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Risk factors of obstructive sleep apnea syndrome in the developmental age

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Summary

Background: Obstructive Sleep Apnea Syndrome (OSAS) is a prevalent respiratory sleep disorder in children, associated with severe health consequences, including hypertension, cardiac dysfunction, and neurocognitive impairment. Despite extensive research on OSAS in adults, the risk factors for pediatric OSAS remain underexplored.

Objective: This literature review aims to identify and present the key risk factors associated with pediatric OSAS based on contemporary studies.

Methods: A systematic search of the PubMed and Scopus databases was conducted for literature published between 2016 and 2024. Search terms included “obstructive sleep apnea,” “children,” and “risk factors.” A total of 93 relevant studies were reviewed after excluding non-pediatric and irrelevant papers from an initial pool of 283.

Results: The most commonly identified risk factors for pediatric OSAS include adenoid and tonsillar hypertrophy, obesity, craniofacial abnormalities, and asthma. Additional risk factors

such as allergic rhinitis, recurrent upper respiratory infections, nasal stenosis, congenital diseases, low vitamin D levels, and preterm birth were also noted.

Conclusion: Pediatric OSAS is influenced by multiple factors, including anatomical, physiological, and genetic components. Further research is required to explore emerging risk factors, such as role of vitamin D deficiency and microbiota, and to clarify the impact of variables like ethnicity and breastfeeding.

Keywords: obstructive sleep apnea; obstructive sleep apnea syndrome; obstructive sleep apnea risk factors

Introduction and Purpose

Obstructive Sleep Apnea Syndrome (OSAS) is one of the most prevalent respiratory sleep disorders (RSD), characterized by the partial or complete obstruction of the upper airways during sleep. This obstruction disrupts normal gas exchange, leading to fragmented sleep. According to the third edition of the *International Classification of Sleep Disorders* (ICSD-3), OSAS is diagnosed through polysomnography (PSG) when at least five respiratory disturbances occur per hour of sleep (Respiratory Disturbance Index - RDI), accompanied by symptoms such as unrefreshing sleep, excessive daytime sleepiness, fatigue, insomnia, or loud snoring. Alternatively, OSAS can be diagnosed when at least 15 respiratory disturbance events occur per hour, even without symptomatic manifestations. [1] Nevertheless, OSA in children does not fall under this definition or the associated diagnostic criteria. [2]

Despite extensive literature on the pathogenesis of OSAS in adults, research on OSAS in pediatric populations remains limited. The prevalence of pediatric OSAS varies, ranging from 1.2% to 5.7% [3], and is most commonly observed in children aged between 2 and 8 years [4]. The typical symptoms include habitual snoring, intermittent gasps or pauses during breathing, disturbed sleep, and daytime neurobehavioral issues [4].

Pediatric OSAS is a serious condition with potentially severe health consequences, including hypertension, cardiac dysfunction, and neurocognitive impairment. Therefore, it is crucial to identify the risk factors associated with pediatric OSAS, develop effective diagnostic protocols, and initiate timely treatment. This review aims to present the risk factors for pediatric OSAS as identified in contemporary literature.

Materials and Methods

A literature search was conducted using the PubMed and Scopus databases, covering the period from 2016 to 2024. The search utilized the keywords "obstructive sleep apnea," "children," and "risk factors," yielding 283 articles. Of these, 190 studies were excluded due to their lack of relevance to pediatric OSAS or risk factors. Ultimately, 93 papers were included in this review.

Results – Description of the state of knowledge

Various studies have identified a range of risk factors for OSAS in children. The most prevalent include adenoid and tonsillar hypertrophy, obesity, craniofacial abnormalities, and asthma [5]. Other risk factors highlighted include breastfeeding practices [6] , allergic rhinitis, recurrent upper respiratory infections, chronic sinusitis, nasal stenosis [7], and congenital disorders.

Adenoid and Tonsillar Hypertrophy

Adenoid and tonsillar hypertrophy are the most common risk factors for pediatric OSAS. Enlarged tonsils and adenoids can obstruct the upper airway, particularly during sleep when

muscle relaxation exacerbates the blockage. Several studies, including a retrospective analysis by Baker et al., consistently identify adenoid and tonsillar hypertrophy as the leading risk factor for OSAS in children. [8,9] The prevalence of OSAS peaks between the ages of 3 to 6 years, whichh coincides with the maximum size of the adenoids and tonsils relative to airway size. [10]

Obesity

Obesity is another well-documented risk factor for pediatric OSAS. The incidence of OSAS among obese children ranges from 5.7% to 56% [11], with a complex bidirectional relationship between obesity and OSAS. Excess adipose tissue in the upper airway muscles and lumen predisposes the airways to collapse during sleep, contributing to OSAS development. Obesity increases respiratory effort during sleep due to mechanical reasons [12], such as reduced lung volume, making the condition more severe [13]. This intricate relationship is exacerbated by systemic inflammation, oxidative stress, metabolic dysfunction, and alterations in gut microbiota, creating a vicious cycle [14]. Studies have also identified a positive correlation between the Apnea-Hypopnea Index (AHI) and waist circumference, visceral fat area, and neck circumference. [15] Interestingly, research by Glicksman et al. indicates that the neck-to-abdominal fat ratio is a stronger predictor of OSAS severity than total body mass. [16]. Numerous investigations into OSA have demonstrated a strong connection between the condition and chronic, systemic inflammation. White blood cell (WBC) ($P<0.001$), neutrophil (NEUT) ($P<0.001$), neutrophil-lymphocyte ratio (NLR) ($P=0.006$), and fibrinogen (FIB) ($P=0.033$) levels were all greater in obese children with OSA [17]. Early lifestyle modifications and family education are essential to preventing obesity and its effects.

Craniofacial Abnormalities

Craniofacial abnormalities also play a significant role in the development of pediatric OSAS. Children with conditions such as mandibular retrognathia, malocclusion, increased facial height, and abnormal hyoid bone positioning have a higher risk of developing OSAS. [18,19]

Structural features such as a narrow posterior airway space, lengthened soft palate, and mandibular deficiency, maxillary hypoplasia have all been associated with the condition [20]. Furthermore, in a study by Maresky et al. mandibular width has been shown to have a positive correlation with OSA. One idea regarding this mechanism involves the displacement of the parapharyngeal fat pads from the airway and the anterior positioning of the base of the tongue muscles. Another hypothesis is that the dimensions of the mandible affect muscle placement, which may subsequently impact the size and openness of the airway [21]. Another anatomical abnormality associated with obstructive sleep apnea (OSA) in children is the presence of an isolated cleft lip and/or palate (CL/P), with 14.7% of cases also presenting OSA. Children with unilateral cleft lips often develop a deviated nasal septum, commonly as a consequence of surgery. Additionally, Furlow palatoplasty, a surgical procedure used for CL/P, may enlarge and thicken the palate, reducing airway space and leading to OSA. Acute airway obstruction has been observed in patients undergoing posterior pharyngeal flap (PPF) and sphincter pharyngoplasty (SPP), potentially resulting in chronic nasal obstruction and contributing to OSA. [22]

Asthma

The relationship between asthma and OSA is still being discussed in the literature. A cross-sectional study by Fumo-Dos-Santos et al. showed an incidence of OSA of 70% in children with severe mild to moderate asthma and 64% in children with severe asthma. [23]
Another study by He et al. showed an incidence of OSA of 57% in children with persistent asthma included in the study. [24] A questionnaire-based study by Dooley et al. showed an association of the Pediatric Sleep Questionnaire with OSA prevalence and with poorly controlled asthma. [25]
However, other studies have failed to find a direct association between asthma severity and OSAS. [26], but show high presence of OSA in asthmatic patients [27]

Upper Respiratory Infections, Allergic Rhinitis, and Nasal Stenosis

Some studies have shown a correlation between allergic rhinitis and pediatric OSAS [28]

Increased upper airway resistance brought on by nasal blockages can cause sleep disruptions in OSAS patients. A study by Shen L et al. identified nasal stenosis and chronic sinusitis as independent risk factors of OSAS. 70,5%-94,3% (depending on the severity of OSA, from mild to severe) of 338 children with OSAHS included in the study suffered from chronic sinusitis and 42,0%-71,4% had nasal stenosis. [29]

Congenital Diseases

Certain congenital disorders also increase the risk of pediatric OSAS. Children with sickle cell anemia [30] , Prader-Willi syndrome, [31] or Down syndrome are particularly vulnerable. Studies have reported a higher prevalence of OSAS in these populations, with incidences as high as 95% in infants with Down syndrome [32]. These findings highlight the need for early screening and intervention for children with congenital disorders to prevent severe health outcomes.

Perinatal Risk Factors (Preterm Birth)

Preterm birth has been linked to an increased likelihood of obstructive sleep apnea syndrome (OSAS) in children [33]. A study by Tapia IE et al. identified additional perinatal risk factors for pediatric OSA, including chorioamnionitis and multiple gestations [34]. Furthermore, while one study found breastfeeding to be a risk factor for OSAS [35], older studies suggested it may have a protective effect against its development [36]. As a result, the relationship between breastfeeding and OSAS remains an area for further research.

Other Factors

Ethnicity and vitamin D levels have been identified as potential risk factors for obstructive sleep apnea syndrome (OSAS) in children. A Belgian study by Slaats M observed that Black African children exhibited more severe OSAS compared to their Caucasian counterparts [37]. However, the small sample size of only 11 Black African participants limits the broader applicability of these findings. Additionally, vitamin D deficiency has been linked to an increased risk of OSAS. Research by Ozgurhan G et al. indicated that children with low

25(OH)D levels had a significantly higher likelihood of developing OSAS, with 14.16% in the low 25(OH)D group at high risk compared to 5.83% in the control group [38]. Further investigation by Kheirandish-Gozal et al. found that children with both obesity and OSAS exhibited even lower plasma 25(OH)D levels, with a direct correlation observed between 25(OH)D levels and key polysomnographic markers, such as the apnea-hypopnea index (AHI) and oxygen saturation (SpO2) [39].

Discussion

The present study provides a thorough review of risk factors for pediatric OSAS; however, several limitations should be addressed. First, the inclusion criteria for studies were relatively broad, which may have introduced heterogeneity in the quality of the cited research, potentially affecting the overall conclusions. For instance, many studies relied on observational designs or small sample sizes, which limits their ability to establish causality. The lack of longitudinal studies also weakens our understanding of the temporal relationships between risk factors and the development of OSAS. Moreover, certain factors, like breastfeeding, present conflicting evidence across the literature, yet this review does not deeply investigate or critically compare these discrepancies. Additionally, the review underrepresents potential biases, such as geographic or cultural differences in the diagnosis and reporting of OSAS. Finally, while emerging factors like vitamin D levels are highlighted, the clinical relevance and underlying mechanisms are not fully explored, leaving questions about their true impact on pediatric OSAS. A more critical evaluation of the methodologies and conclusions of the cited studies would strengthen the review's contributions to the field.

Conclusions

Pediatric OSAS is a multifactorial condition influenced by a range of risk factors, including anatomical abnormalities, obesity, respiratory diseases, and genetic predispositions. Given the serious long-term health consequences of untreated OSAS, early diagnosis and intervention are critical. Future research should continue to explore these risk factors, especially in underrepresented populations and emerging areas such as the role of vitamin D.

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