening the receptive field area. This changes the normal processing at the higher centers and causes nonpainful information to be perceived as painful.23 The studies concerned with the TMD-associated referred pain are limited in the literature.

In the present study, the prevalence of referred pain in patients diagnosed with TMD was 60.7%. Another study showed a lower prevalence of referred pain (26.4%), where the locations of referred pain were classified into extraoral, intraoral, and joint sites. According to this study, the TMD referred pain was diagnosed at the temporalis muscle (9.6%), masseter muscle (14.3%) and at the mandibular area (8.6%) whereas the joint area was involved in 7.5%.24 The study was based on the RDC/TMD Validation and TMD Impact studies, whereas the present study was based on the modified DC/TMD classification that imposed new pain definitions and localization protocols. In the present study, the referred pain was recorded most commonly in the temporal area (45.2%) followed by the ear (42.1%) then the neck (19.0%). In another study, the TMD referred pain was reported most commonly in the cheek region followed by the ear and the forehead. The author of the study concluded that the pattern of TMD referred pain was consistent and predictable, which agrees to our study.22 Another study reported the prevalence of referred TMD pain in the ear as 51.3%, which is in accordance with our results.13,25

The evaluation of the prevalence of referred pain in different DC/TMD classes has shown that the most common location for referred pain in anterior disc displacement with reduction was in the temporal area (36.8%), in anterior disc displacement with reduction with intermittent locking was in the ear (37.5%), in anterior disc displacement without reduction with limited mouth opening was in the temporal area and the ear equally (36.4%) and in anterior disc displacement without reduction without limited mouth opening was in the temporal area and in the ear equally (29.4%). Referred pain was recorded in the ear and in the temporal area equally in hypermobility (26.1%), and in myofascial pain with referral (29.0%). These results are expected to facilitate the complex diagnostic processes of TMD by elaborating the possible pathways of referred pain related to each DC/TMD class.

In the present study, the association between referred pain and mouth opening was found to be weak. This result was not in accordance with another study that showed strong association between the mouth opening and referred pain in patients with TMD-related migraine.26 There was a weak association in our study between temporalis muscle and masseter muscle tenderness and referred pain, and there was no association between lateral pterygoid muscle tenderness and referred pain. It has been shown that the presence of TMD-associated headaches in patients with myofascial pain does not negatively affect the treatment of pain; however it might change the pattern of pain improvement after the proper management.27

The significant reduction in referred pain levels following different forms of treatment confirms that TMD was the cause of referred pain. Similar results were reported in another study that showed a reduction in the disability scores and referred pain levels following TMD treatment.26

In the present study, the TMD referred pain characteristics were reported as dull pain in 42.5% of patients and as sharp and throbbing pain in 36.2% of patients. In another study, the TMD-related referred pain in the ear was described as severe and unbearable pain in 31.03% of patients, and as mild and bearable pain in 68.97% of patients.25 The inconsistency in describing orofacial pain characteristics among various studies may negatively affect the scientific value of these studies. The authors of the present study recommend the unifying of the pain descriptive terms in different studies to maximize the benefit to the scientific community when comparing the results of these studies.
The main limitation of this study was the small sample size. Therefore, the presented data should be interpreted with caution. However, considering the high prevalence of TMD, the findings of this study might encourage the pursuing of future studies with larger sample sizes.

In conclusion, referred pain is a prominent feature of TMD. The prevalence of referred pain associated with TMD was 60.7%. The most common referred pain location was the temporal area, followed by the ear. Anterior disc displacement with reduction with intermittent locking and myofascial pain with referral were the most common diagnoses associated with referred pain. There was a strong strength association between the different diagnostic subgroups and the presence of referred pain, a moderate strength association between the pain character and the diagnostic subgroups, whereas a weak association was found between the diagnostic subgroups and the referred pain locations. Following treatment, 62.4% of patients reported improvement of their referred pain levels. More studies are required with longer follow-up periods and bigger sample sizes to support the findings of the present study that are expected to significantly improve the diagnostic processes of TMD.

Disclosures
This study is a part of a thesis submitted for partial fulfillment of the requirements of the Masters of Science Degree in Oral Surgery.

Ethical approval
Research Ethics Committee, University of Sharjah.

Consent
Written informed consent for publication of the participants/patients’ details and/or their images was obtained from the participants/patients/parents/guardian/relative of the participant/patient.

Data availability
Repository: Harvard Dataverse: “Replication Data for: Prevalence and characteristics of referred pain in patients diagnosed with temporomandibular disorders according to the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD)”, https://doi.org/10.7910/DVN/GXTCDR

This project contains the following underlying data:

- Data file 1. (Raw date used for assessment of the prevalence and evaluation of the characteristics of referred pain associated with temporomandibular disorders that are diagnosed according to the DC/TMD.)

Data are available under the terms of the Creative Commons “No rights reserved” data waiver (CC0 1.0 Public domain dedication).

References

Open Peer Review

Current Peer Review Status: ? ✓

Version 1

Reviewer Report 17 August 2022

https://doi.org/10.5256/f1000research.121234.r140855

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The submitted manuscript wishes to report the “Prevalence and characteristics of referred pain in patients diagnosed with temporomandibular disorders according to the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD)”. The topic is of interest however at first reading some modifications maybe required to improve the quality of the manuscript. A proper rationale for the outlined hypothesis is not feasible without providing details of the demographic information of the included sample. In addition, authors should mention details of their inclusion and exclusion criteria. It will be surprising if the sample included for examples medically compromised patients who suffer from systematic diseases, on medications, previous surgery or TMJ problems, or diagnosed with bone diseases or osteoporosis.

The reviewer is also wondering whether the case diagnosis, evaluation, and data recording were done by only one investigator and whether the investigators had checked for intra- or inter-rater reliability.

It will also be very useful to the readers if the authors included the power of study analysis or sample size calculation.

Is the work clearly and accurately presented and does it cite the current literature? Yes

Is the study design appropriate and is the work technically sound? Yes

Are sufficient details of methods and analysis provided to allow replication by others? Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Yes

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Orthodontics, 3D imaging, Airway Analysis, Obstructive Sleep Apnea (OSA), Virtual Reality (VR), Augmented Reality (AR), and Artificial Intelligence (AI)

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 02 Sep 2022

Wael Talaat, University of Sharjah, Sharjah, United Arab Emirates

Response to Reviewer 2: Ahmed Ghoneima
The authors would like to express their gratitude for the reviewer for his constructive comments. We are hereby providing a point by point response.

Comment 1:
A proper rationale for the outlined hypothesis is not feasible without providing details of the demographic information of the included sample.
Response:
More demographic details were added in the results section.

Comment 2:
Authors should mention details of their inclusion and exclusion criteria.
Response:
The inclusion and exclusion criteria were elaborated in the Methods Section.

Comment 3:
The reviewer is also wondering whether the case diagnosis, evaluation, and data recording were done by only one investigator and whether the investigators had checked for intra- or inter-rater reliability.
Response:
The TMJ clinical evaluation was carried out by two examiners; an oral and maxillofacial surgeon and a general dental practitioner who did the initial screening. The surgeon was blinded to the outcome of the initial screening procedure as well as to any related outcomes that were evaluated in all questionnaires. Calibration of the examiners based on the DC/TMD protocol was accomplished before the start of the study by asking each examiner to assess the same 20 subjects independently. The results were then analyzed, and any disagreements were resolved through group discussion. Inter-rater reliability was measured using the intraclass correlation coefficients (ICCs). The radiographic evaluations
were analyzed twice, with a 1-week interval, by one specialist in oral radiology. The radiologist was blinded to the clinical evaluation outcomes. Intra-rater reliability was measured using the intraclass correlation coefficients (ICCs). Excellent inter-rater and intra-rater reliability was achieved for the clinical and radiographic diagnosis respectively (ICC=0.95-0.96).

Comment 4:  
It will also be very useful to the readers if the authors included the power of study analysis or sample size calculation.  
Response:  
The formula used for the sample size calculation was added to the Methods Section.  

**Competing Interests:** No competing interests were disclosed.
Please arrange the diagnosis to be the same for figures and tables.

Tables
- Table 1 - mention n(%) in one cell instead of two.
- Figure 3 is not clear, it would be better to remove the figure to avoid confusion.
- Combine table 1 and 2.

Discussion & Conclusion
- First part of the discussion should be in the introduction.
- You need to cite more papers in the discussion unless the information provided is new and has not been conducted in this case state that this clearly.
- Limitations of the study should be stated before conclusion.
- Please re-write your conclusion based on your results.

Is the work clearly and accurately presented and does it cite the current literature?
Partly

Is the study design appropriate and is the work technically sound?
Partly

Are sufficient details of methods and analysis provided to allow replication by others?
Partly

If applicable, is the statistical analysis and its interpretation appropriate?
Partly

Are all the source data underlying the results available to ensure full reproducibility?
Partly

Are the conclusions drawn adequately supported by the results?
Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Dental Public Health

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 02 Sep 2022
Wael Talaat, University of Sharjah, Sharjah, United Arab Emirates
Response to Reviewer 1: Khalifa Sulaiman Al-Khalifa

The authors would like to express their gratitude for the reviewer for his constructive comments. We are hereby providing a point by point response.

Comment 1:
Title: The study was conducted in Sharjah, UAE - this needs to be reflected in the title and aim of your study.
Response: It has been indicated in the title and aim that the study was conducted in Sharjah, United Arab Emirates.

Comment 2:
Introduction: No prevalence studies in the introduction.
Response: The related prevalence studies were added in the introduction.

Comment 3:
Explain Axis-I assessment algorithms for the reader.
Response: Axis-I assessment algorithms have been explained in the Introduction Section.

Comment 4:
Where is the reference for Helkimos clinical dysfunction index?
Response: The reference was added in the Methods Section.

Comment 5:
All instruments used - you need to use references. The author needs to cite all instruments used in the study.
Response: The missing citations were added in the Methods Section.

Comment 6:
Are the tools used in the study validated?
Response: Yes, only validated tools were used in this study. An indication was added in the Methods Section.

Comment 7:
What is the gold standard for TMD?
Response: The DC/TMD (Schiffman E, et al, 2014) is an objective and reliable diagnostic protocol that uses several validated assessment tools with high sensitivity and specificity. Magnetic resonance imaging is usually required to diagnose soft tissue disorders whereas cone beam computed tomography is needed to evaluate the bony changes.

Comment 8:
Spelling mistakes e.g., month vs mouth.
Response: 
The spelling mistakes were corrected.

Comment 9:
Please arrange the diagnosis to be the same for figures and tables.
Response:
The diagnosis was arranged to be the same for figures and tables.

Comment 10:
Table 1 - mention n(%) in one cell instead of two.
Response:
Table 1 was modified and n(%) was mentioned in the same cell.

Comment 11:
Figure 3 is not clear, it would be better to remove the figure to avoid confusion.
Response:
Figure 3 was modified so that it is clearer to the reader.

Comment 12:
Combine table 1 and 2.
Response:
Tables 1 and 2 were combined in one table (table 1).

Comment 13:
First part of the discussion should be in the introduction.
Response:
The authors totally understand and value the comment of the reviewer. In the Introduction Section, the authors define the TMD referred pain as described by the DC/TMD and explain the reason why this type of pain often complicates the diagnosis of TMD. In the discussion section, the authors explain the neuroanatomic and physiologic theories of the referred pain.

Comment 14:
You need to cite more papers in the discussion unless the information provided is new and has not been conducted in this case state that this clearly.
Response:
Although many studies evaluated the pain associated with the different classes of TMD, a limited number of studies were concerned with the TMD-associated referred pain. This was elaborated in the first paragraph in the Discussion Section.

Comment 15:
Limitations of the study should be stated before conclusion.
Response:
The limitations of the study were added before the conclusions.

Comment 16:
Please re-write your conclusion based on your results.
Response:
The conclusions were re-written based on the results.

**Competing Interests:** No competing interests were disclosed.

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