Obstructive Sleep Apnea in Infants During the First Year of Life: What the Pediatrician Needs to Know

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Introduction

Obstructive sleep apnea (OSA) is a relatively common childhood disorder that has been associated with neurocognitive, somatic and cardiovascular morbidity. Changes in cognitive development, temperament and behavior have been attributed to OSA in infants during the first 12 months of life. Infants undergo a rapid change in sleep architecture, airway anatomy and respiratory control during the first year of life. Infants are particularly vulnerable to OSA due to their upper airway structure, disadvantaged pulmonary mechanics, immaturity of ventilatory control, lower arousal threshold, active laryngeal chemoreflex and a REM-predominant sleep state distribution. As many of these factors developmentally improve over the course of infancy, interpreting PSG findings and differentiating pathology from physiology is challenging. Particularly vexing to the clinician is differentiating reversible from fixed airway obstruction and the clinical threshold for intervention. Due to these differences between infants and older children, it is important to separately review the existing literature on OSA using a cut off of 12 months age.

We excluded discussions on apnea of prematurity, central sleep apnea and periodic breathing since they were beyond the scope of this article. The aims of this review are to summarize available literature on OSA in infants less than 12 months of age and highlight best clinical practices. We reviewed prevalence, existing definitions to identify clinically significant OSA requiring intervention, diagnostic methods, various management options as well as sequelae of infant OSA and alluded to knowledge gaps which create clinical predicaments.

A. Epidemiology

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Infant OSA is reported to have a higher prevalence in at-risk populations such as syndromic craniosynostosis, prematurity, laryngomalacia, hypotonia and bronchopulmonary dysplasia (BPD). OSA in the high-risk infant population ranges from 11% -100%\textsuperscript{9,10} using the pediatric definition of OSA (Apnea Hypopnea Index or AHI>1.5 to 2/hr).

B. Clinical Symptoms:

Common presenting symptoms for OSA in infants include snoring, noisy breathing, mouth breathing, restless sleep, stridor and incidentally identified oxygen desaturations. Brief resolved unexplained events (BRUE) can often initiate an evaluation for OSA. There is inconclusive data to determine a strong association between OSA and BRUE.

C. Diagnosis:

Polysomnography:

Polysomnography is the gold standard for diagnosing OSA\textsuperscript{11}. In our experience, polysomnography in infants is not only technically challenging but also difficult to analyze due to short sleep periods from suboptimal maturation of ultradian and circadian rhythms. Therefore center expertise in the performance and interpretation of infant polysomnography is key to quality data for clinical decision making.

Polygraphy and oximetry:

Some investigators have utilized overnight oximetry to diagnose obstructive sleep apnea in infants\textsuperscript{12-14}. While it may be a useful screening tool in high-risk populations, its sensitivity is
premised on more significant oxygen desaturation and therefore does not replace the polysomnogram. A high prevalence of artifacts renders data interpretation more challenging.

**Airway endoscopy:**

Direct visualization methods have been used to assess the severity of upper airway obstruction in infants. The most common includes flexible upper airway endoscopy. This has been successfully utilized in infants with craniofacial anomalies including Pierre Robin Sequence. There is a high prevalence of dynamic airway abnormalities in the infant age group which often improves with age. Laryngomalacia is the most common dynamic abnormality described in infants with OSA. Adenoidal hypertrophy is the most common fixed obstruction. Drug induced sleep endoscopy (DISE) has emerged as a reliable tool for identifying upper airway obstruction in children and has demonstrated more sensitivity in identifying collapse of the lateral pharyngeal walls and base of the tongue compared to awake endoscopy. Consistent methodology of endoscopic evaluation, such as drug induced sleep endoscopy (DISE) is therefore essential for standardizing care in future comparative studies. Furthermore, while endoscopy provides anatomical information at that cross section of time, it does not provide reliable information on physiological consequences or compensation ability for the observed anatomic compromise.

**Airway imaging:**

Although, MRI has been used in the evaluation of upper airway structures in pediatric OSA, no prospective clinical trial has been performed in the infant population. Three dimensional CT head and neck has been utilized by a study on infants with micrognathia
D. Definition of infant OSA:

In clinical practice, the total AHI is commonly utilized to define OSA and guide treatment decisions. Literature suggests that a total AHI in excess of 5/hour, may normally occur in early infancy21-24. This may be due to a high frequency of both central events from immaturity of respiratory control and obstructive respiratory events secondary to physiological dynamic airway collapse. Daftary et al24 reported a median AHI of 14.9/hr with a significant contribution from central events in neonates. Matlen25, Duenas-Meza21 and Brockman et al23 have reported a temporal trend of decreasing AHI with increase in age in healthy neonates. While serial assessments of the AHI over the entire 12 month period of infancy are not available, a cross sectional study with a longitudinal sub-cohort of healthy infants21 suggests a trend towards spontaneous improvement of the AHI with growth. As the infant airway and respiratory control matures, there is a natural decline in the AHI. Due to the heavy influence of central events on the total AHI, this parameter may have lower clinical utility in infant OSA. Brockman et al23’s data suggests that central sleep apnea can improve without intervention. Therefore when making clinical decisions, it may be worthwhile paying attention to the other indices such as obstructive and central AHI as well as time in airway obstruction26. Literature suggests the obstructive AHI (OAHI) may be high in healthy neonates compared to older children (2.3/hr and 2.9/hr)24. OAHI has a wide variability within the first year of life, particularly in infants with co-morbidities. Therefore, the standard criteria of obstructive AHI>1-1.5/hr may not be a suitable definition to define clinically significant obstructive sleep apnea in population at high
risk for OSA. Thus close monitoring and other outcome measures are required to determine
need for intervention.

E. Management:

There is a considerable variation in practice when treating obstructive sleep apnea in infants
less than 12 months of age. Table 2 outlines all the studies on management of infant
obstructive sleep apnea in a heterogenous population. Treatment includes non-surgical
interventions (observation, supplemental oxygen, anti-GERD treatment, nasal corticosteroids
and non invasive ventilation) and surgical interventions (adenotonsillectomy, adenoidectomy
or tonsillectomy alone, supraglottoplasty, correction of craniofacial anomaly and
tracheostomy).

Non-surgical interventions:

A recent metanalysis supports the use of non-invasive ventilation in infants with OSA with
demonstrated improvement in respiratory parameters. Considering the pathophysiology of
infant sleep apnea, studies have reported ability to discontinue PAP therapy, corroborating the
reversible nature of infant OSA. Challenges to PAP therapy in this population include mask
complications, such as pressure ulcers, leaks, midfacial hypoplasia. Non-surgical treatment
is more common, due to the high prevalence of dynamic airway obstruction in this age group.
In the absence of delayed growth, significant sleep disruption or gas exchange disturbances,
watchful waiting may be a reasonable consideration. Comparison of non surgical and surgical
interventions by age showed predominant pursuit of non surgical interventions in infants
(89.3% between 3-5 months) that transitioned to surgical interventions after 12 months of age.
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(65.8% at 12-17 months of age)²⁹. Patient’s tolerance and compliance with PAP should influence choosing this treatment option.

Treatment of OSA in infants with craniofacial anomalies poses a unique challenge. A recent longitudinal study has shown improvement in obstructive apnea index in infants with OSA and Pierre Robin Sequence treated conservatively over time³⁹. Craniofacial growth and maturity of respiratory control were hypothesized to result in spontaneous resolution of OSA. Prone sleep positioning has also been practiced as a treatment option. Positioning interventions in infants are complicated by the increased risk of sudden infant death syndrome in non supine positions. A recent study on 27 infants with cleft palate +/- lip, did not provide evidence of improvement in polysomnographic measures in non supine sleep⁴⁰. Another study on infants without craniofacial anomalies did not find any significant effect of body position on infant OSA ⁴¹. Nasal trumpets have been used in infants with craniofacial anomalies. The trumpet breaks the seal between the soft tissues of the base of the tongue and the pharynx decreasing obstruction. Manual orofacial therapy (CMT) including basic orofacial muscle activation exercises and stimulation of facial motor points by pressure, traction and vibration in specifically defined directions has been developed for children with craniofacial malformations and neurological diseases⁴². Recent studies have combined CMT with use of different kinds of oral appliances and demonstrated feasibility in infants with trisomy 21⁴³ and syndromic Robin Sequence⁴⁴.

Surgical intervention:
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There is improvement after surgical intervention in infants with fixed airway obstruction. Adenoidectomy is the most common surgical intervention. Studies report adenoidectomy at a median age ranging from 10.6 months to 16.9 months. Supraglottoplasty is the other surgical intervention which has been effective in treating infants with laryngomalacia and obstructive sleep apnea. Interestingly, the criteria used to determine need for a surgical intervention are not clearly described in the literature.

Special surgical interventions are performed in infants with unique craniofacial anomalies. Mandibular distraction osteogenesis (MDO) or tongue-lip adhesion are often performed in infants with Pierre Robin Sequence. A recent international survey showed wide variation of management of these infants. A 2016 consensus report recommended endoscopic airway evaluation to confirm glossoptosis and diagnose concomitant airway abnormalities. If concomitant abnormalities cannot be corrected, then tracheostomy is recommended. In infants who have undergone palatal repair and secondary speech surgery (palatoplasty, pharyngeal flap and sphincter pharyngoplasty) OSA may exacerbate as they decrease the cross-sectional area of the airway. In Beckwith-Wiedemann syndrome, tongue reduction surgery is the mainstay of treatment. The earliest reported age of surgery (midline partial glossectomy and uvulectomy) in an infant with Beckwith-Wiedemann syndrome was 2 months. In our experience, a multidisciplinary approach is ideal for infants with craniofacial anomalies. Polysomnographic evaluation along with close monitoring of feeding and growth outcomes are essential components to guide management of these patients.

F. Sequelae:
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OSA in children has frequently been associated with developmental delay, increased systemic blood pressure and health care utilization. Most clinical trials have excluded infants (<1 year old) from their cohorts; therefore it is difficult to understand the sequelae of infant obstructive sleep apnea. No clinical trials have assessed the cardiovascular outcomes of infant OSA.

Table 3 summarizes the publications on neurocognitive outcomes in infants with OSA. Three studies have analyzed a relationship between AHI and neurodevelopmental scores in the infant population. These studies did not find any correlation between the two. Studies have reported lower cognitive scores in infants who snore. Adverse neurocognitive effects have been well described with OSA in older children. Considering the rapid brain growth in infancy, the lack of correlation of AHI with neurodevelopmental testing is intriguing. The literature suggests that the AHI may not be the best predictor of neurocognitive outcomes in infant OSA.

Conclusion

In summary, infants are physiologically more prone to sleep apnea than older children. Due to varying definitions, the reported prevalence of infant obstructive sleep apnea is hard to estimate; yet published literature suggests a higher prevalence of PSG identified obstructive events in infancy than older pediatric age groups. Certain co-morbidities are associated with a higher prevalence of OSA in infants—noteably craniofacial anomalies, neurologic pathology especially with hypotonia, and bronchopulmonary dysplasia. High risk infants may be asymptomatic or present with atypical symptoms like noisy breathing. Polysomnography is the gold standard for diagnosis of OSA. However, this may be supplemented with airway endoscopy to determine management. Observation is a popular choice for management in low risk
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populations due to the high prevalence of dynamic airway obstruction. However, non-invasive positive pressure ventilation, oral appliances, orofacial therapy and surgical interventions may be needed in infants with comorbidities. There is very limited literature on the outcomes of infant OSA. With standardization of testing for sleep apnea in infancy, outcome studies are now required to guide management decisions.
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REFERENCE:

Obstructive sleep apnea in infants during the first year of life—what the pediatrician needs to know


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**Risk Factors**
- Syndromic craniosynostosis (Pierre Robin Syndrome, cleft palate+- lip, Trisomy 21, Beckwith Wiedemann Syndrome)
- Prematurity
- Low Birth weight
- Bronchopulmonary dysplasia
- Laryngomalacia
- Neuromuscular disease with hypotonia

**Presenting signs and symptoms**
- Noisy breathing
- Snoring
- Mouth breathing
- Stridor
- Restless sleep
- Desaturations

**Diagnosis**
- Polysomnography
- Airway Endoscopy
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**Management**

- **Non surgical**
  - Observation
  - Supplemental oxygen
  - Anti-GERD treatment
  - Nasal Corticosteroids
  - Non invasive ventilation
  - Manual orofacial therapy

- **Surgical**
  - Adenoidectomy
  - Supraglottoplasty
  - Tonsillectomy
  - Adenotonsillectomy
  - Correction of craniofacial anomaly (mandibular distraction, tongue reduction surgery)

**Table 1: Key Points for Infant OSA**

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Subjects (N) (age)</th>
<th>Comorbidities</th>
<th>Interventions (frequency)</th>
<th>Interventions (frequency)</th>
<th>Outcomes</th>
</tr>
</thead>
</table>


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<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size</th>
<th>Associated Conditions</th>
<th>Non Surgical</th>
<th>Surgical</th>
<th>Observations</th>
</tr>
</thead>
</table>
| Ramgopal, 2014   | 97 infants (<12 months) | 53% hypotonia, 24% laryngomalacia, 19% T21, 16.5% craniofacial anomalies, 27.8% premature | Non surgical: 48% | Surgical: 37% | • 76% of patients who received surgical intervention had symptom resolution  
• 30% of patients who were observed had symptom resolution  
• 40% of patients who received O2/PAP had symptom resolution |
| Leonardis, 2013  | 126 infants (0-12 months) | 68.3% GERD, 36.5% craniofacial malformation, 28.6% laryngomalacia, 13.5% hypotonia | Non surgical: Observation (26.2%), Supplemental oxygen (24.6%), CPAP/NPPV (14.3%) | Surgical: Adenoidectomy (23.8%), Supraglottoplasty (8.7%) | • Observation was the most subjectively effective intervention according to caregivers with a 65.6% objective reduction in AHI  
• CPAP/NPPV had highest mean % reduction in AHI (67.2%) |
| Robison, 2013    | 295 children (3-11 months) | 15.9% laryngomalacia, 12.9% congenital syndrome, 9.8% hypotonia, 49.8% GERD | Non surgical: 89.3% (3-5 months), 10.7% (6-11 months) | Surgical: 68.1% (3-5 months), 31.9% (6-11 months) | • Reduction in AHI with adenoidectomy was 86.3% (infants 3-5 months) 56.6% (infants 6-11 months)  
• CPAP/biPAP was the most effective non surgical intervention with reduction in AHI of 77.3% (infants 3-5 months) and 94.2% (infants 6-11 months)  
• Observation resulted in decrease in AHI by 63.2% (3-5 months) to 63.8% (6-11 months) |
| Powitzky, 2011   | 20 infants (<1 year old) | 100% laryngomalacia | N/A | Supraglottoplasty | • Preoperative AHI 11.2/hr (4.9-16.2)  
• Post operative AHI 4.7/hr (3.2-8.5) |
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Table 2: Studies on management of infant obstructive sleep apnea in heterogenous population with polysomnographic outcomes

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Subjects</th>
<th>Comorbidities</th>
<th>AHI (median)</th>
<th>Age at neurodevelopmental assessment</th>
<th>Neurodevelopmental outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meerkov, 2019</td>
<td>48 term and near term newborns (39.3+/−1.6 weeks)</td>
<td>At risk for seizures</td>
<td>10.1 (3.3-18.5)/hr</td>
<td>18-22 months</td>
<td>No association between PSG results and BSID-III scores</td>
</tr>
<tr>
<td>Bandyopadhyay, 2017</td>
<td>15 infants (37-46 weeks)</td>
<td>prematurity</td>
<td>17.4 (2.2-41.3)/hr</td>
<td>22 months</td>
<td>Median cognitive score (BSID-III) 90 (65-125), median language score 89 (65-121), median motor score 91 (61-112) were within 1 SD of published norm</td>
</tr>
</tbody>
</table>
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<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size</th>
<th>Diagnosis</th>
<th>Mean Age</th>
<th>Follow-up</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smith, 2014</td>
<td>33 infants</td>
<td>Cleft lip/cleft palate</td>
<td>23.9 (18)/hr</td>
<td>36.7 (1.4) months</td>
<td>Mean end tidal CO2 negatively correlated with cognitive scores; lower percentage of REM associated with lower cognitive score BSID III; more obstructive events associated with lower global behavior ITQOL score (infant/toddler quality of life questionnaire)</td>
</tr>
<tr>
<td>Piteo, 2011</td>
<td>13 infants</td>
<td>none</td>
<td>Not performed</td>
<td>6 and 12 months</td>
<td>Lower cognitive development scores (mean 94.2 SD 3.9) on BSID III compared to infants who did not snore</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Study</th>
<th>Participants</th>
<th>Control Group</th>
<th>Follow-up</th>
<th>Cognitive Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Piteo, 2011</td>
<td>16 infants snoring from birth compared to 88 healthy controls</td>
<td>None</td>
<td>Not performed</td>
<td>6 months</td>
</tr>
<tr>
<td>Montgomery-Downs, 2006</td>
<td>35 infants from community</td>
<td>None</td>
<td>0/hr</td>
<td>8.2 +/- 4 months</td>
</tr>
</tbody>
</table>

Table 3: Neurocognitive outcomes in infant obstructive sleep apnea