Thai Journal of Orthodontics

บทความปริทัศน์

Review article

Risk Factors Related to Obstructive Sleep Apnea Syndrome in Children with Repaired Cleft Lip and Palate

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Abstract

Obstructive sleep apnea syndrome (OSAS) is a common sleep-related breathing disorder frequently detected in children, especially when a craniofacial condition such as cleft lip and palate (CLP) plays a role. Their distinct craniofacial alterations, marked by a diminished midface and a retrusive maxilla compared to non-cleft children, increase the susceptibility of children with CLP to OSAS. These anatomical changes result in a decreased cross-sectional airway volume, increasing the likelihood of OSAS development in children with CLP. Medical procedures like palatoplasty, commonly utilized to address anatomical irregularities, can inadvertently lead to upper airway obstruction. Additionally, various risk factors influence OSAS in children with CLP, making it a multifactorial condition. The ability to identify OSAS in children with CLP is essential because if left untreated it can cause cognitive deficits, behavioral problems, impaired growth, and cardiovascular complications. To minimize the underdiagnosis of OSAS, the related risk factors related to OSAS in children with CLP should be considered. This review article aims to investigate those risk factors in children with repaired CLP to enable early detection, which can prevent unexpected complications through proper interventions.

Keywords: Cleft lip and palate, Obstructive sleep apnea syndrome, Risk factors

Received: 23-July-2023 **Revised:** 11-Sep-2023 **Accepted:** 5-Oct-2023

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Introduction

Obstructive sleep apnea syndrome (OSAS) is known as a common sleep-related breathing disorder marked by prolonged partial upper airway obstruction and/or intermittent complete obstruction during sleep.[1] Its prevalence is 1.2 % -5.7 % in the overall pediatric population.[2] The major risk factors of OSAS in healthy children are adenotonsillar hypertrophy (ATH) and obesity, but other factors should be a concern in children who suffer from such conditions as a history of prematurity, asthma, Down syndrome, sickle cell disease, achondroplasia, neuromuscular disease, and craniofacial abnormalities. Children with cleft lip and palate (CLP), recognized as the most common craniofacial abnormality, are also at an elevated risk of developing OSAS.[2,3]

CLP arises from the deficiency of proper interaction or sustained contact between the medial nasal and the lateral nasal process as well as the maxillary process.[4] The documented incidence of CLP among liveborn babies is 1.7 cases per 1000 births.[5-7] In Thailand, a comparable incidence of 1.6 cases per 1000 live births has been observed for CLP among Thai infants.[8] The presence of CLP in children is significantly related to the diagnosis of OSAS. Abnormal craniofacial structure and anatomic alterations in the nasal cavity, nasopharynx, oropharynx, palate, and maxilla that characterize patients with CLP are factors related to OSAS.[9-11] These alterations in craniofacial structure, notably the underdeveloped midface and retrusive maxilla, lead to a decrease in the cross-sectional airway volume, thereby heightening the likelihood of OSAS development in children diagnosed with CLP.[12] These deformities necessitate various surgical interventions, including primary palatoplasty, to address the cleft anomaly, enhance speech function, and correct facial features.[12] However, these corrective procedures can inadvertently lead to upper airway obstruction.[13] Furthermore, approximately 13 % of children with CLP experience velopharyngeal insufficiency (VPI) following primary palatal repair, leading to hypernasal voice and swallowing challenges.[3] As a consequence, many CLP children require secondary corrective surgeries, often employing techniques like pharyngeal flap, sphincter pharyngoplasty, pharyngoplasty, and Furlow palatoplasty. These interventions have potential complications, with OSAS emerging as a prominent concern.[14] CLP children also suffer from disruptions of the oropharyngeal muscles, with negative effects on speech, swallowing, and airway patency, especially while sleeping.[15]

There is limited existing literature on the risk factors pertaining to OSAS in children with repaired CLP. The objective of this study is to access and explore the risk factors for OSAS in children with repaired CLP, based on the published studies, thus deepening the understanding of the connection between CLP and OSAS; this potentially will give new insights and advance the field's knowledge. The resulting enhanced awareness for early detection of OSAS in CLP children is crucial for preventing complications and alleviating the negative effects on cognitive function, behavior, and cardiovascular health, and attention deficits and delayed development that younger CLP children with OSAS may experience. Finally, the findings of this study will provide valuable information for dental professionals and healthcare providers involved in the care of children with CLP, enabling them to improve their clinical practices and provide better care for these individuals.

Literature review

Risk factors

Several studies have identified potential risk factors that may be related to OSAS in children with CLP. These risk factors include:

1. Cleft type

Orofacial clefts are categorized into various types:[16]

1. Cleft lip without cleft palate (CL): This type affects only the lip and may be unilateral or bilateral.

2. Cleft lip with cleft palate (CLP): This involves both the lip and the primary palate. CLP can be

unilateral or bilateral and may present as a complete or incomplete cleft.

3. Isolated cleft palate (CP): This type affects only the secondary palate and is rarely diagnosed prenatally.

4. Median cleft lip and palate (MCLP): Unlike CL and/or CLP, MCLP is characterized as a midline defect. It is often associated with additional midline brain and facial anomalies and has a high probability of origin in chromosomal abnormalities.

In a research study comparing the prevalence of increased OSAS risk in patients with and without CLP, researchers utilized a validated questionnaire, the Pediatric Sleep Questionnaire (PSQ), as a research tool for identifying OSAS risk; a higher score indicated an increased risk. Compared to patients without CLP, patients with unilateral and bilateral CLP had significantly higher mean Pediatric Sleep Questionnaire scores and a higher prevalence of elevated OSAS risk.[17] However, when individuals with both cleft lip and palate were compared regarding cleft types, encompassing isolated CP, unilateral and bilateral cleft lip and alveolus, no significant correlation was found between cleft type and the prevalence of OSAS risk.[17] Similarly, several prior studies conducted by Silvestre et al. (2014) and MacLean et al. (2009) did not identify a significant association between OSAS risk and cleft classification.[18,19]

In addition to typical CLP, there are other variations, including submucous cleft palate (SMCP) and cleft mandible. However, our literature review did not yield any published information regarding the potential association between these cleft types and the risk of OSAS.

2. Abnormalities of bony anatomy and neuromuscular function

Children diagnosed with non-syndromic CLP commonly exhibit diminished upper airway dimensions attributable to skeletal abnormalities, particularly involving the retrusive maxilla,[20] which is similar to patients with nasal airway obstruction and OSAS.[21] Research has established a strong correlation between maxillary dimensions and upper airway measurements,[11] highlighting the significant impact of a hypoplastic midface and retrognathic maxilla in reducing cross-sectional airway volume in children with CLP.[12] These findings align with another study that reported a significant prevalence of OSAS in children with CLP, further suggesting that children with CLP are more susceptible to symptoms of OSAS.[10,22]

Furthermore, these patients are prone to experiencing neuromuscular dysfunction, specifically affecting the muscles responsible for controlling the soft palate, which heightens the risk of airway collapse and the development of OSAS.[23] Nasal airway obstruction resulting from nasal deformities further contributes to the susceptibility of patients with CLP to OSAS.[24,25]

3. Palatal dimensions

Palatal dimensions refer to the measurements and characteristics of the palate, which is the superior aspect of the oral cavity. These dimensions of width, height, depth, surface area, and volume of the palatal structure collectively determine the size, shape, and overall morphology of the palate. Palatal dimensions are a key contributing factor to the risk of OSAS in children both with and without unilateral cleft lip and palate (UCLP). Several studies have explored the relationship between palatal dimensions and upper airway measurements. Notably, a study conducted by Kecik (2017) compared palatal area, palatal width, and airway volume between patients with OSAS and those without OSAS and found that OSAS patients had significantly smaller palatal dimensions. Additionally, they established a significant correlation between palatal volume and oropharyngeal area, affirming their pivotal role in the development of OSAS.[26] In a recent study by Ciavarella D. et al. (2023), a significant negative correlation emerged between palatal depth and area and the severity indexes of OSAS. This further supports the association between abnormal palatal dimensions and an increased susceptibility to OSAS symptoms.[27]

Significant differences were also observed in comparative analyses of palatal dimensions, including volume and surface area, between children with UCLP and those without. Children with either unilateral or bilateral CLP exhibited significantly smaller palatal volumes compared to non-cleft individuals.[28] Another study utilizing digital dental casts to evaluate the maxillary arch width, palatal surface area, and volume in children with UCLP during mixed dentition and children without UCLP found significantly reduced palatal surface area and volume in the UCLP group compared to the control group.[29] These findings align with the research conducted by Smahel et al. (2003), which analyzed the three-dimensional palatal morphology in children with UCLP. This study revealed an overall palatal narrowing of the palate, specifically in the anterior region. Moreover, it was accompanied by reduced width and height of the palate.[30] Asymmetry in the palatal vault was also observed, with the highest points situated in the front on the clefted side and in the back on the non-clefted side.[31]

While the precise mechanisms underlying the association between diminished palatal dimensions and increased risk of OSAS are not yet fully understood, it is widely believed that the reduced palatal dimensions commonly observed in patients with UCLP can restrict the space available for the tongue. This can lead to airway narrowing and obstruction during sleep, potentially contributing to the development or exacerbation of OSAS-related symptoms.[30] To date, however, evidence is insufficient to support comparative evaluations of palatal dimensions in UCLP children with and without OSAS, or to correlate palatal dimensions with OSAS in children with UCLP. Although craniofacial characteristics are considered predisposing factors for OSAS, the precise role of palatal dimensions in the etiology of OSAS has yet to be accurately described. Further research is necessary to develop evidence-based clinical practices in this area.

4. Age

Aging intensifies the susceptibility to OSAS, with the prevalence of OSAS steadily increasing as individuals advance in years.[32] However, its mechanism remains unclear.[33] It is possible that, as indicated by certain studies, changes in pharyngeal anatomy and biomechanics, alterations in the distribution of body fat, or decline in the function of pharyngeal dilator muscles may lead to variations in the amount, location, and pattern of upper airway obstructions over time.[34] This study showed that age might impact sleep by altering the collapsibility of the pharynx. It has been observed that elderly patients have greater pharyngeal collapsibility during sleep.[35] Another investigation showed that elderly individuals diagnosed with OSAS exhibited a higher frequency of complete velum collapse and a reduced frequency of total lateral wall collapse within the oropharynx, in contrast to their younger counterparts.[36] However, a recent study comprising 351 children and adolescents with non-syndromic CLP found positive OSAS risk to be more common in CLP patients younger than ten years old, based on the Obstructive Sleep Apnea-18 (OSA-18) questionnaires.[37] Conversely, a previous study found that age is not a significant factor in OSAS risk with CLP patients.[19]

5. Gender

Biological sex may represent a potential risk factor for childhood OSAS. A study of otherwise healthy children indicated that boys without CLP have a higher OSAS risk compared to girls.[38] The reasons for this difference remain unclear, but many factors may contribute to the greater OSAS prevalence among males (without CLP), including the distribution of body fat, upper airway length and collapsibility, neurochemical control processes, and arousal response.[38] However, a recent study of children with CLP showed no differences between males and females in terms of OSAS risk,[37] in agreement with previous studies in children with CLP.[17,18]

6. Obesity

Childhood obesity has a significant impact on OSAS. Some cross-sectional studies have indicated that childhood obesity, defined by a body mass index (BMI) equal to or surpassing the 90th or 95th percentile, increases the likelihood of snoring by two to four times.[39] Obesity is an independent risk factor for both snoring and OSAS in children.[40,41] According to a retrospective study, there is a link between BMI and Apnea Hypopnea Index (AHI). In obese children, both the median AHI and the percentage of cases where AHI exceeded 1.5 per hour were significantly higher compared to nonobese children.[42] Several mechanisms establish a connection between obesity and OSAS, including diminished compliance within the respiratory system, elevated airway resistance, reduced lung volumes, modified ventilation patterns, alterations in expiratory flow rate, and disruptions in gas exchange.[43] Despite this association of obesity with an elevated risk for OSAS in children and adolescents without CLP,[44] a review of studies of children with CLP failed to identify a significant link between high BMI and positive OSAS risk.[17,18]

7. Primary palatoplasty techniques and timing of cleft palate repair

Primary palatoplasty is used to treat children diagnosed with CP in developed nations, typically either prior to or around their first birthday.[45] Several primary palatoplasty techniques are used, including two-flap palatoplasty, a straight-line repair, and the double-opposing Z-plasty.[45] Primary palatoplasty in children with CP can result in airway obstruction.[13] However, the precise impact of this procedure on OSAS has not been well-studied. One study suggested that surgical closure of the palate induces upper airway obstruction within the initial 24-hour period post-surgery, mainly attributable to surgical manipulation and consequent complications like swelling of the tongue, postoperative bleeding, or laryngitis following extubation. This obstructive effect is mostly indicated by snoring and other transient symptoms, such as difficulty breathing during sleep, but without breathing pauses.[13] A retrospective study of 64 children with CP repair who underwent polysomnography (PSG) before and after palatoplasty found that OSAS did not develop or worsen as a result of primary palatoplasty; nonetheless, the AHI score increased by five or more events per hour in approximately 20 % of the participants.[45]

The timing of cleft palate repair is a critical factor influencing mid-face growth outcomes in CLP patients;[46] this may, in turn, impact OSAS risk due to reduced airway volume.[12] Early repair has proven benefits for speech development but may potentially restrain maxillary growth.[47] The American Cleft Palate–Craniofacial Association advises that palate repair should ideally be performed by the time a child reaches 18 months of age, with the goal of maximizing favorable long-term speech outcomes.[48] Some researchers argue that delayed palate repair may lead to improved craniofacial morphology, although possibly impairing speech development.[46] However, others find no significant disparities in craniofacial growth between early and delayed cleft repair.[49] In some cases, patients having surgery at the recommended time achieve normal speech abilities despite notable craniofacial morphology differences.[46] Consequently, the ideal timing of cleft palate repair remains a topic of debate, particularly regarding its potential interference with maxillary growth. A study by Rana et al. (2016) revealed no significant differences in pharyngeal airway dimensions between early and late palatal surgery and a control group. Nevertheless, further research is warranted to explore the relationship between the timing of cleft palate repair and OSAS risk in the cleft population.[46]

8. Adenotonsillar hypertrophy

Adenotonsillar hypertrophy (ATH) is one of the predominant causes of pediatric obstructive sleep apnea syndrome (OSAS) in the non-cleft population.[22] A study conducted by Isono et al. (1998) compared the collapsibility of the passive pharynx during anesthesia and skeletal muscle paralysis in non-cleft patients with

and without OSAS. The results indicated that in children with OSAS, upper airway closure occurred at the level of the tonsils and adenoids.[50] In contrast, in non-OSAS children, it occurred at the level of the soft palate. This underscores the influential role of anatomical factors in the pathogenesis of pediatric OSAS and suggests that structural anomalies in the entire pharynx, alongside enlarged adenoids and tonsils, may contribute to the manifestation of OSA.[50]

Children with CLP who additionally suffer from ATH face an elevated susceptibility to OSAS as a result of restricted airways.[23] Enlarged tonsils, aside from their association with OSAS, could partially obstruct the space between the palate and the posterior pharyngeal wall, hindering palatal closure and potentially causing VPI.[23] Significantly, tonsillectomy has been effective in alleviating both OSAS and VPI. On the contrary, adenoid hypertrophy, located on the posterior pharyngeal wall, may act as a cushion against VPI by facilitating velopharyngeal closure.[23] However, after adenoidectomy, this compensatory mechanism may be compromised, potentially leading to VPI. As a result, when necessary, tonsillectomy and/or partial adenoidectomy are effective therapeutic approaches for managing OSAS in individuals with repaired CP who have tonsillar and/or adenoid hypertrophy.[23]

9. Surgical techniques for treating velopharyngeal insufficiency

VPI is defined by inability to achieve proper closure of the velopharyngeal sphincter, which leads to an inadequate separation between the oral and nasal cavities during speech. Thirteen percent of children with CP develop VPI following primary palatal repair, resulting in hypernasal voice and swallowing difficulty.[3] One study has estimated that 5 % to 30 % of patients with CP will require secondary surgical procedures to enhance velopharyngeal closure after receiving the appropriate primary palatal repair and speech therapy.[51] Madrid et al. reported that several surgical techniques for correction of VPI include pharyngeal flap, sphincter pharyngoplasty, pharyngoplasty, and Furlow palatoplasty, but that various surgical techniques have had complications, with OSAS being one of the major concerns.[14] OSAS can develop following posterior pharyngeal flap surgery and is a known occurrence in children with CLP. Moreover, there have been reports of fatalities resulting from upper airway blockage in the postoperative period.[52,53] However, the prevalence and duration of this OSAS are debatable.[54] Some findings demonstrate that post-operative dynamic sphincter pharyngoplasty may increase the incidence of OSAS.[55] Following a Furlow palatoplasty, a slight elevation in upper airway obstruction may be observed in the immediate postoperative period. Nonetheless, it seems to have a lower rate of OSAS complications.[56]

10. Breastfeeding

Several studies indicate that breastfeeding could offer long-term defense against the severity of sleep-disordered breathing in childhood. Children who were breastfed for two to five months had less severe OSAS symptoms than children who had not been breastfed.[57] Breastfeeding contributes to the development of a healthy upper airway structure, and breast milk provides immunologic protection against infections that may trigger OSAS.[57] However, another study reported a positive correlation between breastfeeding and OSAS.[58] Similarly, a different investigation found that breastfeeding was associated with chronic snoring as a risk factor through an unidentified mechanism, which could be immunological in nature. They suggested that the immunological agents from the breast milk promoted airway inflammation, which led to wheezing and snoring.[59] A study was conducted to compare the duration of breastfeeding in patients with and without CLP, which yielded interesting results.

A study reported that children with CLP had had significantly shorter durations of breastfeeding and significantly longer durations of bottle-feeding than children without CLP.[17] This difference could be explained by the fact that newborns with non-syndromic clefts exhibit less effective sucking patterns compared to individuals without CLP.[17] Nonetheless,

according to Palmer, bottle-feeding leads to the development of high palates, narrow dental arches, and retruded chin, which increases the risk of snoring and sleep apnea. In contrast, breastfeeding provides advantages in diminishing malocclusion among children in general.[60] Consequently, a recommendation can be made in favor of breastfeeding over bottle feeding, particularly for children with CLP.

Discussion and Conclusion

Clinicians treating children with CLP should consider the factors associated with OSAS in children with repaired CLP.

1. Cleft type: The research highlights a notable increase in the risk of OSAS among children with unilateral and bilateral CLP when compared to those without CLP.[17] Nonetheless, when comparing individuals with different cleft types, including isolated CP and unilateral and bilateral cleft lip and alveolus, no significant correlation between cleft type and the prevalence of OSAS was observed.[17-19] Therefore, it is recommended that a systematic and thorough assessment for OSAS risk should be an integral part of the routine care for children with CLP of all types.

2. Bony anatomy and neuromuscular dysfunction: Skeletal abnormalities and diminished upper airway structures often accompany CLP, thereby contributing to the development of OSAS.[12,20,21] Dysfunction in the muscles controlling the soft palate and nasal deformities can also increase the risk of OSAS.[23-25] Evaluation of children with CLP should include assessment of anatomy and muscle function.

3. Palatal dimensions: Palatal dimensions play a potential role in the risk of OSAS in children with and without UCLP. Further research is necessary to gain a deeper understanding of the precise mechanisms involved and to develop evidence-based clinical practices in this area.

4. Age: Aging significantly impacts the risk of OSAS, with the prevalence of the condition increasing with age.[32] Elderly individuals tend to have greater pharyngeal collapsibility during sleep.[35,36] Only a limited number of studies have specifically investigated the influence of aging on OSAS risk among individuals with CLP. Even after childhood repair, continuing care should consider patient aging.

5. Gender: The impact of gender on OSAS risk in children with CLP remains uncertain. Therefore, the emphasis should be on conducting personalized assessments and educating families about recognizing OSAS symptoms, particularly in boys.

6. Obesity: Childhood obesity is a recognized risk factor for OSAS.[39-41] However, its association with OSAS in cleft patients is uncertain and inconsistent.[17,18] When dealing with CLP children, this relationship becomes complex and may not always follow the usual pattern. Thus, it is recommended that clinicians should diligently monitor the growth and weight of CLP children, addressing obesity concerns through appropriate interventions like dietary guidance, physical activity, and behavioral changes. Collaborative and individualized approaches involving weight management, multidisciplinary teams, and tailored treatments are essential. Continuous monitoring and family education play crucial roles. Further research is needed to better understand the connection between obesity and OSAS in CLP children.

7. Primary palatoplasty techniques and timing of cleft palate repair: Primary palatoplasty in cleft palate patients may cause temporary symptoms such as snoring. However, its impact on OSAS is not well-studied, and this procedure does not appear to significantly increase or worsen the risk of OSAS.[13] It is advisable to closely monitor the post-surgical population for the emergence of OSAS following palatoplasty. These patients and their families should also be informed that postoperative medical or surgical intervention might become necessary to address OSAS. Cleft palate repair is necessary for functional and aesthetic reasons, and decisions regarding surgical timing should be made in consultation with healthcare

professionals specializing in care of children with this condition. Although the relationship between the timing of cleft palate repair and OSAS risk in the cleft population is still unclear, the potential risk of OSAS should be carefully considered alongside the benefits of timely palate repair for each individual case.

8. Adenotonsillar hypertrophy: Because of the increased risk for OSAS in children with CLP with ATH, a tonsillectomy and/or partial adenoidectomy should be considered for OSAS management. Additional surgical interventions may be necessary to address airway obstruction, especially when there are accompanying comorbidities that complicate the management of OSAS.

9. Surgical techniques for treating velopharyngeal insufficiency: Some surgical techniques to correct VPI may increase the risk of OSAS.[14] Clinicians must be aware of these potential complications when discussing surgical interventions for VPI management in CLP patients. Treatment should be highly individualized, balancing the benefits and risks of surgical techniques, such as Furlow palatoplasty, which may have a lower OSAS complication rate. A multidisciplinary approach involving various specialists is essential, as is educating families about potential risks and symptoms.

10. Breastfeeding: The relationship between breastfeeding and OSAS is complex. While breastfeeding may have protective effects against sleep-disordered breathing, conflicting findings suggest a potential association between breastfeeding and OSAS in certain cases.[57,58] Breastfeeding should be prioritized over bottle-feeding for children with CLP, with support for mothers. We suggest that future longitudinal prospective studies with more validated sampling and diagnostic methods are needed to clarify the relationship between breastfeeding and OSAS.

Despite the valuable insights gathered from various studies compiled in this review, limitations exist. Some studies included in our review employed questionnaires to identify children with OSAS symptoms instead of using PSG, which is the gold standard method for diagnosis of OSAS. Because of the substantial expenses involved and the disparity between demand and available capacity, it is crucial to establish criteria for referring patients for PSG. It is essential to recognize a crucial difference between children clinically diagnosed with OSAS and those identified solely through symptom questionnaires. This difference can affect how we determine the number of children with OSAS among those with CLP. Some children with OSAS might be overlooked because they do not receive a PSG diagnosis. This issue might impact our understanding of the prevalence of OSAS risk in children with CLP.

Nevertheless, this compilation of research sheds light on the multifaceted nature of OSAS risk factors in children with CLP. This review should serve not only as a resource for dental professionals and healthcare providers caring for children with CLP but also as a catalyst for future research. Understanding the intricacies of OSAS risk within this particular population remains limited. Hence, we strongly encourage future research to investigate the risk factors related to OSAS in children with repaired CLP to expand the horizons of knowledge in this vital area of research, contributing to improved care and outcomes for this population.

Author contributions

CP: Conceptualization, Validation, Formal analysis, Investigation, Data Curation, Writing-Original Draft, Visualization and; MC: Conceptualization, Validation Writing-Review & Editing, Visualization, Supervision.

Disclosure statement

No conflict of interest in the study

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