# SYSTEMATIC REVIEW



# Congenital cranio-facial abnormalities in paediatric population: a systematic review on temporomandibular disorders

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### Abstract

The aim of this systematic review was to explore the prevalence of temporomandibular disorders (TMD) in patients affected by congenital craniofacial disorders (CCD). Out of 292 papers, 9 studies were included with 561 participants. The included studies analyzed at least 15 patients treated for temporomandibular disorders, evaluating at least one clinical outcomes such as orofacial pain and/or muscular diseases, malocclusion, skeletal abnormality and/or deformities concerning temporomandibular joint, upper/lower jaw bone malformations. These findings provide an evidence of an association between temporomandibular disorders and congenital craniofacial disorders. The evidence is supported by the findings of a small number of papers in the literature, some of which were of just fair quality. To be definitive in this regard, additional research with a sizable sample size and control group are required.

## Keywords

Cranio-facial abnormalities; Congenital; Orofacial pain; Pediatric; Temporomandibular disorders

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# **1. Introduction**

The temporomandibular joint is a bicondylar joint because of its morphological form, linked in all movements [1, 2]. Retrusion, protrusion and excursion are the three actions that make up the joint's mechanics. The articular surface of the temporomandibular joint, which is coated with avascular fibrocartilage, is what makes it distinctive [1, 3]. Compared to other human joints, the functional and anatomical structure is more complicated [1, 3-5]. The temporomandibular joint develops from two distinct nuclei during a lengthy period of ontogenesis, which sets it apart from other joints [6, 7]. This joint also develops much later than others. The temporomandibular joint and craniofacial development are both significantly influenced by the Meckel's Cartilage, emerging in stage 13 embryos (32 days) [8]. Growth disturbances of the mandible can be a symptom of congenital abnormalities of the temporomandibular joint (TMJ). Agenesis, dysplasia, hypoplasia or hyperplasia of the mandibular condyle are examples of joint structures that can exhibit either hyperplasia or hypoplasia in temporomandibular disorders. They might potentially show up as a cluster of symptoms with a congenital mandibular malformation. The origin and symptoms of temporomandibular joint diseases vary [4, 9-13]. The prevalence of temporomandibular disorders (TMD) ranges between 12 and 60%, according to the most recent literature reviews [14–16]. As a result, the sampling methodology and diagnostic criteria used in the various studies have a significant impact on the results of those studies [17-21]. The following etiologic factors have been proposed for the development of TMD: (I) acquired causes like infection and trauma; (II) iatrogenic factors like surgery and radiation; (III) genetic mutations like osteogenesis imperfecta (OI) affecting the genes responsible for collagen type I production, Williams Syndrome, Fetal Alcohol Syndrome, Cranio-Maxillofacial dysplasia (IV) Habitual factors like bruxism and clenching the jaws, and (V) other variables like muscular spasm, occlusal interferences, stress, systemic disorders and immunological factors [17, 22]. However, there are several challenges in figuring out their genesis [17]. In 1992, the original Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) axis I diagnostic algorithms and Axis II instruments have been performed in order to carry out a TMD classification [23]. Then, in 2004, Schiffman et al. [23] reported a new dual-axis Diagnostic Criteria for TMD (DC/TMD) providing evidence-based criteria for the clinician in order to facilitate communication regarding consultations, referrals and prognosis. There are several disorders that coexist with TMD pain and represent shared etiologic causes and painprocessing pathways. These conditions include neuropathic pain disorders, connective tissue illnesses, joint disk dislocation, osteoarthritis, migraines and tension-type headaches [2427]. Epidemiological studies have supported the theory that TMD is also of a congenital character by demonstrating that its signs and symptoms may occur in people of all ages [5, 13]. In young children, TMD is not very common. It is accompanied by minor signs and symptoms if it is present. However, teenagers and adults experience a rise in its occurrence [4, 10]. Regarding the connection between congenital diseases and TMD, certain abnormalities may take place in utero, most notably at the end of the first trimester [1, 3, 9]. This systematic review focused on the congenital etiology of temporomandibular disorders, aiming to explore the prevalence and features of TMDs in patients affected by congenital craniofacial disorders (CCD).

# 2. Materials and methods

# 2.1 Eligibility criteria

According to the participants, exposure, comparison and outcomes (PECO) model, all papers were evaluated for eligibility:

(P) Participants consisted of patients with a diagnosis of congenital craniofacial disorders.

(E) The exposure consisted of the diagnosis of temporomandibular disorders associated with congenital craniofacial disorders.

(C) The comparison consisted of the patients suffering by diagnosis of congenital craniofacial disorders with no diagnosis of temporomandibular disorders.

(O) The outcome measures consisted of assessing the features of temporomandibular disorders in patients affected by congenital craniofacial disorders, *i.e.*, oro-facial pain and/or muscular diseases, malocclusion, skeletal abnormality and/or deformities concerning temporomandibular joint, upper/lower jaw bone malformations.

Only articles that provided data at the end of the intervention were included. The exclusion criteria were: (1) patients with a history of TMJ trauma; (2) patients with TMD secondary to iatrogenic causes; (3) studies written in a language other than English; (4) review; (5) case series; (6) case report; (7) *in vitro* studies; (8) full-text unavailability (*e.g.*, posters and conference abstracts); (9) studies involving animals.

## 2.2 Search strategy

The PubMed, Web of Science and Lilacs databases were systematically searched for articles published from 1980 until 21 December 2022. Search strategy included Medical Subject Headings (MeSH) terms: temporomandibular disorders OR congenital abnormalities OR craniofacial abnormalities was employed. This systematic review was conducted according to the guidance of the Preferred Reporting Items for Systematic Reviews and Meta-Analyzes (PRISMA) guideline and the Cochrane Handbook for Systematic Reviews of Interventions [28]. The systematic review protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) with number CRD42022315908.

# 2.3 Data extraction

Data from the included studies were retrieved using a customized data extraction on a Microsoft Excel sheet by two reviewers working separately (F.D., G.M.). A third reviewer was used to obtain consensus in cases of dispute. The following information were reported: (1) First author; (2) Year of publication; (3) Study design; (4) Diagnosis of craniofacial congenital disorder (CCD); (5) Number of examined patients with diagnosis of CCD; (6) Number of patient suffering of TMD with diagnosis of CCD; (7) Clinical manifestations of temporomandibular disorders.

# 2.4 Quality assessment

The possibility of bias in the included study was evaluated by two reviewers independently and separately (F.D, G.M). Using the Newcastle-Ottawa Scale (NOS), nonrandomized clinical studies' quality was evaluated [29]. A study is rated on this scale using a star system based on three main criteria: the choice of the study groups (up to 4 points), the comparability of the groups (up to 2 points), and exposure or result of interest for case-control or cohort studies, respectively (up to 3 points). Studies were deemed to be of high quality if they received five or more Newcastle-Ottawa Scale scoring criterion. With the help of a third reviewer, any disagreements were resolved until an agreement was reached (A.L).

# 3. Results

The Fig. 1 reported the flowchart of data selection. The electronic search produced 290 studies. The screening and selection of the studies were done by two separate reviewers (F.D. and G.M.). After analyzing all selected studies, 58 papers were included for reading the abstracts, whereas 9 duplicates were eliminated. The publications that were obviously ineligible were eliminated after the examination of abstracts, obtaining 49 full-text articles. The two independent reviewers applied the inclusion and quality-assessment criteria (F.D, G.M). Finally, 9 full-text articles were included. Features of the included studies are reported in Table 1. The included studies were performed in humans, including at least 15 patients treated for temporomandibular disorders, evaluating at least one clinical outcomes such as oro-facial pain and/or muscular diseases, malocclusion, skeletal abnormality and/or deformities concerning temporomandibular joint, upper/lower jaw bone malformations. There are heterogeneity concerning outcomes among included studies. Poon et al. [30], considering patients affected by Hemifacial microsomia (HM), showed over the 50% of patients affected by HM showed mildly hypoplastic mandibular ramus-condyle with functioning temporomandibular joint. Nevertheless, other four included studies analyzing coronoid locking, Arthrogryposis Multiplex Congenital (AMC) and Fetal Alcohol Syndrome (FAS) reported under the 50% of patients affected by mentioned CCD suffer of TMDs, although patients presented coronoid process hyperplasia, upper/lower jaw bone malformations and limited mouth-opening [31-34]. Furthermore, Ferri et al. [35] in a retrospective studies analyzing 85 patients affected by cranio-maxillofacial dysplasia showed all patients showed



FIGURE 1. Flowchart of search strategy.

mandibular hypoplasia and dysplasia of the mandibular ramus, and consequently TMD disorders. Castro et al. [36] showed some patients affected by Williams syndrome present the phenotypic characteristics that include joint abnormalities. A hypothesis was that the temporomandibular joint of these individuals may be affected. A study showed reduced mandibular movements, functional changes in the TMJ, articular and muscle pains and Angle III class malocclusion [36]. In a cross-sectional investigation by Bendixen et al. [37] of temporomandibular disorders and dental occlusion in a sample of patients affected by Osteogenesis Imperfecta (OI), it was discovered that 25.0% of those with moderate-to-severe OI and 8.9% of those with mild OI had decreased jaw opening ability. It was suggested by Malgorzata et al. [38] that the significant incidence of disk displacement in asymptomatic TMJs may be a congenital normal anatomic variation. According to the current study, only children with OI type I had improved cervical spine and TMJ mobility, whereas children with OI types III and IV had restricted motion in both the cervical spine joints and the TMJ. The results of the research indicated that acoustic complaints from the TMJ occurred more frequently in children with OI than in healthy children; as a result, TMD preventive programs should include activities for tongue-mandibular synchronization in addition to cervical

spine stability exercises.

The results of the quality assessment of included studies are reported in Fig. 2. The analysis of the NOS reported scores ranging 5 to 9, whereas studies that met five or more of the NOS score criteria were considered as good quality. Apart from four papers [30, 31, 34, 37], all papers lost two points due to lack of control for age or other factors relating to comparability and outcome. Four studies were deemed to be at a low risk of bias overall [30, 31, 34, 37] and five were at high risk of bias overall [32, 33, 35, 36, 38]. The studies at high risk of bias had an overall NOS ranging from 5 to 7 [32, 33, 35, 36, 38] (Fig. 2).

# 4. Discussion

The two main types of temporomandibular joint diseases are functional problems (such as tetany and myofascial pain syndrome) and anatomical abnormality [39]. Depending on which portion of the anatomy is most damaged (*e.g.*, muscles, mucosa and glands *vs.* joints and skeleton), anatomical illnesses are further categorized into soft-tissue or skeletal deficiencies [40]. An important portion of the viscerocranium illnesses are temporomandibular joint problems. An estimated one in five people worldwide experience some degree of temporo-

TADELE 1. Main characteristics of the included studies.									
Authors	Publication Year	Study Design	Diagnosis of CCD	No. Examined Patients with diagnosis of CCD	No. patient suffering of TMD with diagnosis of CCD	Features of TMD relating to CCD			
Malgorzata <i>et al.</i> [38]	2021	Prospective study	Osteogenesis Imperfecta	57	34	Myofascial pain with limited mouth-opening Disk displacement with reduction			
Ferri <i>et al.</i> [35]	2021	Retrospective study	Cranio- Maxillofacial Dysplasia	85	85	Mandibular Hypoplasia Dysplasia of the mandibular ramus			
Castro <i>et al</i> . [36]	2018	Retrospective study	Williams Syndrome	52	25	Articular pain Muscle pain Angle Class III malocclusion			
Bendixen <i>et</i> al. [37]	2018	Prospective study	Osteogenesis Imperfecta	75	17	Myofascial pain with limited mouth-opening Disc displacement with reduction			
Poon <i>et al</i> . [30]	2003	Retrospective study	Hemifacial Microsomia	65	37	Hypoplastic condyle Hypoplastic of the mandibular ramus			
Church <i>et al.</i> [31]	1997	Retrospective study	Fetal Alcohol Syndrome	22	4	Upper/lower jaw bone malformations Limited mouth-opening			
Steinberg <i>et al.</i> [34]	1996	Prospective study	Arthrogryposis Multiplex Congenital	23	5	Skeletal open-bite Mandibular Hypoplasia Limited mandibular opening			
Isberg <i>et al</i> . [32]	1990	Prospective study	Coronoid Locking	19	8	Limited mandibular opening Coronoid process hyperplasia			
Isberg <i>et al</i> . [32]	1987	Prospective study	Coronoid Locking	163	4	Limited mouth-opening Coronoid process hyperplasia			

TABLE 1. Main characteristics of the included studies.

CCD: congenital craniofacial disorders; TMD: temporomandibular disorders.

mandibular joint dysfunction [41]. All illnesses that affect these structures are typically accompanied by excruciating pain and great discomfort. It's critical to have a thorough understanding of the temporomandibular joint illnesses' symptoms when practicing dentistry [42]. Church *et al.* [31], analyzing the FAS, showed TMDs can be associated with dental malocclusions, highlighting that the existence of TMDs was probably due to such jaw malformations. In fact, all four patients suffering of TMDs had class II malocclusions with overjets [31]. The relationship between dental malocclusions and TMDs has been reported by different articles [39–41]. However, a diagnosis of TMD has not been performed assuming only certain signs such as malocclusions, but a complete examination of the patient and the current diagnostic criteria have been carried out. Nowadays, the recommendation is to apply various tests that will lead us to an accurate diagnosis in order to define a TMD, applying diagnostic criteria for TMD (DC/TMD) providing evidence-based criteria for the clinician in order to facilitate communication regarding consultations, referrals and prognosis, according to Schiffman *et al.* [23]. It is crucial to take into account a much larger variety of illnesses when diagnosing temporomandibular joint problems since they all exhibit symptoms that are comparable in the head and neck region [40]. First, it's important to determine whether intracranial pathologies and systemic disorders are present [43]. This method, which focuses entirely on treating temporomandibular joint disorders, is crucial from a therapeutic standpoint because it reduces the possibility of situations in which the dentist fails to notice life-threatening problems [44]. After cleft lip and palate, hemifacial microsomia (HM)

	D1	D2	D3	OVERALL
Malgorzata et al	+	+	-	×
Ferri et al	+	×	+	×
Castro et al	+	×	+	×
Bendixen et al	+	+	+	+
Poon et al	+	+	+	+
Church et al	+	+	+	+
Steinberg et al	+	+	+	+
Isberg et al	+	×	+	×
Isberg et al	+	×	+	×

Risk of bias domains

D1: Bias due to Selection-Domain scoring:0-1(High); 2( Some concerns); 3+ ( Low) D2: Bias due to Comparability-Domain scoring:0-1(High); 2( Some concerns); 3+ ( Low) D3: Bias due to Outcome-Domain scoring:0-1(High); 2( Some concerns); 3+ ( Low)



FIGURE 2. Risk of bias assessment using Newcastle-Ottawa score Risk of bias assessment for each study according to NOS. Plots created using risk-of-bias visualization (robvis) tool.

is the second most prevalent congenital facial skull deformity, resulting in mandibular and condylar hypoplasia [30]. Mandibular body and rami underdevelopment is frequently linked to condylar hypoplasia [45]. Mandibular hypoplasia or micrognation, is characterized by an unusually tiny mandible [35]. It can happen as a deformity brought on by intrauterine mandibular compression, on the one hand, in most of the cases is asymmetrical. On the other side, it can also have a malformation-like quality. Poon et al. [30], considering patients affected by HM, showed that over the 50% of patients affected by HM reported mildly hypoplastic mandibular ramus-condyle with functioning temporomandibular joint with no diagnosis of TMD. This aspect reflects the dubious relationship between jaw malformations and TMD. Then, a typical congenital mandibular malformation may reflect correct joint function through musculoskeletal and dental compensatory mechanisms. However, jaw malformations must be identified and intercepted at the earliest stage in order to have the possibility of intervening with an orthodontic-surgical approach. Condylar hypoplasia, which can be congenital or acquired, is described in the literature as abnormal mandibular condyle growth. Congenital condylar hypoplasia is linked to head and neck syndromes include hemifacial microsomia, oculoauriculo-vertebral syndrome, and mandibulofacial dysostosis (Goldenhar syndrome). Agenesis of the whole condyle or branch (condylar aplasia) can be reported in the most severe cases. However, acquired condylar hypoplasia is brought on by issues with the condyle's growing growth center. The most frequent cause is condylar trauma during the early and second decades of life. Other reasons include infections, radiation therapy and rheumatoid or degenerative arthritis [35, 45]. On the other hand, condylar hyperplasia is an uncommon condition marked by an abnormal increase in bone mass [46]. The fovea, which adjusts to the aberrant shape of the skull,

might be negatively impacted by over-enlargement or less frequently distortion of the mandibular head. Most frequently, it happens unilaterally, which causes asymmetry. The most frequent cause for early-stage patient visits to the doctor is an unattractive look. Additionally, myofascial discomfort in the face, occlusion issues and pain around the temporomandibular joint are all brought on by unilateral hyperplasia. Overactive cartilage is mostly linked to the etiology. Injuries, genetic predispositions and endocrine problems are among the variables thought to increase the risk of condylar hyperplasia. Typically, excessive mandibular growth will stop after bone formation is complete [47]. Due to the physical complexity of the malformation, mandibular asymmetry is particularly challenging to diagnose and cure. Before arriving at a final diagnosis and treatment strategy, clinical findings must be supported by radiography. Determine whether growth is still occurring because the surgical and orthodontic therapies are influenced by the patients' growth [48, 49].

# 5. Conclusions

According to this systematic review, temporomandibular disorders and congenital craniofacial problems are related. The findings of a small number of articles in the literature, some of which are of simply average quality because they lack a control group or have a tiny sample size are nonetheless, what the evidence is built on. However, given that nearly all of the studies showed a high prevalence of TMD in CCD patients, all medical physicians should be aware of this link in order to refer CCD patients to dentists for screening when they complain of symptoms suggestive of TMD. To clearly identify the relationship between congenital craniofacial deformities and temporomandibular disorders, future research with a significant sample size and a control group is required.

### AVAILABILITY OF DATA AND MATERIALS

The data are contained within this article (and supplementary material).

### **AUTHOR CONTRIBUTIONS**

GM, MMM and MC—designed the research study. GM, FDF, GC and GM—performed the research. AL and MMM—analyzed the data. GM, MMM and FDF—wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

# ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

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# **CONFLICT OF INTEREST**

The authors declare no conflict of interest. Giuseppe Minervini is serving as one of the Editorial Board members of this journal. We declare that Giuseppe Minervini had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to GAF.

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