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A Comparative Evaluation of Malocclusion and Associated Risk Factors in Patients Suffering with Temporomandibular Disorders: A Systematic Review and Meta-analysis of Observational Studies

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Abstract

An association of malocclusion as potent risk factor to temporomandibular disorders (TMDs) has been under question since ages. A systematic review and meta-analysis of case–control and cohort studies was performed following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses)guidelines to compare the prevalence of TMDs in subjects with malocclusion to patients with normocclusion. The study was registered on the PROSPERO database (identifier: CRD42022315863). An elaborate electronic database (PubMed, DOAJ, and Google Scholar) and manual search resulted in 325 articles, among which 7 and 3 articles were shortlisted for qualitative and quantitative review, respectively, for articles published from January 2000 until December 2021. A total of 4,183 participants were included in this review with age range of 5 to 75 years. New–Castle Ottawa tool was employed for quality assessment, while I^2 statistical value for meta-analysis was interpreted in accordance with the Cochrane Handbook for Systematic Reviews of Interventions. Fixed effect model was applied as, $I^2 = 0$. Pooled odds ratio with 95% confidence interval for all three studies was 14.64 [4.43, 48.36] suggesting that TMDs were 14.64 times more associated in patients with malocclusion (cases) than patients without malocclusion (controls). Within the limitations and fair quality of evidence of the current review and analysis, TMDs and associated symptoms are more prevalent in patients with malocclusion with or without more associated factors.

Keywords
- malocclusion
- meta-analysis
- systematic review
- temporomandibular disorders
- temporomandibular joint

Introduction

Temporomandibular disorders (TMDs) are a group of disorders that affect the masticatory muscles, the temporomandibular joints (TMJ), and associated tissues accompanied by joint and muscle pain, abnormal joint sounds, and mandibular dysfunction.[1,2] TMD has a complex etiology ranging from biomechanical, biopsychosocial, neurobiological, and neuromuscular factors. These factors are classified as predisposing conditions, initiating, and aggravating.[2–4] Risk factors such as

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sex, age, stress, depression, trauma, certain dental treatments, and parafunctional habits are known to cause TMJ pathologies.[3,4]

There is a link between malocclusion and TMD since years, yet it has never been scientifically concluded as different parameters present different results.[5] The significance of dental occlusion in TMD development is currently unknown and is still debatable.[4,5] Indeed, the results of studies evaluating the association between the development of TMD and malocclusion diverge.[1,6–10]

But why is this correlation important? Appropriate therapy cannot be commenced unless the correct diagnosis is established. The clinician's essential job is to detect the type of occlusal parameter strongly correlated with TMD.[6] It will aid in detailing the etiology of TMDs.

Many occlusal parameters have been evaluated in the current study to study and establish them as predisposing factors to TMD.

The objective was to conduct a systematic review and meta-analysis of case–control and cohort studies to comparatively evaluate the malocclusion traits to normal occlusion and predict their cause to effect relationship to the TMJ disorders.

Methods

A systematic review and meta-analysis of observational studies was performed to evaluate the correlation of TMDs in patients with normo-occlusion and malocclusion. This study followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses, 2020) guidelines, the Cochrane Handbook for systematic reviews of interventions, version 5.1.0. and 4th edition of the JBI reviewer's manual.[11,12] This study was registered on the PROSPERO database (identifier: CRD42022315863).

Search Strategy

Studies were selected based on the PECOS (population, exposure, comparison, outcome and study design) inclusion criteria in the review protocol. Three independent reviewers (TA, AS, and GI) assessed titles and abstracts to identify potentially eligible studies. Any queries were discussed with a fourth reviewer (MA). The exposure was malocclusion while outcome was the presence of TMDs. The electronic data resources consulted for elaborate search were PubMed, DOAJ, and Google Scholar with controlled vocabulary and free text terms (►**Table 1**). Apart from the electronic databases, a manual search of the references of the relevant articles was done. Articles published from January 1, 2000, until December 1, 2021 were searched, without any restriction concerning the publication's language (Google Translate was used for translation).

Following keywords and MeSH terms were used in combination with Boolean operators in the advanced search option.

Search Strategy in PubMed

("malocclusion, angle class i"[MeSH Terms] OR ("malocclusion"[All Fields] AND "angle"[All Fields] AND "class"[All Fields] AND "ii"[All Fields]) OR "angle class ii malocclusion"[All Fields] OR ("class"[All Fields] AND "ii"[All Fields] AND "malocclusion"[All Fields]) OR "class ii malocclusion"[All Fields]) AND ("temporomandibular joint disorders"[MeSH Terms] OR ("temporomandibular"[All Fields] AND "joint"[All Fields] AND "disorders"[All Fields]) OR "temporomandibular joint disorders"[All Fields] OR ("temporomandibular"[All Fields] AND "disorders"[All Fields]) OR "temporomandibular disorders"[All Fields])) AND ("case-control studies"[MeSH Terms] OR ("case-control"[All Fields] AND "studies"[All Fields]) OR "case-control studies"[All Fields] OR ("case"[All Fields] AND "control"[All Fields] AND "study"[All Fields]) OR "case control study"[All Fields])) AND ("adult"[MeSH Terms] OR "adult"[All Fields] OR "adults"[All Fields])

Entry terms in Google Scholar:
Malocclusion
Temporomandibular disorders

Selection of Studies

The title and the abstract of each study were reviewed and critically assessed by three reviewers. Any disagreement was solved by the fourth reviewer. The integration of the searched outcomes was accomplished by deleting the duplicate entries. Recovery of the full text of potentially relevant articles was completed to examine and verify the degree of compliance that the studies had with the eligibility criteria. The inclusion and exclusion criteria assessed for the final decision was as follows:

Eligibility Criteria

1. Inclusion criteria
   - Population: Studies including patients with one or more symptoms of TMDs such as pain, clicking, deviation, tenderness, and palpation.

Table 1 Terms imported in the search strategy

Population	Exposure	Comparison	Outcome	Study design
Adult, adolescents, children, child	Class I, Class II, Class III, anterior open bite, anterior deep bite, increased overjet, increased overbite	Without exposure No malocclusion	Temporomandibular disorders, temporomandibular joint pain, clicking, deviation,	Case–control, cohort

- Exposure: Studies including patients with malocclusion, i.e., Class I malocclusion, Class I with anterior open bite, Class I with anterior deep bite, Class II malocclusion, and Class III malocclusion.
- Comparison: Studies comparing patients with and without the exposure.
- Outcome: Studies providing information about the prevalence of malocclusion in patients with TMDs, odds ratio, and risk ratio.
- Study design: Studies with case control and cohort designs.

2. Exclusion criteria
   - Studies involving patients not providing informed consent.
   - Studies with study design other than case–control and cohort.
   - Review reports, case series, in-vitro and animal studies will be excluded.
   - Studies providing only abstract and not full text.

Risk of bias of retrieved studies

Quality assessment of included studies was done using the New–Castle Ottawa tool for case–control and cohort studies.[13] This tool contains three domains, namely, Selection, Comparability, Outcome or Exposure.

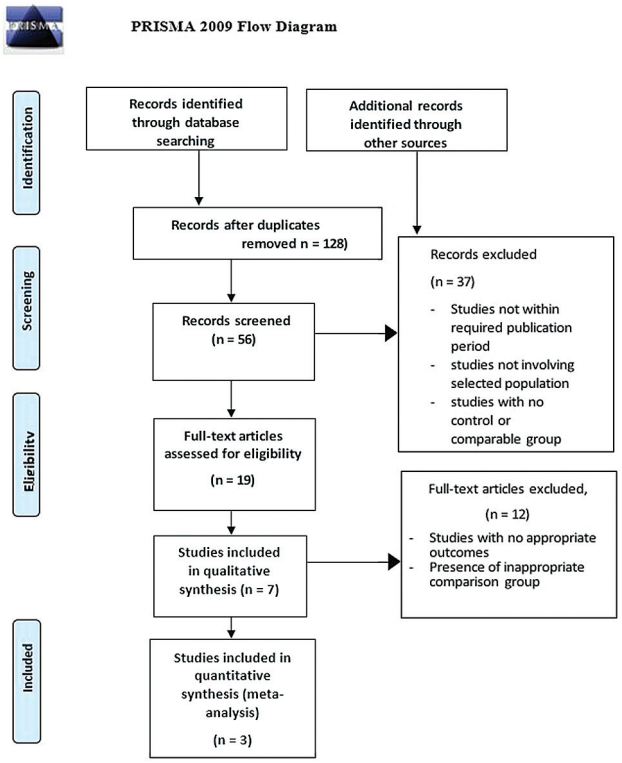

Fig. 1 PRISMA flow chart. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analyses.

Results

Study Selection

The initial electronic database search on PubMed/Medline, Directory of Open Access Journals (DOAJ), and Google Scholar, and manual search resulted in 325 titles. One hundred twenty-eight articles were cited as duplicates. After screening the abstracts, 19 relevant titles were selected by three independent reviewers, and 37 were excluded for not being related to the topic. Following examination and discussion by the reviewers, 19 articles were selected for full-text evaluation. Hand searching of the reference lists of the selected studies did not deliver additional papers. After prescreening, application of the inclusion and exclusion criteria and handling of the PECO questions, seven studies were shortlisted and included in the qualitative synthesis, which were subjected for data extraction and statistical analysis. Out of these seven studies, three were included for meta-analysis, which was conducted using the Review Manager version 5.3 software. ►**Fig. 1** gives detailed study selection process.

Data Extraction

After narrowing down to the articles from all the databases, a verification list of all items for data extraction was made. The data were tabulated under the following contents- authors, year and title of study, place of study, study design, sample size, age group of participants, gender, prevalence of TMDs, odds ratio, risk ratio, and conclusion of study.

Details regarding the publication and the study, participants, settings, interventions, comparators, outcome measures, study design, statistical analysis, and results, and all other relevant data (funding, conflict of interest, etc.) were carefully and accurately extracted from all included studies. Data extraction was done and accurately recorded in the excel sheets for all primary outcomes separately.

Study characteristics

Seven studies were selected for qualitative synthesis whose general characteristics are presented in ►**Table 2**.[14–19] The study designs for all included studies were analytical studies: case–control and cohort. A total of 4,183 participants were included in this review with age range of 5 to 75 years. The prevalence of malocclusion was the highest in case group as compared with control group for all included studies.

Risk of Bias Applicability

Quality assessment of included studies was done using the New Castle Ottawa tool[8] for case–control and cohort studies as mentioned in ►**Table 3** and ►**Table 4**, respectively. The domains and scoring criteria for both the tools was same; however, the questions under the domains were different for both the tools.

Among the case–control studies,[6,16–19] three studies were showed a good risk of bias, two were fair and one was poor. The main domain responsible for poor risk of bias was the Selection domain.

Two studies[14,15] with cohort study design showed good risk of bias applicability.

Meta-analysis

Three studies[16,18,19] gave comparable values of odds ratio for quantitative synthesis and less heterogeneity compared with

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Table 2 Characteristics of included studies

Sr. No.	Study Id	Place of study	Study design	Sample size	Age (y)	Method of data collection	Prevalence of malocclusion In case group	Prevalence of malocclusion In control group	Odds ratio
1	Henrikson and Nilner (2003)[14]	Sweden	Cohort	118	–	Clinical examination at each visit	100%	30%	–
2	Mohlin et al (2004)[15]	The United Kingdom	Cohort	1018	11–19	Plaster casts, past records	>50%	–	–
3	Lambourne et al (2007)[16]	The United States	Case control	100	8–16	Plaster casts, past records	60%	36%	9.35
4	Paolo et al (2013)[17]	Italy	Case control	2375	5–70	Retrospectively from medical records	25.5	–	–
5	Haralur (2017)[6]	India	Case control	100	18–35	Occlusal analysis using T-scan	66%	34%	–
6	Mélou et al (2021)[18]	France	Case control	114	Case: 18–73 Control: 21–75	Interviews, medical records	100	96	11.95
7	Zúñiga-Herrera et al (2021)[19]	Mexico	Case control	358	25.26 ± 11.79	Research diagnostic data for TMD	48.04	–	19.85

Table 3 Risk of bias applicability according to New Castle–Ottawa tool for case–control studies

Study Id	Selection				Comparability		Outcome			Total score	Quality
	Case definition	Representativeness of case	Selection of controls	Definition of controls	Main factor	Additional factor	Ascertainment of exposure	Same method of ascertainment for cases and controls	Non-response rate		
Lambourne et al (2006)[16]	*	*	–	*	*	–	*	*		7	Good
Paolo et al (2013)[17]	*	–	–	*	*	–	*	*	*	6	Fair
Haralur 2017[6]	*	*	*	*	*	–	*	*	*	8	Good
Mélou et al (2021) 2021[18]	*	–	–	–	*	–	*	*	–	4	Poor
Zúñiga-Herrera et al (2021)[19]	*	*	*	*	*	–	*	*	*	8	Good

Table 4 Risk of bias applicability according to Newcastle–Ottawa tool for cohort studies

Study Id	Selection					Comparability		Outcome			Total score	Quality
	Representativeness of cohort	Selection of non-exposed cohort	Ascertainment of exposure	Outcome of interest present at start of study		Main factor	Additional factor	Assessment of outcome	Was follow-up enough	Loss to follow-up		
Henrikson and Nilner (2003)[14]	*	*	*	*		*	—	*	*	*	8	Good
Mohlin et al (2004)[15]	*	—	*	*		*	—	*	*	*	7	Good

other included studies. Hence, these were included in meta-analysis. The statistic test used to quantify the inconsistence between studies was the I^2. It was interpreted in accordance with the Cochrane Handbook for Systematic Reviews of Interventions. I^2 value was less than 50% hence fixed effect model was applied.

Effect sizes

Effect sizes refer to quantitative indicators of the direction and magnitude of effects of the interventions on outcomes. Odds ratio with 95% confidence interval and the number of participants in each group were used.

Three studies were included in the meta-analysis. The pooled odds ratio (►**Fig. 2**) for all three studies was 14.64 [4.43, 48.36], suggesting that TMDs were 14.64 times more associated in patients with malocclusion (cases) than patients without malocclusion (controls).

Heterogeneity

Among the different statistical approaches for investigating heterogeneity, the standard Chi-squared test, the I^2 statistic, and Tau-squared were used in this meta-analysis.

If $I^2 = 0\%$, this indicates that all variabilities in effect size estimates is due to sampling error within studies. If $I^2 = 50\%$, it indicates that half of the total variability among effect sizes is caused not by sampling error, but by true heterogeneity between studies. I^2 is a percentage and its values lie between 0% and 100% according to Higgins et al.[20] A value of 0% indicates no observed heterogeneity, and larger values show increasing heterogeneity.[20]

Discussion

In the current study, the association of occlusal parameters between individuals having malocclusion and normocclusion was done. These were comparatively evaluated for prevalence of TMD.

A prospective study by Henrikson et al[14] concluded a general prevalence of TMDs bending toward subjects having class II malocclusion compared with the normal group. Supporting this, the study also suggested that patients who underwent orthodontic treatment suffered from decreased prevalence of masticatory muscle tenderness after a period of 2 years. This result suggested that the type of occlusion plays a pivotal role in advancement of TMJ disorders that is in agreement to the meta-analytical result. However, Henrikson et al[14] have not quantified these factors. Eriksson and Rönnerman[21] suggested that the decrease in muscle tenderness was due to a decreased muscle function during orthodontic tooth movement because of tender teeth. Therefore, he concluded in this study that there was a decrease in the prevalence of tenderness of TMJ due to the altered activity of masticatory muscles during orthodontic movement. Orthodontic treatment achieved harmony in the TMJ during functional movements due to minimal interferences as opposed to malocclusion, which preceded the orthodontic treatment.[21,22]

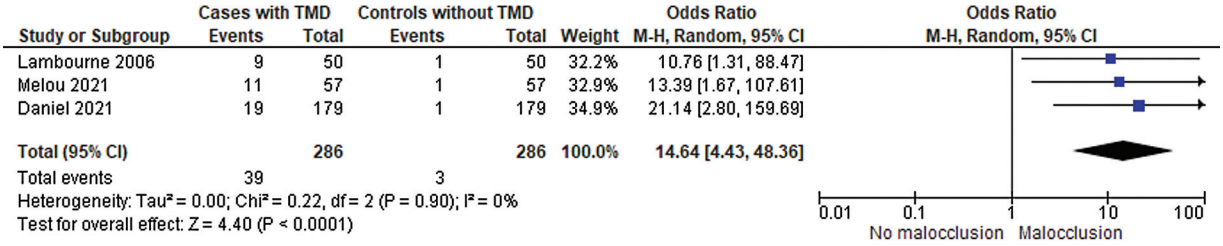

Fig. 2 Forest plot for quantitative analysis of included observational studies.

Over a period of 3 years, notable fluctuations were observed in TMJ clicking. Because this was detected in all three groups in the current study, it could be concluded that the malocclusion did not influence the presence of clicking.[14] A previous study by Brooke et al[23] stated that TMJ clicking is progressive in coherence to the finding of this study. Magnasson et al[24] support this evidence, suggesting TMJ clicking over a period of 2 years increased through childhood to adolescents, to higher prevalence in adults. Therefore, collective evidence suggested that clicking may spontaneously appear and disappear without necessarily associating with other TMJ anomalies.[24–28] No evidence regarding this finding is present in the classic literature, and more studies must be performed to substantiate the same.

Evidence-based research suggests a strong association of TMD with occlusal interferences.[29] Researchers have proven occlusal disturbances to cause orthopaedic instability of TMJ and hyperactivity of masticatory muscles causing TMD.[30] Haralur et al[6] presented their study, in which occlusal parameters were evaluated by both conventional and digital methods to understand the risk factors leading to TMD. Results concluded that subjects in positive TMD group (group II) had group-function occlusion (66.0%), while Group I control group had predominantly canine-guided occlusion. Canine-guided occlusion has shown its superiority over group function in significantly reducing load on joint structures and subsequent permanent structural damage.[6] Akoren et al[31] suggested that this may occur as canine-guided occlusion disoccludes the posteriors during excursive movements. This helps to minimize muscle activity and alleviate the load off the joints.

According to Donegan et al,[32] the prevalence of canine guidance in nonpatients and symptomatic patients was 30 and 22%, respectively. However, Kahn et al[33] presented conflicting results to the present study depicting that no predominance of canine-guided occlusal scheme in symptomatic patients. Thus, it can be assumed that no single occlusal feature is the etiologic factor in the development of TMD.

Within a 2-year prospective cohort, a case–control study by Marklund et al,[34] the 2-year cumulative incidence, and duration of TMD symptoms increased due to self-reported bruxism and crossbite. In their study population, cases with TMJ signs or symptoms mainly comprised those reporting TMJ clicking sounds and cases with myofascial symptoms. Crossbite presented as a morphological factor in occlusion related to both the incidence and persistence of TMJ dysfunction in comparison to neutral transversal relationships.[34,35]

Discrepancies in the intercuspal position (ICP) were considered a risk factor for mandibular instability. Therefore, patients with ICP in either anterior segment/unilaterally or bilaterally were linked to the persistence of TMJ and masticatory muscle disorder. The former situation is a potential class III, and the latter a class II lever. The prevalence of TMD in both can be explained by an increased intra-articular pressure on the TMJ. The observation to be emphasized upon was that the negative predictive value was high. This indicated that the lowest risk of TMD was seen in stable ICP.[34]

In an experimental study by Kuboki et al,[36] it was established that a class II lever situation caused a frontal rotation of the mandible. This may be an etiological factor for TMD due to a calculated increased pressure on the TMJ.

Mohlin et al[15] supported Henrikson's[14] findings that patients who had received orthodontic treatment were less severely affected by TMD. However, the effect of orthodontic therapy on clicking and locking of the TMJ varies largely among studies.[37–43] It was proposed that the difference in population sample age and quality of treatment may be causative reasons.

It has been proposed that more extended head posture is seen in Angle Class II cases.[44] A few studies showed an association of large overjet in Class II patients to TM joint disc displacement. Sagittal discrepancies in malocclusion such as Class III bilateral crossbite patients has found an association to TMDs in the literature.[44–47]

Deep bite has been witnessed mostly in cases with anterior growth rotation, and a greater muscular strength is seen in this category of craniofacial morphology. An interesting observation was made in subjects of TMD regarding the prevalence of deep bite.[15] Increased muscular strength of deep bite patients may have led to a higher prevalence of TMD, thus establishing an association of malocclusion to the TMJ.[48]

Women in greater numbers than men showed a tendency toward the development of muscle pain and fatigue when clinically assessed. It was supported by the tendency of women to reach their maximal bite force easily, signaling periodontal receptor overload. On the contrary, men hesitated to use their full bite capacity.[49] Men may use less than 50% of their maximal bite force in general, and cause versus effect is difficult to contemplate.[49] Nilsson et al[50] found that the incidences of limited mandibular function and overall force impact were found to be significantly higher on the TMJ in

women than in men. The paucity of definitive conclusions, and a higher rate among women may occur as a result of biological, psychological, hormonal, and physical factors and more research needs to be conducted in this regard.

Daniel et al[19] performed a case–control study and demonstrated a strong association between TMD signs and symptoms and malocclusion complexity. A critical outcome of their analysis showed 80% of the study participants with TMD had high malocclusion complexity values. These two variables were directly proportional, i.e., increasing malocclusion complexity posed the highest risk for developing TMD (OR = 19.85). Mohlin et al[15] in their study supported this evidence comparing patients with TMD signs and symptoms to controls, and concluded that the PAR index of malocclusion severity appeared to be the highest in most severe TMJ dysfunctions. Paolo et al[17] debated that TMD dysfunction poses a threat for some headache development forms (probably tensive type) and vice versa. Both Lambourne and Daniel suggested that a combination of factors such as posterior crossbite and > 5 mm overbite alone are associated with an increased risk of headache and as reviewed in the literature, such patients are directly or indirectly affected with TMDs.[16,19] Some studies that disagree to an association of malocclusion with TMD symptomatology are based on the evaluation of individual traits rather than combined.[5,51] This could explain the inconsistency of results.

There is substantial scientific evidence that malocclusion adversely effects the quality of life (QOL) in terms of psychosocial well-being of a patient.[51–54] In addition, the correction of misaligned teeth with orthodontic therapy was beneficial on the QOL.[52,53] The psychological wellness and psychosocial satisfaction degrade probably due to the disparity in normal mastication, speech, and appearance. It may cause social anxiety that indirectly leads to joint and muscular pain. This sets the onset of chronic development of TMJ dysfunction with a complex etiology, wherein each and every trait mentioned previously has a weak or a strong association to it.

Lambourne et al[16] studied the relationship between factors of malocclusion and headaches in children and adolescents. Two extensive reviews by Pullinger et al[55] and McNamara et al[56] pointed out five occlusal risk factors for headache and TMJ disorders. The factors were, skeletal open bite, centric relation to centric occlusion discrepancy >4 mm, overjet >6 mm, unilateral posterior crossbite, and the missing or non-replaced 5 or more posterior teeth. Pullinger et al[55] concluded that occlusal factors affecting TMDs must not be overemphasized as they presented a weak association. Gesch et al[57] supported it by showing inconsistent findings to prove significant association among the two factors. Similarly, in the research published by Lambourne et al,[16] malocclusion traits previously considered to be problematic contributed little to the change in risk in the multiple-factor chi-square analysis. However, overjet, overbite, and posterior crossbite were statistically significant.

Melou et al[18] stated that a combination of several malocclusion traits were potential risk factors to TMD rather than a single factor to which a patient could adapt in time. Multivariate analysis in their study revealed the evidence of a link between TMD and laterotrusive interferences. It was also observed that the protrusive interferences were not deleterious owing to their significantly higher prevalence in the control group than in the case group. In conclusion to the multivariate analysis, overbite >4 mm, interferences in laterotrusion, and absence of Class I showed significantly higher association with TMD.

Fantoni et al[58] also provided evidence to these results linking interferences in laterotrusion to TMD. Some authors[2] have stated that Angle's Class II and Class III have an association to myofascial pain. However, Angle's class I normoclussion does not. Other variables, such as crossbite, anterior open bite, and overjet, significantly linked to TMD in the literature were not significant in this study.[7,61] These varied results may occur because all the studies had different design protocols. Some used both conventional and digital methods to assess occlusion. Another reason for the difference was that some studies' sample population included children or adolescents, others only included women. TMD is complex and multifactorial and includes malocclusion, psychological parameters as etiology ,which is evident from previous data and current review.[62]

A few more insights have been discussed by Melou et al[18] in their study such as the adverse effect of iatrogenic malocclusions as a result of orthodontic treatment. They also suggested that because many patients suffer from parafunction, these activities must be taken into consideration when evaluating the effect on TMD. These factors were not taken into account in the current review, and further investigation must be performed to establish their relationship to TMJ.

Conclusion

Over the ages, there is the presence of sufficiently powered evidence linking occlusion to the TMDs; yet, no conclusions have been reached. Within the limitations and parameters of the current systematic review, the class I normal occlusion posed least threat to the development of disorders of TMJ. In addition to it, the meta-analytical data concluded that TMDs and related symptoms were more commonly associated with patients having malocclusion including Class II, Class III, anterior open or deep bite, increased overjet or overbite. Malocclusion is detrimental to the temporomandibular joint and associated structures. It can pose a threat to the normal functioning of the masticatory system. However, it is recommended that these results are in tandem with the constraints of the current study and more elaborate research is needed.

Conflict of Interest
None declared.

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