# Craniofacial and Upper Airway Morphology in Pediatric Obstructive Sleep Apnea Patients: A Systematic Review

Ann Chianchitlert[1], Nithivoot Luengthamchat[1], Thanakorn Saengphen[1], Irin Sirisoontorn[1]*

1. Department of Clinical Dentistry, Walailak University International College of Dentistry, Bangkok, Thailand.

**Abstract**

The crucial influencing factor in the development and progression of pediatric obstructive sleep apnea might be the disharmony of craniofacial structure. The objective of this systematic review is to explain the association between craniofacial structure disharmony and pediatric obstructive sleep apnea.

Citations of potentially relevant published trials were located by searching PubMed, Scopus, the Cochrane Central Register of Controlled Trials and Web of science. Inclusion criteria were (1) randomized controlled trials, retrospective study, cross-sectional, case-series, or cohort studies with controls; (2) studies in nonsyndromic children from birth to 19 years of age with a diagnosis of obstructive sleep apnea by either a screening questionnaire, or polysomnography; and (3) principal outcome measures of craniofacial or upper airway dimensions or proportions with various modalities of cephalometric analysis for the craniofacial and neck regions. The quality of the studies selected was evaluated by assessing their methodologies.

Through the electronic searches, 1290 titles and abstracts were identified. From these, 241 met the inclusion criteria. This resulted in 6 studies from cross-sectional trials that were included in this systematic review. 1 case series reported the association between craniofacial disharmony and obstructive sleep apnea.

There is statistical support for an association between craniofacial disharmony and obstructive sleep apnea. There was significant correlation between upper airways dimensions and maxillomandibular discrepancy expressed by a significantly larger ANB angle. The upper airway measurement showed a significant difference between OSA group and non-OSA group.

**Review (J Int Dent Med Res 2022; 15(1): 412-421)**

**Keywords:** Airway, Craniofacial, Obstructive Sleep apnea.

**Received date:** 03 December 2021 **Accept date:** 04 January 2022

## Introduction

Sleep apnea according to American Association of Orthodontists in 2012, is defined as a temporary suspension of breathing which occurs repeatedly during sleep. It occurs when there is an increase of collapsibility of the upper airway.[1] Obstructive sleep apnea (OSA) gains more attention in the field of pediatrics. The symptoms lie behind a spectrum of disorders of sleep-breathing. It can negatively impact health if left untreated. Patients are not usually diagnosed with sleep-disordered breathing (SDB) or obstructive sleep apnea (OSA) until approximately 40 years of age.[2] Obstructive sleep apnea (OSA) in children is a respiratory disorder characterized by upper airway collapse during sleep. Obstructive sleep apnea syndrome (OSAS) is a common circumstance in children. If it is left untreated, it can lead to severe complications.[3]

Children with mild OSA are not always diagnosed since the symptoms of the disorder are not obviously seen. But suspected SDB children are commonly seen in dental practice.[4] There are increasing incidences of pediatric OSA in some races such as African-Americans.[5]

The components of upper airway structures consist of the oral cavity, pharynx, and larynx. The growth and development of the head and neck from the neonatal period till the end of adolescence is significantly influenced by the upper airway.[6]

***Corresponding author:***
Dr. Irin Sirisoontorn
Department of Clinical Dentistry, Walailak University International College of Dentistry,
Bangkok, Thailand'
E-mail: irin.sirisoontorn@gmail.com

In this review, we focus on upper airway dimension in pediatric obstructive sleep apnea with partial or complete upper airway obstruction.

Predisposing factors for pediatric OSA

There are several causes of pediatric sleep apnea. They might be due to a complex interaction of neuromuscular, anatomic and inflammatory factors.[7]

Adenotonsillar hypertrophy

Adenotonsillar hypertrophy (AH) is considered as one of the most common disorders and sources of upper respiratory obstruction among children and influences the upper airway morphology. The correlations between adenotonsillar size and polysomnographic features remain diverse and controversial.[8]

The effects of adenotonsillar on pediatric obstructive sleep apnea may be altered by factors including obesity and age.[9] Kang et al. in a 2013 study found that adenotonsillar size of OSA does not differ between obese and non-obese children, but differ in children of different ages, and the influence of adenoid size decreases in adolescence.

Adenotonsillar hypertrophy is the most common disorder in the pediatric population. It can cause symptoms such as mouth breathing, nasal congestion and snoring. It is also the source of obstructive sleep apnea (OSA) in children.[3]

Obesity

The pediatric obesity population is increasing. 18 % of childhood obesity has tripled during the past several decades.[10] Obesity is one of the important risk factors for pediatric obstructive sleep apnea in both children and adolescents.[5,6].

Craniofacial morphology

The etiology of craniofacial morphology may result from both genetics and the environment.[11] Studies reported that sleep disordered breathing and obstructive sleep apnea conditions increased in retrognathic mandible individuals.[12] The maxillary transverse constriction is also a signal for a decrease in transverse upper airways dimension which may indicate an increase in nasal resistance.[13]

Role of cephalometric radiographs

The lateral cephalometric radiograph might be used as a screening method for measuring dimension of both nasopharyngeal and palatopharyngeal upper airways. There is a correlation between the three-dimensional magnetic resonance imaging and the lateral cephalometric radiograph.[14]

The lateral cephalometric radiograph of the upper airway dimension may be an important screening tool for pediatric obstructive sleep apnea. There is no systematic review of the relation between pediatric obstructive sleep apnea and upper airway dimension.

The aim of this study is to conduct a systematic review of the published literature and elucidate the association between upper airway morphology and pediatric obstructive sleep apnea.

## Materials and methods

Protocol and registration

The PRISMA-P statement was used as a specific protocol developed and piloted guidelines for the outline of this systematic review.[15] Moreover, the Cochrane Handbook for Systematic Reviews of Interventions was used as a guideline for the procedure.[16] The reporting complied with the PRISMA statement's guideline.[17]

| Criteria | Definition |
|---|---|
| Study characteristics | The study should be prospective, retrospective, or case control in design. Included study designs will be randomized controlled trials, case-control trials, cohort studies, case series. |
| Patient characteristics | Nonsyndromic children, 0-19 years old with a diagnosis of obstructive sleep apnea by a sleep disorder unit, screening questionnaire or polysomnography. |
| Study method characteristics | Studies with various analysis of lateral cephalometric radiograph for the craniofacial region. |
| Outcome characteristics | Trials reporting outcome measures:<br>• Craniofacial dimension<br>• Upper airway dimension |

**Table 1.** Study selection criteria.

Eligibility criteria

This systematic review and meta-analysis was conducted based on the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) guidelines. [18] Title-abstract-full text of each article was checked independently by three authors based on the PRISMA chart.

The inclusion criteria were restricted to (1) randomized control trials, cohort studies or case series; (2) studies of nonsyndromic children from birth to 19 years of age with a diagnosis of obstructive sleep apnea by a screening questionnaire, sleep disorders unit, or polysomnography; and (3) main measurement of

craniofacial and upper airway dimensions in various lateral cephalometric analysis of the craniofacial regions. The selection criteria for this study is described in Table 1.

Outcomes

The primary outcome was the cephalometric measurement variables from lateral cephalograms of pediatric obstructive sleep apnea patients as measured by various modalities. The measurements included 3 angles of craniofacial skeletal and 4 linear measurements of upper airways as described in table 2.

| Cephalometric measurements | Definitions |
|---|---|
| SNA | Angle between sella, nasion, and A-point |
| SNB | Angle between sella, nasion, and B-point |
| ANB | Difference of SNA and SNB angles |
| PNS-AD1 | Distance from the posterior nasal spine to the nearest adenoid tissue measured along the PNS- basion line |
| PNS-AD2 | distance from the posterior nasal spine to the nearest adenoid tissue measured along the line perpendicular to the sella-basion line |
| MinRPA | Minimal width of airway behind soft palate perpendicular to posterior pharyngeal wall |
| PPW1 | Linear distance from anterior to posterior pharyngeal wall |

**Table 2.** The measurements of upper airways.

Study selection

Types of studies

Modalities of lateral cephalometric analysis of upper airway dimension in diagnosing OSA in children were included. Cross-sectional and case series were also considered in order to compare their bibliographic references with the results of our literature search.

Participants

Non syndromatic obstructive sleep apnea patients of 19 years of age and under were eligible for inclusion. Studies that included adults or syndromatic pediatric patients were excluded. Only studies where subjects confirmed as having pediatric obstructive apnea by performing obstructive sleep apnea questionnaire or polysomnography were included.

Search strategy

Searching was performed using the appropriate databases (PubMed, Embase, Scopus, and Cochrane Central Register of Controlled Trials) for potentially related published journals. The strategy used several combinations of searches related to the specific patient population, index test, and the reference standard for the target condition. All references were managed by reference manager software and duplicate hits removed. Only English studies were considered.

Further searching in the references of the reviewed articles was also performed. The search period was from November 20, 2020, across all databases, until December 31, 2020.

Study selection and data extraction

Three authors individually reviewed the titles and abstracts of all discovered citations. Any studies that did not meet the inclusion criteria were excluded from further assessment, and the full articles were reprocessed for those that fulfilled the criteria. The three authors (A.C, N.T, T.S) individually reviewed all full articles.

Data abstraction was executed independently by the three authors using Excel (Microsoft, Redmond, Wash). The characteristics of the included studies were publication year, the details of the study design, the details of the patients' demographic, the characteristics of participants, the method of pediatric obstructive sleep apnea diagnosis, the analysis modalities, an assessment of quality of the study, and the statistical details. The eligible abstracts from three authors were pooled for providing supplementary details on their studies. Citations from eligible journal and review articles were double-checked to identify more studies.

Any uncertain issues were settled by discussion and communal agreement between the three authors. Angular variables were detailed in degrees and linear variables were detailed in millimeters.

| Strong evidence | Moderately strong evidence | Limited evidence |
|---|---|---|
| • Randomized controlled trials, prospective study with numbers of sample size<br>• Well-defined and clinically related variables<br>• Clearly defined and adequate control group<br>• Low dropout samples<br>• Quality statistical analysis | • Prospective study, cohort, controlled-clinical trial, retrospective study with numbers of sample size<br>• Well-defined and clinically related variables<br>• Low dropout samples<br>• Quality statistical analysis | • Cross-sectional study, case series<br>• No control<br>• High dropout sample<br>• Inadequate statistical analysis |

**Table 3.** Criteria for study evaluation.

Quality assessment and risk of bias of the selected study

The methodologies from each study were used to evaluate the quality of every study. Assessment of the methodological quality was conducted according to guidelines recommended by the evaluation criteria from the Centre for Reviews and Disseminations in York, United Kingdom.[19] A methodological quality scored the

studied as 'strong evidence', 'moderate evidence' and 'limited evidence' for each quality assessment item. The criteria are presented in Table 3.

Risk of bias was evaluated by using Cochrane Collaboration's tool:

Our review categorized the general risk of bias according to the following items. (Table 4.)

1. Low risk of bias (plausible bias unlikely to seriously alter the results) if all criteria were met.
2. Unclear risk of bias (plausible bias that raises some doubt about the results) if at least 1 criterion was assessed as having an unclear risk.
3. High risk of bias (plausible bias that seriously weakens confidence in the results) if at least 1 criterion was assessed as having a high risk.

| Article | Judgement |
|---|---|
| **Ahmed et al** (Journal of Oral Biology and Craniofacial Research, 2020) | |
| Random sequence generation | Low risk |
| Allocation concealment | Low risk |
| Blinding of participants or personnel | High risk |
| Blinding of outcome assessment | High risk |
| Incomplete outcome data addressed | Low risk |
| Selective reporting | Unclear risk |
| Other bias | Unclear risk |
| **Ahn et al** (Journal of Oral and Maxillofacial Surgery, 2015) | |
| Random sequence generation | Unclear risk |
| Allocation concealment | Low risk |
| Blinding of participants or personnel | High risk |
| Blinding of outcome assessment | High risk |
| Incomplete outcome data addressed | Unclear risk |
| Selective reporting | High risk |
| Other bias | Unclear risk |
| **Bergano et al** (Journal of Oral Biology and Craniofacial Research, 2014) | |
| Random sequence generation | Low risk |
| Allocation concealment | Low risk |
| Blinding of participants or personnel | Low risk |
| Blinding of outcome assessment | Low risk |
| Incomplete outcome data addressed | Unclear risk |
| Selective reporting | Unclear risk |
| Other bias | Unclear risk |

**Table 4.** Assessment risk of bias.

Statistical analysis

Data was analyzed using SPSS version 25.0 (SPSS Inc., Chicago, IL, USA). The pooled analysis was performed for the common of data categories among the studies. A random effects model was selected due to the presumed variability in the trials. The intersection of the 95% confidence intervals for the outcomes of individual study was clearly checked for categorizing heterogeneity.

3 angles and 4 linear measurements of cephalometric variables from pediatric obstructive sleep apnea patients were collected as described in table III.

## Results

The restrictions were assigned on the patients' ages and English language. In the initial investigation, 1,290 citations through the 4 databases were found. We identified 1,290 citations from electronic databases: 347 from PubMed/Medline, 302from COCHRANE, 355 from SCOPUS and 286 from Web of Science. 1,241 were duplicates. The exclusion of seven citations in foreign languages from this review were executed. The remaining 241 abstracts were further investigated. 26 journals were studied as full text. Studies included in qualitative synthesis resulting in a total of 7 studies in this systematic review.

The Prisma-Flow diagram in Figure 1 illustrates the searching process.

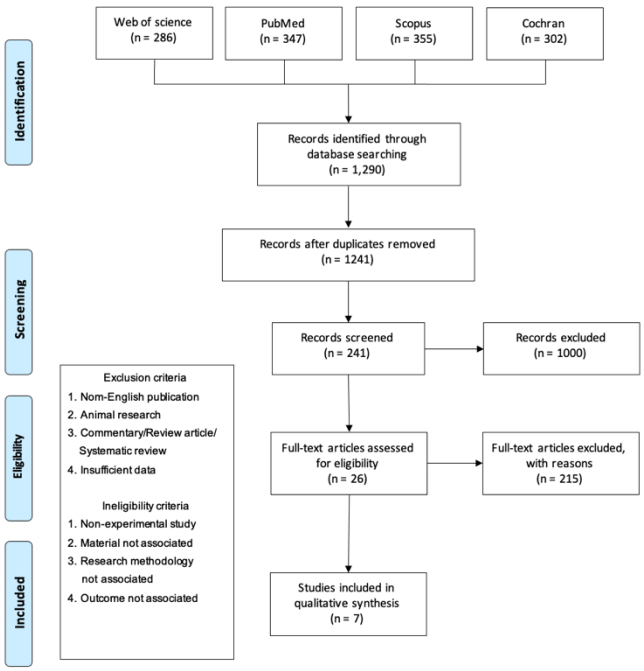


**Figure 1.** The picture of PRISMA flow diagram.

The characteristics of the 7 included trials, including their methodologic quality, are summarized in Table 5.[20-26]

Ahmad et al, studied obstructive sleep

apnea (OSA) risk in adolescent population and its association with the subjects' craniofacial and upper airway morphologies. From 60 subjects, 30 subjects were in in OSA risk group and 30 subjects were in non-OSA-risk group. Modified STOP-BANG questionnaire was used for screening OSA-risk in adolescent orthodontic patients (10–19 years). The mean age of participants in the current study was 16 ± 3.4. The sex distribution of participants was 19 girls and 11 boys for participant group and 20 girls and 10 boys for control group. Cephalometric analysis was performed to define skeletal and upper airway variables. Cephalometrically, the upper airway measurement by PNS-AD1 =16.5 mm. ± 3.8 in OSA group, 20.2 mm. ± 3.4 in Non-OSA group. The lower airway measurement by PNS-AD2 = 13.7mm. ± 3.6 in OSA group, 17.2 mm. ± 3.9 in Non OSA group. The results showed a significant difference between OSA-risk and non-risk. Parameters PNS-AD1 and PNS-AD2 exhibit statistically significant differences of 3.7 and 3.43 respectively ($p < 0.001$) between OSA-risk and non-OSA risk. Other cephalometric variables (SNA 82.9 ± 4.5, SNB 78.7 ± 4.9 ANB 4.3 ± 2.9 in OSA group and 79.5 ± 4.0, 82.8 ± 3.8, 2.8 ± 2.2 in non-OSA group, respectively), exhibit higher values in OSA-risk than non-risk but are not highly significant.[20]

Ahn et al., in the present report was to evaluate the treatment efficacy and stability of modified MMA surgery in an obstructive sleep apnea growing patient. They used the follow-up results from the questionnaire and polysomnography to confirm the obstructive apnea. The cephalometric analysis used the result from 2-dimensional cephalometry and 3-dimensional cone-beam computed tomography measurements. The sample in this case report was an 11.1-year-old girl. Lateral cephalometric analysis was performed to evaluate the presence of craniofacial morphologic anomalies which was a retrognathic mandible (SNB=77°) and parapharyngeal soft tissue abnormalities (Superior posterior airway space= 9, Ad1-PNS=24, Ad2-PNS=19.5) which are considered risk factors for OSA. This patient also had a skeletal type II with hyperdivergent pattern and class II malocclusion. [21]

Bergamo et al, studied adenoid hypertrophy, craniofacial morphology in apneic children. In their study, they selected the OSA group from the Mouth Breathing Center from the Pedodontic Clinic, followed by an otorhinolaryngologic evaluation on each patient to confirm the breathing pattern. The children with suspected OSA underwent nocturnal diagnostic polysomnography according to American Academy of Sleep Medicine (AASM). Only children with an AHI > 1 were included in the OSA group, 21 children (10 girls, 11 boys) with obstructive sleep apnea (OSA) between 6 and 10 years of age (mean age 8.15) and 22 children (10 girls, 12 boys) nasal breathing (control group) between 6 and 9 years of age (mean age 7.47) were included. Using the cephalometric analyses, the maxilla was in the orthognathic range (SNA) and the mandible showed a slight retrognathic tendency (SNB). The OSA and control group showed skeletal class I characteristics (ANB) with no statistical differences. The airway measurement in the palatine plane (PPW1; linear distance from the anterior to posterior pharyngeal walls) was statistically different between the groups (16.31 for OSA vs. 20.84 for the controls).[22]

Geleotti et al, in the study in the correlation between the cephalometric variables and obstructive sleep apnea index in pediatric patients investigated the correlation between upper airway dimensions and maxillomandibular skeletal discrepancy. The sample selection based on the inclusion criteria are as follows: reported OSA symptoms (such as snoring, gasping of air, apnea events during the night), significant obstructive apnea events (Obstructive Apnea Hypopnea Index - OAHI - ≥1.5. The sample size was 47 obstructive sleep apnea patient children (mean age±SD= 5.75±1.99 years). The subjects were 23 males (48.9%) and 24 females (51.1%). Cephalometric analysis was performed to define skeletal and upper airway variables. Positive associations with statistical significance were found between OAHI (events/h) and maxillomandibular discrepancy expressed by the ANB angle ($p=0.023$). There was significant correlation between upper airways dimensions and maxillomandibular discrepancy expressed by the ANB angle.[27]

In the study of Lee et al, they examined craniofacial, dental arch morphology, and characteristics in preschool children with mild obstructive sleep apnea. They selected the children who passed the inclusion criteria for the test group with primary dentition and a diagnosis

of mild OSA confirmed by overnight polysomnography. The test group comprised of 16 preschool children (11 boys, 5 girls; mean age: 5.14 years old; mean ahi: 2.02) with confirmed polysomnographic diagnosis of mild OSA. 10 control subjects also underwent polysomnography (5 boys, 5 girls; mean age: 5.18 years old; median ahi: 0.43). Lateral cephalometric radiographs were measured and found that in the mild OSA group, there was a significantly larger anteroposterior maxilla and mandible discrepancy (ANB angle, p = 0.015) and a reduced SNB angle (p = 0.045). The dimensions of the upper airway, soft palate and tongue, and the position of the hyoid bone There were not significantly difference in upper airway between the mild obstructive sleep apnea and controls group. But The significantly larger discrepancy between the anteroposterior maxilla and mandible was found between mild obstructive sleep apnea children and control group. The mild obstructive sleep apnea group also had a bigger overjet and a more retrognathic mandible. [24]

Purwanegara et al., studied the correlation between snoring and apnea with Obstruction of Upper Respiratory Tract (OURT). The inclusion criteria were; living in Jakarta with the Deutro-Malay race, age 9-15 years, generally good health, diagnosed OSA by ENT and questionnaire. The total subjects were 285 OURT patients divided into two groups of age, first group was 12-15 years old (165 subjects), and the second was 9-11 years old (120 subjects). The measurement of nasopharyngeal space was performed based on lateral cephalometric radiography. The McNamara modification line indicated no significant difference between apnea and no apnea during sleep in both age groups of OURT participants.. [25]

Quo et al., performed a preliminary study to investigate the use of bone anchored maxillary protraction (BAMP) as a strategy to treat maxillary retrusion, malocclusion and children with OSA. The subjects were 15 children, ages 9-16 years with maxillary retrusion and a resulting malocclusion using titanium bone anchored miniplate implants to protract the maxilla forward. All children were screened for OSA by the American Academy of Sleep Medicine (AASM) guideline for sleep and wakefulness and the respiratory variables: apnea, hypopnea, lowest oxygen saturation and calculation of an apnea-hypopnea index (AHI). Lateral cephalograms were taken on all subjects. Cephalometric measures included skeletal and pharyngeal airway dimensions by Dolphin imaging software. When compared to an age and sex matched untreated control group, BAMP treatment improved respiratory and airway parameters in OSA children, with a very significant shift in the forward position of the upper jaw and expansion of the nasopharyngeal to oropharyngeal junction. In the OSA group with BAMP, the anterior-posterior length at the nasopharyngeal/oropharyngeal transition region increased substantially. They indicated that BAMP might help OSA patients with maxillary retrusion because of the expansion of the nasopharyngeal airway. [26]

Uslu-Akcam et al. compared the dimensions of nasopharyngeal and oropharyngeal in skeletal class II, division 1 and division 2 patterns individuals during the growth periods for comparison with a skeletal class I individuals. One hundred and twenty-two lateral cephalograms from 47 subjects of skeletal class I; 45 subjects of skeletal class II, division 1; and 32 subjects of skeletal class II, division 2. The growth periods were in the duration of pre-peak, peak, and post-peak puberty. The measurement included Thirteen landmarks, 4 angle and 4 linear dimensions. The final 4 proportional calculations were obtained. The SNB angle was different among the groups. There was significant difference in ANB for all 3 groups. The nasopharyngeal airway space presented the significant increase in the skeletal class II group. The naso-oropharyngeal airway dimensions showed a statistically significant difference among the class II, division 1; class II, division 2; and class I groups during different growth periods. During different growth stages, the naso-oropharyngeal airway dimensions exhibited a statistically significant difference between the class II, division 1; class II, division 2; and class I groups. [28]

## Discussion

There have been several lateral cephalometric studies in OSA. Galeotti et al. analysed the correlation between cephalometric variables and OSA severity in children. According to their findings, increased obstructive sleep apnea index was linked to skeletal discrepancy

as measured by the ANB angle. The ANB angle was a crucial cephalometric statistic for determining the maxillomandibular discrepancy in both sagittal and vertical directions. In sagittal direction, a skeletal Class II malocclusion was defined by an increased in the ANB angle. In the vertical direction, it showed a clockwise rotation of mandible. [27] Schiffman et al. investigated the size of the mandible in children with obstructive sleep apnea syndrome. They found that the size of mandible was not a distinguishing characteristic in children with obstructive sleep apnea with no visible craniofacial deformities. The mandible's position might still be a significant anatomical occurrence of children with obstructive sleep apnea. [29] There was an observing a positive correlation of an increased ANB and the pharyngeal airway bone. [30] Ahmad et al reported significant association of reduced PNS- AD1 and PNS- AD2 distance in pediatric OSA patients from a lateral cephalometric parameters study. [20] Furthermore, children with obstructive sleep apnea may have a narrower upper airway anteroposteriorly at the level of the posterior nasal spine. However, when adenotonsillar hypertrophy is combined with additional variables such as craniofacial abnormalities, lower upper airway muscle tone, and neural reflexes, obesity, or heredity, a clinically substantial dynamic airway blockage may exhibit.[31]

Many of the clinical characteristics of pediatric OSA and the determinants of its epidemiology differ from those of adult OSA. The diagnostic criteria for OSA in adults have been determined by expert consensus and often include an AHI of 5 or greater on the nocturnal polysomnogram and evidence of disturbed or unrefreshing sleep, daytime sleepiness, or other daytime symptoms. AHI cut points of 5, 15, and 30 events per hour have been suggested to indicate mild, moderate, and severe levels of OSA. However, the rationale for specific AHI diagnostic criteria for children suffers from less available data and more heterogeneity across the studies. As yet, no international consensus has been reached regarding the AHI cutoff values for therapy initiation. At present, an AHI 1 to 5 events per hour has been most often used in research to identify children with OSA.[32] An unequal male to female ratio in sample size, an unequal male to female ratio in sample size may also have an effect on the results. However, in the study of Angela Galeotti et al., they found that OSA showed the same prevalence in male and female patients similar to previous findings reporting that, in the prepubertal period, there is no gender difference in the incidence of OSA.[33]

The lateral cephalogram, which was recorded in an upright position with the teeth in occlusion while the patient was aware, was one possible complicating factor in evaluating craniofacial morphology. Sleep-disordered breathing in children was studied under supine circumstances, where muscular tone loss might occur during sleeping. It was unclear whether the variation in orientation had a little influence in children with sleep-disordered breathing and whether the state of awareness affects upper airway measures. It is suggested that research techniques be standardized even further. In addition, while polysomnography, the gold standard for confirming OSA, is costly and time-consuming, questionnaires and lateral cephalograms are a feasible, cost-effective, conveniently accessible, and more practical approach for screening OSA risk. However, in recent years, 3-dimensional cone-beam computed tomography (3-D CBCT) has been rated superior in terms of airway visualization and image processing, although 3-D CBCT is still not as common as 2-D cephalograms due to the greater cost and radiation dosage.

Limitations

From PRISMA 2009 Flow Diagram, we found only 7 of 1,290 studies in this systematic review that were included in qualitative synthesis. 1 of 7 studies were rated as having a moderately strong evidence level. 5 of 7 studies were rated as having a limited evidence level. No study was assessed as providing strong evidence. Limited evidence level could have biased the results at the final summary.

The sample size is relatively small because of the low prevalence of the disease and the challenge in getting patients of young age to cooperate. It is more difficult to reach a level of difference that is statistically significant.

There are some limitations of the study. Cephalometric analysis was used in all studies to define skeletal and airway dimensions. Because of lateral cephalograms are 2-D images of a 3-D anatomical complex, the changing from upright to supine position alters the upper airway space in OSA patients. It was reported that the pharyngeal airway area on a lateral cephalogram strongly

correlates with volumetric data on cone-beam computed tomography (CBCT) images but lateral cephalogram can provide precise information in estimating tongue and pharynx volumes with a lower radiation dose.

We hope that this systematic review will be assist future studies in pediatric obstructive sleep apnea related to dental field which can be another screening procedure.

## Conclusions

Under limited evidence level of this review, we concluded that there is statistical support for an association between craniofacial disharmony and pediatric sleep-disordered breathing. There was significant correlation between upper airways dimensions and maxillomandibular discrepancy. Maxillomandibular discrepancy expressed by a significantly larger ANB angle. The maxilla was in the orthognathic range (SNA). The mandible showed a slight retrognathic tendency (SNB). The upper airway measurement showed a significant difference between OSA group and non-OSA group.

## Declaration of Interest

The authors report no conflict of interest.

**Table V. Characteristic of included studies**

| **Study** | Ahmad et al., (2020) | Ahn et al., (2015) | Ana Z.N. Bergamo et al., (2014) | Angela Galeotti et al., (2019) | Yu-Hsuan Lee et al., (2019) | Miesje Karmiati Purwanegara et al., (2017) | Stacey Quo et al., (2019) |
|---|---|---|---|---|---|---|---|
| **Country** | India | Korea | Brazil | Italy | Taiwan | Indonesia | United States |
| **Setting** | A Government dental hospital | Kyung Hee University School of Dentistry | The School of Dentistry of Ribeirao Preto | The "Bambino Gesù" Children's Hospital | The Chang Gung Memorial Hospital | Universitas Indonesia | UCSF School of Dentistry |
| **Design and participant characteristics** | Prospective, cross-sectional study | Case series | Cross-sectional study | Cross-sectional study | Cross-sectional study | Cross-sectional study | Pilot study |
| **Total number of subjects** | 60 patients: OSA (n=30) Non-OSA (n=30) | 1 patient | 43 children: OSA (n=21) Control group (n=22) | 47 patients | 26 children: OSA (n=16) Control subjects (n=10) | 285 patients: 9 to 11 years (n=120) 12 to 15 years (n=165) | 15 children: OSA (n=8) Control group (n=7) |
| **Mean age +/- SD** | 16±3.4 | | | | | | 9-16 years |
| Participant | 10-19 years | 11.1 | 8.15 | 5.75±1.99 | 5.14±0.79 | (1) 9-11 years (2) 12-15 years | none |
| Control | 10-19 years | - | 7.47 | - | 5.18±0.62 | - | none |
| **Sex distribution of subjects** | | | | | | | |
| Participant | 19 girls, 11 boys | 1 girl | 10 girls, 11 boys | 24 girls, 23 boys | 5 girls, 11 boys | none | none |
| Control | 20 girls, 10 boys | - | 10 girls, 12 boys | - | 5 girls, 5 boys | - | none |
| **Body Mass Index** | | | | | | | |
| Participant | none | 21.7 | none | none | 15.38 | none | none |
| Control | none | - | none | - | 15.19 | - | none |
| Control matched for age and sex | Yes | none | none | none | none | none | none |

| **Methods used** | | | | | | | |
|---|---|---|---|---|---|---|---|
| Method of sleep-disordered breathing diagnosis | STOP-BANG questionnaire | Polysomnography | Polysomnography; Apnea-hypopnea-index (AHI) Otorhinolaryngologic evaluation | Polysomnography; Apnea-hypopnea-index (AHI) Otorhinolaryngologic evaluation | Polysomnography; Apnea-hypopnea-index (AHI) Characteristics and quality of life survey | Medical records and questionnaire | Polysomnography Apnea-hypopnea-index (AHI) |
| Measurement tool: NHP, natural head position | Cephalogram | Cephalogram | Cephalogram | Cephalogram | Cephalogram | Cephalogram | Cephalogram |
| Error of the method: NS, not significant | NS | none | none | none | none | none | none |
| **Study quality appraisal** | | | | | | | |
| Evidence level (Strong, Moderately strong, Limited) | Moderately strong | Limited | Limited | Limited | Limited | Limited | Limited |
| Comments | Small sample size with an unequal male to female ratio. High sensitivity and specificity for OSA-risk of Modified STOPBANG questionnaire but no comparison with others. No confirmation of OSA with PSG has been done after screening OSA-risk. | none | none | Pharyngeal airway area on a lateral cephalogram strongly correlates with volumetric data on cone-beam computed tomography (CBCT) | The sample size is relatively small, 2-D cephalometric measurements; inherent structural limitations, such as error of projection and error of identification | none | none |

**Table 5.** Characteristic of included studies.

## References

1. Behrents RG, Shelgikar AV, Conley RS, Flores-Mir C, Hans M, Levine M et al. Obstructive sleep apnea and orthodontics: An American Association of Orthodontists White Paper. Am J Orthod Dentofacial Orthop 2019;156:13-28 e11.
2. Guilleminault C, Sullivan SS, Huang YS. Sleep-Disordered Breathing, Orofacial Growth, and Prevention of Obstructive Sleep Apnea. Sleep Med Clin 2019;14:13-20.
3. Marcus CL, Brooks LJ, Draper KA, Gozal D, Halbower AC, Jones J et al. Diagnosis and management of childhood obstructive sleep apnea syndrome. Pediatrics 2012;130:e714-755.
4. Guilleminault C, Khramtsov A. Upper airway resistance syndrome in children: a clinical review. Semin Pediatr Neurol 2001;8:207-215.
5. Lofstrand-Tidestrom B, Hultcrantz E. Development of craniofacial and dental arch morphology in relation to sleep disordered breathing from 4 to 12 years. Effects of adenotonsillar surgery. Int J Pediatr Otorhinolaryngol 2010;74:137-143.
6. Carroll JL. Obstructive sleep-disordered breathing in children: new controversies, new directions. Clin Chest Med 2003;24:261-282.
7. Pirelli P, Saponara M, Guilleminault C. Rapid maxillary expansion in children with obstructive sleep apnea syndrome. Sleep 2004;27:761-766.
8. Major MP, Flores-Mir C, Major PW. Assessment of lateral cephalometric diagnosis of adenoid hypertrophy and posterior upper airway obstruction: a systematic review. Am J Orthod Dentofacial Orthop 2006;130:700-708.
9. Dayyat E, Kheirandish-Gozal L, Sans Capdevila O, Maarafeya MMA, Gozal D. Obstructive sleep apnea in children: relative contributions of body mass index and adenotonsillar hypertrophy. Chest 2009;136:137-144.
10. Brietzke SE, Gallagher D. The effectiveness of tonsillectomy and adenoidectomy in the treatment of pediatric obstructive sleep apnea/hypopnea syndrome: a meta-analysis. Otolaryngol Head Neck Surg 2006;134:979-984.
11. Friedman M, Wilson M, Lin HC, Chang HW. Updated systematic review of tonsillectomy and adenoidectomy for treatment of pediatric obstructive sleep apnea/hypopnea syndrome. Otolaryngol Head Neck Surg 2009;140:800-808.
12. Pirila-Parkkinen K, Lopponen H, Nieminen P, Tolonen U, Pirttiniemi P. Cephalometric evaluation of children with nocturnal sleep-disordered breathing. Eur J Orthod 2010;32:662-671.
13. Fauroux B, Lavis JF, Nicot F, Picard A, Boelle PY, Clement A et al. Facial side effects during noninvasive positive pressure ventilation in children. Intensive Care Med 2005;31:965-969.
14. Spruyt K GD. Pediatric sleep questionnaires as diagnostic or epidemiological tools: a review of currently available instruments. Sleep Med Rev. 2011:9-32.
15. Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ 2015;350:g7647.
16. Higgins JP, Altman DG, Gotzsche PC, Juni P, Moher D, Oxman AD et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011;343:d5928.
17. Swartz MK. The PRISMA statement: a guideline for systematic reviews and meta-analyses. J Pediatr Health Care 2011;25:1-2.
18. Moher D LA, Tetzlaff J, Altman DG; . PMID: 19723669. Reprint--preferred reporting items for systematic reviews and

meta-analyses: the PRISMA statement. Phys Ther. 2009;9:873-880.
19. Khan KS. Undertaking systematic reviews of research on effectiveness : CRD's guidance for those carrying out or commissioning reviews. York: University of York, NHS Centre for Reviews & Dissemination; 2001.
20. Ahmad L, Kapoor P, Bhaskar S, Khatter H. Screening of obstructive sleep apnea (OSA) risk in adolescent population and study of association with craniofacial and upper airway morphology. Journal of Oral Biology and Craniofacial Research 2020;10:807-813.
21. Ahn HW, Lee BS, Kim SW, Kim SJ. Stability of Modified Maxillomandibular Advancement Surgery in a Patient With Preadolescent Refractory Obstructive Sleep Apnea. Journal of Oral and Maxillofacial Surgery 2015;73:1827-1841.
22. Bergamo AZN, Itikawa CE, De Almeida LA, Sander HH, Fernandes RMF, Anselmo-Lima WT et al. Adenoid hypertrophy, craniofacial morphology in apneic children. Pediatric Dental Journal 2014;24:71-77.
23. Galeotti A, Festa P, Viarani V, Pavone M, Sitzia E, Piga S et al. Correlation between cephalometric variables and obstructive sleep apnoea severity in children. Eur J Paediatr Dent 2019;20:43-47.
24. Lee YH, Huang YS, Chen IC, Lin PY, Chuang LC. Craniofacial, dental arch morphology, and characteristics in preschool children with mild obstructive sleep apnea. Journal of Dental Sciences 2020;15:193-199.
25. Purwanegara MK, Sugiarto RH, Abdurachman H, Sutrisna B. Correlation between snoring, apnea and obstruction of upper respiratory tract: (population study in Jakarta and its vicinity). Journal of International Dental and Medical Research 2017;10:284-291.
26. Quo S, Lo LF, Guilleminault C. Maxillary protraction to treat pediatric obstructive sleep apnea and maxillary retrusion: a preliminary report. Sleep Med 2019;60:60-68.
27. Galeotti A, Festa P, Viarani V, Pavone M, Sitzia E, Piga S et al. Correlation between cephalometric variables and obstructive sleep apnoea severity in children. European Journal of Paediatric Dentistry 2019;20:43-47.
28. Uslu-Akcam O. Pharyngeal airway dimensions in skeletal class II: A cephalometric growth study. Imaging Science in Dentistry 2017;47:1-9.
29. Schiffman PH, Rubin NK, Dominguez T, Mahboubi S, Udupa JK, O'Donnell AR et al. Mandibular dimensions in children with obstructive sleep apnea syndrome. Sleep 2004;27:959-965.
30. Iwasaki T, Suga H, Yanagisawa-Minami A, Sato H, Sato-Hashiguchi M, Shirazawa Y et al. Relationships among tongue volume, hyoid position, airway volume and maxillofacial form in paediatric patients with Class-I, Class-II and Class-III malocclusions. Orthod Craniofac Res 2019;22:9-15.
31. Neelapu BC, Kharbanda OP, Sardana HK, Balachandran R, Sardana V, Kapoor P et al. Craniofacial and upper airway morphology in adult obstructive sleep apnea patients: A systematic review and meta-analysis of cephalometric studies. Sleep Medicine Reviews 2017;31:79-90.
32. Ruehland WR, Rochford PD, O'Donoghue FJ, Pierce RJ, Singh P, Thornton AT. The New AASM Criteria for Scoring Hypopneas: Impact on the Apnea Hypopnea Index. Sleep 2009;32:150-157.
33. Alsubie H, Bahammam A. Obstructive Sleep Apnoea: Children are not little Adults. Paediatric Respiratory Reviews 2017;21.