

Obstructive Sleep Apnea in Infants and Children in Review

Raniyah Embarak Alharbi^{1*}, Hisham Fayiz Alkhuzaie², Kholoud Mohammed Bakheet³, Mlouk Bassam Shabrawishi⁴, Ghadeer Jaffar Al-Esmaeil⁵, Saud Mohammed Al Amri⁶, Noura Sabah Alibrahim⁷, Mohammed Saud Aljohani⁴, Sultan Mohamed Qattan⁴, Saud Faisal Nahhas⁴, Hussam Mohammed Algarni⁸ and Azhar Jamal Nasef⁹

¹Consultant of Pediatric, Hera General Hospital, Mecca, Saudi Arabia

²Security Forces Hospital, Mecca, Saudi Arabia

³King Abdulaziz University, Jeddah, Saudi Arabia

⁴Ibn Sina National College for Medical Studies, Jeddah, Saudi Arabia

⁵Maternity and Children Hospital, Dammam, Saudi Arabia

⁶Al Yamamah Hospital, Riyadh, Saudi Arabia

⁷The University of Jordan, Jordan

⁸King Saud Bin Abdulaziz University for Health Sciences, Jeddah, Saudi Arabia

⁹University of Debrecen Medical School, Hungary

***Corresponding Author:** Raniyah Embarak Alharbi, Consultant of Pediatric, Hera General Hospital, Mecca, Saudi Arabia.

Received: November 21, 2020; **Published:** January 18, 2021

Abstract

Background: Obstructive sleep apnea is described as a breathing problem during sleep associated with partial or full airway obstruction that disturbs normal sleeping breathing resulting in oxygen desaturation and hypercapnia, which causes increase in respiratory activity and other changes in intrathoracic pressure, which eventually lead to culminating in subcortical or cortical arousal then the infant wanders back to sleep and the cycle continues to happen all night resulting in disturbed sleep.

Aim: In this review, we will look into the pathophysiology, symptoms, risk factors, diagnosis and treatment of OSA in children and infants.

Conclusion: OSA is prevalent among children and infants and underdiagnosed by both parents and clinician until now. Junior physicians should be educated to be familiar with symptoms of OSA because children have various clinical symptoms and signs according to their developmental stages. Risk factors of OSA should be further studied to prevent increased incidence and further complication of untreated OSA. Untreated OSA in children is correlated with neuropsychiatric impairment, hyperactivity and cardiovascular impacts and sometimes can be correlated with sudden infant death syndrome.

Keywords: *Obstructive Sleep Apnea in Children; OSA in Infants; OSA in Children, Diagnosis of OSA; Management of OSA*

Introduction

Obstructive sleep apnea is described as a breathing problem during sleep associated with partial or full airway obstruction that disturbs normal sleeping breathing resulting in oxygen desaturation and hypercapnia, which causes increase in respiratory activity and other changes in intrathoracic pressure, which eventually lead to culminating in subcortical or cortical arousal then the infant wanders

back to sleep and the cycle continues to happen all night resulting in disturbed sleep [1]. Obstructive apnea is rated if the case is associated with an absence or more than 90% of airflow decreased for 2 or more missing breaths and increased effort for respiration [2]. The prevalence of apnea in infants is unidentified since many parents do not notice the child during sleep. The incidence of apnea is inversely related to gestational age due to the poor development of mechanisms of respiratory control and has apnea of prematurity in preterm infants. In preterm infants younger than 28 weeks gestation 50% of infants have apnea episodes. The incidence of apnea in the full-term infant is almost one per 1000 [3].

Anatomical and physiological predisposition to airway obstruction as well as congenital airway defects and causes such as gastroesophageal reflux are common known risk factors in this age group [4]. The most common cause of obstructive sleep apnea in children is enlarged tonsils or adenoids. Obesity is also one of the most significant risk factors for OSA in children. Children with asthma and obesity have a 4-fold increased risk of developing OSA, particularly if they have weak pharmacological control. Other risk factors identified include a history of prematurity or multiple pregnancy, craniofacial defects, neuromuscular problems, prolonged exposure to smoke, asthma and allergic rhinitis [5].

Popular nighttime signs and symptoms include snoring, heavy sweating, disturbed sleep, breathing of the mouth, apnea, gasping, labored or paradoxical breathing, and hyperextension of the neck during sleep. Daytime signs most often include attention disturbances, behavioral and mood disorders, daily fatigue, prolonged daytime sleepiness (EDS) and inability to thrive [6]. It is estimated that up to 1 in 7 children snore [7].

Untreated OSA may result in serious morbidity in neurobehavioral, cardiovascular, and somatic growth and development [8]. The standard gold test for diagnosis of obstructive sleep apnea is Nighttime in-laboratory Level 1 polysomnography (PSG). Patients are evaluated during the procedure with EEG leads, pulse oximetry, temperature and pressure monitors for nasal and oral ventilation, respiratory impedance plethysmography or equivalent resistance belts across the chest and abdomen for motion monitoring, ECG lead, and EMG monitors for muscle movement in the chin, chest, and legs [9].

Management with montelukast and nasal steroids may be enough to reduce the apnea-hypopnea index to goal in mild cases. While the primary treatment for obstructive sleep apnea in a child is tonsillectomy and adenoidectomy. The consideration for surgery should be balanced with the severity of symptoms, physical exam, and age [10].

In this review, we will look into the pathophysiology, symptoms, risk factors, diagnosis and treatment of OSA in children and infants.

Pathophysiology

When the child is awake, increased pharyngeal neuromuscular tone prevents upper airway collapse. This muscle tone is attenuated during sleep and is lowest during REM sleep, predisposing the upper airway to collapse. Children with OSA were observed to have slightly more collapsible upper airways with increased (i.e. lower negative) Pcrit during sleep than children without OSA [11].

Many patients with OSA have upper airway obstruction either at the level of the tongue, the soft palate, enlarged tonsils, large volume of the tongue in case of down syndrome, abnormal maxilla position and a decrease in the cross sectional area of the upper airways [12]. Micrognathia, achondroplasia, trisomy, Beckwith Wiedemann syndrome, and mucopolysaccharidoses, macroglossia and midface hypoplasia are other anatomical features which result also in upper airway narrowing found in children with craniofacial syndromes Treacher Collins syndrome, Crouzon syndrome, Apert syndrome, Pierre Robin sequence [13].

OSA symptoms

Primary snoring, the mildest and most prevalent manifestation, which is defined as habitual snoring for more than 3 nights per week without apneas, hypopneas, frequent arousals or gas exchange abnormalities. Its estimated population prevalence is 7.45% (95% confi-

dence interval: 5.75 - 9.61%) [14]. Other commonly reported symptoms in young children with OSA are mouth breathing, frequent upper respiratory tract infections, urinary incontinence, hearing and speech problems, recurrent ear infections, nausea, vomiting, and difficulty swallowing. Children also appear to be very restless during the night, frequently changing sleep positions to those promoting airway patency and hyperextending the neck [15]. Neurocognitive abnormalities and behavioral symptoms are also prevalent and are thought to be the result of prolonged exposure to recurrent hypoxemia and sleep disturbances attributable to sleep disturbance. Behavioral characteristics in children with OSA can be somewhat similar to those of attention deficit hyperactivity disorder [16]. Several studies illustrate the deleterious association between OSA and cognitive ability, with IQ indicated being up to 10 points lower than the average population except in those with moderate OSA. Other neurological symptoms include hyperactivity, aggression, irritability, and somatization [17].

OSA risk factors

- Adenotonsillar hypertrophy leads to a narrowing of the upper airway which, when superimposed on decreased muscle tone for example, may lead to clinically relevant dynamic blocking of the airway during sleep. It is the most common condition associated with childhood OSA [18]. There is correlation between the size of tonsils and the intensity of the OSA. Multiple studies have studied the association between adenotonsillary hypertrophy (ATH) and OSA [19].
- Obesity has been known as one of the most important risk factors for OSA in children. Per 1 kg/m² rise in body mass index above the 50th percentile (adjusted for gender and age) is correlated with a 12% increase in OSA risk [20]. In several previous trials, the neck circumference \geq 30 cm, the neck/height ratio \geq 0.25 and the waist/hip ratio \geq 0.95 were correlated with OSA [21].
- Breastfeeding has been generally linked with OSA. The potential explanations for this association included decreased access to health services, disparities in health-related habits and environmental exposure to pollutants [22]. Previous study confirmed that breastfeeding is a defensive factor for OSA. Children who were breast fed for 2 to 5 months showed less OSA severity than children who had not been breast fed [23].
- Preterm delivery has also been studied as a risk factor for OSA. Preterm infants could be at elevated risk for SDB partially on the basis of their perinatal exposure; such conditions could affect the development of respiratory function or upper airway size [24].
- Genetic risk factors in the production of OSA have been established. Previous studies have reported OSA in children with Beckwith-Widemann syndrome. Symptoms of OSA have also been associated with Joubert Syndrome, Marfan syndrome and Cornelia de Lange Syndrome [25].
- Inflammation: OSA can encourage the activation and spread of systemic inflammatory reactions. Latest studies have demonstrated a link between OSA and inflammation [26]. Increased development of various pro-inflammatory mediators in obese children such as leptin, interleukin 6 (IL-6) and tumor necrosis factor alpha (TNF- α) due to insulin resistance and hepatic steatosis [27].
- Craniofacial abnormalities include dentofacial defects (i.e. ogival palate) and severe craniofacial malformations (i.e. maxillary hypoplasia, retro-micrognathia and macroglossia). Craniofacial anomalies can lead to sleep apnea in children due to the overcrowding of upper airway structures [28]. Children with severe cranio-facial malformations have regular multi-level airway obstruction and must be closely examined by fibroscopy and drug-induced sleep endoscopy (DISE). Children with OSA had improved collapsibility at soft palate and retroglossal levels, indicating a substantial change in pharynx collapsibility compared to standard control subjects [29]. In a retrospective case-control study involving 1,203 children less than 18 years of age with obstructive sleep apnea, craniofacial anomalies were closely correlated with obstructive sleep apnea, a result which was particularly significant in children with Down syndrome and orofacial clefts [30].

- Neuromuscular abnormalities are associated with OSA due to inadequate pharyngeal motor functions, but also are at possibility of hypoventilation due to respiratory muscle weakness. Neuromuscular conditions typically coexist with Down syndrome, which is accompanied by hypoplasia of the upper jaw, ogival palate, macroglossia and muscular hypotonia [31]. OSA is frequently associated with Down's syndrome (81%). The neurologic disorders included cerebral palsy, meningomyelocele, severe global delay, Prader-Willi syndrome, tuberous sclerosis, Duchenne muscular dystrophy, Crouzon syndrome, and microcephaly with seizures [32].

Evaluation and diagnosis

The clinical assessment of the pediatric OSA patient consists of a careful history assessment, diagnostic examination and endoscopic and instrumental assessment. History-taking is the foundation of the diagnosis of any disorder [33]. Questions about sleep habits at night like snoring, breathing (resistance, sweatiness, and fading growth), if child sleeps with the mouth open, morning thirst and the presence of apnea by questioning when the child feels 'strangled' throughout sleep, or if there is a time where the child's breathing goes silent which then overcomes with a sigh [34]. Also, history taking also may be done using the Pediatric Sleep Questionnaire proposed by Chervin especially in its short version of 22 questions, which has been validated in several languages [35].

Physical examination is variable in children with OSA and begins with a general observation of the patient. Many children with OSA have enlarged tonsils and adenoids and not certainly demonstrate breathing difficulties during the examination [36]. The breathing of the mouth and the adenoidal facies should be noticed. Hyponasal tone is a hint of nasal obstruction. The nose is tested for septal deviation, mucosal thickening, polyps, and patency of each vestibule with opposite naris occluded. The oral cavity should be observed for the size and appearance of the tongue and soft palate: a broad tongue and/or a high arched or elongated palate or a low dependent palate can predispose to SDB [37]. For retrognathia, micrognathia, or mid-facial hypoplasia, the lateral facial profile should be investigated [38].

Flexible optical fiber endoscopy enables the measurement of nasal cavity like lower turbinate hypertrophy, occurrence of septal or choanal atresia and adenoid hypertrophy also tongue base tropism, or potential presence of laryngomalacia [39]. Polysomnography (PSG) was recommended by the AAP as the only gold standard method for the diagnosis of pediatric OSA. Also, the American Academy of Sleep Medicine (AASM) recommended a guideline for PSG for diagnosis of OSA [40]. The purpose of PSG is to detect, distinguish and measure obstructive apnea, mixed apnea, central apnea, to define and recognize hypopnea and high resistance syndromes and finally to assess sleep fragmentation. PSG recordings in children can be longer than adults, due to their longer sleep and should cover at least two complete nocturnal sleep cycles [41].

Treatment of OSA

Management of pediatric OSA is still challenging and each task should always be carefully evaluated. The backbone of OSA treatment is surgical adenotonsillectomy (AT), then comes medical treatments although respiratory support with CPAP, and the of airway adjuncts using [42].

AT is the main treatment for pediatric OSA in children with adenotonsillary hypertrophy. Tests have demonstrated substantial changes in obstruction of follow-up sleep studies, as well as in quality of living, actions and school success following surgery. Obese children have been reported to have less favorable outcomes following AT [43]. A research evaluating the effects of OSA tonsillectomy in children less than 3 years of age and another study evaluating similar outcomes in children less than 5 years of age noted that although substantial improvement in the respiratory distress index was observed after surgery, symptoms may recur after treatment and follow-up tests are necessary [45].

(CPAP) has also been suggested for the treatment of paediatric OSA, although its position is controversial, particularly after adenotonsillectomy. CPAP is recommended for the treatment of uncomplicated moderate to extreme OSA although it remains optional for mild

OSA [46]. The required CPAP time is assumed to be more than 4 hours a night and the appropriate CPAP implementation are calculated to be greater than 70% of the times. The use of CPAP has been correlated with increased concentration, somnolence, school success and global quality of life experience [45].

Nasopharyngeal airway (NPA) fashioned from an endotracheal tube (ETT) is often used to bypass upper airways obstruction in infants. Some anti-inflammatory drugs were also reported to be beneficial in treatment of OSA in children [47].

Conclusion

OSA is prevalent among children and infants and underdiagnosed by both parents and clinician until now. Junior physicians should be educated to be familiar with symptoms of OSA because children have various clinical symptoms and signs according to their developmental stages. Risk factors of OSA should be further studied to prevent increased incidence and further complication of untreated OSA. Untreated OSA in children is correlated with neuropsychiatric impairment, hyperactivity and cardiovascular impacts and sometimes can be correlated with sudden infant death syndrome.

Bibliography

1. Chang SJ and Chae KY. "Obstructive sleep apnea syndrome in children: epidemiology, pathophysiology, diagnosis and sequelae". *Korean Journal of Pediatrics* 53.10 (2010): 863-871.
2. Berry RB., *et al.* "Rules for scoring respiratory events in sleep: update of the 2007 AASM Manual for the Scoring of Sleep and Associated Events. Deliberations of the Sleep Apnea Definitions Task Force of the American Academy of Sleep Medicine". *Journal of Clinical Sleep Medicine* 8 (2012): 597-619.
3. Regenbogen E., *et al.* "Epidemiological trends among preterm infants with apnea. A twelve-year database review". *International Journal of Pediatric Otorhinolaryngology* 107 (2018): 86-92.
4. Katz ES., *et al.* "Obstructive sleep apnea in infants". *American Journal of Respiratory and Critical Care Medicine* 185 (2012): 805-816.
5. Tapia IE., *et al.* "Caffeine for apnea of prematurity - Sleep Study Group. Perinatal risk factors associated with the obstructive sleep apnea syndrome in school-aged children born preterm". *Sleep* 39 (2016): 737-742.
6. Kheirandish-Gozal L and Gozal D. "Sleep Disordered Breathing in Children A Comprehensive Clinical Guide to Evaluation and Treatment". New York, NY: Springer Science (2012).
7. Schechter MS. "Section on Pediatric Pulmonology, Subcommittee on Obstructive Sleep Apnea Syndrome. Technical report: diagnosis and management of childhood obstructive sleep apnea syndrome". *Pediatrics* 109 (2002): e69.
8. Tietjens JR., *et al.* "Obstructive Sleep Apnea in Cardiovascular Disease: A Review of the Literature and Proposed Multidisciplinary Clinical Management Strategy". *Journal of the American Heart Association* 1 (2019): e010440.
9. Miller BJ and Gupta G. "Adenoidectomy". StatPearls. StatPearls Publishing; Treasure Island (FL) (2020).
10. Green KK., *et al.* "Drug-Induced Sleep Endoscopy and Surgical Outcomes: A Multicenter Cohort Study". *Laryngoscope* 129.3 (2019): 761-770.
11. Pham LV and Schwartz AR. "The pathogenesis of obstructive sleep apnea". *The Journal of Thoracic Disease* 7 (2015): 1358-1372.
12. Pirelli P., *et al.* "Rapid maxillary expansion in children with obstructive sleep apnea syndrome". *Sleep* 27 (2004): 761-766.

13. Villa MP, *et al.* "Rapid maxillary expansion in children with obstructive sleep apnea syndrome: 12-month follow-up". *Sleep Medicine* 8 (2007): 128-134.
14. Rigatto H and Brady JP. "Periodic breathing and apnea in preterm infants. II. Hypoxia as a primary event". *Pediatrics* 50 (1972): 219-228.
15. Friedman BC, *et al.* "Adenotonsillectomy improves neurocognitive function in children with obstructive sleep apnea syndrome". *Sleep* 26 (2003): 999-1005.
16. Guilleminault C, *et al.* "A review of 50 children with obstructive sleep apnea syndrome". *Lung* 159 (1981): 275-287.
17. Stein MA, *et al.* "Sleep and behavior problems in school-aged children". *Pediatrics* 107 (2001): E60.
18. Marcus CL, *et al.* "Diagnosis and management of childhood obstructive sleep apnea syndrome". *Pediatrics* 130 (2012): 576-584.
19. Dayyat E, *et al.* "Obstructive sleep apnea in children: relative contributions of body mass index and adenotonsillar hypertrophy". *Chest* 136 (2009): 137-144.
20. Redline S, *et al.* "Risk factors for sleep-disordered breathing in children. Associations with obesity, race, and respiratory problems". *American Journal of Respiratory and Critical Care Medicine* 159.5-1 (1999): 1527-1532.
21. Bhatia R, *et al.* "Body fat composition: a predictive factor for sleep related breathing disorder in obese children". *Journal of Clinical Sleep Medicine* 11 (2015): 1039-1045.
22. Montgomery-Downs HE, *et al.* "Snoring in preschoolers: associations with sleepiness, ethnicity, and learning". *Clinical Pediatrics* 42 (2003): 719-726.
23. Montgomery-Downs HE, *et al.* "Infant-feeding methods and childhood sleep-disordered breathing". *Pediatrics* 120 (2007): 1030-1035.
24. Rosen CL, *et al.* "Prevalence and risk factors for sleep-disordered breathing in 8- to 11-year-old children: association with race and prematurity". *The Journal of Pediatrics* 142 (2003): 383-389.
25. Fitzgerald DA, *et al.* "Severity of obstructive apnoea in children with Down syndrome who snore". *Archives of Disease in Childhood* 92 (2007): 423-425.
26. Kheirandish-Gozal L, *et al.* "Elevated serum aminotransferase levels in children at risk for obstructive sleep apnea". *Chest* 133 (2008): 92-99.
27. Redline S, *et al.* "Association between metabolic syndrome and sleep-disordered breathing in adolescents". *American Journal of Respiratory and Critical Care Medicine* 176 (2007): 401-408.
28. Arens R and Marcus CL. "Pathophysiology of upper airway obstruction: a developmental perspective". *Sleep* 27 (2004): 997-1019.
29. Isono S, *et al.* "Comparison of static mechanical properties of the passive pharynx between normal children and children with sleep-disordered breathing". *American Journal of Respiratory and Critical Care Medicine* 157 (1998): 1204-1212.
30. Lam DJ, *et al.* "Pediatric sleep apnea and craniofacial anomalies: a population-based case-control study". *Laryngoscope* 120 (2010): 2098-2105.
31. Masters IB, *et al.* "Clinical versus polysomnographic profiles in children with obstructive sleep apnoea". *Journal of Paediatrics and Child Health* 35 (1999): 49-54.
32. Bull MJ. "Committee on Genetics Health supervision for children with Down syndrome". *Pediatrics* 128 (2011): 393-406.

33. Carroll JL, *et al.* "Inability of clinical history to distinguish primary snoring from obstructive sleep apnea syndrome in children". *Chest* 108 (1995): 610-618.
34. Kadmon G, *et al.* "I'M SLEEPY: a short pediatric sleep apnea questionnaire". *International Journal of Pediatric Otorhinolaryngology* 78 (2014): 2116-2120.
35. Chervin RD, *et al.* "Pediatric sleep questionnaire (PSQ): validity and reliability of scales for sleep-disordered breathing, snoring, sleepiness, and behavioral problems". *Sleep Medicine* 1 (2000): 21-32.
36. Marcus CL, *et al.* "Determinants of growth in children with the obstructive sleep apnea syndrome". *The Journal of Pediatrics* 125 (1994): 556-562.
37. Mallampati SR, *et al.* "A clinical sign to predict difficult tracheal intubation: a prospective study". *Can Anaesth Soc Journal* 32 (1985): 429-434.
38. Friedman M, *et al.* "Staging of obstructive sleep apnea/hypopnea syndrome: a guide to appropriate treatment". *Laryngoscope* 114 (2004): 454-459.
39. American Academy of Pediatrics. "Clinical practice guideline: Diagnosis and management of childhood obstructive sleep apnea syndrome". *Pediatrics* 109 (2002): 704-712.
40. Iber C, *et al.* "The AASM manual for the scoring of sleep and associated events: rules, terminology and technical specifications". Westchester, IL: American Academy of Sleep Medicine (2007).
41. Berry RB, *et al.* "The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications". American Academy of Sleep Medicine, Darien, IL (2017).
42. Marcus CL, *et al.* "A randomized trial of adenotonsillectomy for childhood sleep apnea". *The New England Journal of Medicine* 368 (2013): 2366-2376.
43. Merrell JA and Shott SR. "OSAS in Down syndrome: T and A versus T and A plus lateral pharyngoplasty". *International Journal of Pediatric Otorhinolaryngology* 71 (2007): 1197-1203.
44. Sheldon SH and Jacobsen J. "REM-sleep motor disorder in children". *Journal of Child Neurology* 13 (1998): 257.
45. Marcus CL, *et al.* "Adherence to and effectiveness of positive airway pressure therapy in children with obstructive sleep apnea". *Pediatrics* 117 (2006): e442-e451.
46. Anzai Y, *et al.* "[Treatment of sleep apnea syndrome in a Down syndrome patient with behavioral problems by noninvasive positive pressure ventilation: a successful case report]". *No To Hattatsu* 38 (2006): 32-36.
47. Urquhart DS, *et al.* "Sleep-disordered breathing in a 4-year old child with Down syndrome". *British Medical Journal* 337 (2008): a1229.

Volume 17 Issue 2 February 2021

© All rights reserved by Raniyah Embarak Alharbi, *et al.*