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Cephalometry as an aid in the diagnosis of pediatric obstructive sleep apnoea: A systematic review and meta-analysis

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ABSTRACT

Background: Obstructive sleep apnoea (OSA) is part of a spectrum of sleep disorders causing snoring, gasping, and choking while sleeping. In children, OSA can also lead to behavioural issues, hyperactivity, and poor academic performance. Thus, early identification and management of OSA in children is crucial in preventing long-term health problems. The gold standard test for diagnosis is an overnight in-lab polysomnography (PSG). However, due to certain constraints associated with PSG, such as lack of accessibility, high expenses incurred, as well as the need for hospitalization, alternative diagnostic tools are needed. Cephalometry is a non-invasive, affordable diagnostic tool that may offer useful information in the evaluation of OSA. The present systematic review and meta-analysis aimed to evaluate the various cephalometric parameters associated with the diagnosis of OSA in children.

Methods: A structured literature search was performed using the search engines PubMed, Scopus, Web of Science, Cochrane, and Google scholar from inception till July 2022. The weighted mean difference (z-test) was calculated using a random effects method (REM).

Results: 16 studies were included in the review and meta-analysis was executed for each cephalometric parameter. The parameters of significance ($p < 0.05$) in Pediatric OSA with lower heterogeneity were associated with McNamara's and Linder-Aronson's analysis, the hyoid bone position, a retrognathic mandible, and an acute cranial base angle.

Conclusions: Certain parameters in craniofacial morphology may be reliable diagnostic parameters. Further long-term studies are needed in order to shed more light in this area.

1. Introduction

Obstructive sleep apnoea (OSA) is a condition which could affect all age groups, including children. It occurs when a person's airway is blocked while sleeping, resulting in repetitive pauses in breathing that can last anywhere from a few seconds to more than a minute.[1] OSA can cause snoring, gasping, and choking while sleeping, as well as tiredness, irritability, and trouble concentrating during the day in children. OSA can also lead to behavioural issues, hyperactivity, and poor academic performance in children.[2] OSA is predicted to impact 2–5% of all children, and its occurrence is increasing as obesity and other lifestyle factors are on the rise.[3] Hence, early identification and management of OSA in children is critical to prevent potential future consequences such as high blood pressure, heart disease, stroke, and cognitive impairment.[4]

The diagnosis of OSA involves various diagnostic tools. Medical history and physical examination are the first steps in identifying risk factors and symptoms of OSA.[5] An overnight in-lab polysomnography (PSG) that records numerous physiological factors during sleep, such as breathing patterns, oxygen saturation, and brain activity, is the gold standard test in identifying OSA. The PSG is comprised of multiple components such as the electroencephalogram (EEG), electrooculogram (EOG), chin electromyogram (EMG), airflow, oxygen saturation, respiratory effort, and electrocardiogram (ECG) or heart rate. Other recommended parameters include body position and leg EMG.[6] The diagnosis of OSA via a PSG is done using the apnoea hypopnea index (AHI), which is the number of apneic and/or hypopneic events per hour. As per the

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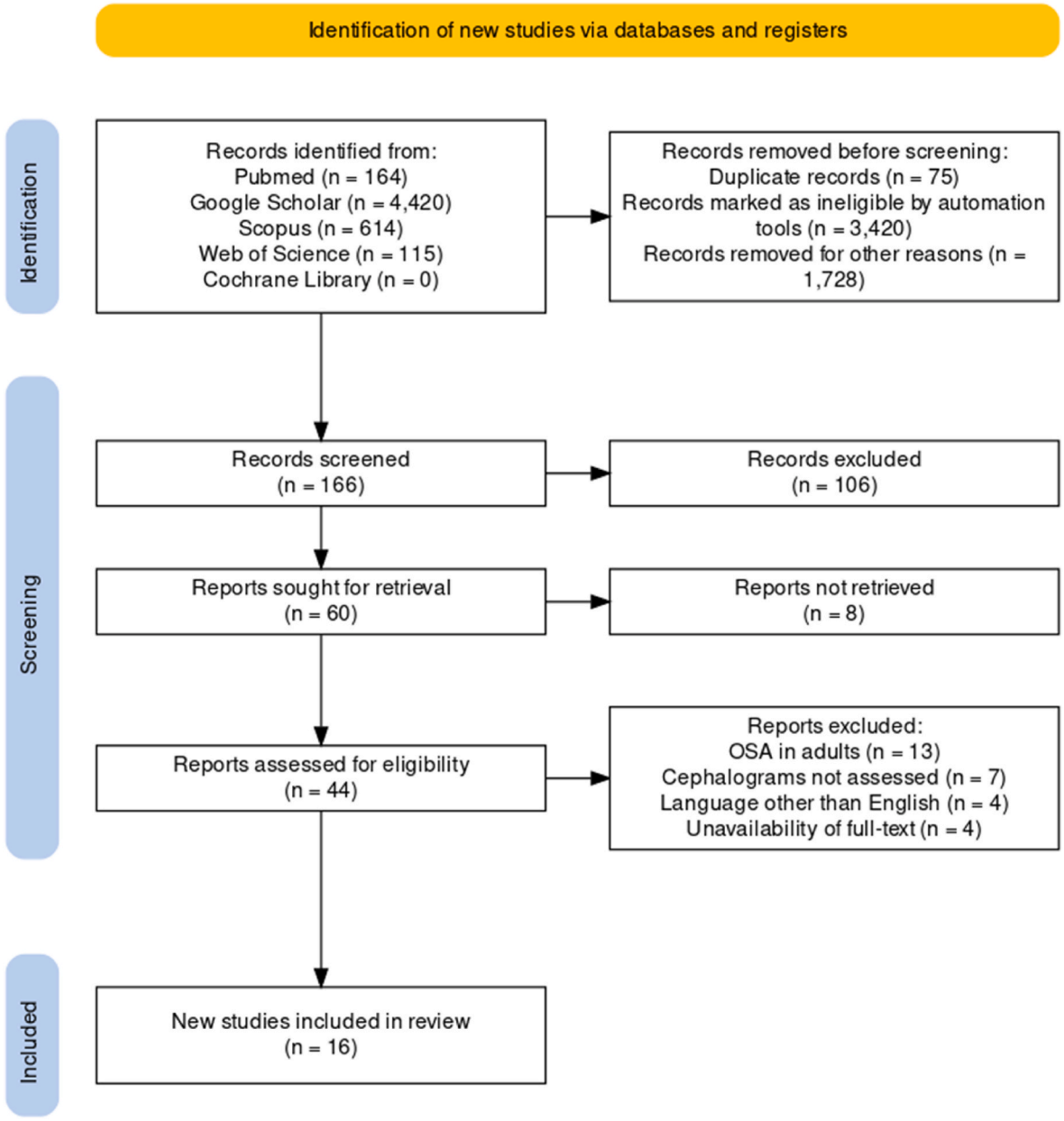

Fig. 1. Flowchart defining search strategy as per PRISMA 2020 guidelines.

American Academy of Sleep Medicine criteria, an AHI index >1 is considered to be pediatric OSA. However, PSG is associated with various constraints such as the high expense, limited access, and the need for hospitalization. Furthermore, the child may experience increased discomfort due to the multiple leads required for the assessment. The future prospects of PSG include a shorter duration of evaluation instead of an overnight procedure. It also includes the development of portable equipment which could enhance the applicability of the procedure. Other tests to assess OSA include oximetry, which quantifies oxygen levels in the blood, and the Epworth Sleepiness Scale, which evaluates daytime sleepiness. Individual patient factors such as the severity of symptoms, the involvement of chronic conditions, and the ease of access to testing facilities all impact the selection of screening tools.[7,8]

Cephalometry is a diagnostic instrument that uses X-rays to provide data on the dimension and location of upper airway structures, which can aid in the diagnosis and classification of the severity of OSA. Cephalometry can direct treatment planning by focusing on the areas of the upper airway that may gain from corrective surgery or other therapies by recognising anomalies or obstructions that contribute to OSA. Despite being a static imaging technique that cannot capture dynamic changes in airway structure, cephalometry is an economical, non-invasive diagnostic tool that could offer useful data in the assessment of the presence of OSA.[9,10]

The pharyngeal airway space, hyoid bone position, mandibular plane angle, and craniofacial dimensions are all cephalometric landmarks commonly used to assess OSA.[11] The distance between the posterior pharyngeal wall and the base of the tongue is measured as the pharyngeal airway space. A narrow pharyngeal airway space increases the risk of airway collapse during sleep.[12] The location of the hyoid bone can influence the position and support of the upper airway structures, whereas the mandibular plane angle can suggest the inclination of the mandible and the upper airway's stability.[13] Further, craniofacial parameters offer useful data regarding the dimension and form of the upper airway and can be employed to recognise abnormal development that contributes to OSA. The McNamara and Ricketts analyses are the two commonly used cephalometric assessments for evaluating OSA. The

McNamara analysis determines the orientation of the maxilla as well as the mandible with respect to the cranial base, whereas the Ricketts analysis determines the position of the jaws and dentition with respect to the cranial base.[14,15] Healthcare professionals can better identify and manage OSA by using cephalometric landmarks to evaluate the upper airway, ultimately improving patient outcomes.[11]

Several studies have found an association between OSA and abnormal orofacial morphology.[16–21] As a result, the current research goal was to evaluate the effectiveness of cephalometry in diagnosing OSA through a systematic review. This review could aid in the timely identification and treatment of pediatric OSA cases.

2. Methods

This review was registered in PROSPERO (CRD number: CRD42022330353) and was executed following the guidelines as per the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

2.1. Selection criteria

The following PICO question was put together:

Participants – Children diagnosed with obstructive sleep apnoea.

Index - Any study that scrutinized, from an accuracy analysis position, a minimum of one or more objectively measurable parameters to identify obstructive sleep apnoea using a lateral cephalogram.

Comparator/Control – Children without a diagnosis of obstructive sleep apnoea and without a history of oral habits.

Outcomes – Measurements of the cephalometric parameters associated in participants and controls.

Inclusion criteria: Studies meeting the following criteria were selected

1. Children diagnosed with obstructive sleep apnoea
2. Children with no history of medical and/or syndromic conditions
3. Children with no history of treatment for obstructive sleep apnoea
4. Children with no oral habits

Exclusion criteria: Studies meeting the following criteria were eliminated from this review.

1. Individuals above the age of 18 years
2. Children diagnosed with medical and/or syndromic conditions
3. Studies conducted in vitro or ex vivo, studies conducted on animals, and narrative reviews.
4. Studies published in languages other than English.

2.2. Search strategy

A systematic literature search was conducted via the databases, namely, PubMed, Scopus, Web of Science, Cochrane, and Google scholar from inception till July 2022 (Fig. 1). The key words, Sleep Apnoea Syndrome, Sleep Apnoea, Obstructive, Children, Humans, Cephalometry were utilised to run the search engines with the Boolean operator AND and OR. The title and abstract were recovered for the identified studies by two autonomous reviewers (SS and KP) for the initial assessment. All conflicts were resolved via mutual discussion involving a third reviewer (SW). The studies to be assessed for full-text screening were identified using the inclusion criteria and exclusion criteria. Studies that met the inclusion criteria were selected for further analysis.

2.3. Data extraction

The following data from the above chosen studies were extracted: Title of study, author, year of publication, number of patients included in the study and control groups, age of the patients included, body mass index (BMI) if recorded, diagnostic method utilised to identify obstructive sleep apnoea, age/sex matching of the control group, race/ethnicity of the included patients, standardization method for recording of the lateral cephalogram, as well as the parameters assessed (Table 1) such as nasopharyngeal parameters, oropharyngeal parameters, hyoid bone measurements, other cephalometric landmarks used in each study and the values obtained for the same.

The data was recorded and summarized using Microsoft Excel spreadsheet.

Table 1
Cephalometric Landmarks and reference planes for areas analyzed.

S. No.	Area assessed	Linear cephalometric parameters (mm)	Angular cephalometric parameters (degree)
1	Cranial Base	S–N S–Ba N–Ba	N–S–Ba
2	Facial parameters: Anterior facial height Upper anterior facial height Lower anterior facial height Posterior facial height Gonial Angle Upper gonial angle Lower gonial angle Facial axis Facial taper	N–Me N-ANS ANS-Me S-Go	Ar-Go-Gn Ar-Go-N N-Go-Gn BaN-PmGn NPog-GoGn
3	Maxilla and Mandible Maxilla to cranial base Mandible to cranial base Maxilla and mandible Maxillary plane Mandibular plane Mandibular arc	ANS-PNS Go-Gn	SNA SNB ANB Sn-Go-Gn Sn-Go-Me PmXi-XiDC
4	Pharyngeal Airway Linder-Aronson Analysis McNamara's Analysis Pharyngeal airway space	PNS - AD-1 PNS - AD-2 PTV-AD Upper pharynx Lower pharynx	Ba-S-PNS
5	Soft Palate & Tongue	SPT SPL Tongue length	
6	Hyoid Bone	C3–H H-MP H – Posterior wall of pharynx H – Palatal plane MP-H/Go-Gn	Gn-Go-H

Cephalometric parameters which have been analyzed and evaluated in the included studies for diagnosing pediatric sleep-disordered breathing.

2.4. Quality assessment (Risk of bias) of the included studies

The studies meeting the inclusion criteria were appraised by two autonomous appraisers (SW and JJ) using the Quality Index.[22] The Quality Index[22] was modified according to the need of the present review and the studies assessed were segregated into low, medium, and high risk of bias as per the scores obtained post assessment.

2.5. Statistical analysis

JBI SUMARI (in collaboration with the Joanna Briggs Institute) was employed for performing the statistical analysis. The heterogeneity test

Table 2
Study characteristics.

Author (Year)	Study design	Diagnostic method	Age {Range (Yr)/Mean SD (Yr)} (n)		BMI		Cephalometric tracing technique used
			OSA	Control	OSA	Control	
Caprioglio et al. (1999)	CC[a]	PSG[c]	4.5 (13)	5 (13)	–	–	Manual
Pirilä-Parkkinen et al. (1999)	CS[b]	PSG[c]	7.1 ± 1.71 (20)	8.5 ± 1.39 (10)	–	–	Digital
Zucconi, M et al. (1999)	CS[b]	PSG[c]; Questionnaire	4.6 ± 1.5 (26)	5.1 ± 0.5 (26)	–	–	Digital
Kawashima et al. (2000)	CS[b]	PSG[c]	4.7 (15)	4.7 (30)	16.5	NA[d]	Manual
Cozza et al. (2004)	CC[a]	PSG[c]; Questionnaire	5.91 ± 1.14 (20)	6 ± 0.71 (20)	16.02 ± 3.40	20.98 ± 0.48	Manual
Zettergren Wijk (2006)	Cohort	PSG[c]	10.9 (17)	10.7 (17)	–	–	Manual + Digital
Pirilä-Parkkinen et al. (2010)	CS[b]	PSG[c]; Questionnaire	7.3 ± 1.72 (70)	7.3 ± 1.78 (70)	OSA-16.6 ± 3.46; UARS - 16 ± 3; Snoring - 16.8 ± 2.52	16.6 ± 2.23	Manual
L. Perillo et al. (2012)	CS[b]	PSG[c]; Questionnaire	8.95 (40)	9.4 (40)	–	8.5 ± 1.39 (10)	Digital
Di Francesco et al. (2012)	CS[b]	PSG[c]	M – 5.5(48); F - 6 (29)	NA[d]	M – 14.61; F - 14.86	NA[d]	Digital
Kawashima et al. (2012)	CS[b]	PSG[c]	4.8 ± 0.8 (15)	4.9 ± 0.8 (15)	14.790 ± 1.125	15.993 ± 1.303	Digital
Deng & Gao (2012)	CC[a]	PSG[c]	9.5 ± 1.0 (15)	9.6 ± 1.8 (15)	–	–	Manual
Vieira et al. (2013)	CS[b]	PSG[c]; Questionnaire	5.18 (14)	5.07 (15)	–	–	Manual
Au et al. (2018)	CS[b]	PSG[c]	OAHI 1–5: 9.4 ± 1.3; OAHI >/ = 5: 9.0 ± 1.9 (47)	8.9 ± 1.6 (43)	OAHI 1–5: 19.1 ± 4.7; OAHI >/ = 5: 17.7 ± 3.4	16.4 ± 2.6	Digital
Zhao et al. (2018)	CC[a]	PSG[c]	12.6 ± 1.2 (23)	12 ± 1.2 (23)	–	–	Digital
Hwang et al. (2019)	CS[b]	PSG[c]	5.9 ± 2.2 (21)	7.2 ± 1.9 (18)	16.6 ± 2.3	16.9 ± 2.3	Manual
Yuen et al. (2022)	CS[b]	PSG[c]	8.4 ± 1.7 (48)	8.2 ± 1.7 (34)	0.16 ± 0.92	0.24 ± 0.80	Manual

Footnotes.
[a] CC- Case control.
[b] CS – cross-sectional.
[c] PSG – Polysomnography.
[d] NA – Not available.

and Chi-squared test were carried out to evaluate the heterogeneity and inconsistency, for which 95 % confidence interval was calculated and illustrated in the form of forest plots. The overall test for significance (z-test) was performed and weighted mean difference was calculated for all the cephalometric parameters. Random effect method (REM) was chosen in order to reduce the existing variability, and forest plots were produced to graphically represent the weighted mean difference and overall test for significance.

3. Results

3.1. Characteristics of the included studies

5313 studies were obtained from the initial search, of which 249 titles and abstracts were qualified for screening post elimination of duplicates. After further analysis, 44 studies were selected for full-text review. Of these, a final pool of 16 studies were selected for this systematic review.

From those studies included in this review, three studies dated back to 1999[23–25] and one study published in 2021.[26] Four studies were performed in a Chinese population,[16,17,26,27] three in Italy,[19,23,25] two in Brazil[20,28] and Japan[21,29]; and one each in Sweden,[30] and Korea.[18] A majority of the studies had a cross-sectional study design[16,18–21,23,24,26,28,29,31] with the rest having a case-control[17,25,27,32] while one study had a cohort study design.[30] The sample sizes for the OSA group ranged from 13[25] to 77[20] and the age from 4.5 years[25] to 12.6 years.[27] All studies comprised of children as the study sample (age <18 y). The cephalometric tracing technique used varied amongst the studies where 8 studies[17,25,26,28,29,32–34] employed a manual technique, 7[16,19–21,24,27,35] employed a digital software, and 1[30] used both. The assessment of BMI was executed in only half of the included studies.[16,19–21,26,29,31,32,34]

The characteristics of the included studies are summarized in Tables 2 and 3.

3.2. Risk of bias analysis of the included articles

The quality assessment of inter-reviewer reliability as per Cohen's kappa was 0.94. As none of the articles were of low quality of evidence, all the included articles were involved in the meta-analysis. Of the 16 studies found to be relevant (Tables 4 and 5), 10 studies had a low-risk and 6 had a moderate risk of bias.

3.3. Study outcomes and measurements

Three studies analyzed the cephalometric measurements relating to tongue length and soft palate length between OSA and control group[16,17,32] of which two studies found no significant association between the position of the tongue and OSA.[17,32] Two studies compared the thickness of the soft palate[17,32] of which one study found a significant association between OSA and the ratio of the radius of the tonsil (T) to the width of the pharyngeal airway.[17]

Nine studies assessed different pharyngeal parameters[16,17,19,21,23,25,29–31] where evaluation of the pharyngeal airway was done via McNamara's analysis by two studies,[16,17] Linder-Aronson analysis by two studies[30,31] and both by four

Table 3
Study characteristics (contd.).

Author (Year)	OAHI index recorded	Controls matched to age and/or sex?	Error of method checked	Lateral cephalogram standardization
Caprioglio et al. (1999)	No	Yes	Yes	S[b]
Pirilä-Parkkinen et al. (1999)	Yes	Yes	No	NS[c]
Zucconi, M et al. (1999)	Yes	Yes	Yes	NHP[a]; S[b]
Kawashima et al. (2000)	Yes	No	No	NHP[a]; NS[c]
Cozza et al. (2004)	Yes	No	Yes	S[b]
Zettergren Wijk (2006)	Yes	Yes	Yes	S[b]
Pirilä-Parkkinen et al. (2010)	Yes	Yes	Yes	NHP[a]; S[b]
L. Perillo et al. (2012)	No	Yes	Yes	S[b]
Di Francesco et al. (2012)	Yes	No	No	S[b]
Kawashima et al. (2012)	Yes	No	No	S[b]
Deng & Gao (2012)	Yes	Yes	Yes	NHP[a]; S[b]
Vieira et al. (2013)	Yes	Yes	No	NS[c]
Au et al. (2018)	Yes	Yes	No	S[b]
Zhao et al. (2018)	Yes	No	Yes	NHP[a]; S[b]
Hwang et al. (2019)	Yes	No	No	S[b]
Yuen et al. (2022)	Yes	No	No	S[b]

Footnotes.
[a] NHP – Natural head position.
[b] S – Standardized.
[c] NS – Not Standardized.

studies.[21,25,29,35] The pharyngeal airway space was assessed by three studies[17,19,31] of which two found a significant reduction in pharyngeal airway space in children with OSA.[19,31] Five studies assessed various parameters associated with the hyoid bone[16–19,28] of which three studies[16,17,19] found a significant association between an inferiorly positioned hyoid bone and OSA. Five studies assessed parameters related to the cranial base[16,17,19,29,31] of which only one study found a significant association between cranial base angle and OSA.[19] Nine studies assessed measurements pertaining to different facial parameters[16,17,19,23–25,27–29] of which two studies found a significant association between anterior facial height, lower anterior facial height, and OSA[17,19]; four studies found a significant association between the lower gonial angle and OSA.[25,27,29,35] Seven studies assessed parameters related to maxillary and mandibular measurements[16,25,27,29–31,35] of which only one study found a significant association between SNA and OSA.[31]

All of the studies used healthy children without OSA as the control group. The children of the study group were recruited via the polysomnographic diagnostic method. Measurements for the cephalometric analysis were completed using either manual[17,18,26,28,29,31,32] or digital[16,19–21,23,24,27] or both[29] tracing techniques.

3.4. Meta-analysis

Meta-analysis was performed on the basis of various parameters included in the studies like tongue length, soft palate length and thickness, pharyngeal airway parameters, hyoid bone parameters, cranial base parameters and facial height parameters (Table 6).

Statistical significance for overall effect was found to be significant (i.e., $p < 0.05$) for the Linder-Aronson analysis, McNamara's analysis, Hyoid bone parameters such as H-MP, H-posterior pharynx, cranial base angle (Na–S–Ba), Posterior facial height, and parameters related to maxilla and mandible such as SNB, ANB and ANS-PNS.

Data from six studies[21,23,29–31] was included to compare cephalometric measurements of the Linder-Aronson Analysis for both AD 1 mm and AD 2 mm. The weighted mean difference for AD 1 mm was −3.86 (95 % CI: −5.04 to −2.67) with a low degree of heterogeneity ($I^2 = 17$; df = 5; p = 0.335). The weighted mean difference for AD 2 mm was −2.40 (95 % CI: −4.32 to −0.49) with a high degree of heterogeneity ($I^2 = 84$; df = 5; p = 0). Data from four studies[21,23,25,29] was included in the meta-analysis to compare cephalometric measurements of the PTV- AD mm. The weighted mean difference was −3.12 (95 % CI: −4.64 to −1.61) with a moderate degree of heterogeneity ($I^2 = 59$; df = 3; p = 0.057). Data from four studies[16–19,28] was incorporated in the meta-analysis to compare cephalometric measurements of the H-MP. The weighted mean difference was 3.60 (95 % CI: 2.60–4.59) with no degree of heterogeneity ($I^2 = 0$; df = 4; p = 0.901). Data from three studies[16,19,28] was included in the meta-analysis to compare cephalometric measurements of point H to the posterior wall of the pharynx. The weighted mean difference was 1.41 (95 % CI: 0.22–2.60) with a moderate degree of heterogeneity ($I^2 = 54$; df = 2; p = 0.11). Data from five studies[16,17,19,24,29] was included to compare cephalometric measurements Na–S–Ba. The weighted mean difference was −1.59 (95 % CI: −2.68 to −0.49) with a low degree of heterogeneity ($I^2 = 32$; df = 4; p = 0.123). Data from seven studies[16,17,19,23,25,31,32] was included in the meta-analysis of cephalometric measurements of SNB. The weighted mean difference was −1.09 (95 % CI: −2.13 to −0.04) with a moderate degree of heterogeneity ($I^2 = 57$; df = 6; p = 0.021). Data from seven studies[16,17,19,23,25,31,32] was included in the meta-analysis of cephalometric measurements of ANB. The weighted mean difference was −1.17 (95 % CI: 0.55–1.80) with a moderate degree of heterogeneity ($I^2 = 52$; df = 6; p = 0.056). Data from five studies[16,17,19,21,32] was included in the meta-analysis of cephalometric measurements of ANS-PNS. The weighted mean difference was −1.62 (95 % CI: −2.66 to −0.58) with no heterogeneity ($I^2 = 0$; df = 3; p = 0.587).

4. Discussion

Lateral cephalometry has been in use as a diagnostic aid in analyzing soft tissue and skeletal relationships such as the length of soft palate, posterior airway space (PAS) and hyoid position.[36] It has previously been acknowledged as a reliable screening tool in cases of upper airway obstruction.[37] It is a comparatively economical tool while considering other imaging techniques such as cone-beam computed tomography, magnetic resonance imaging, etc.

The meta-analysis of this systematic review identified various parameters used in lateral cephalometry in conditions wherein this radiographic imaging technique was utilised as an adjunct to identify pediatric obstructive sleep apnea.

Of the parameters assessed, the following inferences could be obtained.

4.1. Cranial base

The development of the head and neck is influenced by the growth of the dentofacial complex where the cranial base plays a significant role.[38] The Na–S–Ba parameter, representing the cranial base flexure angle is correlated with pharyngeal airway dimensions.[39] A significantly acute angle was found to be associated with OSA in the present study, indicating that it could be a potentially reliable parameter in the assessment of pediatric OSA.

Table 4
Quality assessment of the included studies.

S. No.	Questions	Author (Year)							
		Yuen et al. (2022)	Hwang et al. (2019)	Au et al. (2018)	Zhao et al. (2018)	Vieira et al. (2014)	Perillo et al. (2013)	Deng et al. (2012)	Di Francesco et al. (2012)
1	Is the hypothesis/aim/objective of the study clearly described?	1	1	1	1	1	1	1	1
2	Are the main outcomes to be measured clearly described in the Introduction or Methods section?	1	1	1	1	1	1	1	1
3	Are the characteristics of the patients included in the study clearly described ?	1	1	1	1	1	1	1	1
4	Are the interventions of interest clearly described?	1	1	1	0.5	1	1	1	1
5	Are the main findings of the study clearly described?	1	0.5	1	0.5	1	1	1	1
6	Does the study provide estimates of the random variability in the data for the main outcomes?	1	1	1	0	1	1	1	1
External validity:									
7	Were the subjects asked to participate in the study representative of the entire population from which they were recruited?	1	1	1	1	1	1	1	1
8	Were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of patients receive?	1	1	1	1	1	1	1	1
Internal validity – bias:									
9	Was the OAHI index used to grade the patients enrolled?	1	1	1	1	1	0	1	1
10	Was the standardization of the lateral cephalogram specified?	1	1	1	1	1	1	1	1
11	If any of the results of the study were based on "data dredging", was this made clear?	0.5	0.5	0	0	0.5	0.5	0.5	0.5
12	Were the statistical tests used to assess the main outcomes appropriate?	1	1	1	0	1	1	1	1
13	Were the main outcome measures used accurate (valid and reliable)?	0.5	1	1	0.5	1	1	1	0.5
Internal validity – confounding (selection bias)									
14	Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population?	1	1	1	1	1	0	1	1
15	Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?	1	1	1	1	1	1	1	1
16	Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?	0.2	1	1	0	1	1	1	1
17	Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5 %?	1	0	0	0.5	0	0.5	1	0
	Total	**15.2**	**15**	**15**	**11**	**15.5**	**14**	**16.5**	**15**
	Risk of Bias assessment	**Low**	**Low**	**Low**	**Medium**	**Low**	**Low**	**Low**	**Low**

Risk of bias assessment of the included studies using the Quality Index Tool.

4.2. Maxilla and mandible

The parameters used in the assessment of the maxilla and the mandible have been previously described. Both maxillary as well as mandibular retrusion, especially the latter, have been identified as key features in OSA. The findings of this study suggest that reduced SNB and ANB angles, as well as ANS-PNS length were found to be significantly associated with OSA with a moderate degree of heterogeneity. These findings correspond with previous meta-analysis done in this field.[40,41]

A steep mandibular plane as well as a clockwise rotation of the mandible were both found to have a statistically significant relationship with OSA in previous studies.[17,19,27,40] However, the present study reports no significant correlation between these parameters and pediatric OSA. A small maxilla has been associated with a reduced upper airway space.[42] Patients with a retrognathic mandible are suggested to be more predisposed to developing OSA as it causes narrowing of the pharyngeal airway dimensions. The findings of the present study support this hypothesis.

4.3. Facial height

A longer face is associated with OSA. Also known as the "adenoid facies" often discovered in mouth breathing, a longer facial height has been an indicative risk factor of OSA.[43,44] While a previous meta-analysis in adults had found a significant association with the posterior facial height and OSA to be of a low heterogeneity, a high degree of heterogeneity was found in the present study indicating that the same measures may not be reliable in identifying children with OSA.[40]

4.4. Hyoid bone

The position of the hyoid bone plays a significant role in identifying OSA. It has been previously stated that an inferiorly positioned hyoid bone presents with an increased risk of developing OSA.[17,18,45] An inferiorly positioned hyoid bone tends to pull the tongue backwards, further narrowing the pharyngeal airway and reducing airway patency.[46] It has been shown that adult patients with obstructive sleep apnoea syndrome often present with changes in hyoid bone position.[35]

Table 5
Quality assessment of the included studies (contd.).

S. No.	Questions	Author (Year)							
		Kawashima et al. (2012)	Pirila-Parkkinen et al. (2010)	Zettergren et al. (2008)	Cozza et al. (2004)	Kawashima et al. (2004)	Caprioglio et al. (1999)	Zucconi et al. (1999)	Pirilä-Parkkinen et al. (1999)
1	Is the hypothesis/aim/objective of the study clearly described?	1	1	1	1	1	0	1	1
2	Are the main outcomes to be measured clearly described in the Introduction or Methods section?	1	1	1	1	1	1	1	1
3	Are the characteristics of the patients included in the study clearly described ?	0.5	1	1	1	1	1	1	1
4	Are the interventions of interest clearly described?	1	1	1	1	1	1	0	1
5	Are the main findings of the study clearly described?	1	1	0	1	1	1	1	1
6	Does the study provide estimates of the random variability in the data for the main outcomes?	1	1	0.5	1	1	1	1	1
External validity:									
7	Were the subjects asked to participate in the study representative of the entire population from which they were recruited?	0	1	0.5	1	1	1	0	1
8	Were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of patients receive?	1	1	1	1	1	1	0	0.5
Internal validity – bias:									
9	Was the OAHI index used to grade the patients enrolled?	1	1	1	1	1	0	1	1
10	Was the standardization of the lateral cephalogram specified?	0.5	0.5	0	1	0	1	0	0
11	If any of the results of the study were based on “data dredging”, was this made clear?	0	0	0	0.5	0	0	0	0
12	Were the statistical tests used to assess the main outcomes appropriate?	1	1	1	0	0	1	1	1
13	Were the main outcome measures used accurate (valid and reliable)?	1	1	1	1	1	1	1	1
Internal validity – confounding (selection bias)									
14	Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population?	0	1	1	0.5	0.5	0.5	1	1
15	Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?	1	0.5	0	0	0.5	0.5	0.5	0.5
16	Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?	0	0	0	1	0	0	1	1
17	Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5 %?	0	0.5	0.5	1	0.5	0	0.5	0
	Total	**11**	**13.5**	**11**	**14**	**11.5**	**11**	**11**	**13**
	Risk of Bias assessment	**Medium**	**Low**	**Medium**	**Low**	**Medium**	**Medium**	**Medium**	**Low**

Risk of bias assessment of the included studies using the Quality Index Tool.

The present study reports a significant association between the position of the hyoid bone and OSA, namely an inferiorly positioned hyoid bone and its distance from the pharyngeal airway. These results indicate that the parameters used in this assessment could be reliable markers for pediatric OSA.

4.5. Tongue length and soft palate

An inferiorly positioned tongue could be associated with a retrognathic mandible and thus play a role in OSA.[26,47] The tongue is attached to the soft palate by the palatoglossus muscles, hence mandibular advancement may increase muscle tension resulting in changes in the velopharyngeal region. However, the findings of the present study indicate no significant association between the tongue length and OSA as well as soft palate and OSA. Potential reasons for this could be the difficulties associated with reproducing tongue position on lateral cephalograms.[48,49] Therefore, while it may not be a reliable radiographic parameter, it could still play a significant role clinically.

4.6. Pharyngeal airway

A reduced pharyngeal airway is a landmark feature of OSA.[20,50–52]

Table 6
Pooled results for cephalometric variables in individuals with obstructive sleep apnoea compared with the healthy controls.

Cephalometric variable	Weighted weighted mean difference (OSA-control)	95 % CI	Heterogeneity (I^2; P (significant <0.05)	Statistical significance for overall effect (P)
Tongue Length	1.65	−0.36 – 3.67	16; 0.26	0.108
Soft Palate				
- Length	0.15	−1.76 – 2.06	49; 0.15	
- Thickness	−0.32	−2.04 – 1.41	80; 0.02	0.879
Pharyngeal Airway				
- Ba-S-PNS	1.12	−2.08 – 4.32	89; 0	0.494
- Linder-Aronson	−3.86	−5.04–−2.67	17; 0.33	**0.000**[a]
- AD	−2.40	−4.32–−0.49	84; 0	**0.014**[a]
- PTV-AD	−3.12	−4.64–−1.61	59; 0.05	**0.000**[a]
- McNamara's Analysis	−3.10	−4.42–−1.79	69, 0.008	**0.000**[a]
- PAS	−1.15	−3.28 – 0.19	71; 0.02	0.080
Hyoid bone				
- C3H	1.24	−0.05 – 2.99	58; 0.009	0.163
- H-MP	3.60	2.60–4.59	0; 0.901	**0.000**[a]
- H-posterior pharynx	1.41	0.22–2.60	54; 0.11	**0.020**[a]
- H-palatal plane	−0.23	−0.8.87–8.42	97; 0	0.959
Cranial Base parameters				
- SN	0.48	−3.42 – 4.39	89; 0	0.808
- S–Ba	−0.47	−1.85 – 0.90	47, 0.71	0.501
- Na–S–Ba	−1.59	−2.68–−0.49	32, 0.12	**0.005**[a]
Facial Height				
- N–Me	2.61	−1.38 – 6.59	76, 0.01	
- Upper anterior facial height	−0.12	−1.44 – 1.19	19, 0.11	0.852
- Lower anterior facial height	2.23	−2.10 – 6.57	90, 0	0.313
- Posterior facial height	1.16	0.07–2.25	0, 0.83	**0.038**[a]
- Gonial angles	2.32	0.79–5.43	81, 0.001	0.143
- Upper gonial angles	4.70	−0.10 – 9.50	91, 0	0.055
- Lower gonial angles	2.37	−0.59 – 5.33	66, 0.04	0.116
- Facial axes	−1.25	−2.66 – 0.17	0, 0.82	0.084
- Facial taper	0.46	−5.12 – 6.05	92; 0.001	0.870
- SNA	0.09	−1.21 – 1.38	71, 0.001	0.896
- SNB	−1.09	−2.13–−0.04	57, 0.021	**0.041**[a]
- ANB	1.17	0.55–1.80	52, 0.05	**0**[a]
- ANS-PNS	−1.62	−2.66–−0.58	0, 0.58	**0.002**[a]
- Mandibular plane	0.05	−2.72 – 2.83	69, 0.02	0.97
- Sn-Go-Gn	2.01	−0.02 – 4.03	70, 0.005	0.052
- Sn-Go-Me	2.44	−2.00 – 6.89	68, 0.07	0.28
- Mandibular arc	−0.04	−1.84 – 1.75	27, 0.262	0.962

Footnotes.
[a] $P < 0.05$ – statistically significant.

The assessment of the pharyngeal airway via lateral cephalometry is a long tried and tested method.[33,49,53,54] Various cephalometric analyses have been described for tracing the pharyngeal airway on a lateral cephalogram.[14,55–57] Of these, the most commonly used is the McNamara analysis (1984), which was employed in 5 studies in this meta-analysis.[14,16,17,21,25] Two parameters evaluated the upper and lower pharyngeal airways. Linder Aronson's analysis (1973) of the nasopharynx and the adenoids uses a triangle based on three anatomic points, pterygomaxillary, hormion, and basion, to describe the bony nasopharynx. A total of 6 measurements are used within the triangle. In this meta-analysis, 6 studies had used the Linder Aronson analysis for airway assessment.[21,23,25,29,30,33]

Older studies have used Linder Aronson's analysis which is accurate, but involves multiple measurements which could be tedious. At present, McNamara's analysis is more widely used for airway assessment. The Linder-Aronson analysis[55] (AD-1, AD, AD-2) and the McNamara's analysis[14] were both found to be significant with a moderate degree of heterogeneity. Although various airway analyses exist, their reliability is an important factor to consider during diagnosis. Therefore, these two analyses could be reliably used in pediatric OSA assessment.

On an overall note, the parameters found to be of significance in Pediatric OSA with lower heterogeneity were McNamara's and Linder-Aronson's analysis, the hyoid bone position, a retrognathic mandible, and an acute cranial base angle. However, a random effects model was used instead of a fixed model due to the significant amount of heterogeneity amongst the studies. The interpretation of these results cannot be applied to individual patients in cases of significant heterogeneity as these are results based on the weighted mean difference.

Possible reasons attributed to the high degree of heterogeneity with various parameters are the lack of a suitable sample size, homogenous study designs, samples not representative of the population, etc. These factors need to be controlled in order to provide a systematic review with greater accuracy. Most of the studies reported in the current review were observational studies. There is a need for more clinical trials to be conducted in the diagnostic arena of pediatric OSA. Other factors influencing the parameters could be the lack of standardization of natural head position[53,58–60] as well as the tracing techniques employed. Manual tracing could be associated with greater error in comparison to digital tracing.[61,62]

The limitations of the present study are that publications in only English language were searched for, grey literature was not included, and that although various databases were included, a few more could have been included.

Future developments in the arena of cephalometric radiography include the application of artificial intelligence (AI) in the automated positioning of landmarks on cephalometric radiographs with a high degree of accuracy. AI is now a promising tool that enables the identification of cephalometric landmarks in daily clinical practice which may facilitate diagnosis and treatment planning for clinicians with easier radiological examination in orthodontics. However, legalities concerning the application of AI in the diagnosis and monitoring of orthodontic treatment will have to be formulated and endorsed.

5. Conclusion

From the current review, it cannot be concluded that craniofacial morphology has a significant association with pediatric OSA. Although there are certain parameters identified which have been of significance, an overall assumption that craniofacial parameters as measured via lateral cephalometry will provide a reliable diagnosis for sleep-disordered breathing cannot be made. There is a need for further research in this field in order to justify the same. The recommendations of the present study are to conduct more clinical trials using cephalometric parameters, which could preferably correlate with polysomnographic findings in order to discover more predictive and reliable parameters. The future development of OSA diagnosis using cephalometric radiography could eventually comprise of a specific set of values which could enable the clinician to potentially identify children with OSA at a much earlier stage.

Data availability

Data are available upon request.

Patient's/guardian's consent

Not applicable as the present study is a systematic review and meta-analysis

Ethical clearance

Not applicable as the present study is a systematic review and meta-analysis

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None declared.

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