RARE OROFACIAL CLEFTS AND DENTAL PHENOTYPES ASSOCIATED: A SYSTEMATIC REVIEW

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Pollyana Pereira Teotonio dos Santos[1]
Ana Laura Herrera Farha[2]
Lucimara Teixeira das Neves[3].

ABSTRACT

Orofacial Cleft (OC) represents one of the most common craniofacial malformations. The rare clefts of the face are malformations that affect other parts of the face and skull other than the most common locations, such as the lip and palate. The rare orofacial clefts may be associated with other deviations, including dental anomalies. **Objective:** The objective of this paper was to carry out a systematic review of the literature to investigate and describe the dental phenotypes diagnosed in subjects with rare orofacial clefts, determining the most frequent. **Method:** This systematic review's protocol and guidance checklist followed PRISMA guidelines (*Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement*.) The PICo criterion ("population", "interest" and "context") was used for research orientation. A broad literature search strategy was carried out, without date limitation, via four online databases: PUBMED, EMBASE, SCOPUS and WEB OF SCIENCE. Using the research strategies, 153 records were retrieved. Two examiners carried out the systematic selection of studies in two phases. **Results:** Of the 153 records identified in the databases, 12 studies were selected to compose this systematic review. As for the characterization of the sample, the total number of cases evaluated in these studies was 53 subjects; 27 were male, and 26 were female. The mean age of the evaluated patients ranged from newborns to a patient aged 25 years old. Among the rare cleft types diagnosed in the selected studies, type 7 cleft was the most reported. The type 11 cleft and the transverse/oblique cleft were reported in only one study. Regarding dental phenotypes, one or more dental anomalies were diagnosed in 18 (34%) of the 53 subjects. Of these 18 subjects, 10 had one or more dental agenesis (55.5%), and 6 had only supernumerary teeth (33.3%). The association of two different dental phenotypes, tooth absence and supernumerary teeth, was observed in only one patient (5.6%), and hypomineralized teeth were found in 1 patient (5.6%). **Conclusion:** Dental agenesis and supernumerary teeth are the most frequent dental phenotypes in cases of rare orofacial clefts.

Keywords: Atypical clefts. Rare clefts. Tessier. Dental anomalies.

[1] DDS,Master in Rehabilitation Sciences, PhD student in Rehabilitation Sciences Hospital for Rehabilitation of Craniofacial Anomalies - University of São Paulo (HRAC/USP)
[2] DDS,Master in Rehabilitation Sciences, PhD student in Rehabilitation Sciences, Hospital for Rehabilitation of Craniofacial Anomalies - University of São Paulo (HRAC/USP)
[3] DDS, MSC, PhD, Associate Professor, Department of Biological Sciences, Bauru School of Dentistry, University of São Paulo and Post-Graduation Program in Rehabilitation Sciences, Hospital for Rehabilitation of Craniofacial Anomalies, University of São Paulo (HRAC/USP)

FISSURAS OROFACIAIS RARAS E FENÓTIPOS DENTÁRIOS ASSOCIADOS: UMA REVISÃO SISTEMÁTICA

RESUMO

A Fissura Orofacial (FO) representa uma das malformações craniofaciais mais comuns. As fissuras faciais raras são malformações que afetam outras partes da face e do crânio além das localizações mais comuns, como lábio e palato. As fissuras orofaciais raras podem estar associadas a outras anomalias, incluindo anomalias dentárias. Objetivo: O objetivo deste artigo foi realizar uma revisão sistemática da literatura para investigar e descrever os fenótipos dentários diagnosticados em indivíduos com fissuras orofaciais raras, determinando os mais frequentes. Método: O protocolo e o checklist de orientação desta revisão sistemática seguiram as diretrizes PRISMA (Itens Preferenciais para Relato de Revisões Sistemáticas e Meta-Análises: A Declaração PRISMA). O critério PICo ("população", "interesse" e "contexto") foi utilizado para a orientação da pesquisa. Uma ampla estratégia de busca bibliográfica foi realizada, sem limitação de data, em quatro bases de dados online: PUBMED, EMBASE, SCOPUS e WEB OF SCIENCE. Utilizando as estratégias de pesquisa, 153 registros foram recuperados. Dois examinadores realizaram a seleção sistemática dos estudos em duas fases. Resultados: Dos 153 registros identificados nas bases de dados, 12 estudos foram selecionados para compor esta revisão sistemática. Quanto à caracterização da amostra, o total de casos avaliados nesses estudos foi de 53 indivíduos, sendo 27 do sexo masculino e 26 do sexo feminino. A média de idade dos pacientes avaliados variou de recém-nascidos a um paciente com 25 anos de idade. Dentre os tipos raros de fissura diagnosticados nos estudos selecionados, a fissura tipo 7 foi a mais relatada. A fissura tipo 11 e a fissura transversa/oblíqua foram relatadas em apenas um estudo. Em relação aos fenótipos dentários, uma ou mais anomalias dentárias foram diagnosticadas em 18 (34%) dos 53 indivíduos. Desses 18 indivíduos, 10 apresentavam uma ou mais agenesias dentárias (55,5%) e 6 apresentavam apenas dentes supranumerários (33,3%). A associação de dois fenótipos dentários diferentes, ausência dentária e dentes supranumerários, foi observada em apenas um paciente (5,6%), e dentes hipomineralizados foram encontrados em 1 paciente (5,6%). Conclusão: Agenesia dentária e dentes supranumerários são os fenótipos dentários mais frequentes em casos de fissuras orofaciais raras.

Palavras-chave: Fissuras atípicas. Fissuras raras. Tessier. Anomalias dentárias.

HENDIDURAS OROFACIALES RARAS Y FENOTIPOS DENTALES ASOCIADOS: UNA REVISIÓN SISTEMÁTICA

La hendidura orofacial (CO) es una de las malformaciones craneofaciales más comunes. Las hendiduras faciales poco frecuentes son malformaciones que afectan otras partes de la cara y el cráneo, además de las localizaciones más comunes, como el labio y el paladar. Estas hendiduras pueden estar asociadas con otras anomalías, incluyendo anomalías dentales. Objetivo: El objetivo de este artículo fue realizar una revisión sistemática de la literatura para investigar y describir los fenotipos dentales diagnosticados en individuos con hendiduras orofaciales poco frecuentes, determinando los más frecuentes. Método: El protocolo y la lista de verificación de la guía para esta revisión sistemática siguieron las directrices PRISMA (Ítems de Informe Preferidos para Revisiones Sistemáticas y Metaanálisis: La Declaración PRISMA). Los criterios PICo (población, interés y contexto) se

utilizaron para guiar la investigación. Se realizó una búsqueda bibliográfica exhaustiva, sin restricciones de fecha, en cuatro bases de datos en línea: PUBMED, EMBASE, SCOPUS y WEB OF SCIENCE. Mediante estas estrategias de búsqueda, se recuperaron 153 registros. Dos revisores realizaron una selección sistemática de estudios en dos fases. Resultados: De los 153 registros identificados en las bases de datos, se seleccionaron 12 estudios para esta revisión sistemática. Con respecto a la caracterización de la muestra, el número total de casos evaluados en estos estudios fue de 53 individuos, 27 hombres y 26 mujeres. La edad media de los pacientes evaluados varió desde recién nacidos hasta un paciente de 25 años de edad. Entre los tipos raros de fisura diagnosticados en los estudios seleccionados, la fisura tipo 7 fue la notificada con mayor frecuencia. La fisura tipo 11 y la fisura transversal/oblicua se notificaron en un solo estudio. Con respecto a los fenotipos dentarios, se diagnosticaron una o más anomalías dentarias en 18 (34%) de los 53 individuos. De estos 18 individuos, 10 tenían una o más agenesias dentarias (55,5%) y 6 tenían solo dientes supernumerarios (33,3%). La asociación de dos fenotipos dentales diferentes, ausencia dentaria y dientes supernumerarios, se observó en solo un paciente (5,6%), y se encontraron dientes hipomineralizados en otro (5,6%). Conclusión: La agenesia dental y los dientes supernumerarios son los fenotipos dentales más frecuentes en casos de fisura orofacial poco frecuente.

Palabras clave: Fisuras atípicas. Fisuras raras. Tessier. Anomalías dentales.

1 INTRODUCTION

Cleft lip and/or palate are considered the most common craniofacial malformations, with an average prevalence of 1:650 live births. They can occur in association with other alterations as part of a syndrome, known as syndromic clefts, or in isolation, when they are called non-syndromic clefts (FREITAS et al., 2012).

Morphologically, it can affect several anatomical structures, determining different types of clefts. Considering this morpho-anatomical heterogeneity and to facilitate diagnosis and especially establish rehabilitation treatment protocols, numerous classifications of oral clefts have been proposed. The Hospital for Rehabilitation of Craniofacial Anomalies (HRAC/USP) adopts the classification proposed by Spina et al., 1972, modified by Silva Filho, 1992. This classification uses the incisive foramen as an anatomical reference, grouping the different types of cleft into 4 main groups: Group 1- Pre-foramen clefts (cleft lip - unilateral, bilateral or median; complete or incomplete), Group 2- Transforamen clefts (cleft lip and palate - unilateral, bilateral or median), Group 3- Post-foramen clefts (cleft palate - complete or incomplete), Group 4- Rare clefts of the face. The latter do not necessarily involve the incisive foramen and occur in areas distant from those embryologically determined as areas of fusion between the facial processes for the formation of the lip and palate (FREITAS et al., 2012;NEVES et al., 2024).

Rare clefts, also known as atypical facial clefts, can involve both soft and hard tissue and affect other parts not defined in the typical pattern (BELLO et al., 2019). They can present clinically in varying degrees of complexity, from a mere notch in the lip, nose, or other facial structure to a complete separation of all layers of the facial structures (ADEOSUN; OGAH, 2017).

Several specific classifications have been proposed to categorize rare clefts. The most commonly used is the Tessier classification, which uses the orbit as an anatomical reference point for categorization and comprises a numerical system that is almost universally used by craniofacial surgeons. It is demarcated by a horizontal axis that crosses both orbits, with clefts above and below this line (FEARON, 2008) that are numbered from 0 to 14 (Figure 1) (MAEDA et al., 2014; Fijałkowska & Antoszewski, 2015; RACZ et al., 2018). Clefts located below the orbit are considered facial clefts and are numbered from 0 to 8, depending on the location of the cleft, with 0 being that located in the midline and 8 being that which affects the external lateral corner of the orbit. The clefts located above the orbit are called cranial clefts

and are numbered from 9 to 14 (Figure 1). The median cleft of the lower arch is designated with the number 30. It is also important to highlight that, among the rare orofacial clefts, there may be an association of a cranial and a facial cleft on a single side (unilateral), or in both sides (bilateral).

Figure 1
Tessier Classification

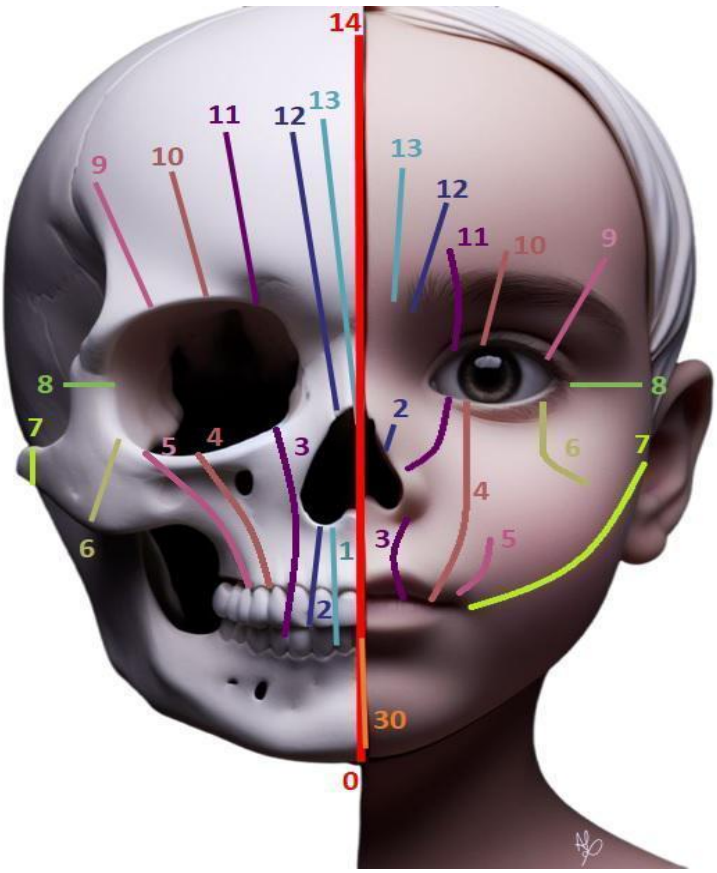


Image: created by the author A.L.H.Farha

The severity of rare clefts varies according to their location and the structures affected. Often, soft tissue clefts do not correspond in severity to corresponding hard tissue clefts (RAMANATHAN et al., 2012).

In general, orofacial clefts, whether typical (cleft lip, cleft lip and palate, and isolated cleft palate) or atypical (rare), can lead to various consequences depending on the tissues involved. The most common are aesthetic, functional, and emotional changes (MAEDA et al., 2014; BALAJI, 2018; LEE et al., 2019; CHUNG et al., 2020). Furthermore, other anomalies associated with clefts are also frequently observed, and in some cases, these associated dysmorphologies involve the oral cavity, determining altered dental phenotypes, also known as dental anomalies.

Dental alterations associated with typical clefts have been widely investigated in the literature. Highlighting that hypodontia, microdontia, taurodontism, and supernumerary teeth

are some of the most prevalent anomalies among subjects with cleft lip, cleft lip and palate, and isolated cleft palate and have a clinical impact on the treatment approach considering the rehabilitation tripod: aesthetic, functional, and emotional (WECKWERTH et al., 2016; NEVES et al., 2022; NEVES et al., 2024).

In the context of rare clefts, there are only a few studies evaluating dental phenotypes. This is probably due to the low prevalence of this type of cleft, making it more difficult to obtain a data set from a larger number of subjects with this specific type of cleft. In this context, the few published studies refer to case reports, pointing out the diagnosed dental anomalies in isolation. However, none of them presents conclusive data on which dental phenotypes are most prevalent among subjects with rare orofacial clefts. Nor has a systematic review of the literature on this topic been carried out.

Thus, this study proposed to carry out a systematic literature review to answer the research question: What are the dental phenotypes described among subjects with rare clefts, and which are the most frequent?

This study is justified, since the aesthetic and functional impairment is extensive in rare clefts, and dental anomalies represent an additional factor in terms of the impact they can have on the comprehensive rehabilitation process of these cases. Thus, knowing which are the most common dental phenotypes among individuals with rare orofacial clefts enables, especially for the dentistry team, preventive action towards the best and most effective planning for dental rehabilitation, both from an aesthetic and functional point of view, contributing to improving quality of life.

2 METHODS

2.1 PROTOCOL

The protocol and guidance checklist for this systematic review followed the PRISMA guidelines (*Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement* (PAGE *et al*., 2021)).

The PICo criterion ("*population*", "*interest*" and "*context*") was used to construct the research orientation, with the following inclusion criteria: (i) *Population*: subjects with rare non-syndromic orofacial clefts; (ii) *Interest*: dental phenotypes; (iii) *Context*: prevalence of dental phenotypes diagnosed in the context of aesthetic and functional rehabilitation of rare non-syndromic orofacial clefts, regardless of the type of rare cleft.

2.1.1 Eligibility criteria

The eligibility criteria used to select studies included in the review were: (1) only complete articles without language limitations; (2) that investigated any type of dental phenotype in subjects with rare non-syndromic orofacial clefts, regardless of the type of rare orofacial cleft according to the Tessier classification.

2.1.2 Exclusion criteria

Studies were excluded for the following reasons: (1) population not following the previously established PICo criterion; (2) lack of information regarding the interest of the study or in disagreement with the established criterion; (3) full article not located; (4) other types of publications other than full research articles, such as: letter to the editor, note, conference abstract,etc.

2.1.3 Search strategies

A broad literature search strategy was carried out, without date limitations, in 4 online databases: PUBMED, EMBASE, SCOPUS, and WEB OF SCIENCE. The following terms were included in the search strategy: “dental anomalies” OR “tooth malformation” OR “dental disorders” OR “tooth agenesis” OR “dental agenesis” OR “hypodontia” OR “supernumerary” OR “taurodontism” OR “hyperdontia” OR “microdontia” OR “macrodontia”; “Tessier classification” OR “atypical facial clefts” OR “rare facial clefts” OR “oblique facial clefts” OR “Tessier cleft”. Boolean operators represented by the terms AND and OR were used, which allow searching by combination of terms, expanding or restricting the search, with OR used for additive combination and AND for restrictive combination.

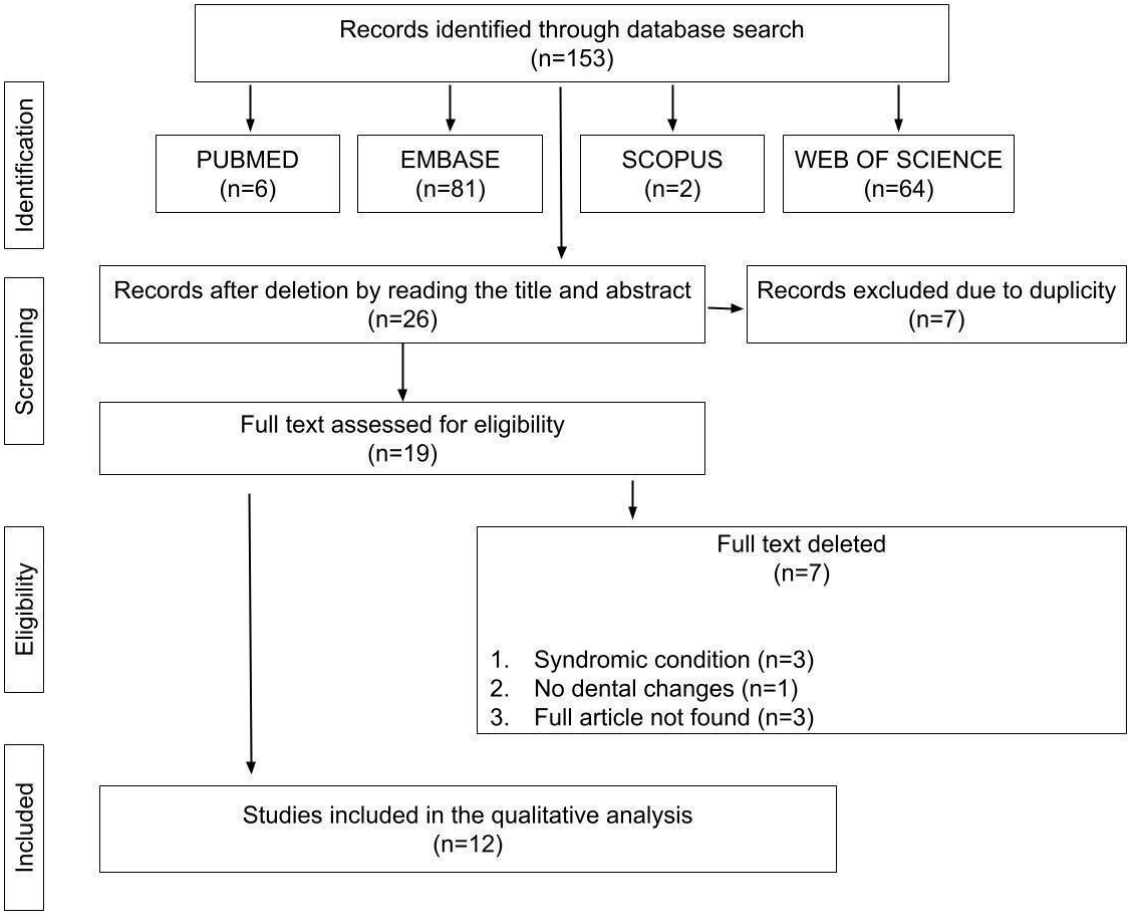
2.1.4 Study selection

Using the search strategies described, 153 records were retrieved. The systematic selection of studies was carried out in two phases. In the first phase, two examiners (PPTS and LTN) reviewed titles and abstracts, excluding titles that were not relevant according to the scope of this review, that is, those that involved syndromes or that did not present data related to any type of rare cleft or even did not present information on dental phenotypes. The second phase was initiated after retrieving all the full texts of all the works considered relevant and selected in the first phase. At this stage, these full texts were read and those that did not meet the previously established eligibility/exclusion criteria were excluded. If there were discrepancies in each of the phases, these were discussed and the disagreement

resolved by consensus between the two examiners. The flowchart of the search and selection process is presented in Figure 2.

This research strategy was designed to balance sensitivity and precision. Sensitivity is characterized by the identification of the largest possible number of records of interest and precision by the ability to exclude the largest possible number of irrelevant articles.

Figure 2
Flowchart of the study selection process, following the checklist adapted from PRISMA.



2.1.5 Mining for data collection

The two examiners (PPTS and LTN) systematically mined, collected and reviewed the following information from the included articles: title, authors, year, journal, type of study, objective of the study, number of participants, profile of participants (age and sex), type of rare orofacial cleft according to the Tessier classification, diagnosed dental phenotypes, teeth or groups of teeth affected by the phenotypes, methodology used and ethnic origin of the sample. Any discrepancies were resolved through discussion and mutual agreement between the two authors. The mined and collected data were tabulated in a spreadsheet using Microsoft Excel.

2.1.6 Statistical analysis

A descriptive statistical analysis was performed and presented in tables and graphs, in absolute numbers and percentages. Data synthesis was performed by grouping studies according to the type of rare orofacial cleft described, presenting the reported dental phenotypes. The teeth affected by the phenotypes were also described when this information was included in the article.

3 RESULTS

Of the 153 records identified in the searches in the databases described, 12 studies were selected to compose this systematic review, and these studies were published between 2011 and 2020 (Table 1). Of the 12 studies selected to integrate this systematic review, 10 (83%) are case reports only, or case reports with literature review, and only 2 studies (17%) analyzed a set of cases through retrospective cross-sectional studies with analysis of characteristics of the group of subjects. The regions with the most studies were China (3), India (2), and Korea (2). The other studies were carried out in Japan, Türkiye, Malaysia, the United States, and France.

Table 1
Selected articles

TITLE	AUTHORS	YEAR	JOURNAL	TYPE OF STUDY	N. OF STUDY PARTICIPANTS	LOCATION
A rare bilateral Tessier no. 6 and 7 clefts	Hou *et al*.	2011	Journal of Cranio-Maxillofacial Surgery	Case report	1	China
A Rare Case of Multiple Oblique Facial Clefts with Supernumerary Teeth: Case Report	Ramanathan *et al*.	2012	Craniomaxillofacial Trauma and Reconstruction	Case report	1	India
A rare case of accessory maxilla and bilateral Tessier no. 7 clefts, a 10-year follow-up	Borzabadi-Farahani *et al*.	2013	Journal of Cranio-Maxillofacial Surgery	Case report	1	United States (Los Angeles)

Tessier 30 symphysea l mandibular cleft: Early simultaneo us soft and hard tissue correction - A case report	Ladani *et al*.	2013	Journal of Cranio-Maxillofacial Surgery	Case report	1	India
Combinatio n of Tessier clefts 3 and 4: Case report of a rare anomaly with 12 years' follow-up	Maeda *et al*.	2014	Journal of Cranio-Maxillofacial Surgery	Case report	1	Japan
Lateral facial cleft associated with accessory mandible having teeth, absent parotid gland and peripheral facial weakness	Özçelik *et al*.	2014	Journal of Cranio-Maxillofacial Surgery	Case report	1	Turkiye
Lateral or oblique facial clefts associated with accessory maxillae: Review of the literature and report of a case	Hou *et al*.	2015	Journal of Cranio-Maxillofacial Surgery	Case report and literature review	1	China
Orthodontic and orthopedic treatment for a growing patient with Tessier number 0 cleft	Baek *et al*.	2018	Korean Journal of Orthodontics	Case report	1	Korea
Phenotypic spectrum of Tessier facial cleft number 5	Racz *et al*.	2018	Journal of Cranio-Maxillofacial Surgery	Retrospec tive study of medical records and image	4	France

				analysis		
Bifid Tongue and Cleft Palate With and Without a Tessier 30 Facial Cleft: Cases of Rare Congenital Anomalies and a Review of Management and Literature	Lee *et al*.	2019	The Cleft Palate-Craniofacial Journal	Case report	2	Malaysia
Distribution, side involvement, phenotype and associated anomalies of Korean patients with craniofacial clefts from single university hospital-based data obtained during 1998–2018	Chung *et al*.	2020	Korean Journal of Orthodontics	Longitudinal retrospective study	38	Korea
A rare case of accessory maxilla: a case report and literature review of Tessier no. 7 clefts	Sun *et al*.	2020	Journal of International Medical Research	Case report	1	China

Regarding the characterization of the casuistry of these 12 selected works, the total number of cases evaluated in these studies was 53 subjects, 27 males and 26 females. The average age of the patients evaluated ranged from newborns (LADANI; SAILER; SABNIS, 2013; MAEDA et al., 2014; ÖZÇELIK et al., 2014; LEE et al., 2019) to a 25-year-old patient (SUN et al., 2020).

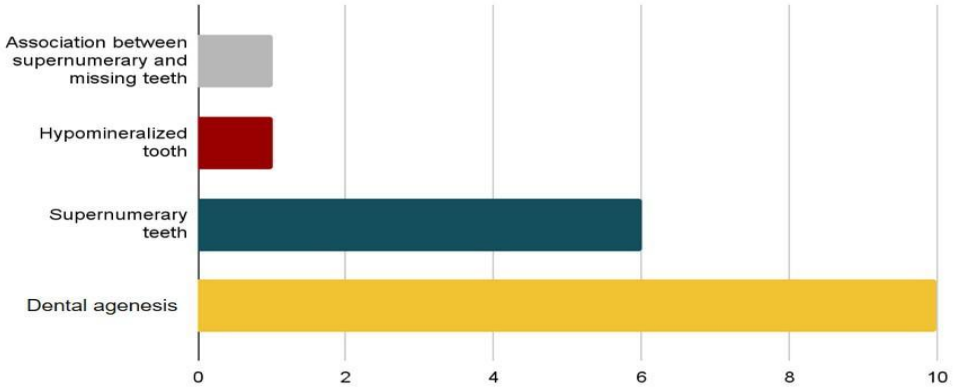
The rare cleft types described in these selected works were Tessier n° 0 (BAEK et al., 2018; CHUNG et al., 2020), Tessier n° 3 (MAEDA et al., 2014; CHUNG et al., 2020), n° 4 (MAEDA et al., 2014; RACZ et al., 2018; CHUNG et al., 2020), n° 5 (RAMANATHAN et al., 2012; RACZ et al., 2018), n° 6 (HOU et al., 2011; RAMANATHAN et al., 2012; RACZ et al., 2018), n° 7 (HOU et al., 2011; RAMANATHAN et al., 2012; BORZABADI-FARAHANI et al., 2013; ÖZÇELIK et al., 2014; SUN et al., 2020), n° 11 (MAEDA et al., 2014) and Tessier cleft n° 30 (LADANI; SAILER; SABNIS, 2013; LEE et al., 2019; CHUNG et al., 2020). A transverse/oblique cleft was also reported, but was not classified in the study using the Tessier classification. (HOU et al., 2015)

Among the types of rare clefts diagnosed in the selected studies, type 7 cleft according to the Tessier classification was the most reported, with 5 of the 12 studies, that is, 41.6% of the studies presenting a patient with this type of rare cleft. While cleft n° 11 and the transverse/oblique cleft, which did not have the Tessier classification, were only reported in one study each. It is worth noting that the same patient could present more than one type of rare Tessier cleft, or even different clefts on each side of the face.

Regarding dental phenotypes, one or more dental anomalies were diagnosed in 18 of the 53 subjects that comprised the general sample of this systematic review. Thus, the overall prevalence of dental anomalies in this sample was 34%.

Analyzing only the 18 subjects with some type of dental anomaly (n=18), the distribution of prevalence by type of alteration was: 55.6% (n=10) with dental agenesis (LADANI; SAILER; SABNIS, 2013; MAEDA et al., 2014; BAEK et al., 2018; RACZ et al., 2018; CHUNG et al., 2020); 33.4% (n=16) with supernumerary teeth (HOU et al., 2011, 2015; RAMANATHAN et al., 2012; ÖZÇELIK et al., 2014; RACZ et al., 2018; SUN et al., 2020); 5.5% (n=1) with association between missing teeth and supernumerary teeth (BORZABADI-FARAHANI et al., 2013) and 5.5% (n=1) with hypomineralization (Figure 3).

Figure 3
Distribution of dental phenotypes by number of subjects.



Regarding the teeth or group of teeth affected by each type of dental anomaly, for dental agenesis, a group of incisors (central and lateral), premolars and molars were affected, both in the deciduous and permanent dentition, with some studies showing a correlation between the type of fissure and its location with dental agenesis.

Supernumerary teeth were diagnosed in most studies in posterior teeth, both in the deciduous and permanent dentitions. Some studies only described that there were supernumerary teeth, without detailing how many teeth or even which teeth were affected. In one case report study, 14 supernumerary teeth were diagnosed, of which four were impacted.

In the only case that presented an association of dental agenesis and also supernumerary teeth, these anomalies occurred respectively in the upper left first molar and the upper right. This patient had a bilateral Tessier 7 cleft.

Another unique case involved tooth hypomineralization in the lower median region, and the patient had a Tessier 30 cleft.

4 DISCUSSION

Rare or atypical clefts have a prevalence of around 1.43 to 4.85 per 100,000 births (HOU et al., 2011; MAEDA et al., 2014; BAEK et al., 2018), a lower occurrence than that of typical clefts, and therefore, cases with this type of cleft, as the name suggests, are rare. Still in line with this epidemiological data, which could also be seen in the process of selecting the studies to be included in this systematic review, most published studies addressing this topic are case reports, describing the facial and/or surgical characteristics of the cases. Furthermore, in the vast majority of these studies, other associated phenotypes associated with this type of cleft are not analyzed. Thus, the present study proposed a systematic review to investigate the most frequent dental phenotypes associated with rare orofacial clefts. By describing the most common dental phenotypes in rare clefts, this study aims to contribute to oral diagnosis and dental treatment planning. Depending on the type and frequency of these anomalies, they may represent an additional factor to be considered in the comprehensive rehabilitation process, including aesthetic, functional, and emotional aspects. As it is an atypical condition and involves a wide spectrum of changes, early diagnosis is important for a good prognosis. The management of these patients requires a multidisciplinary team for treatment and monitoring, including a dentist and a plastic surgeon (MAEDA et al., 2014; SUN et al., 2020).

The cases of the 12 studies selected to compose this systematic review, a total of 53 subjects were evaluated. There was a balanced distribution regarding the sex of this sample,

as 27 (50.9%) were male and 26 (49.1%) were female, which coincides with the distribution found in the study by Chung et al., 2020. Through the evaluation of this data, there is apparently no gender predilection when it comes to rare orofacial clefts, regardless of the specific type of rare cleft.

Regarding the type of rare cleft, the Tessier 7 cleft was the most prevalent in the studies analyzed. A retrospective longitudinal study carried out by Chung et al., 2020, also found the Tessier 7 cleft as the most prevalent among the rare clefts evaluated in that study. On the other hand, the least prevalent cleft in this series that comprised this review was Tessier 11 and transverse/oblique. In the literature consulted, no studies were found that addressed a possible justification for these findings.

Regarding dental phenotypes, the prevalence of one or more types of dental anomalies in this sample of subjects with rare clefts was 34%. One limitation to be pointed out here is that through the literature review of the results of the studies included in this study, it was not possible to know whether these studies diagnosed all dental anomalies present in the cases analyzed or whether they only reported the most common alterations or those that attracted the most attention.

A possible explanation for this prevalence could also be related to methodological differences or approaches used in studies for these diagnoses. Or even the issue of the patient's age at the time of the examination, since the age range profile, considering all the studies included, was quite broad, ranging from a 1-week-old baby to a 25-year-old subject. This broad age range makes it very difficult to assess possible dental anomalies, which preferably depend on clinical and radiographic evaluation for a conclusive diagnosis. Furthermore, there is an ideal age range for diagnosing some specific types of dental phenotypes, especially in permanent dentition, such as hypodontia and structural alterations of dental enamel, among others. This fact may lead to an underestimation of the prevalence of dental anomalies in this population, especially when patients are evaluated at very early ages.

Considering these 18 subjects with some type of dental anomaly, the most common phenotype was dental agenesis and supernumerary teeth. Analyzing the prevalence of each of the alterations individually, it is possible to verify that the prevalence of missing teeth was 55.5%, with a predominance of missing central and lateral incisors, permanent and deciduous, both in the maxilla and mandible. Missing premolars and unusual findings of missing permanent molars are also described. In general, regarding these findings, it is important to highlight that many of the studies use the term dental absences instead of dental agenesis or hypodontia, which would be the most appropriate term to designate the

congenital absence of a tooth. This fact may be associated with the impossibility of a conclusive diagnosis of whether the absence of a tooth is due to true dental agenesis or due to tooth loss of unknown cause prior to the patient's examination.

In individuals with typical orofacial clefts, hypodontia is also very common, with the absence of the lateral incisor on the cleft side being the most commonly found dental phenotype (RIBEIRO et al., 2003; TEREZA; CARRARA; COSTA, 2010). This fact can also be observed in the results found in the present study, in which, in many cases, the region that presented the missing teeth coincided with the location of the atypical cleft. For these missing teeth close to the cleft region, some cause-and-effect hypotheses are raised, such as the deficiency of blood supply triggered by the presence of the defect or even the manipulation of tissues in reconstructive surgical procedures. Furthermore, genetic factors have also been identified as an etiological factor associated with these dental anomalies in patients with orofacial clefts (OLIVEIRA SÁ et al., 2015; Neves et al., 2022).

Patients who presented supernumerary teeth represented 33.4% of the sample. This type of dental anomaly is also frequently found in the population with typical clefts (OLIVEIRA SÁ et al., 2015) and with a lower frequency in patients without craniofacial anomalies (ANEGUNDI et al., 2014). Interestingly, retained or impacted teeth, which represent another type of dental anomaly, were diagnosed in association with supernumerary teeth, all of which were reported in one of the studies selected in this review (RAMANATHAN et al., 2012). Looking at the data on supernumerary teeth from another perspective, and considering a possible correlation between cleft type and dental anomaly, studies that reported Tessier type 7 clefts (n=5), representing 41.67% of all studies included in this review, most commonly described the presence of supernumerary teeth as the associated dental phenotype.

The association between supernumerary teeth and dental agenesis was reported in only one of the selected studies, representing 5.5%. This type of association between dental agenesis and supernumerary teeth, although not common, was also reported in the study by Küchler et al., 2011 in a series of subjects with typical clefts.

The occurrence of hypomineralization of lower incisors was reported in only one isolated case with Tessier 30 cleft. This may have occurred as a result of the presence of the cleft itself in the mandible, with consequent impairment of irrigation to this region of incisors and to the teeth in formation, compromising the mineralization process of the dental structure during odontogenesis. However, the main focus of this work was the description of the clinical characteristics as well as the surgical procedure for the rehabilitation of two cases with congenital bifid tongue associated with Tessier 30, which does not allow us to conclude that this was the only dental phenotype present in these clinical cases.

Finally, the results of this systematic review indicate that dental agenesis and supernumerary teeth are the most frequent dental phenotypes in cases of rare orofacial clefts. However, it is important to consider the limitations of the present study, particularly those inherent to systematic reviews. Even when conducted following standardized and validated protocols, such reviews are subject to bias, including methodological differences in the diagnostic criteria used across the included studies, which may affect the results. Furthermore, some of the selected studies did not report how many or which teeth were affected by the described dental phenotypes, making it difficult to identify a consistent pattern suggesting that these anomalies are exclusively associated with the cleft area.

We recommend that future studies involving dental anomalies should include this type of information. The clinical impact of the number and which teeth are involved has consequences on the clinical prognosis and can indicate whether there is an expected pattern or even a chance of prediction. Sometimes it is possible to anticipate clinical conduct to minimize this impact on the rehabilitation process. Thus, through a broader diagnostic approach, it will be possible to improve the characterization of the phenotypic spectrum in rare cleft cases. This will increase diagnostic accuracy and, more importantly, provide data for a more effective overall treatment plan, aiming at comprehensive rehabilitation, resulting in better quality of life and socioemotional integration for individuals with rare orofacial clefts.

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