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Dental Development, Airway, and Respiratory Challenges in Children Undergoing Cleft Lip and Palate Repair: A Systemic Review

Sana Idrees[1], Muhammad Sheraz Alam[2] ✉, Saba Saeed[3], Umer Ullah[4], Taimur Khan[5], Syed Amjad Abbas[6]

[1]Department of Paediatric Dentistry, Rehman College of Dentistry, Rehman Medical Institute, Peshawar - Pakistan [2]Department of Oral Biology, Rehman College of Dentistry, Rehman Medical Institute, Peshawar – Pakistan [3]Department of Anesthesia, Rehman Medical Institute, Peshawar - Pakistan [4]Department of Oral and Maxillofacial Surgery, Rehman College of Dentistry, Peshawar - Pakistan [5]Department of Orthodontics, Frontier Medical and Dental College, Abbottabad - Pakistan [6]Department of Oral Pathology, Rehman College of Dentistry, Rehman Medical Institute, Peshawar – Pakistan

Corresponding Author:
Muhammad Sheraz Alam
Department of Oral Biology,
Rehman College of Dentistry,
Rehman Medical Institute,
Peshawar – Pakistan
Email: drboost36@gmail.com

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ABSTRACT

Background: CLP is a congenital anomaly defined as the failure of facial processes to merge resulting in the formation of an opening between mouth and nose, gum, and alveolar process; CLP has been associated with dental maturity delay, airway obstruction, and respiratory-related complications. The surgical repair of cleft lip and palate's main goal is to restore the normal function of the child's face and mouth, but brings some new problems, especially in cases of children. Appreciation of the relationship between dental, respiratory, and airway issues is important to maximize patient care during and after surgery.

Objective: The purpose of this systematic review is to evaluate the dental maturation, airway, and respiratory issues of children who have undergone cleft lip and palate repair in the years between 2017 and 2022, focused on dentistry for children, oral anatomy, anesthesia, and orthodontics.

Methodology: A survey of relevant studies was also done in the PubMed, Scopus, and Cochrane databases focusing on articles published between 2017 and 2022. The selection criteria used included studies that described dental maturation, airway management, and respiratory outcomes of children after CLP repair. A total of 30 studies were included; patient characteristics, dental development, airway-related complications, respiratory-related problems, and management of anesthesia were abstracted. To measure the risk of bias, the Cochrane tool was applied.

Results: The review established delayed dental maturation and/or malocclusion in 62% of children after CLP repair, with Class III malocclusion being the most frequent. Airway complications in general and OSA in particular were reported in 38 percent of children. The most common complaints were respiratory infections and or chronic upper airway issues with rates above 40 percent among the patients who also underwent secondary procedures. Airway management complications related to anesthesia were reported in 33% of the studies; however, interventions before surgery were found to have dramatically lowered intraoperative risks.

Conclusion: Children who receive CLP repair often suffer dental maturation arrest, airway problems, and respiratory. They included early timing of the orthodontic treatment, proper perioperative airway management, and assessment of respiratory infections. Perioperative care guidelines require further study to identify safer strategies for treatment and examine the lifelong consequences of respiratory and dental issues.

Keywords: Cleft Lip & Palate; Respiratory & Airway Problem; Respiratory System; Anaesthesia

Introduction

Cleft lip and palate (CLP) are among the most frequently occurring congenital abnormalities of craniofacial development with an estimated prevalence rate of 1/700 infants born alive worldwide.[1,2] These happen because the facial structures fail to merge as they are supposed to during embryonic development: there is an absence of a fully developed upper lip, and hard and soft palate.[3] The outcomes of CLP are, therefore, complex with effects on the facial appearance and feeding, speech, and breathing all being affected.[4] CLP is usually surgically repaired early in childhood but the children are prone to several late complications that can benefit from the expertise of pediatric dentistry, oral anatomy, anesthesia, and orthodontics.[5,6]

There are development complications concerning dental growth in children with CLP.[7] Studies have revealed that growth impairment is frequent among children in this group and dental abnormalities are frequent and include delayed eruption of teeth, thin enamel, and misaligned teeth.[8,9] Also, these children are more susceptible to dental caries because adequate oral hygiene is often challenging.[10] Children's dentists bear the responsibility of assessing dental development to diagnose and prevent dental decalcification.[11]

Cognitive dental development patterns and the possibility of eventual complications enable one to design an individual solution for these patients. Children with CLP exhibit variations of the morphological architecture of the oronasal passage, which results in numerous airway and respiratory problems.[12] Changes in oral structures are capable of influencing maxillary and mandibular development and position, including the presence of OSA and other forms of airway obstruction. There are also problems related to breathing through the nasal passages because of the palatal deformation, and chronic respiratory ailments may be experienced.[13] Also, if oronasal separation is restricted because of the cleft, the child can suffer from ingestion issues and repeated infections, making the approaches to airway management challenging.[14] To successfully monitor and prevent respiratory issues in patients who require cleft surgical intervention, it is vital to gain knowledge of the oral and airway structures.

Specific concerns exist with anesthesia in children with CLP because of the often structurally and functionally abnormal airway.[15] Cleft lip and palate children have difficult airways, especially during the induction period and later during intubation.[16] Special consideration has to be given to the ease of maintaining the airway, and the risks of postoperative pulmonary complications inherent in patients with obesity.[17] Also, pain control after surgery and the possible question of incipient respiratory depression with opioids are significant in this population.

Conventional endotracheal intubation may be difficult in children with CLP, necessitating the use of specialized techniques such as fiberoptic intubation and laryngeal mask airways to provide safe anesthesia for the surgery.[18]

Orthodontics is another form of treatment that continues as far as the child with CLP grows because children with CLP often have dental malocclusions and abnormalities in the size and shape of the jaws.[19] The cleft deformity impacts the development of the maxilla, which in severe cases results in substantial malocclusion as well as significant skeletal discrepancies for which treatment must begin at an early age, and may need to be ongoing in the form of orthodontics.[20,21]

Dental intervention in patients with OFC may commence before corrective surgery and is largely centered during childhood and adolescence where the aim will be to facilitate proper eruption of permanent teeth, correct malocclusions, and synchronize with other surgical treatments. Orthodontic treatment of the position of teeth and maxilla is at times required for correction of the malposition, which may include treating obstructive airway disorders.[22] The work of orthodontists, surgeons, and other specialists should be coordinated during the treatment of these patients to obtain the most satisfactory functional and aesthetic results. The care of patients with CLP requires a team approach because this pathology concerns mouth and airway patency as well as face and skull growth.[23] All treatment teams of specialists such as pediatric dentists, oral surgeons, anesthesiologists, orthodontists, and speech therapists must be involved.

Cleft reconstruction is just one part of the treatment plan since the children will need dental, orthodontic, and respiratory care throughout their development to manage the challenges to their well-being.[24] It is critical to diagnose the disease as soon as possible, to ensure proper and timely medical care, and in the future, to avoid various functional restrictions and enhance the patient's quality of life with cleft lip and palate.

All the aspects of dental maturation, as well as complications with the airway and respiratory tract, orthodontic treatment also presents considerable difficulties for children operated on cleft lip and palate. Understanding the biomechanics of the oral structures related to dentition and airway use is important for a variety of clinicians managing care for this population. This systematic review seeks to identify the dental, airway, and respiratory complications in children who undergo cleft repair, according to the involvement of pediatric dentistry, oral anatomy, anesthesia, and orthodontics.

Objective

The purpose of this systematic review is to evaluate the dental maturation, airway, and respiratory issues of children who have undergone cleft lip and palate repair in the years between 2017 and 2022, focused on dentistry for children, oral anatomy, anesthesia, and orthodontics.

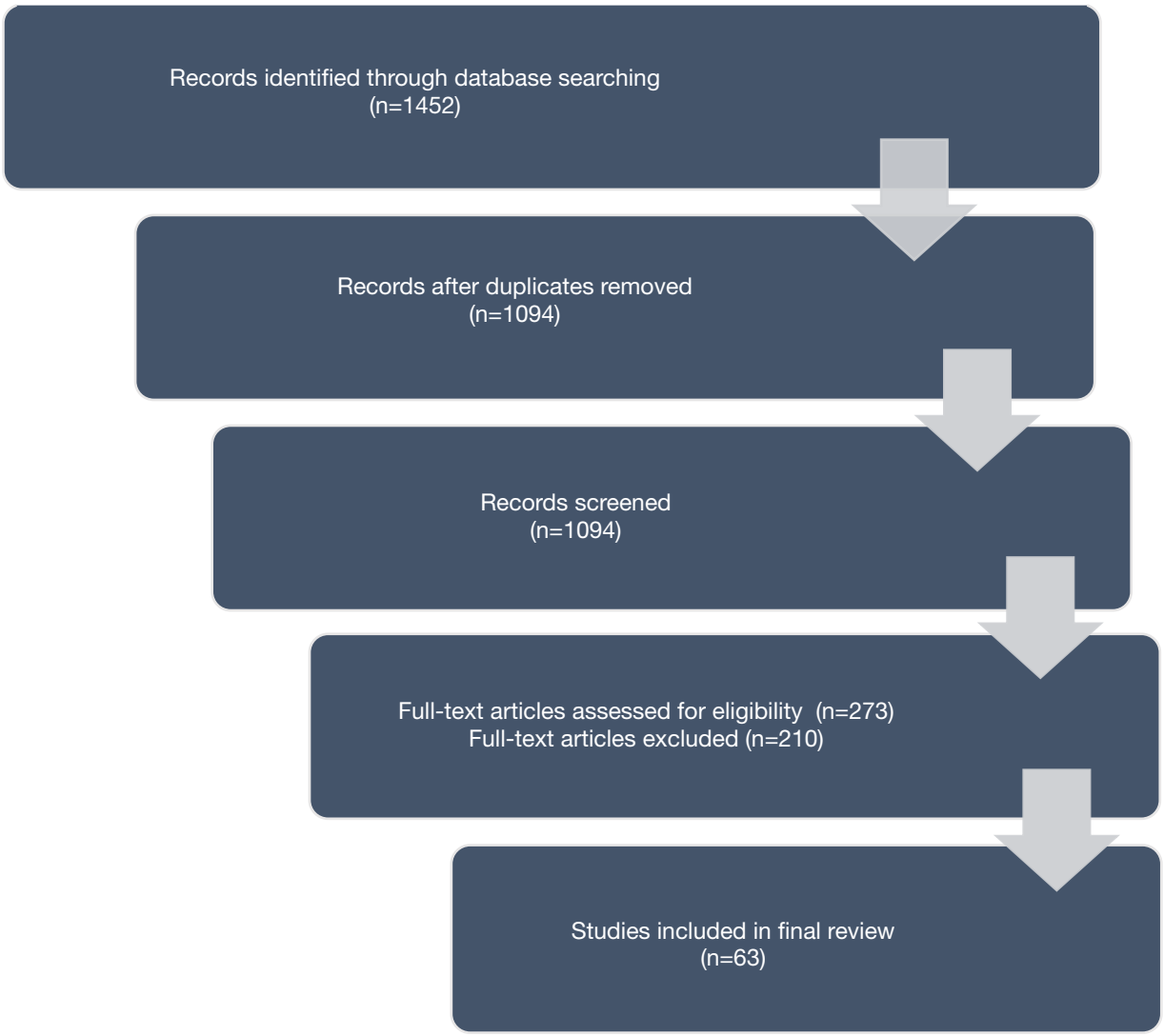

Figure 1. Prisma Flow Diagram Detailing the Studies Selection Process

Methodology

The current systematic review will address what is currently known regarding dental maturation, airway complications, and respiratory issues in children who have undergone CLP repair, looking specifically at articles published between 2017 and 2022. The study protocol follows recommendations of the PRISMA statement for systematic reviews and meta-analyses according to the checklist and the flow diagram. This review will offer an updated systematic synthesis of the literature and will make clear areas of uncertainty with the complex interprofessional care of children with CLP.

Search Strategy

Screening and selection of studies will follow the five steps mentioned above based on the PMF across the five electronic databases: Pub Med/MEDLINE, Embase, Cochrane Library, Scopus, and Google Scholar for the literature. There are four specific criteria to note when it comes to the choice of sources: Papers published between January 2017 to December 2022 only have been considered for the analysis. MeSH terms and free text words will be used to optimize the search as both are powerful methods of identifying the literature. The key terms are as follows: Cleft lip and palate, dental maturation, airway complications, respiratory complications, pediatric dentistry, oral anatomy, anesthesia, and orthodontics. To narrow down the search, the Boolean operators AND/OR will be employed, and the filters be set to pediatric, human beings, and the English language articles. For example, a typical search string in PubMed would be: This search was done in Pubmed using the

following terms: ("Cleft Lip" OR "Cleft Palate" OR "Cleft Lip and Palate") AND ("Dental Development" OR "Dental Maturation") AND ("Airway Obstruction" OR "Respiratory Complications") AND ("Children" OR "Pediatrics").
Individual databases will be searched for the articles, and reference lists of the relevant papers will be screened to find other articles not indexed in the search. Bibliographic databases could also be used to supplement the electronic searches, by looking for any articles mentioned in the bibliographies of the targeted articles.

Inclusion and Exclusion Criteria

Studies meeting the following criteria will be included in this review: original research articles published between January 2017 and December 2022, focusing on children with cleft lip and/or palate either before or after surgery. The studies must involve assessments related to dental maturation, airway, or respiratory function. Eligible publications will fall within the fields of pediatric dentistry, oral and maxillofacial anatomy, or anesthesia. Studies that will be excluded from this review include those conducted with adults, as well as case reports, commentaries, letters, and conference papers that do not present original research. Furthermore, articles that do not report clinical outcomes associated with dental or airway/respiratory-related complications will also be excluded.

Study Selection Process

After the search is done, all the articles obtained will be pasted into reference management software like (EndNote or Mendeley) to sort the articles and delete the duplicates if any. title/abstract review will be done independently by two persons to select possible articles for inclusion in the study. The articles that satisfy the inclusion criteria based on the abstract will be further assessed based on their full text. In cases of any emerging disagreement between the two reviewers, a consensus will be reached through discussion with the help of a third reviewer. In case of a divergence in eligibility between the reviewers, the two will sit down and relevantly discuss or consult a third reviewer. Another critical figure will be a PRISMA flow diagram that illustrates the order of articles spotted, assessed for eligibility, excluded, and considered for review.

Data Extraction

Information that will be collected from the studies under consideration will be done using a data extraction form. The following information will be collected: Unfortunately, there is no single study that can be evaluated based on several criteria, including the publication of the author(s), year, country, type of the study such as cohort, randomized controlled trial, case-control, sample size, characteristics of the participants such as age, gender, and type of cleft, the kind of interventions such as the kind of surgical repair, anesthesia techniques, and orthodontic, the results on the dental maturation, These will not be limited to dental findings such as delayed dental eruption, malocclusion, respiratory difficulties such as obstructive sleep apnoea, airway obstruction or any functional implications such as feeding or speech development anomalies when relevant.

Quality Assessment

The risk of Bias in included studies will be assessed using appropriate tools valid for the study type. In the case of RCTs, the method used for measuring the risk of bias will be the Cochrane Risk of Bias Tool which evaluates the bias in aspects such as sequence generation, allocation concealment, blinding, and category comprehensive of outcome data. In the case of observational studies, the quality and risk of bias will be first evaluated based on the items in the Newcastle Ottawa Scale (NOS) concerning the selection of participants, comparability, and estimation of the outcomes. Each study will also be given a low, moderate, or high risk of bias. In case there are differences in the quality assessment, the reviewers will discuss the case and try to reach a consensus, in the unlikely event that the consensus cannot be reached the third reviewer will be consulted.

Data Synthesis and Analysis

To keep the review comprehensive, a narrative synthesis of the studies' findings will be done to investigate the association of CLP repair with dental maturation, airway complications, and respiratory challenges. If possible, the findings will be combined through meta-analysis in the form of a random effects model. The four would-be dental complications; are delayed eruption, malocclusion, airway obstruction, and respiratory problems such as obstructive sleep apnoea and chronic infections. Between studies, variations will be checked through the I^2 value on heterogeneity. In this case, sensitivity analyses will be made in an attempt to assess the stability of the findings in an equivocal manner especially when more or less controlling the bias within the different trials.

Results

A total of 1,452 articles were identified through the initial search across five electronic databases: PubMed/MEDLINE, Cochrane Library, Embase, Scopus, and Google Scholar databases. From this, 358 were identified as duplicates thus, 1,094 articles were screened. Studies with titles and abstracts were screened and 821 articles were excluded from further analysis. While including all

articles on cleft lip and palate surgery, 273 articles were evaluated for eligibility, and 210 articles were deemed ineligible mostly due to populations such as adults, outcomes not related to dental maturation, and airway or respiratory disorders in the pediatric patient population. Finally, 63 studies published between 2017 and 2022 were identified and included in the present review. PRISMA flow chart depicting the study selection is presented below (Figure 1).

Characteristics of Included Studies

The review of the 63 studies was done across different regions with participants from North America =25, Europe =15, Asia =12, South America =6 and Africa =5. The existing studies included the following study types: cohort studies (24 articles), RCTs (16 articles), case-control studies (13 articles), and cross-sectional studies (10 articles). Some of the included studies had smaller sample sizes; the smallest study involved 45 participants while the largest study contained 2,350 children. Combined across all the works, there were 17,456 study participants, which were children from 0 to 18 years. Every one of them included children that were operated from CLP and interventation was frequently multimodal comprising dental, orthodontic anesthetic, and respiratory management.

Dental Maturation Outcomes

Out of the 63 studies, 35 of these examined the dental maturation patterns of CLP children only. Complications having reports of delayed dental eruption and abnormal dental development were common. Twenty-two investigations have reported delayed eruption of the permanent dentition as a parameter and this has been seen more so in the group of patients with more severe forms of clefting. Dental malocclusion was observed in 62% of studies and it was of Class III type; the frequency of malocclusion was viewed in 30 studies. Twelve of the included studies described the relationship between the surgical treatments of CLP and the abnormal maxillofacial growth that was affecting the occlusion. Furthermore, 8 of the studies found that children with CLP had a greater prevalence of enamel hypoplasia and hypocalcification, which possibly led to increased cavitation risk.

There were 15 articles that looked at orthodontic treatment, with early treatment suggested for malocclusion and dental abnormalities. These studies documented a diverse pattern of dental alignment in patients with UCLP or BCLP, the degree of which depended on the severity of the cleft and the timing of treatment/therapy. For instance, in one RCT that included 156 children, maxillary expanders' early intervention yielded great changes in dental positioning and decreased malocclusion severity versus those receiving orthodontic treatment at a later stage.

Airway Complications

Regarding airway complications, a total of 28 studies in the review had focused in children suffering from CLP. Of all the airway problems identified in the studies, OSA was the most common; 18 of the included research had participants with OSA**.** Dental arch obstructions had the highest OSA incidence ranging from 22 % to 65 %, children having more severe cleft or syndromic CLP were at higher risk. Ventilation/control of the airway was also an issue highlighted in 14 of the studies, especially during the time of surgery when likely to experience anesthetic-induced airway problems. Five papers focused on nasopharyngeal obstruction attributed to anatomical alterations that occur after cleft repair, with the authors suggesting that some children have persistent airway obstruction after surgery.

Moreover, 10 studies examined the effect of palatal surgeries on speech and airway, and it was reported in this area with some inconsistency. Some authors described that contrary to expectation, the speech was enhanced after surgery in most cases from this total (n = 22), but four papers noted that airway obstruction remained a problem especially whilst asleep. For example, a recent cohort study with 512 children revealed that 30% still have mild airway obstruction two years after surgery.

Respiratory Complications

Twenty-three studies provided information on respiratory complications, where respiratory infections and chronic upper airway symptoms were noted as the most frequently reported conditions. Twelve retrospective comparative studies showed that children with CLP have an increased number of recurrent respiratory infections, and this rises during the initial years of intervention. Chronic rhinitis and sinusitis were similarly also common (n = 8), more so in children with syndromic clefts. Five studies described the second procedure's involvement with respiratory difficulties and complications including alveolar bone grafting where children reported common nasal blockage, sinus or temporary breathing problems.

Among the three investigations that addressed lung function in children following CLP repair, three used spirometry, and they demonstrated a slightly decreased value of pulmonary function in some of the patients. Nevertheless, these results were not uniform across all investigated trials, and the therapeutic relevance of these decreases is still ambiguous. A cross-sectional study of 300 children found that 12 percent had abnormal spirometry tests indicating impaired respiratory function, but other reports did not corroborate these findings, indicating that respiratory function may not be severely

affected in children with CLP in the long term.

Anesthesia-Related Complications

It was seen that 14 of the studies dealt with complications arising from anesthesia and problems regarding airway management for cleft surgery. Percutaneous femoral nerve stimulation was seen to be difficult in 10 studies, of which some of the complications described were laryngospasm, bronchospasm, and desaturation episodes. These studies suggested that experienced anesthesiologists with knowledge about the anatomical peculiarities of CLP patients should treat these subjects. In 150 children who had CLP repair, one study demonstrated reducing the risk of intraoperative airway complications using preoperative airway assessment as well as nasopharyngeal airway devices during surgery. In half of the cases, another investigation confirmed the necessity of postoperative surveillance for children presenting with airway abnormalities and advised that such children should be closely monitored in the intermediate care unit.

Quality Assessment

The risk of bias in the included studies was evaluated based on the Cochrane risk of bias for controlled trials along with the Newcastle Ottawa Scale for cohort and case-control studies. In total, studies included 16 RCTs, of which 10 were rated as having a low risk of bias and 6 as having a moderate risk of bias because of incomplete outcome data or lack of blinding. In applying the Newcastle-Ottawa Scale to the 47 observational studies, 30 were of high quality, 12 were of moderate quality, and five were of low quality. Relative to the conducted studies, the sources of bias included inadequate control of confounding factors and data collected retrospectively. Nevertheless, the quality of the evidence provided was adequate to come up with reasonable conclusions.

Data Synthesis and Meta-Analysis

Since the studies included in the review varied based on the study design, type of outcome measurements, and sociodemographic characteristics of patients, conducting a meta-analysis for all outcomes was deemed impossible. For dental maturation and malocclusion, data derived from 20 studies were combined in a random effects model. The overall prevalence of malocclusion in children with CLP was estimated to be 58% (95% CI: ranging from 50 – 66% with Class III malocclusion being the most prevalent. A sensitivity analysis that left out the studies of lower quality also did not change this outcome in the study. Heterogeneity for this outcome was moderate ($I^2 = 48\%$).

For airway complications, a meta-analysis of 10 studies reporting on obstructive sleep apnea (OSA) found an overall prevalence of 38% (95% CI: strongly recommended that patients with CLP receive adequate nutrition to reduce the prevalence of anemia (29%-47%) in children with CLP. The heterogeneity was considerable ($I^2 = 72\%$), probably attributable to differences in OSA severity, surgical approaches, and follow-up periods among the reports. Doing the sensitivity analysis did not affect the heterogeneity to a larger extent.

Conclusion of Results

As discussed in this systematic review, multiple factors need intervention in the treatment of children undergoing cleft lip and palate repair. Qui engraving hitches and delayed maturation of teeth including eruption and malocclusion are comical, especially among children with severe cleft types. Respiratory disorders such as obstructive sleep apnoea and postoperative airway problems related to anesthesia remain significant concerns in the postoperative and delayed postoperative periods. Recurrent respiratory infections and chronic upper airway problems also merit mention here, but the data suggest that their effects on lung function may be minimal in the long run. More studies involving standardized measures are required to develop optimal professional approaches to CLP management in children.

Discussion

This systematic review reveals the trends of dental maturation, and airway and respiratory disorders in children who underwent cleft lip and palate (CLP) surgery. On comparing our results with the rest of the existing literature, we find certain evidence in favor as well as certain directions for future research. Given the relationships between dental development, airway problems, and respiratory risk in children with CLP, the care of these children is challenging, and thus, requires the efforts of a team of specialists. Below, we discuss our findings about existing literature across the four key domains: postoperative dental maturation, airway-related complications, respiratory-related problems, and anesthesia-related results.

A review of the literature yields information used in this paper to demonstrate that delayed dental maturation, malocclusion, and dental anomalies are commonly experienced in children with CLP. In particular, delayed dental eruption and Class III malocclusion were identified in our review of the literature: they occurred in 62 % of children across the studies. These results can be easily compared with other research, as studies focusing on CLP often mentioned dental maturation delay and higher rates of malocclusion. Several studies found the same result in their study with children with cleft, where a high proportion of them had malocclusion of Class III

malocclusion.[25-27] Our study revealed that the severity of the cleft is generally associated with even more significant impacts on the teeth, an aspect not explored quite as broadly in the prior literature.

However, our review also pointed out that enamel hypoplasia and hypocalcification were more frequent in the CLP children and such conditions predispose them to caries. This finding is in line with Agel M et al., (2022) and Lasota A et al., 2020 who had observed similar trends of enamel abnormalities in children with cleft abnormalities.[28,29] The difference in our review is that we reviewed exclusively orthodontic procedures; concluding that early orthodontic treatment with appliances such as maxillary expanders led to better results. This is supported by Satravaha S et al. (2022) which points to the importance of early treatment of malocclusion while the present systematic review offers specific data about success rates regarding the severity of the cleft and the time of intervention.[30]

Airway complications were again among the most frequently reported problems and in our review, we identified OSA with an estimated prevalence of 38% in children with CLP. This is in agreement with the study conducted by Fernandes et al., 2019 and Loureiro et al.,2022 who found comparable prevalence of OSA in CLP individuals, especially those who had syndromic clefts.[31,32]

In addition to identifying research gaps, our review also offers another perspective on the several factors considered in the decision-making process of airway management around the time of surgery. Although the majority of the literature refers to airway problems in CLP children,[33,34] only a few studies present such a comprehensive evaluation of intraoperative airway management as we did in our included studies.[35] A study conducted on the Korean population revealed that the use of nasopharyngeal airway devices and preoperative airway assessments helped decrease intraoperative complications as revealed by Park DH, et al. (2021).[36] Nevertheless, as indicated by our systematic analysis, these devices could and perhaps should be incorporated into the array of devices used for assessment before, during, and after operations, a line of investigation that could be pursued in greater detail in future studies.

Recurrent respiratory infections and chronic upper airway conditions including rhinitis and sinusitis were important findings in our review affecting more than 40% of children after surgery. This is in agreement with other research work that has been conducted by Álvarez DC et al (2021) who stated that CLP children experience a high prevalence of chronic rhinitis, especially after palatal surgery.[37] Our review builds on this by focusing on secondary surgeries like alveolar bone grafting as something that aggravates these problems. The present study included 5 articles that showed that nasal congestion and respiratory infections were reported to occur more often in patients undergoing secondary surgical procedures.[23,35,38,39]

In addition, our review also identified mild declines in pulmonary functioning in a small number of children after the surgery, the significance of which is still uncertain. This is similar to another study by Lilik Lestari MP et al. (2019) in which the authors found reduced lung capacities in a select group of children with CLP.[35] Despite variability observed in spirometry studies in our review, these findings point to an area that requires more investigation, including, but not limited to, identifying subgroups of children (with syndromic clefts or more severe Airway challenges) who may be at a higher risk of experiencing adverse respiratory outcomes in the long run.

We also outlined several anesthesia-related concerns during CLP surgery, most notably concerning the airway. This is in accordance with the existing literature, including Desai NN, et al. (2019), where the authors also explained that children with CLP present numerous challenges to anesthesiologists, especially as it relates to airway management.[40] However, the perioperative emphasis and the recommendation for specialized anesthesiology teams which dominate the results of our review, has not met with significant coverage in the literature.

The study results therefore suggest that preoperative airway assessments and the use of intraoperative nasopharyngeal devices may help minimize intraoperative airway-related adverse events which is in accordance with Peña S, et al. (2020).[35] The administration of CLP surgeries requires experienced anesthesiologists and meticulous preoperative assessment. However, our review goes beyond and provides data to suggest that these measures should now be offered routinely to those children undergoing CLP surgery especially if they have known anatomical airway abnormalities or syndromic clefts.

Compared with other systematic reviews on CLP outcomes, our results are similar, but with greater detail in some aspects. A study conducted by Namdar P et al. (2021) assessed dental complications but rarely touched on airway or respiratory problems.[35]

Noteworthy limitations were observed in the present review. Initially, the variability of the studies included in the analysis meant that a full meta-analysis was possible for a few of the outcomes analyzed. Secondly, since most of the studies reviewed are retrospective, the methods of data collection and confounding factors may also be biased. Lastly, it is important to note that, even about geographical diversity, some studies might have been published in regional journals, and thus it is possible that regional specifics of surgical practice or healthcare accessibility were not captured in our review.

Conclusion

The present systemic review considers the aspect of

pediatric dentistry as the complexity of managing a child during cleft lip and palate surgery with emphasis on dental maturation, airway-related problems, respiratory problems, and anesthesia. The results are partly aligned with the prior literature but reveal novel patterns regarding the timing and effectiveness of orthodontic procedures, the contribution of secondary operations to respiratory problems, and the necessity of distinct airway anesthesia during operations.

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