Original Article

Systematic Review of Craniofacial Phenotyping in Pediatric Obstructive Sleep Apnea: An Approach to Standardization of Methods

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Sleep Sci

Abstract

Craniofacial phenotyping methods are pivotal in understanding and diagnosing pediatric obstructive sleep apnea (OSA). However, the lack of standardized methods often leads to inconsistencies, hindering the reliability and validity of quantitative analyses in this field. This systematic review aims to evaluate existing craniofacial phenotyping methodologies and their key parameters to propose standardization measures to enhance the reliability and validity of future quantitative analyses on this topic. A comprehensive search of electronic databases was conducted following PRISMA guidelines, resulting in the inclusion of 13 studies. Data extraction focused on the types of phenotyping methods and the parameters or measurements used. Our findings revealed a variation in the phenotyping techniques and a wide array of parameters used across studies, highlighting the need for standardization. The authors proposed a framework of parameters for future evaluation of craniofacial morphologies of pediatric OSA. By standardizing the assessment of these craniofacial morphologies, future research efforts can ensure consistency, facilitating more reliable and valid quantitative analyses in this critical area of study.

Keywords
- craniofacial phenotype
- pediatric
- obstructive sleep apnea
- phenotyping methods

Introduction

Obstructive sleep apnea (OSA) is characterized by recurrent episodes of partial or complete upper airway obstruction during sleep leading to episodes of hypopnea and/or apnea and sleep disruption. In pediatric patients, these lead to daytime symptoms such as hypersomnolence, mood changes, enuresis, hyperactivity, trouble focusing, and poor performance in school. This represents a significant health concern in the growing patients as it may negatively impact neurocognitive development, cardiovascular health, and overall quality of life later in adulthood.[1,2] The cause of OSA in pediatric patients is commonly associated with abnormalities in the anatomical form of the upper airway.[3,4] Several craniofacial features of the developing patients were found to play a crucial role in the pathophysiology of pediatric OSA.[5–7] Identifying these factors would give some guidance to frontline clinicians, such as family

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physicians, dentists, and other healthcare practitioners, to detect and screen for OSA risks. This allows for an early interceptive intervention before using more complex or invasive diagnostic approaches, like polysomnography (PSG) or drug-induced sleep endoscopy (DISE).

One of the main objectives of phenotyping is to minimize and manage the heterogeneity of presenting symptoms, etiopathophysiology, diagnostic variations, and treatment outcomes in pediatric OSA associated with craniofacial phenotypes. Classifying the disorder into a systematic characterization of craniofacial morphology will provide a more homogenous phenotype.[8,9] This phenotyping has emerged as a valuable tool in pediatric OSA research and clinical practice which can provide insights into the underlying mechanisms of airway obstruction and facilitate risk stratification, diagnosis, and treatment planning. Given the crucial role of dental surgeons and orthodontists in addressing the craniofacial phenotype associated with pediatric OSA, it is imperative for medical professionals across disciplines to adeptly identify patients who stand to benefit from early interceptive dental treatments through comprehensive craniofacial phenotyping.[10–13]

Current methods in identifying craniofacial phenotypes for pediatric OSA encompass a range of approaches aimed at characterizing anatomical features of the hard and soft tissues in terms of size, shape, and position, that may contribute to airway obstruction during sleep. These features involve graded and structured clinical assessment of the facial structures, such as Mallampati score and the Friedman tongue position, Brodsky grading and nasofiberendoscopy (NFE) scoring of the adenotonsils,[14–18] the dentofacial relationship and morphology,[19–21] as well as the adipose tissue under the chin. Other important craniofacial assessment includes a comprehensive dental and occlusal assessment with classification of dental occlusion, arch width, and palatal vault. Recent studies found that malocclusion with restricted maxilla, retruded mandible, and distal molar occlusion were predictive factors of OSA in children.[22,23]

Several imaging techniques were also employed in craniofacial phenotyping to accurately assess craniofacial morphology and its relationship to OSA risk. Lateral cephalometric analysis evaluates the cranial base angle, mandibular plane angle, and pharyngeal airway dimensions through several landmarks in the cephalogram.[24–27] Current technology of imaging such as cone-beam computed tomography and surface-based 3D imaging (photometry /3D photographic analysis) can provide detailed representation of the craniofacial morphology allowing precise quantification of landmarks and volumes that may predispose to OSA.[17,28–30]

Despite the wealth of available methods, there exists a notable lack of standardization of methods across studies, in particular, the research methodology, and the data collection such as appropriate cephalometric measurements leading to variability and inconsistency in phenotypic assessment.[5,7,31] The importance of standardization in these assessment methods for craniofacial phenotyping in pediatric OSA cannot be overstated. Standardization refers to the establishment of uniform protocols, criteria, and measurement techniques to ensure consistency, reproducibility, and comparability of results across studies and clinical settings.[32] Multiple benefits can be achieved in standardizing the assessment of craniofacial phenotyping methods in pediatric OSA.[8,9,33] Of paramount advantage is the ability of these phenotyping methods to increase the statistical power, as well as reduce the risk of measurement error and bias, thereby facilitating comparison across studies. These attempts lay the groundwork to establish craniofacial phenotypes in OSA while advancing precision medicine in pediatric OSA. A one-treatment-fits-all approach of CPAP in the management of OSA should not be the standard approach in pediatric OSA.

Considering the benefits, the standardization of phenotyping methods for craniofacial assessment in pediatric OSA represents a critical imperative for advancing research, clinical practice, and patient care in this field. This systematic review aims to 1) explore the current landscape of phenotyping methods, 2) identify existing gaps and challenges in standardization efforts, and 3) provide recommendations for future research and clinical practice to promote uniformity and consistency in craniofacial phenotyping approaches for pediatric OSA.

Methods

This systematic review protocol on the methods of craniofacial phenotyping in pediatric OSA was developed following PRISMA reporting guidelines.[34]

Search Strategy and Eligibility Criteria

A comprehensive search strategy using multiple databases was employed to find relevant studies up to the year 2023. A consultation with a specialized health-sciences librarian was done to ensure resources were suitable. Electronic searches using a series of keywords and keyword combinations based on the knowledge of the subject-area controlled vocabulary, free-text terms, and use of Medical Subject Headings were done. Reference lists in the selected articles were also reviewed during the article screening process. The databases searched include MEDLINE via PubMed, the Cochrane Central Register of Controlled Trials, BMJ Online Journals, ScienceDirect, and Scopus. The search syntax consisted of three concepts: obstructive sleep apnea (OSA), pediatric population, and craniofacial phenotype. The MeSH term used for OSA included “sleep apnea, obstructive,” “obstructive sleep apnea” and “obstructive sleep apnea syndrome”; for the pediatric population included “child” and “adolescent” and for craniofacial phenotype included “craniofacial abnormalities” and “facial bones.” These concepts were used during the search by adding the Boolean operator AND. ►**Table 1** shows the search strategy with the MeSH and terms used.

The inclusion and exclusion of articles were guided by the PICO question: “In nonsyndromic pediatric patients diagnosed with obstructive sleep apnea, how are the craniofacial and dental phenotypes being assessed?” The articles focused on (P) nonsyndromic pediatric patients below the age of 18, (I) who were diagnosed with obstructive sleep apnea, with their craniofacial phenotypes identified, and (C) compared

Table 1 Concepts, MeSH terms and Keywords used for search strategy

Concept	MeSH Term	Keywords
Obstructive sleep apnea	"Sleep Apnea, Obstructive" [MeSH] "Obstructive Sleep Apneas" [MeSH] "Obstructive Sleep Apnea Syndrome" [MeSH]	"Obstructive Sleep Apnea"[tiab] OSA[tiab] OSAHS[tiab] "Syndrome, Sleep Apnea, Obstructive"[tiab] "Sleep Apnea Syndrome, Obstructive"[tiab] "Apnea, Obstructive Sleep"[tiab] "Sleep Apnea Hypopnea Syndrome"[tiab] "Syndrome, Obstructive Sleep Apnea"[tiab] "Upper Airway Resistance Sleep Apnea Syndrome"[tiab] "Syndrome, Upper Airway Resistance, Sleep Apnea"[tiab]
Pediatric population	"Child"[MeSH] "Adolescent"[Mesh]	Adolescen*[tiab] Teen*[tiab] Teenage*[tiab] Youth*[tiab] "Adolescent*, Female"[tiab] "Female Adolescent*"[tiab] "Adolescent*, Male"[tiab] "Male Adolescent*"[tiab] Preschool[tiab] Child*[tiab]
Craniofacial phenotype	"craniofacial abnormalities" [MeSH] "Facial bones" [MeSH]	"Craniofacial morpholog*"[tiab] "Craniofacial featur*"[tiab] Dentofacial[tiab] "Facial skeletal"[tiab] "Maxillomandibular"[tiab] "Jaw*"[tiab]

with the non-obstructive sleep apnea pediatric patients as control, evaluating the (O) variations in the method of assessment of the craniofacial and dental features through clinical and imaging (►**Table 2**).

Study Selection

The review process for the searched articles involved two phases and two reviewers (I.N.I and N.D.I). Initially, the articles underwent evaluation based on their titles and abstracts. Subsequently, those selected proceeded to a thorough examination of their full texts. Following these stages, further citations were identified by analyzing the reference lists of all previously chosen articles. The articles identified went through a similar review process for the selection. Lastly, the eligibility criteria, which encompassed the specified PICO strategy and study types, were meticulously applied during the analysis of articles.

Table 2 PICO Strategy for eligibility criteria

PICO	Description
Population	Non-syndromic pediatric patients, below 18 years
Intervention/Exposure	Diagnosed with OSA
Comparison	Non OSA as control
Outcome	Method of assessment of craniofacial and dental assessment

Data Extraction and Outcome Synthesis

Data extraction was conducted meticulously to assess various types of phenotyping methods employed across studies which was represented in a table together with other important details such as the author, year of publication, and demographic features, as well as their main results (►**Table 3**). To ensure consistency and comparability across studies, rigorous standardization measures were implemented during data extraction, encompassing predefined criteria for inclusion, data abstraction protocols, and quality assessment tools. This extraction was performed by 2 reviewers (I.N.I and N.D. I). The outcome synthesis involved a comprehensive analysis of the extracted data, synthesizing findings across studies to elucidate trends, patterns, and discrepancies in phenotyping methodologies and their respective outcomes.

Results

Study Selection

Following the electronic search across databases and adhering to PRISMA guidelines, the study selection process generated a total of 462 articles from the year 2004 to 2023. After removing duplicates, 431 articles were subjected to title and abstract screening, leading to the exclusion of 339 studies deemed irrelevant for data evaluation. Next, a total of 92 articles were sought for retrieval from the database for full-text reading. However, 77 articles were not retrieved due to unavailable access to full text. The remaining 31 articles underwent full-text review, of which 13 met the predefined

Table 3 Study Characteristics

Authors, Year, Type of Study	Age in Range or (Mean ± SD)	Body mass index (BMI)	Ethnicity	Control group	Criteria adopted to define or diagnose OSA	Methods used to assess craniofacial features
Manrikyan, 2023, CS (35)	Mean 15.8 (1.08)	22.49 ± 4.25 (5 cases BMI >30)	Indo-European and Armenian	Nil	PSG (AHI ≥ 5)	Lateral cephalometry Adenotonsillar assessment Nasal septum Oral breathing
Xu, 2023, CC (38)	5–7 years and 8–10 years	BMI z-score 0.29 ± 1.03 and 0.92 ± 0.20 (OSA vs control)	Chinese	Low risk of PSQ and underwent lateral cephalogram	Pediatric Sleep Questionnaire (PSQ) >8 PSG (AHI >1)	Lateral cephalometry
Wang, 2023, CC (39)	5–12 years	BMI z score (0.88 OSA group*) significant	Chinese	No snoring and OAHI ≤ 1/h	PSG (AHI >1) OSA-18 questionnaire	Friedman tongue position Brodsky tonsil grading NFE adenoid grading Craniofacial photogrammetry
Bozzini, 2022, CS (36)	4–9 years	BMI z-score categorization	Brazilians	Mild OSA	Level 2 PSG (AHI >1) SDSC Questionnaire	Nasopharynx obstruction Tonsil enlargement (Brodsky's grades 2, 3, 4) Orthodontic assessment Lateral cephalometry
Emsaeili, 2022, CC (40)	8–12 years (9.25 ± 1.08)	NR	Iranian	Healthy subject	Berlin questionnaire	CBCT Assessment
Lumbau, 2021, CS (37)	3–8 years	NR	Italian	PSG revealed no OSAS	Clinical sleep record PSG	Dental assessment
Marino, 2021, OS (44)	5.2 - 6.1 years (5.8 ± 0.2)	NR	Caucasian	Nil	PSG with AHI >1	Dental impressions for dental assessments
Murakami, 2021, CC (41)	(10 ± 2.1)	BMI 17.4 ± 2.6	Japanese	ANB >4 (mandibular retrusion vs normal) Basal arch <65 (narrow vs normal)	Out-of-center sleep testing REI >1 and 3% ODI	Lateral cephalograms Dental models
Hsu, 2021, CC (17)	4–16 years (7.9 ± 2.8)	18.4 ± 4.4	Taiwanese	No OSA with AHI ≤ 1	PSG with AHI >5	CBCT Parameters
Lee, 2020, CC (28)	(5.14 ± 0.79)	15.38 ± 2.24	Taiwanese	Normal (AHI <1)	PSG (Mild OSA = <5 (AHI) >1)	Digital measurements of scanned model Lateral cephalometry

Table 3 (*Continued*)

Authors, Year, Type of Study	Age in Range or (Mean ± SD)	Body mass index (BMI)	Ethnicity	Control group	Criteria adopted to define or diagnose OSA	Methods used to assess craniofacial features
Ahmad, 2020, CC (42)	10–19 years	NR	Indians	Non OSA risk (STOP BANG≤2)	STOP-BANG 3–8	Extra and intra-oral examination Lateral cephalometry
Inoshita, 2018, RS (18)	3–15 years	BMI and BMI z-score	Japanese	Gender comparison	PSG with AHI > 1	Tonsillar size Lateral neck radiographs
Smith, 2016, CC (43)	2–12 years (4.7 ± 2.1)	BMI z score (0.45 ± 1.7 vs 0.37 ± 0.7)	Mixed ethnicities (White, Black, Hispanic, Asian, Mixed)	Healthy subjects, non-snoring	PSQ PSG (AHI > 1)	Dental casts

Abbreviations: CC, case control; CS, cross sectional; NR, not recorded; OS, observational study.
Other abbreviations, refer to list of abbreviations.

eligibility criteria and were incorporated into the systematic review (►**Fig. 1**).

Study Characteristics

►**Table 3** reported the characteristics of the included studies, with details of the author, year of publication, and the type of study; the demographic features including age, body mass index, and ethnicity; control group description, criteria adopted to define OSA, and methods used to assess the craniofacial features, and the upper airway were systematically represented.

Among the 13 included studies, 3 presented a cross-sectional design,[35–37] 8 were case-control studies,[17,28,38–43] and one was an observational study.[44] There was a variability in the age range of patients in the studies, ranging from 2 to 19 years old. 5 articles used BMI z scores to classify the different degrees of weight status.[18,36,38,39,43] Each of the articles has almost similar comparison groups where children with no OSA (AHI≤1) were used as control. The criteria for the diagnosis of OSA used include overnight polysomnography as well as multiple other types of questionnaires. The craniofacial and airway assessment includes otolaryngological examination, extra-oral and dental assessment, clinical photos, lateral cephalograms, and CBCT.

Craniofacial Phenotyping Methods

►**Table 4** describes the clinical assessments done to assess the airway and the skeletal and dental features that would contribute to OSA. Four studies assessed the airway patency through adenotonsillar assessment using various scoring and grading scales, e.g., Brodsky tonsil grading and nasofiberendoscopy (NFE) adenoid grading.[18,35,36,39] Most articles that investigated the adenotonsills had positive significance in the OSA group. The nasal and nasopharynx features were also recorded but none had any positive findings that would contribute to OSA in children.[35,36] Tongue position was assessed in one article but did not show any significance in the pediatric OSA group.[39]

Skeletal and dental assessment was mainly assessed by dentists and orthodontists. Seven articles investigated the orthodontic aspects of the OSA in children.[28,36,37,41–44] The extraoral skeletal examination involved the clinical assessment from the frontal and profile, which includes anterior facial height, facial convexity on profile, and the mandibular plane angle. Cumulatively, a convex profile with a steep mandibular plane angle showed significance in the OSA group. Four studies used the dental models for the accurate assessment of the dentition, measuring the horizontal distances between teeth across the arch.[28,41,43,44] It was found that a reduced intermaxillary distance showed positive significance toward pediatric OSA in four studies.

►**Table 5** summarizes the imaging techniques used, the hardware and software involved, the landmarks used for the assessment, and the significant positive findings that showed statistical significance when comparing OSA children with the control group.

Seven studies evaluated craniofacial and airway features through lateral cephalometry with similar measuring

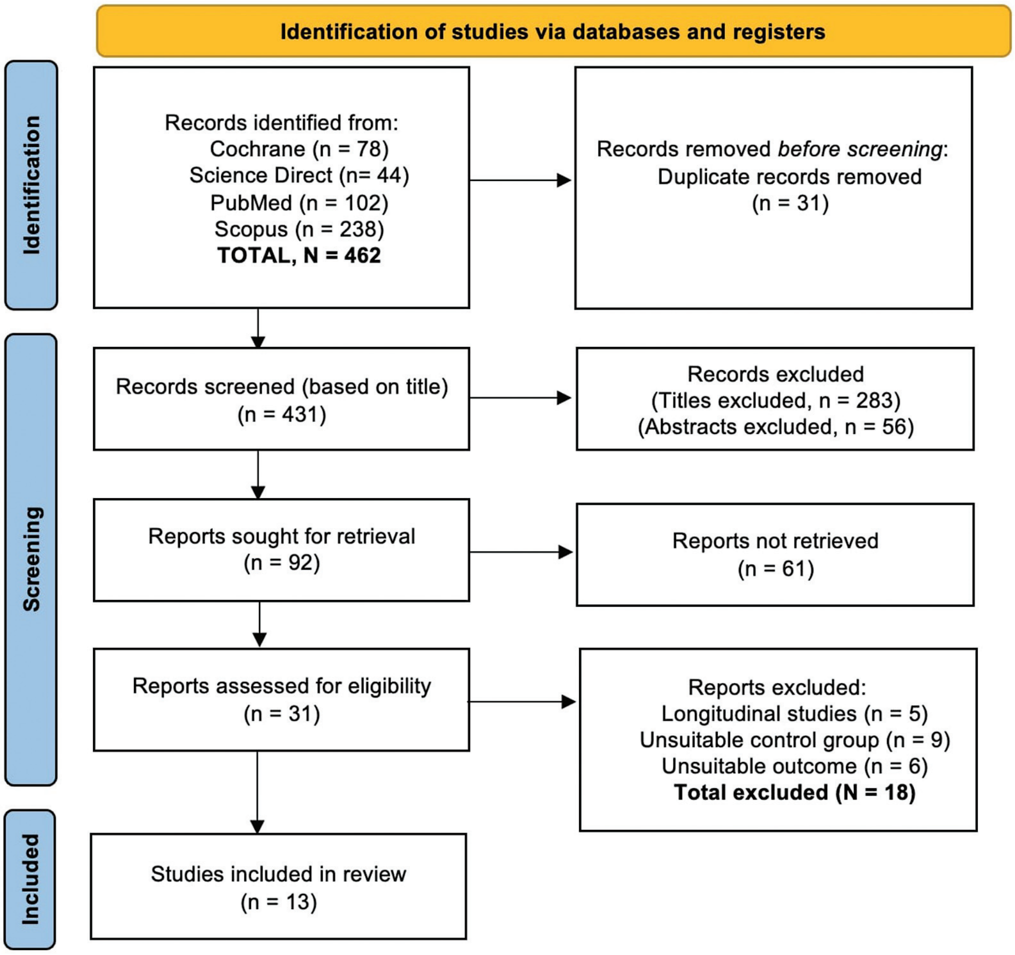

Fig. 1 Flowchart of study selection according to PRISMA guidelines.

instruments (Maxilla and mandible position about the anterior cranial base: SNA, SNB, ANB, BaSN, ArGo, SnMP, MMPA; Facial height; Airway dimension: PAS, NP space, OP space, linear distance between hyoid and spine, and tongue and pharynx).[18,28,35,36,38,41,42] Craniofacial features that yielded significant findings in pediatric obstructive sleep apnea include the retrusive mandible, the high maxillomandibular plane angle, the adenoid size, and the posterior airway space. One study assessed the craniofacial features through photogrammetry and looked at the facial heights, convexity, and maxillomandibular angle.[39] This method produced similar positive findings to pediatric OSA. Two studies assessed the craniofacial features using CBCT with similar landmarks for assessing the airway space and volume.[17,40]

Discussion

Obstructive sleep apnea (OSA) is a multifactorial disorder influenced by a complex interplay of genetic, anatomical, and physiological factors. Understanding the craniofacial phenotype is crucial for identifying individuals at higher risk, as specific anatomical features can significantly contribute to the development and severity of OSA. Accurate detection of these phenotypic characteristics enhances early diagnosis and personalized treatment strategies. The key findings from this qualitative examination of 13 articles highlighted the diversity in methodologies and variables employed in appraising craniofacial attributes among pediatric patients with obstructive sleep apnea. While both clinical examination and imaging techniques for evaluating craniofacial features exhibit similarities, the specific criteria and landmarks utilized vary significantly across methodologies. Despite these methodological differences, certain variables demonstrate consistent significance in pediatric OSA. Notably, these craniofacial characteristics encompass a convex facial profile associated with a downward rotation of the maxillomandibular complex, resulting in mandibular retrusion and an elevated maxillomandibular plane angle.[41,42] These skeletal morphological features contributed to the constriction in the pharyngeal space, evident through diminished horizontal distances between the base of the tongue to the posterior pharynx, and the hyoid bone to the cervical vertebra. Furthermore, dental characteristics predisposing children to OSA include a narrow maxillary arch, with or without crossbite.[37,41,43,44] The validity of these findings has been reinforced by several systematic reviews and meta-analyses, as documented by Fagundes[5] and Brockman.[45]

The importance of standardizing methodologies to identify and screen for risks of pediatric obstructive sleep apnea (OSA) through craniofacial phenotyping cannot be

Table 4 Clinical assessment of the airway, skeletal and dental

Authors (Year)	Airway Assessment	Skeletal and Dental Assessment	Positive findings
Manrikyan et al. (2023) (35)	Adenotonsillar assessment Nasal septum Oral breathing	NI	Tonsillar hypertrophy (14.6%) Adenoid hypertrophy (51.2%) Adenotonsillar hypertrophy (7.3%) Bruxism (22%) Oral breathing (34.1%)
Wang et al. (2023) (39)	Friedman tongue position Brodsky tonsil grading NFE adenoid grading	NI	NFE adenoid grading (0% in grade 1 and 39.6% in grade 4 for OSA group) Tonsil hypertrophy (64.2%) in OSA group
Bozzini et al. (2022) (36)	Nasopharynx obstruction Tonsil enlargement (Brodsky's grades 2, 3, 4)	Orthodontic assessment: Facial profile Lip seal Overjet Distoocclusion (Angle Class II) Crossbites	No significance
Lumbau (2021) (37)	NI	Dental assessment: Angles classification Molar relationship Open bite Crossbite Overjet Narrow palate	Crossbite Narrow palate
Marino (2021) (44)	NI	Dental models: Inter-canine and Inter-molar, Arch length on upper and lower arches.	Reduced upper inter-canine and inter-molar distance
Murakami (2021) (41)	NI	Dental models: Based on Enoki and Motohashi measuring points (cite Enoki 1974)	Mandibular retrusion (ANB <4) Reduced transverse maxillary dimensions
Lee et al (2020) (28)	NI	Digital measurements of scanned model (3shape Dental System D640, 3shapre A/S, Copenhagen, Denmark) Molar relation, Inter-canine width, Intermolar width, Upper arch length, Lower arch length, Palatal height	No significance
Ahmad (2020) (42)	NI	Facial profile Facial height Mandibular plane Faucial pillars and soft palate Shape of upper and lower arch Molar classification	Convex profile Steep mandibular plane Type 3 and 4 faucial pillars Class II molar relationship Ovoid upper arch form
Inoshita (2018) (18)	Tonsillar size	NI	Nil significance
Smith (2016) (43)	NI	Dental measurements: Inter-tooth distance at D, E and 6 Palate height	Reduced inter-tooth distances for D, E, 6

Abbreviations: 6, first permanent molar; D, first primary molar; E, second primary molar; NI, not indicated.
Other abbreviations, refer to list of abbreviations.

overstated. While numerous studies have delineated craniofacial phenotypes associated with pediatric OSA, recent meta-analyses[5,24] have failed to detect significant differences in six skeletal features between OSA and non-OSA patients in lateral cephalometry, including SNA, SNB, ANB, BaSN, U1-L1, and U1-SN. This could be attributed to the fact that these 2-dimensional images represent a single static snapshot of the dynamic upper airway structure and did not

Table 5 Imaging techniques

Imaging techniques	Author	Hardware and software	Landmarks	Positive findings
Lateral cephalometry	Manrikyan et al. (2023) (35)	Planmeca ProMax Type 3D+ (Planmeca) set at 12mA, 90 kV, and exposure time of 0.30 minute at natural head position Romexis viewer 5.4.1 with manual tracing	Angles: SNA, SNB, ANB, BaSN, ArGoGn, MxPl/MdPl Linear: Hyoid and C3 (horizontal distance) Mandibular plane and hyoid (vertical distance) Vertical position of tongue, U1NA, L1NB, OJ, OB, Posterior airway space (PAS)1, PAS2, PAS3, PASmin	SNB 79.4 ± 3.1 (distal position of mandible relative to anterior cranial base) ANB 4.3 ± 1.9 ArGoGn 130.47 ± 8.99 AH-C3H 32.69 ± 5.8
	Xu et al (2023) (38)	ORTHOPHOS XG 3D Ceph, Sirona Dental Systems GmbH Digital cephalometric analysis	Skeletal variables: SNA, **SNB**, ANB, SN, S-Ar, **Ar-Go**, Go-Me, NSAr, SArGo, NMeGo, SumAngles Upper airwar, adenoid and hyoid: **NP space**, **OP space**, A-B **Absolute value of adenoid**, **Linear dimension of bony nasopharynx**, **Ratio A-N (relative adenoid size)**, Distance hypoid-RGn, H-FP	SNB, Ar-Go (ramus height) NP, OP, A(absolute value of adenoid), N (linear dimension of bony nasopharynx), Relative adenoid size
	Bozzini et al (2022) (36)	Orthophos XG 5 DS Ceph, Sirona, Brazil regulated to 12mA, 90kV and 0.30 second of time exposure at natural head position Easy Ceph (Anne Solutions ®Brazil)	Rickets's cephalometric analysis: Facial axis Facial depth Mandibular plane angle Lower facial height Mandibular arch Jarabak's analysis: Posterior and anterior facial height	Facial depth angle on Ricketts (87 ± 2.8 vs 84.1 ± 4.6)
	Murakamai et al (2021) (41)	Not mentioned	Lateral cephalograms SNA, SNB, ANB, FMPA, UIA, LIA Nasopharyngeal and oropharyngeal airway dimension	Mandibular retrusion (ANB <4) Lower pharynx
	Lee et al (2020) (28)	Hardware not mentioned PACS software	Lateral cephalometry: Skeletal: SNA, SNB, ANB, SN-PP, SN-MP, AFH Teeth: OJ, OB Upper Airway: MinRPA, MinRGA Soft palate: SPL, MPT Tongue: TGL, TGH Hyoid bone: MPH	SNB, ANB, Overjet
	Ahmad (2020) (42)	CS 2200-Carestream Health® machine at 30mA, 70 kVp Manual tracing with RK LED X-Ray View	Cephalometric analysis SNA, SNB, ANB, SN-MP, BaSN, PNS-AD1, PNS-AD2	ANB, SN-MP, BaSN, PNS-AD1, PNS-AD2
	Inoshita et al (2018) (18)	NI	Lateral neck radiographs: Airway area, Diameter of adenoids and nasopharynx Ratio of adenoids and nasopharynx (A/N) ANS, PNS, H, Eb, TAA, UNG,	Upper airway area A/N ratio

Table 5 (*Continued*)

Imaging techniques	Author	Hardware and software	Landmarks	Positive findings
Craniofacial photogrammetry	Wang et al (2022) (39)	Smartphone camera to photograph frontal and profile with a scale plate. Image analysis software (Image J version 1.8.0, NIH, Bethesda, Maryland, United States)	Facial landmarks: **Facial heights** and widths **Facial convexity angle,** Eyes and Nose: Inner and outer canthus width **Nose width** Nasal convexity angle Mouth: Lip **width** and height Maxilla and mandible: Maxillary length, mandibular length, Posterior mandibular height, **Maxillomandibular angle**, Mandibular angle	**Upper face width, lower face width, lower facial height, maxillary-mandibular relationship angle** effective and sensitive in predicting OSA in children
CBCT Assessment	Emsaili (2022) (40)	NewTom VGi cone-beam CT unit (Verona/Italy) NNT Viewer software version 2.21	SNA, SNB, ANB, SN-MP, PP-MP, BaSN, PNS-AD1, PNS-AD2	UA width, UA AP dimension, SNB, Shortest distance between PNS-Ad1
	Hsu et al (2021) (17)	i-CT (Imaging Sciences International, LLC, Hatfield, PA) regulated at 120kV, 5mA, 0.25mm voxel size, scanning time of 20 seconds. Dolphin Imaging, Chatsworth, CA	Nasopharyngeal, oropharyngeal volume, Airway length Minimal airway locus – AP and lateral distances Adenoid and tonsil size	Nasopharynx: Volume, Minimal airway area, AP distance, Mean airway area Oropharynx: Volume, Minimal airway area, Lateral distance, airway length, mean airway area

Abbreviations: AP, anteroposterior; NI, not indicated.
Other abbreviations, refer to list of abbreviations.

reflect adequate anatomical contributions that could risk for OSA. For example, the tongue position when standing or lying supine during cephalometric assessment via CBCT or CT may greatly influence the upper airway space.[46] Therefore, a definitive diagnosis of obstructive sleep apnea (OSA) should not be based solely on this single radiographic assessment, as it only suggests potential risks for OSA. Further investigation to show the dynamic function of the upper airway during sleep is indicated to confirm the presence of OSA. Similarly, other associated craniofacial features of pediatric OSA, such as cranial base length,[11] adenotonsillar hypertrophy,[21,47] and lateral pharyngeal wall thickness[9] have not demonstrated a strong association with pediatric OSA. The authors suggest that the inconsistencies in the literature could be due to the varying methodologies used in different studies, making it difficult to conduct reliable qualitative and quantitative analyses.

Given the diversity in methodologies, variables, and instruments used for the assessment of craniofacial morphology, the initial set of craniofacial phenotypes was found to be extremely broad.[7–9,24] Nonetheless, the significant craniofacial morphologies from the skeletal, dental, and pharyngeal assessment ultimately contributed to the narrowing of the pharyngeal space. From here, identifying the key craniofacial parameters or measurements that led to this finding should be standardized across studies. Clinical examination of the facial profile, facial height, and lateral cephalometric analysis which would determine the position of the mandible about the cranial base, the pattern of growth, and the angle of the maxillomandibular complex are important parameters to be assessed.

Introducing a framework for conducting craniofacial assessments in the context of pediatric OSA serves as more than just a mere suggestion; it offers a structured guide essential for researchers navigating the complexities of pediatric OSA and craniofacial phenotyping.[5,7,48] This proposed framework not only outlines standardized parameters but also emphasizes the importance of consistency and uniformity in research practices. By advocating for the adoption of this framework among clinicians and researchers, the authors hoped to ensure a harmonized approach to data collection, analysis, and interpretation across studies. This not only enhances the credibility and reliability of research findings but also facilitates meaningful comparisons and meta-analyses

►**Fig. 2** illustrates the proposed framework of the important parameters that contributed to the craniofacial phenotyping in pediatric OSA that should be evaluated. Key landmarks for these parameters include clinical facial convexity, SNA, SNB, ANB, Ar-Go, Ar-Go-Gn, and MMPA, and therefore need to be included and standardized across studies. Other studies in adult OSA have also confirmed the significance of these parameters.[49–51] In addition to that, adenotonsillar assessment using Brodsky and NFE grading would provide more accurate information regarding the pharyngeal space[52–54] than a Mallampati score or the Friedman tongue position. On the other hand, a crucial characteristic that can often be overlooked is the dental and occlusal status of these children. It was known that a narrow and high-arched palate would contribute to the constriction of the airway at the nasal and nasopharyngeal levels. Hence, measurement of the palate in transverse,

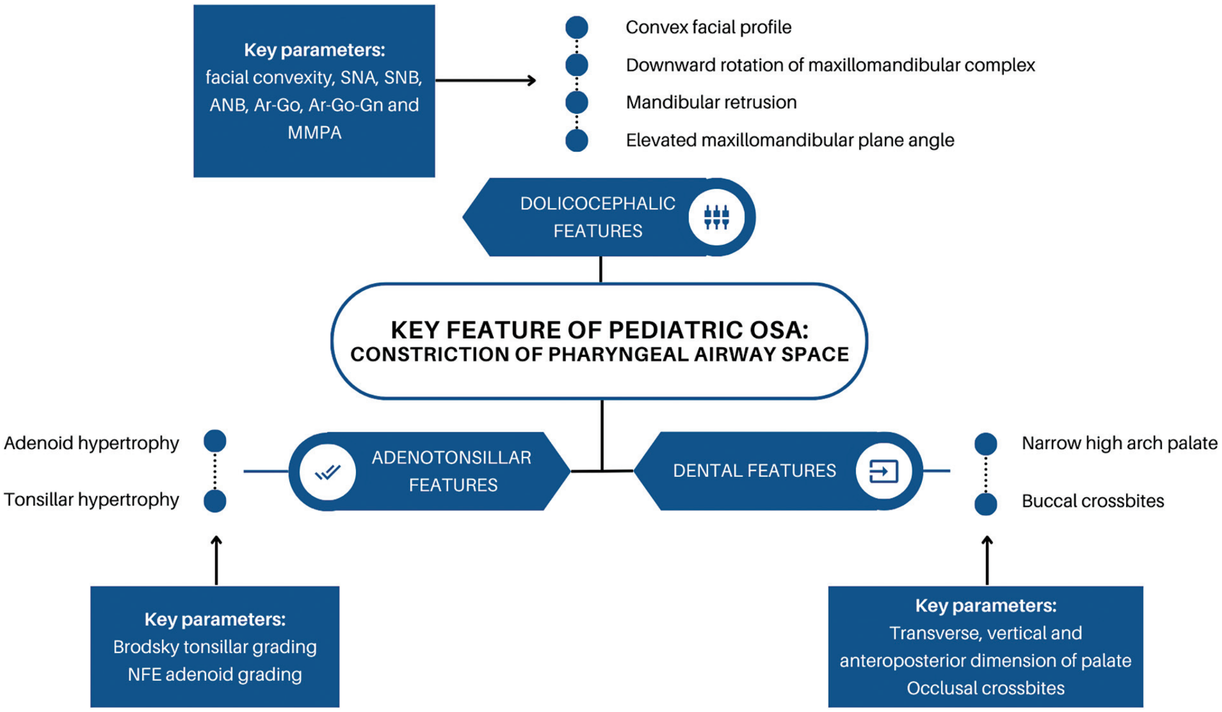

Fig. 2 Proposed framework for parameters to evaluate pediatric obstructive sleep apnea.

vertical, and anteroposterior would benefit the researchers in confirming this component of the craniofacial phenotype for pediatric OSA.

The attempt by the authors to report on the heterogeneity of articles evaluating pediatric OSA will strengthen the need for standardized methodologies to ensure that clinicians in the field can consistently identify and diagnose craniofacial features associated with pediatric OSA while enabling the reproducibility and reliability of results. The present study has systematically gathered and qualitatively reviewed data concerning the methodologies employed to ascertain the craniofacial phenotype of pediatric OSA. The diversity in these methodologies has constrained the ability to establish a uniform approach. Nevertheless, the framework suggested for standardizing evaluated parameters was developed by identifying commonalities among the noteworthy positive findings.

Conclusion

In conclusion, this approach to standardization will facilitate comparison across studies and meta-analyses. Without standardized protocols, variations in methodologies have led to discrepancies in results, making it challenging to draw meaningful conclusions or establish consensus in phenotyping pediatric OSA. Moreover, embracing this framework fosters collaboration and knowledge exchange within the research community, ultimately advancing our understanding of pediatric OSA and improving clinical outcomes for affected individuals.

List of Abbreviations

Abbreviation	Description
NFE	Nasofiberendoscopy
CPAP	Continuous positive airway pressure
BMI	Body mass index
AHI	Apnea/Hypopnea Index
CBCT	Cone-beam computed tomography
REI	Respiratory event index
ODI	Oxygen desaturation index
Lateral cephalometric analysis abbreviations and its description	
SNA	Angle between the sella/nasion plane and the nasion/A-plane
SNB	Angle between the sella/nasion plane and the nasion/B-plane
ANB	Angle between the A-plane and B-plane
BaSN	Angle between the cranial base and the mid-sagittal plane
ArGo	Line between the condyle and the gonial angle of the mandible
Ar-Go-Gn	Angle between the condyle/gonion plane and the gonion/gnathion plane
SNMP	Angle between the sella/nasion plane and the maxillary plane
MMPA	Angle between the maxillary and mandibular plane
PAS	Posterior airway space
NP	Nasopharynx
OP	Oropharynx
U1-L1	Angle between the upper incisor and lower incisor
U1-SN	Angle between the upper incisor and the sella/nasion plane

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Conflict of Interest
The authors report no conflict of interest.

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