

Review Article

A systematic scoping review of dental anomalies associated with cleft lip and palate patients

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Abstract

Objective: The aim of this systematic scoping review is to explore the data regarding dental anomalies related to oral clefts. **Methodology:** A systematic literature search was conducted by two independent reviewers focusing on all types of dental anomalies in cleft lip and palate (CLP) patients. A search string was developed and searched through the PubMed and Scopus database to identify the relevant articles. Identification for additional relevant studies was performed through a manual search of the reference lists of the selected articles. Each selected article was then qualitatively analyzed using Atlas's software. **Results and Discussion:** Eight studies that stated the prevalence of dental anomalies in CLP patients were included and no language restrictions were imposed. Despite lack of standardization in reporting, dental anomalies regarding the tooth form or shape, number of teeth, structural disturbances, and eruption sequence were noted. **Conclusion:** Among cleft group, agenesis was found as the most common dental anomaly with lateral incisor being most commonly involved. The use of standardized classifications and protocols to report cleft types and dental anomalies will be beneficial for clinicians and researchers for identification and better management of the conditions.

Keywords: cleft lip and palate; dental anomalies; hypodontia; tooth agenesis, scoping review; qualitative analysis

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Introduction

Approximately 65% of malformations affecting the head and neck are mainly involve the lip, the palate, or both¹. Cleft lip and palate CLP represent a

breakdown in the normal embryological development of the face which clinically reflects as an orofacial cleft². Genetic and environmental factors contribute to the multiple factors known to cause CLP³. Based

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on geographic origin, socioeconomic status and race, the incidence of CLP ranges from 1 in every 500 to 1000 live-births with the highest incidence rates observed amongst Asian population and the lowest rates amongst African populations^{3,4}.

The embryonic development of tooth germs and orofacial region are not only have a close anatomic relationship but they are also share similar developmental timeline^{5,6}. Genetic malformation causing cleft formation is also shown to affect the dental lamina and tooth development⁷. Dental anomalies including hypodontia, supernumeraries, hypoplasia, and abnormalities in tooth size and shape have been associated with CLP⁸. The prevalence of hypodontia in patients with CLP has been reported to range from 31.6% to 77%⁹⁻¹¹. In addition, the prevalence of hypodontia also increases with severity of the cleft^{8,12,13}. Apart from the commonly missing lateral incisor, other teeth frequently involved are the upper and lower second premolars^{10,12,14-19}, with the maxillary second premolar being the most frequently missing tooth^{17,18}. Meanwhile, it was reported that the prevalence of a supernumerary lateral incisor in patients with CLP ranged from 5.1% to 22.1%^{10,18,20,21}. Other dental anomalies associated with CLP include anomalies in shape and size of permanent teeth, especially at the anterior maxillary region. These malformations frequently manifest as microdontia or macrodontia^{10,20,21}. Cleft-sided central incisors are often found to be rotated, with a prevalence of 68.6%¹⁸ to 78.1%²⁰. This type of malocclusion has been attributed to the lack of space at the end of the alveolar segment²².

Even though it has been well documented that patients with CLP often present with dental anomalies, there are controversies regarding the teeth most affected, and the position of the affected teeth. Moreover, treating CLP patients successfully is often a clinically challenging task, especially when dental anomalies add further complexity to the condition²³. Gaining a better understanding of the relationship between such anomalies and CLP would be helpful in providing timely and appropriate interceptive treatment in cleft patients²⁴. Thus, the specific aims of this systematic scoping review are: (1) to study the frequency and distribution of dental anomalies in CLP, and (2) to highlight different standards and protocols used in literature to classify cleft types and dental anomalies.

Methodology

Preferred reporting of items for systematic reviews and meta-analyses (PRISMA) and the Arksey and O'Malley's methodological framework for scoping studies were utilized for the current study²⁵. After considered various systematic approaches available for reviewing literature, a five-stage approach under the Arksey and O'Malley's scoping review framework outlines are discussed below.

Stage 1: Identifying the research questions

Research questions identified for this scoping study are:

What are the commonly reported dental anomalies associated with CLP patients?

Were there any other notable findings being commonly reported in multiple CLP studies?

Stage 2: Identifying relevant studies

A systematic literature search of the prevalence studies focusing on the co-occurrence of dental anomalies and CLP affected patients was carried out. A combination of MeSH terms and keywords to formulate the search string were used. The search was conducted on the PubMed and Scopus database to identify the relevant published articles.

The search string used for PubMed:

“(cleft palate[MeSH Terms]) OR cleft lip[MeSH Terms]) OR cleft lips[MeSH Terms]) OR cleft palates[MeSH Terms]) OR “cleft”[Other Term]) OR (“cleft lip and palate”) OR “cleft lip and/or palate”) OR “cleft lip palate”) OR “orofacial clefts”) OR “cleft palate”)) AND abnormalities, tooth[MeSH Terms]) OR abnormality, tooth[MeSH Terms]) OR “dental anomalies”) OR “tooth anomalies”) OR “tooth apex/abnormalities”) OR “tooth anomaly”) OR “dental abnormality”) OR “dental anomaly”)) AND ((((((“cross sectional study”) OR “observational study”) OR “case control study”) OR “cohort study”) OR “cross sectional”) OR “observational”) OR “prospective”)) AND (((“non syndromic/cleft”) OR “non syndromic”) OR (“non syndromic cleft lip with or without cleft palate”) OR “non syndromic cleft”))”.

The search string used for Scopus database:

“ALL(“cleft” OR “cleft lip and palate” OR “cleft lip and/or palate” OR “cleft lip palate” OR “orofacial clefts” OR “cleft palate”) AND ALL(“dental anomalies” OR “tooth anomalies” OR “tooth apex/abnormalities” OR “tooth anomaly” OR

“dental abnormality” OR “dental anomaly”) AND ALL(“cross sectional study” OR “observational study” OR “case control study” OR “cohort study” OR “cross sectional” OR “observational” OR “prospective”) AND ALL(“non syndromic/cleft” OR “non syndromic” OR “non syndromic cleft lip with or without cleft palate” OR “non syndromic cleft”)

Manual search in particular handsearching and perusing reference lists of the retrieved articles from the search string was performed to examine and identify further relevant studies. We included the observational studies that reported the dental anomalies in CLP patients specifically exploring the prevalence/occurrence of various dental anomalies.

No language restrictions were imposed. To be included in the review, the study must report the study design, patient age ranges, sociodemographic variables, and at least one type of statistical analysis of tooth anomalies. All other study designs including textbooks, dissertations, case reports, review articles, and abstracts were excluded.

The process of article selection for the current study followed the PRISMA statement²⁶(Figure 1). VOSviewer software (version. 1.6.14) was used to illustrate the network analysis of indexed keywords retrieved from the selected research articles. Each of the selected publication was then qualitatively analyzed using ATLAS.ti software (version 8.1).

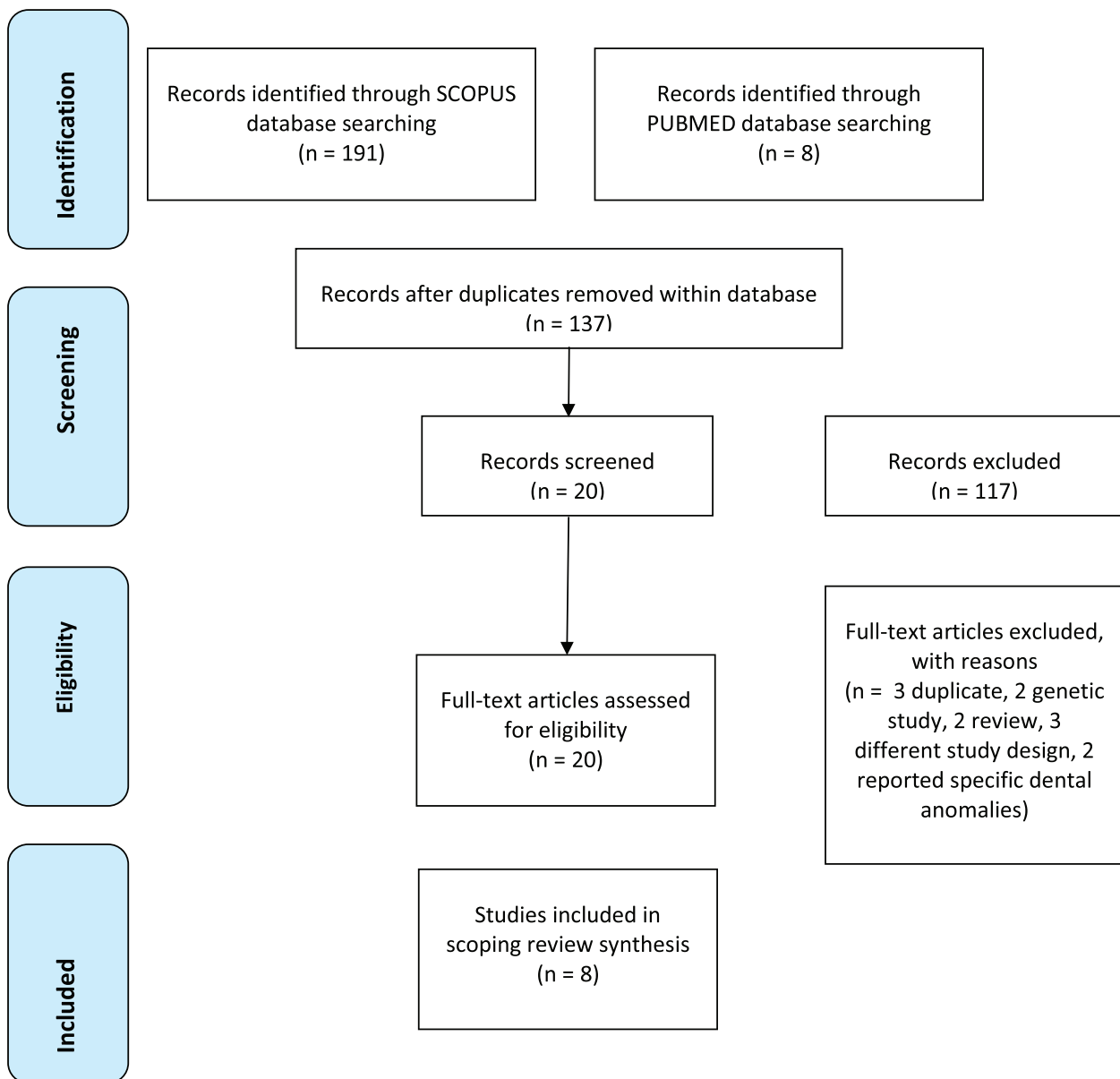


Figure 1. Flow chart of the PRISMA guidelines for study selection²⁶.

Stage 3: Study Selection

Two examiners independently reviewed the title, abstract, keywords and methodology of the selected articles. The published articles were re-examined upon identifying a conflict until a consensus was achieved. The total number of articles identified for this study was 191 from SCOPUS database, 8 from PUBMED after being confirmed by the two independent reviewers. After removing duplicates, 20 full text articles were assessed for their eligibility. However, after reviewing full text articles, genetic studies, reviews, different study designs and articles reported specific dental anomalies, only 8 articles were included in this current review.

Stage 4: Charting the data

The summary of findings from the literature about

the dental anomalies, comparison of percentages of dental anomalies in cleft affected to healthy subjects and odds ratio of occurrence of respective dental anomalies are shown in Table 1 and Table 2.

A total of 74 keywords were identified from the selected literature. A graphical presentation of the most frequently occurring keywords which included tooth malformations, dental anomalies and hypodontia is shown in Figure 2. These commonly occurring keywords are linked through the colorful nodes. Meanwhile, a word cloud presentation created using Atlas's software is displayed in Figure 3. A larger font size represents a greater frequency of commonly occurring words which included "anomalies", "agenesis", "microdontia" and "supernumerary teeth".

Table 1: Summary of findings from selected literature

Author, Year	Location	Study design	Sample size and ethnicity	Age range	Classification according to cleft type	Data collection	Period of Data collection	Exclusion	Inclusion
[27]	Cleft Lip and Palate Clinic of Orthodontics Department of Yeditepe University, Faculty of Dentistry	Retrospective	88 affected and 250 unaffected Turkish	Cleft patient 14.1±6.4 years Normal patient 15.2±7.2 years	Unilateral right CLP, unilateral left CLP, bilateral CLP, and cleft palate	Intraoral and extraoral photographs, panoramic radiographs, and dental casts	2009-2014	The patients with syndromes, incomplete clefts, poor quality/ incomplete records, or missing dental and medical history	Three Turkish generation history, mixed or permanent dentition stage, no orthodontic, no extraction, no restorations and non-syndromic
[28]	Reference center of cleft patients in Rio de Janeiro, Brazil (Nossa Senhora do Loreto Municipal Hospital)	Case-control	321 affected and 321 unaffected, Brazil	9.53±2.1 years	Complete, incomplete, left, right, median, Cleft lip, Cleft lip and palate and Cleft palate were further divided in to complete and incomplete and unilateral left, right and bilateral	Standardized diagnostic records, panoramic and periapical radiographs, dental casts, intraoral photographs, and dental histories	1990-2009		No history of syndrome or family history
[29]	Severcraniofacial medical centers located in the four most populated cities in Colombia-Bogota', Medellin', Cali, and Pereira	Analytical matched case-control	210 affected and 210 unaffected, Colombian	5-12 years	Right unilateral cleft lip, alveolus, and palate, Left unilateral cleft lip, alveolus, and palate, and Bilateral cleft lip, alveolus, and palate	Panoramic radiographs	2014-2016	Patients with history of extraction	Non-syndromic patients

Author, Year	Location	Study design	Sample size and ethnicity	Age range	Classification according to cleft type	Data collection	Period of Data collection	Exclusion	Inclusion
[30]	Department of Orthodontics and Paediatric Dentistry of the University of Florence, Italy	Cross-sectional	150 affected and 1000 unaffected Italian-Caucasian	10 years and 4 months	Right Unilateral CLP, Left Unilateral CLP, and Bilateral CLP	Clinical examination, dental casts, intraoral photographs, and radiographic material (panoramic X-rays, occlusal and/or periapical radiographs) of all subjects were examined	Not specified	Patients with history of any orthodontic treatment, inadequate dental records, craniofacial syndromes, or other medical disorders	Non-syndromic
[31]	Tawanchai Cleft Center (TCC), Thailand	Cross-sectional	280 affected Thai	10.3±3.2 years	Cleft lip only, Cleft lip and alveolus, Unilateral CLP, Bilateral CLP, Cleft palate	Standardized records comprised of panoramic radiograph, intraoral photographs, dental casts, and orthodontic clinic charts	1990-2011		No history of permanent teeth extraction, endodontic, prosthodontic, or orthodontic treatments
[32]	Referral Centre for rare craniofacial malformations of Lille Regional University Hospital Center (Lille, France) and Henri Mondor-Albert Chenevier Hospital Group (Créteil, France)	Retrospective	74 affected, French-Caucasian	6-16 years	Left UCLP, Right UCLP, BCLP, and CP	History records and panoramic radiographs	2010-2015	Previous extraction or orthodontic treatment	
[33]	Combined Clinic at Kota Bharu Dental Clinic (KBDC), Malaysia	Comparative cross-sectional	98 affected and 107 unaffected, Malaysian	5-12 years	Unilateral CLP, and Bilateral CLP	Intra-oral and extra-oral clinical examination of CLP children	6 months		Non-syndromic cleft lip and palate children
[34]	Three referral centers in Brazil: Instituto MaternoInfantil de Pernambuco, in Pernambuco (Northeast region), Hospital Municipal Infantil Menino Jesus, in São Paulo (Southeast region), and Centrinho Prefeito Luis Gomes, in Santa Catarina (South region)	Retrospective	524 affected Brazilian	≤18 years	Unilateral right CL/P, Unilateral left CL/P, Bilateral CL/P, and Cleft palate only	Panoramic radiographs, periapical radiographs, and intra oral pictures	2000-2014	Records with previous tooth extractions and incomplete CL/P description, radiographs with poor image quality	

Table 2. Dental anomalies, percentage of affected-unaffected and odds ratio of respective dental anomalies as calculated by authors.

Author, Year	Dental anomalies reported	Percentage of affected-unaffected (Odds ratio)
Cakan, Yilmaz [27]	Tooth agenesis	77.3-7.2 (5.2)
	Supernumerary tooth	4.6-0.8 (5.9)
	Microdontia	25-0.4 (83)
De Lima Pedro, Daniel Brito Faria [28]	Agenesis	(2.34)
	Microdontia	(1.20)
	Supernumerary teeth	(2.39)
	Malposition	(1.86)
	Impaction	(0.40)
	Taurodontia	(0.25)
	Multiple Anomalies	(5.13)
Total with anomalies	(1.65)	
Yeziro-Rubinsky, Eslava-Schmalbach [29]	Agenesis	50.9-5.71 (8.6)
	Supernumerary teeth	32.3-0.95 (10.5)
	Dilaceration	2.86-0.48 (7)
	Taurodontism	2.38-3.33 (0.71)
	Impaction	12.3-2.38 (6.2)
	Transposition	9.05-0.95 (12.5)
	Rotation of maxillary central incisor	51.9-3.21 (16.8)
	Microdontia of maxillary lateral incisors	51.9-2.38 (17.2)
Camporesi, Baccetti [30]	Agenesis lateral incisors	38.5-4.4 (13.68)†
	Agenesis second premolars	6.4-5.8 (0.12)†
	Supernumerary incisors	21.8-3.9 (8.37)†
	Anomaly size-shape incisors	35.3-3.8 (13.28)†
	Enamel hypoplasia incisors	26.3-4.2 (9.77)†

Wangsrimongkol, Manusudprasit [31]	Agenesis	60.4
	Microdontia	41.4
	Dilaceration	6.4
	Supernumerary teeth	6.1
	Taurodontism	0.4
	Fusion	0.4
	Dens-evaginatus	0.4
Mangione, Nguyen [32]	Gemination	0.4
	Agenesis	83.8
	Supernumerary teeth	8.1
	Incisor rotation	25.7
	Impacted canine	18.9
	Shape anomalies	21.6
Abd Rahman, Abdullah [33]	Morphology	24.5-10.1 (2.9)
	Number of teeth	44.9-7.3 (10.3)
	Alignment	79.6-27.5 (10.3)
Menezes, de Arruda [34]	Facial profile	26-10 (3.58)
	Tooth agenesis	62.0
	Rotated tooth	32.4
	Supernumerary teeth	23.7
	Impacted teeth	17.8
	Microdontia	13.0
	Ectopic tooth	6.4
	Hypoplasia	3.2
	Dilacerations	0.9
	Hypercementosis	0.6

Stage 5: Collating, summarizing and reporting of the notable findings

Four main themes were identified after performing literature review by using Atlas's software with each of the theme discussed below.

Types of Anomalies

Left sided unilateral CLP occurred more frequently in comparison to the right side^{31,34}. When CLPcases and controls were compared, it could be observed that individuals born with clefts presented with more dental anomalies outside the cleft area than noncleft individuals²⁹. However, no gender differences in

term of the frequency of dental anomalies was noted in many different studies^{27,31,33}. Regarding gender difference on cleft type, De Lima Pedro, Daniel Brito Faria²⁸ noted that complete left and complete bilateral clefts were notably common in males whereas cleft palate only were more common in females. There was one study reported the socioeconomic status of the cleft patients were from both low and moderate family income²⁷.

De Lima Pedro, Daniel Brito Faria²⁸ noted in their study that significantly higher number of dental anomalies on the outside the cleft area of the CLP affected cases when compared to unaffected cases. While

Yeziro-Rubinsky, Eslava-Schmalbach²⁹ proclaimed microdontia of upper lateral incisors, rotation of the upper central incisor outside the cleft area, and agenesis as the most frequent dental anomalies. Menezes, de Arruda³⁴ reported that tooth agenesis was the most common dental anomaly followed by rotated teeth most commonly involving upper central incisors. Moreover, according to Wangsrimgkol, Manosudprasit³¹, agenesis of upper lateral incisors was the most common dental anomaly followed by microdontia, however it is noteworthy that the authors did not consider rotation of teeth as a dental anomaly but they considered it as a consequence of having cleft. Another interesting finding was the higher number of dental anomalies in the left side of the palate. also noted left side predilection of dental anomalies, reporting agenesis as the most common followed by rotation of teeth and microdontia. According to cleft type, the occurrence of dental anomalies was highest in bilateral CLP and the least was found in case with cleft palate only^{27,32}. Higher number of dental anomalies in bilateral CLP patients was also noted by Abd Rahman, Abdullah³³.

Dental anomalies in the form of shape, structure and position can increase chances of creating dental biofilm leading to dental caries^{35,36}. Thus, counselling and follow up are important to maintain tooth integrity, even rotated or malpositioned teeth, in order to maintain the supporting structures, which may be defective in the cleft area. It was noted that different studies have described dental anomalies according to the occurrence, without using any standardized system to include radiographs, intraoral photographs and study models. Moreover, various studies applied separate criteria, varying sample size, classifying cleft separately or jointly as shown in Table 1. Standardized classifications should be utilized to improve reporting standards and uniformity of available data to facilitate clinicians and researchers.

Agenesis

Cakan, Yilmaz²⁷ reported that lateral incisor agenesis is the most frequent dental anomaly with premolar as the second most common agenesis. Camporesi, Baccetti [30] also reported that lateral incisor agenesis as the most frequent dental anomaly on the cleft side, followed by supernumerary teeth. Agenesis of teeth was also identified as the most frequent dental anomaly occurring in combination with other dental defect^{28,37}.

The frequency of right lateral incisor agenesis was

found to be significantly higher in right unilateral CLP while the frequency of left lateral incisor agenesis was found to be significantly higher in left unilateral CLP. Furthermore, bilateral lateral incisor agenesis was observed in bilateral CLP which was statistically significant²⁷. De Lima Pedro, Daniel Brito Faria [28] found that the agenesis of the left and right lateral incisors and left second premolar were commonly missing on the outside of the cleft area. Meanwhile, Yeziro-Rubinsky, Eslava-Schmalbach²⁹ shown that maxillary second premolar agenesis was the most common finding outside the cleft area (12 times more odds). Canine was identified as the least affected tooth in agenesis²⁷ where mandibular second premolar agenesis was more commonly found in healthy control cases. Maxillary teeth were more frequently found missing regardless of the cleft type³¹.

Knowledge regarding the frequency, magnitude of agenesis will be beneficial to prevent risk of other dental problems (drifting of the adjacent teeth, supra-eruption of opposing tooth, malocclusion)³⁵; [29], and will be helpful for orthodontist to ensure adequate diagnosis and treatment planning²⁷.

Positioning of teeth

Different opinion has been debated in regard to the malpositioning of teeth in CLP. One school of thought considers malpositioning as a consequence of agenesis or disturbance in the arch form hence they do not report teeth malpositioning as dental anomalies^{27,30,31} whereas for the other group, tooth malposition is considered as part of dental anomalies^{28,29,32-34}. In either case, tooth malpositioning in CLP patients should be monitored by orthodontist to correct malocclusions in order to maintain the supporting bone structures thus preventing periodontal diseases²⁹.

Classification of cleft type

Facilitating international communication and multi-disciplinary discussions are among the reasons for devising classifications which can clearly and precisely describe different phenotypes of a clinical presentation. Allori, Mulliken³⁸ reviewed various classification which are available to describe different phenotypes of orofacial clefts, and they noticed that even the highest quality of studies did not consistently follow any specific classification. Although the use of any available classification system to document various phenotypes in CLP is subjected to the discretion of clinicians and researchers, more standardized system is warranted.

Conclusion

This current review found that agenesis of lateral incisor is the most common dental anomalies in CLP among various abnormalities in the tooth form or shape, number of teeth, structural disturbances, and eruption sequences that were reported. This review also highlighted the need for universally standardized classifications systems, statistical analyses, and diagnostic protocols in the reporting of cleft types and dental anomalies, to ensure internationally recognized methods of discussion and interpretation.

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author Contributions

Conceptualization, S.J., M.F.K., and M.K.A.; methodology, S.J. and M.F.K.; software, A.I.A.; validation, S.J. and M.F.K.; formal analysis, A.I.A. and M.Q.; investigation, A.I.A.; resources, M.Q.S. and H.K.; data curation, M.K.A.; writing - original draft preparation, A.I.A. and M.Q.; writing - review and editing, S.J., M.F.K., M.K.A., M.Q.S., and H.K. All authors have read and hereby agree to the submitted version of the manuscript

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