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GENETIC AND ENVIRONMENTAL INFLUENCES ON UPPER AIRWAY MORPHOLOGY AND ITS RELATIONSHIP WITH CRANIOFACIAL STRUCTURES

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LIETUVOS SVEIKATOS MOKSLŲ UNIVERSITETAS

Monika Šidlauskienė

GENETIKOS IR APLINKOS ĮTAKA VIRŠUTINIŲ KVĖPAVIMO TAKŲ MORFOLOGIJAI IR JOS SĄSAJA SU KAUKOLĖS IR VEIDO STRUKTŪROMIS

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CONTENTS

ABBREVIATIONS

a^2 – additive genetic factors
ACE – additive genes, common and specific environment
c^2 – common environmental factors
CS – cervical stage
CVM – cervical vertebral maturation
CBCT – cone-beam computed tomography
d^2 – dominant genetic factors
DNA – deoxyribonucleic acid
DZ – dizygotic twin
e^2 – specific environmental factors
GSEM – genetic structural equation modeling
LC – lateral cephalometric (imaging)
LSMU – Lithuanian University of Health Sciences
MARPE – miniscrew-assisted rapid palatal expander
MZ – monozygotic twin
OSA – obstructive sleep apnea
RME – rapid maxillary expansion

PREFACE

„For every theory, there has to be counterevidence –
otherwise, science wouldn't progress. "

Haruki Murakami

Curiosity and a strong desire to overcome obstacles motivate new scientific discoveries. At every stage of my education, I have tried to untangle the most complex problems regarding human health and disease.

As an odontology student, I learned about the connection between body posture, breathing, and dental malocclusion in clinical management and even in casual conversations. While walking around the city of Kaunas, I noticed many children with slouched shoulders and dental disorders who did not seem to comprehend the impact of their posture on their health. This awareness sparked my scientific interest and made me want to study the topic more thoroughly.

My residency enabled me to explore this relationship in greater depth, and the data I collected was startling. Many children have poor posture, altered facial form of the dental arch, and abnormal breathing, which damages their oral health and physiological well-being. Breathing is an effortless activity in which a human engages. However, a person may breathe inadequately as many as six hundred million times, settling into a state of being that can harm their development.

While investigating craniofacial anatomy and airway function, I was struck by the potential for orthodontic treatment to improve breathing health. This led to my research question: What causes respiratory dysfunction, and how can orthodontic treatment facilitate the development of efficient breathing patterns during childhood?

This study strives to extend patient management beyond aesthetic concerns to include oral and general health by combining orthodontics, airway physiology, and posture physiology. It is not merely about treating malocclusion; it is about treating well-being.

INTRODUCTION

Ideal occlusion in orthodontics refers to the optimal alignment and functional contact between teeth, ensuring efficiency, stability, aesthetics, and appropriate oral and airway health [1]. In recent years, the relationship between airway function and craniofacial development has attracted considerable attention, mainly due to the increasing prevalence of respiratory disorders reported in pediatric populations [2–4]. Specific estimates indicate that between 11 % to 56 % of children mostly breathe through their mouths [5–7], while orthodontic intervention is necessary for around 21 % to 27 % of children [8,9].

Malvina Moss' functional matrix theory offers essential explanations relevant to the relationship between soft tissues and bones, suggesting that adjunct soft tissues play a significant role in the development and growth of bones [10,11]. Malocclusions like mandibular retrusion and narrow palates are known to cause obstruction to the airway, thereby affecting oral activities and the entire maxillofacial development. This relationship is complicated and subject to the integration of cranial and skeletal systems. [12–22]. Interestingly, children who are mouth breathers tend to have some particular craniofacial characteristics, such as greater facial angles and dental protrusion, which leads to restricted airway space and impaired oral functions [17,23].

Although earlier investigations sought to understand separately the processes of breathing, maxillofacial development, and the growth of teeth alongside orthodontic treatments, there are no consolidated studies of genetic and environmental factors in a single model for the airway obstruction and malocclusion pathogenesis [12,24,25]. Twin study research has notably assisted in disentangling the craniofacial morphology's genetic and environmental influences [26,27]. The malformation of the airway and occlusion is understood through comparisons of monozygotic twins, who are genetically identical, and dizygotic twins, who share part of their genetics and are subjected to a similar environment [28–31]. Knowing how much malocclusion results from genetic inheritance versus environmental change largely determines treatment and prognosis, which features a genetically changed structure of the jaws that are often less responsive to traditional orthodontic treatment [32–35]. Even with progressive knowledge, there is still an insufficient understanding of the effectiveness of therapeutic interventions such as palatal expansion or repositioning of the mandible in enhancing respiratory function over time [20,36–40]. In addition, the impacts from the environment, which include changes in diet, the swallowing and non-nutritive chewing behaviors common to infants, and even climate change, all require

additional scrutiny concerning their contributions to postural craniofacial growth and the incidence of malocclusion [7,23,41–46].

There is also a population genetic covariate that will most certainly affect craniofacial configuration and is likely to increase the incidence of orthodontic treatment needs [47–49]. As difficult as this sounds, understanding the interactions between the shape of the airway, the craniofacial elements, and the body's posture is vital for developing orthodontic and orthopedic corrective measures.

This dissertation addresses several parts of this perspective by using twin comparisons, sophisticated postural photography, and cephalometry. It provides a systematic and novel view of the morphology of the airway and its development together with other structures, which is still a significant deficit in the literature on orthodontic subjects.

The aim of the study

The aim of the study was to assess the impact of genetics and environment on the upper airway morphology and related craniofacial structures, with the following assessment of interconnections between the upper airway, occlusion, and body posture.

Objectives of the study

1. To evaluate interactions between nasopharyngeal obstruction, craniofacial characteristics, and body posture.
2. To assess the genetic and environmental impact on cephalometric parameters of the airway morphology and related craniofacial structures.
3. To assess the genetic and environmental influences on maxillary dental arch and palate morphology after completed maxillary growth.
4. To evaluate relationships between upper dental arch morphology, palate dimensions, and upper airway parameters.

Scientific novelty

1. **Multidisciplinary integration of airway obstruction, malocclusion, and body posture**
   This is the first study to examine the interplay between airway obstruction, occlusal pathologies, and body posture in a comprehensive, multidisciplinary approach. Incorporating cephalometric, orthopedic, and otorhinolaryngological assessments adds to our understanding of how environmental influences contribute to skeletal and functional adaptations in growing individuals.

2. **Genetic and environmental determinants of airway morphology**
   This is the first study to analyze genetic and environmental influences on airway morphology's cephalometric parameters using monozygotic (MZ) and dizygotic (DZ) twins. Unlike previous research, this study employs DNA-based zygosity determination with 15 specific DNA markers and the amelogenin gene fragment**,** ensuring highly accurate genetic comparisons**.**
3. **Advancement in zygosity determination**
   Unlike previous studies that relied on indirect methods, this research employs molecular genetic techniques to determine zygosity with 99.9 % accuracy. This methodological advancement ensures more precise differentiation between genetic and environmental factors influencing craniofacial and airway morphology.
4. **Refined genetic modeling for airway and craniofacial traits**
   Traditional twin studies primarily relied on classical correlation approaches to estimate heritability, often neglecting shared environmental influences. This study introduces an improved structural equation modeling (GSEM) framework, allowing for a more detailed partitioning of additive genetic effects, non-additive genetic effects, common environmental factors, and unique environmental influences on airway morphology and craniofacial structures.
5. **Post-growth analysis for enhanced genetic insights**
   Previous twin studies primarily focused on growing individuals, limiting the ability to distinguish genetic predispositions from ongoing craniofacial development. By selecting post-growth subjects, this study ensures that genetic determinants of maxillary and mandibular morphology are assessed without confounding effects from active growth processes.
6. **Comprehensive assessment of palatal morphology**
   Unlike earlier research focused on linear palatal measurements, this study pioneers by including three-dimensional parameters such as palatal surface area and volume. Integrating advanced morphometric techniques offers a more detailed understanding of how genetic and environmental factors shape palatal development.
7. **Investigation of upper airway-palatal interactions**
   No previous twin studies have explored the correlation between upper airway morphology and palatal dimensions. This study bridges this knowledge gap by elucidating how genetic and environmental factors simultaneously influence palatal width, height, and airway volume, providing novel insights into these structural interactions.

1. LITERATURE REVIEW

1.1. Relationship between upper airway morphology and malocclusion

The interplay between respiratory function and craniofacial development has been extensively studied, particularly regarding the impact of mouth breathing on skeletal growth patterns [4] (Table 1.1.1), (Fig. 1.1.1). Moss' functional matrix theory further supports this relationship, emphasizing that soft tissue function directly influences skeletal development [11].

Chronic mouth breathing is commonly associated with structural abnormalities, such as adenoid and tonsil hypertrophy, maxillary or mandibular retrognathism, inferior mandibular rotation, open bite, hyperdivergent growth patterns, proclined upper incisors, increased lower facial height and gonial angles, all of which contribute to airway narrowing and increase the risk of obstructive sleep apnea (OSA) [13,16,41,50,51]. Specifically, individuals with Class II skeletal patterns tend to exhibit reduced upper airway dimensions, with studies demonstrating that Class II malocclusion patients frequently have a narrower upper pharyngeal width, predisposing them to airway obstruction [52]. While some studies suggest that Class III patients have shorter nasopharyngeal airways due to maxillary retrusion [14], others found no significant airway differences across skeletal patterns [53]. These discrepancies highlight the complexity of airway morphology and the need for further longitudinal studies. Similarly, some authors argue that no significant correlation exists between sagittal jaw relationships and upper airway volume [54].

Table 1.1.1. *Craniofacial skeletal and soft tissue components related to airway function*

Skeletal structures	**Associated soft tissue components**
Nasal airway	**Nasal soft tissue**
- Maxilla	- Turbinates
- Pyriform aperture	- Nasal septum
- Hard palate	- Alar valve
Pharyngeal airway	**Oropharyngeal soft tissue**
- Mandible	- Tongue and tongue-tie
- Hyoid bone	- Tongue base
- Epiglottis	- Adenoids
- Maxilla (posterior)	- Tonsils

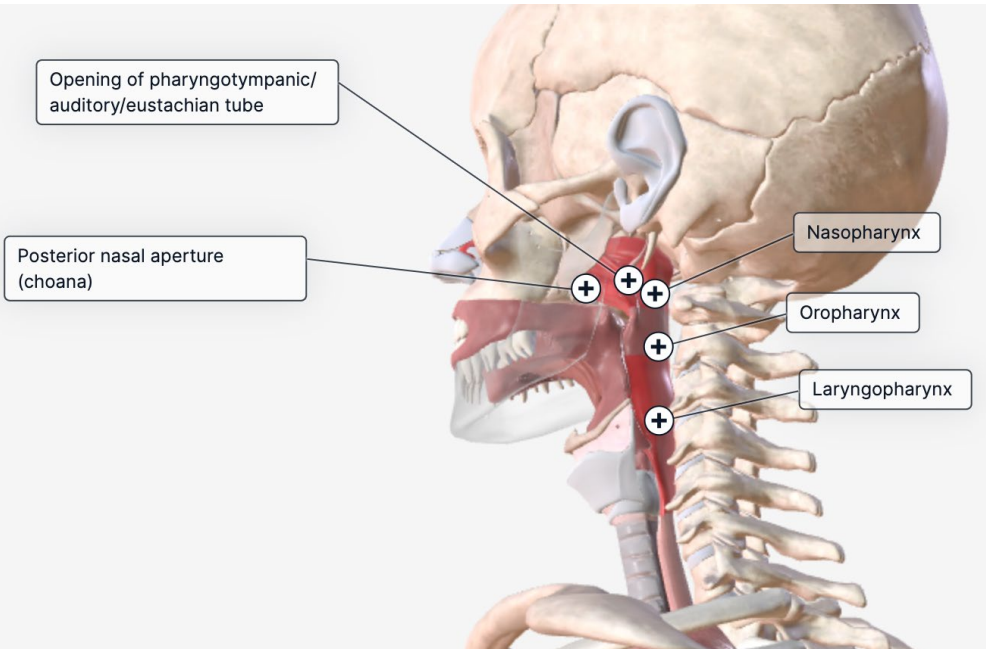

Fig. 1.1.1. *Upper airway anatomy, source: https://www.biodigital.com/*

Airway narrowing is clinically significant due to its association with systemic health concerns, including chronic fatigue, heightened sympathetic nervous system activity, and increased blood pressure [32,55]. Masutomi et al. reported that nasal obstruction leads to prolonged chewing time and reduced masticatory efficiency [23]. Furthermore, mouth breathing has an effect on chewing as well as on the functioning of the orofacial muscles, which leads to skeletal and dental changes [24]. Obesity worsens airway obstruction by adding more tissues to the tongue, uvula, and throat, which greatly reduces airflow [56]. In light of these factors, orthodontic treatment planning cannot be limited to achieving esthetic objectives but must also incorporate functional and systemic health issues. This review of the literature analyzes the intricate relations among the genetic predispositions, the environment, and orthodontic treatment in craniofacial and airway development for the purpose of developing clinical orthodontic practice.

1.2. Relationship between malocclusion, nasopharyngeal pathology and body posture

Craniofacial development, posture, and respiratory function are closely linked**,** influencing each other through neuromuscular and skeletal adaptations [57]. The relationship between dental occlusion and body posture is complex

and bidirectional. A large-scale study in China involving 595,057 students reported that 65.3 % of children exhibited incorrect posture, with a higher prevalence in older children [58]. The study highlights the widespread nature of postural imbalances and their association with malocclusions. Class II malocclusions and retrognathic mandibles are associated with postural adaptations: forward head posture is commonly observed in patients as a compensatory mechanism to maintain airway patency and increased cervical spine lordosis, reinforcing the functional link between stomatognathic structures and postural control mechanisms [22,59,60]. This altered posture can lead to musculoskeletal imbalances, affecting the entire body alignment (Fig. 1.2.1). Several studies suggest that correcting malocclusions can positively influence body posture: orthodontic and orthopedic interventions, including functional appliances, have improved head posture and enhanced postural stability [25,61].

Breathing patterns significantly affect neuromuscular coordination and postural alignment [62–66]. Chronic mouth breathing is associated with open-mouth posture, which leads to anterior head displacement, cervical spine misalignment, and compensatory changes in the thoracic and lumbar regions [67,68]. Orofacial myofunctional therapy helps strengthen and synchronize orofacial muscles, readjust tongue positioning, enhance breath intake through the nose, body and head alignment, and reinforce long-term effectiveness of orthodontic treatment. [57,62].

Early identification of risk factors for malocclusions, posture deviations, and breathing dysfunctions can lead to preventive and therapeutic interventions tailored to individual patient needs.

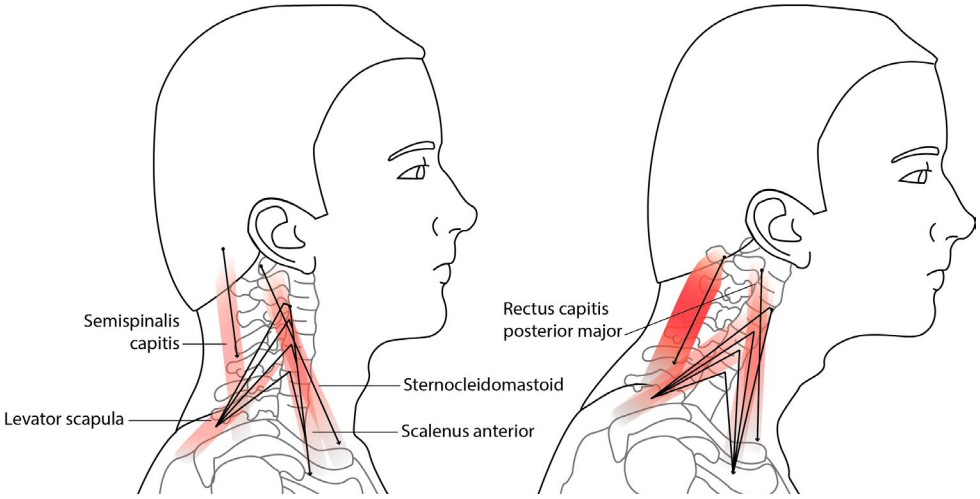

Fig. 1.2.1. *Head posture: correct and habitual*

1.3. Genetic and environmental influences on upper airway morphology

Understanding upper airway morphology, assessing heritability, and identifying craniofacial growth patterns in healthy populations is crucial for detecting individuals at risk of respiratory conditions such as snoring, OSA, and mouth breathing [33,37,43,69,70]. Treatment outcomes in orthodontic and orthopedic interventions largely depend on distinguishing genetically determined malocclusions from those influenced primarily by environmental factors [47]. Malocclusions with a strong genetic component may show limited responsiveness to conventional treatment [26]. Although genetic factors lay the foundational blueprint for craniofacial morphology, environmental factors and their interactions with genetics critically shape these structures [3,26,29,71,72].

Studies demonstrate a strong genetic component underlying airway structure, with variations in craniofacial anatomy such as mandibular size and pharyngeal airway volume significantly influenced by genetic factors [15,43]. Billing et al. [43] conducted a twin study on pharyngeal space variations, examining 19 monozygotic and 23 dizygotic twin pairs. Their findings demonstrated a significant genetic influence on pharyngeal space size, posterior nasopharyngeal wall thickness, and nasopharyngeal airway dimensions. Similarly, Kang et al. [72] analyzed pharyngeal parameters using lateral cephalograms in adult monozygotic and dizygotic twins, reinforcing that airway structures are under substantial genetic control. Jokkel et al. conducted a study using magnetic resonance imaging (MRI) to quantify the impact of heritable and environmental factors on upper airway dimensions in twins [73]. The results demonstrated strong genetic determination in the anteroposterior diameter of the tongue and the thickness of submental fatty tissue. Other parameters of the tongue, soft palate, and uvula showed moderate heritability. At the same time, the thickness of the parapharyngeal fatty tissue, pharyngeal wall, and the minor diameter of the posterior upper airways were primarily influenced by environmental factors [73].

Aspects like lifestyle choices and exposure to pollution have a major impact on the environment, which in turn, affects craniofacial development. For instance, environmental pollutants have been linked to epigenetic modifications influencing craniofacial development, particularly nasal obstruction and altered respiratory function [13,16,23,24,45,51]. These findings underline the complexity of airway morphology, emphasizing the need for further longitudinal research.

1.4. Genetic and environmental influences on palatal development

The size and position of the maxilla are key determinants in the development of malocclusion [74, 75]. Except for Class III malocclusion, which is relatively rare and primarily hereditary, maxillary abnormalities can lead to functional shifts at an early age. A narrow palate, for instance, can contribute to the posterior positioning and underdevelopment of the mandible, resulting in crowding of both upper and lower dentition [75]. Evidence suggests that genetic variables are most significant when defining who has greater palatal dimensions, with deep palates and wide maxillary transverse dimensions noted as some of the most inheritable traits [33,76-79]. Nevertheless, external factors in addition to the robust genetic component still have a profound impact on maxillary evolution. Soft tissue improper functions, like mouth breathing and abnormal tongue position or some parafunctional activities, have been associated with variations of palatal form, which include narrower dental arches along with higher palatal and lower intermolar width dimensions due to tongue displacement and modified orofacial muscular activity [80]. Given the significant impact of orofacial functions – particularly breathing and tongue posture – on maxillary development, a multidisciplinary approach combining orthodontics, myofunctional therapy, and otolaryngology may yield optimal treatment results for individuals with palatal deformities [19,38].

In recent years, research has increasingly focused on the impact of maxillary expansion on airway morphology [20]. Although expansion therapies demonstrate short-term improvements in airway dimensions, long-term outcomes remain controversial [81]. A systematic review and meta-analysis evaluating rapid maxillary expansion (RME) in pediatric populations showed a significant reduction in nasal resistance and an increase in nasal airflow, supporting the potential of expansion therapies to enhance nasal breathing efficiency [20].

Heritability studies have demonstrated that palatal dimensions and dental arch widths are strongly influenced by genetic factors, which suggests that individual responses to expansion therapy may vary [77,78]. Moreover, the timing of intervention is crucial, as palatal suture fusion occurs progressively with age. Research suggests that the midpalatal suture begins ossifying around puberty, typically by age 13, rendering conventional RME less effective in older adolescents and adults [82,83]. In such cases, alternative expansion methods such as surgically assisted rapid maxillary expansion (SARME) or miniscrew-assisted rapid palatal expansion (MARPE) may be required to achieve stable skeletal changes and minimize relapse (Fig.1.4.1) [82].

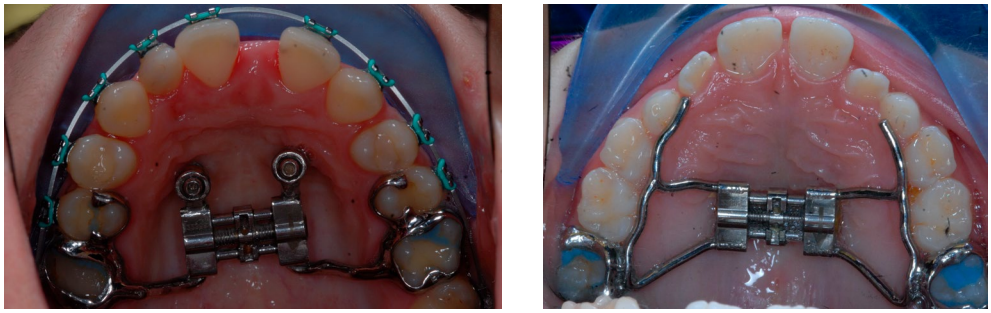

Fig.1.4.1. *MARPE vs conventional RME*

1.5. Relationship between maxillary dimensions and upper airway cephalometric measurements

The relationship between maxillary dimensions and upper airway morphology has been extensively studied in the context of obstructive sleep apnea (OSA), mouth breathing, and craniofacial development. However, very few studies focus specifically on the respiratory function in twins [43,72,73].

A retrospective study investigated the correlation between the palatal index and pharyngeal airway dimensions across different skeletal patterns [84]. Findings revealed that Class II patients had a higher palatal index (indicating a deep, high-arched palate) and reduced upper and lower pharyngeal airway dimensions compared to Class I and Class III. This suggests that Class II malocclusion is significantly associated with airway restriction due to more posteriorly positioned hyoid bone supporting the tongue [84,85]. In another study, Aluru et al. reported that Class II patients (with a retruded lower jaw) exhibited deeper palates and smaller airway spaces**,** suggesting that increased palatal depth may contribute to airflow limitation [83].

Similarly, Kecik et al. and Johal et al. analyzed the palatal morphology of OSA patients compared to that of a control group [86,87]. Their results demonstrated that OSA patients exhibited significantly smaller oropharyngeal volumes and narrower maxillary arches [86-88]. Habumugisha et al. found that mouth-breathing children had narrower maxillae and smaller airway volumes than nasal breathers, further linking maxillary constriction to compromised airway function [17]. A study on children at risk for sleep-disordered breathing found that they had significantly smaller intercanine, interpremolar, and intermolar widths and narrower airways than controls [89].

Despite strong evidence supporting the link between palatal morphology and airway size, some studies challenge this association. For instance, a CBCT study found that vertical facial growth (long face pattern)

substantially impacted depth alone [84]. Similarly, Tepedino et al. concluded that mandibular length – not maxillary sagittal dimensions – was the most significant cephalometric predictor of OSA severity [89]. These findings suggest that lower jaw position and vertical facial proportions may influence airway volume more than maxillary dimensions alone. However, Kecik et al. and Ciavarella et al. suggested that maxillary dimensions continue to play a role in airway function, especially when combined with mandibular positioning [21,86].

1.6. Genetic and environmental influences on mandibular morphology and its relationship with the upper airway

Twin studies have been instrumental in distinguishing genetic and environmental contributions to mandibular morphology. Studies involving monozygotic and dizygotic twins have demonstrated that mandibular length is under substantial genetic control, with higher similarity observed in monozygotic twins than in dizygotic twins [90,91]. Cephalometric twin studies confirm that ramus height and gonial angle exhibit significant genetic determination, suggesting that vertical mandibular growth patterns are primarily inherited [91,71].

Recent genome-wide association studies (GWAS) and whole-exome sequencing have expanded our understanding of the genetic basis of mandibular morphology: Several single-nucleotide polymorphisms (SNPs) have been associated with mandibular prognathism [92]. Studies have also implicated growth hormone receptor (GHR), fibrillin-3 (FBN3) and ectodysplasin A receptor (EDAR) in determining mandibular dimensions, highlighting the polygenic nature of mandibular development [93].

Although genetic factors predominantly shape mandibular morphology, environmental factors critically modify its development and positioning. Dysfunctions of soft tissues, especially mouth breathing and altered tongue posture, considerably impact the development of the mandible. Chronic mouth breathing has been linked to mandibular retrognathism and increased gonial angles, illustrating environmental impacts on mandibular positioning and development [6].

The interaction between mandibular positioning and airway dimensions is a crucial area of study, particularly in Class II malocclusions, which are often characterized by mandibular retrusion and reduced pharyngeal airway space. Advancing the mandible has increased airway dimensions, particularly in the oropharyngeal and hypopharyngeal regions [94,95]. Functional appliances such as the Twin Block and Herbst appliances (Fig. 1.6.1.) can modify mandibular positioning and influence airway dimensions [95,96]. Pavoni et

al. found that pharyngeal airway space improvements following Twin Block therapy remained stable in Class II patients**,** suggesting that skeletal changes persist beyond active treatment [97]. Unlike the Twin Block, Forsus primarily produces dentoalveolar changes rather than accurate skeletal modifications, which may result in less stable airway improvements over time [98,99].

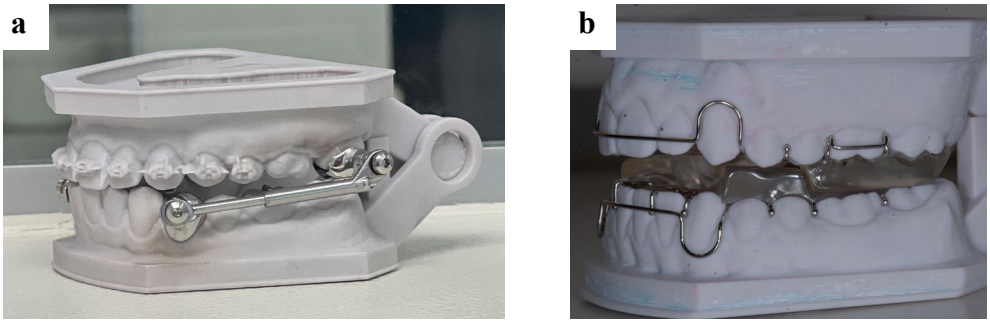

Fig. 1.6.1. *Functional appliances a. Herbst appliance, b. Twin block*

Studies emphasize the interplay between genetic and environmental factors in airway morphology**:** the sagittal position of the mandible is influenced by the cranial base morphology, with saddle angle (NSBa) variations affecting mandibular positioning and airway space [100-102]. Dunn et al. examined nasopharyngeal airway size in monozygotic twins and found a strong genetic component in mandibular morphology and airway dimensions**.** Their findings support the hypothesis that nasopharyngeal obstruction contributes to gonial angle modifications and mandibular width alterations [103].

1.7. Cephalometric analysis in airway assessment

Cephalometric radiography continues to be a cornerstone in assessing craniofacial morphology and upper airway dimensions in orthodontic diagnosis and treatment planning. Among the available imaging techniques, lateral cephalometric radiographs (LCRs) are particularly valued for their accessibility, low radiation exposure, and diagnostic reliability. While cone-beam computed tomography (CBCT) offers advanced three-dimensional visualization of the craniofacial structures, including volumetric assessment of the upper airway, its application in routine clinical settings is often constrained due to higher radiation doses, more significant cost, and limited availability of specialized equipment.

Lateral cephalograms, in contrast, are widely used and provide accurate and reproducible linear and angular measurements, which are particularly useful for evaluating skeletal structures. Practitioners can utilize these

images to analyze the dimensions of the upper respiratory tract's inflow and outflow regions, which is critical in detecting potential airway obstruction or pathological narrowing [42]. Despite being a two-dimensional modality, LCRs have demonstrated strong clinical utility. Studies report high levels of reliability in cephalometric measurements of the upper airway and hyoid bone, with intraclass correlation coefficients (ICCs) consistently exceeding 0.8, confirming their reproducibility and diagnostic value [104].

Nevertheless, certain limitations of LCRs must be acknowledged. While skeletal structures can be measured with high precision, evaluating soft tissue components such as the tongue, soft palate, and pharyngeal wall shows only moderate reliability. This is primarily due to the inherent limitations of two-dimensional imaging in capturing complex three-dimensional anatomical relationships and tissue density variations. As such, LCRs are best suited for analyzing skeletal landmarks and general airway space, whereas detailed evaluation of soft tissues may require complementary imaging modalities.

Furthermore, cephalometric projection techniques have proven useful in assessing airway patency. The narrowing of the airway can be visualized and quantitatively assessed through standardized cephalometric landmarks and linear measurements. These evaluations provide valuable information for interdisciplinary collaboration, particularly when managing patients with suspected airway compromise or craniofacial anomalies that may impact respiratory function.

While CBCT remains the gold standard for comprehensive airway analysis, especially when precise volumetric data is necessary, its higher radiation burden restricts its use in pediatric and longitudinal studies. In this context, LCRs represent a practical and efficient alternative, allowing clinicians to conduct preliminary screening and longitudinal monitoring of airway morphology with minimal patient exposure. They are especially beneficial in large-scale epidemiological studies and in populations requiring repeated imaging.

Although CBCT offers superior three-dimensional analysis, LCRs remain an indispensable tool in clinical orthodontics and airway evaluation due to their low radiation, cost-effectiveness, ease of use, and acceptable diagnostic accuracy for skeletal and selected soft tissue structures. Integrating both imaging modalities – when necessary and feasible – can provide a more holistic approach to diagnosis, treatment planning, and outcome assessment in craniofacial and airway-related disorders.

2. MATERIALS AND METHODS

The study protocols were approved by the Regional Biomedical Research Committee (BE-2-41 and BE-2-48). Relevant guidelines and regulations were followed. Informed consent was obtained from each participant and, for participants younger than 18 years, from their parents.

2.1. Study sample

The twins who participated in this study were recruited from the Twin Centre register of the Lithuanian University of Health Sciences. All twins of this register were offered DNA testing based on zygosity determination as well as medical consultations, including dental and orthodontic consultations, free of charge. Digital dental casts and standardized lateral head cephalograms were taken as part of dental and orthodontic examinations.

The study sample which evaluated the impact of nasopharyngeal obstruction on occlusal development and body posture was obtained from consecutive patients attending the LSMU Department of Orthodontics.

The study sample numbers as well as inclusion/exclusion criteria varied depending on the objectives of the study. The inclusion and exclusion criteria are presented in Table 2.1.1.

***Table 2.1.1**. Study sample inclusion and exclusion criteria*

Study objectives	**Inclusion criteria**	**Exclusion criteria**
To evaluate relationships between nasopharyngeal obstruction**,** occlusal characteristics and body posture	Children at the age 7–14 years	Maxillofacial trauma/ surgery, syndromes, clefts, prior orthopedic, orthodontic, treatments, spine or pelvis injury
To assess the genetic and environmental influences on cephalometric parameters of the airway morphology and related craniofacial structures	Twins of the European descent, CVM stage 6, available lateral head cephalograms	Previous orthodontic treatment, permanent teeth extractions, dental/facial trauma, systemic diseases
To assess the genetic and environmental influences on maxillary dental arch and palate morphology after completed maxillary growth	Twins of the European descent with a full set of permanent dentition (except third molars) and completed maxillary growth (age > 13 years)	Previous orthodontic treatment, permanent teeth extractions, dental restorations interfering with the assessment landmarks, excessive dental wear, poor-quality dental arch and palate models, dental/facial trauma, systemic diseases
To evaluate relationships between occlusal characteristics, upper dental arches morphology, palate dimensions and upper airways parameters.	Twins of the European descent, available lateral head cephalograms and dental arch models	Previous orthodontic treatment, permanent teeth extractions, dental/facial trauma, systemic diseases

The sample's age and sex characteristics are shown in Table 2.1.2.

***Table 2.1.2.** Study sample age and gender characteristics*

Study objective and group	**N (individuals)**	**Mean age (years)**	**SD (years)**
Evaluation of nasopharyngeal obstruction impact on occlusal development and body posture	94	11.90	2.10
- Male	44	-	-
- Female	50	-	-
Assessment of genetic and environmental influences on upper airway and related craniofacial structures (twin pairs)	94	18.85	4.92
Monozygotic (MZ) twins	50	-	-
- Male	15	-	-
- Female	35	-	-
Dizygotic (DZ) twins	44	-	-
- Male	19	-	-
- Female	25	-	-

Table 2.1.2 cont.

Study objective and group	N (individuals)	Mean age (years)	SD (years)
Assessment of craniofacial structures (twin pairs)	141	21.73	5.24
Monozygotic (MZ) twins	90	-	-
- Male	29	-	-
- Female	61	-	-
Dizygotic (DZ) twins	51	-	-
- Male	20	-	-
- Female	31	-	-
Assessment of genetic and environmental influences on maxillary dental arch and palate morphology after completed maxillary growth (twin pairs)	85	17.95	2.83
Monozygotic (MZ) twins	50	-	-
- Male	19	-	-
- Female	31	-	-
Dizygotic (DZ) twins	35	-	-
- Male	19	-	-
- Female	16	-	-
Evaluation of relationships between occlusal characteristics, upper dental arch morphology, palate dimensions, and upper airway parameters (twin pairs)	53	17.82	3.05
Monozygotic (MZ) twins	27	-	-
- Male	8	-	-
- Female	19	-	-
Dizygotic (DZ) twins	26	-	-
- Male	13	-	-
- Female	13	-	-

2.2. Cephalometric analysis

The cephalometric analysis measures the airway, skeletal dimensions, and mandibular variables (Fig 2.2.1). The cephalograms were obtained under standard conditions using digital X-ray equipment (Kodak 8000C). A cephalostat stabilized the subject's head in a constant position. The ALARA (As Low as Reasonably Achievable) principles were followed to minimize radiation exposure.

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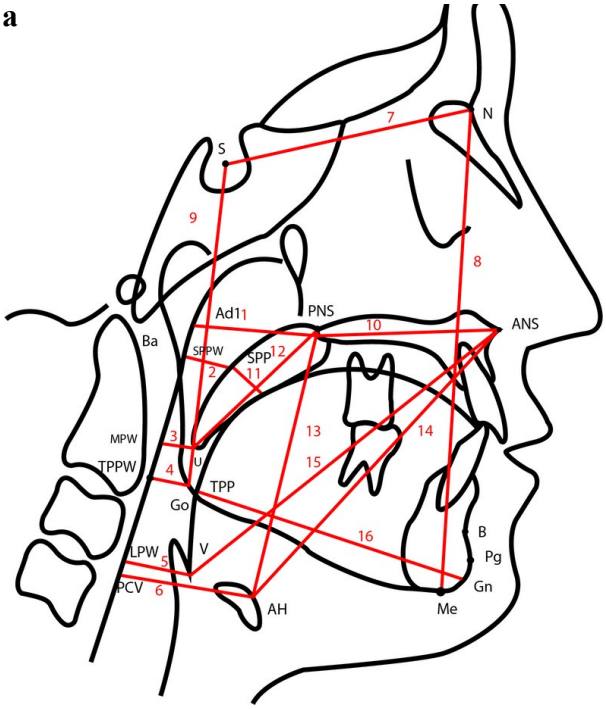
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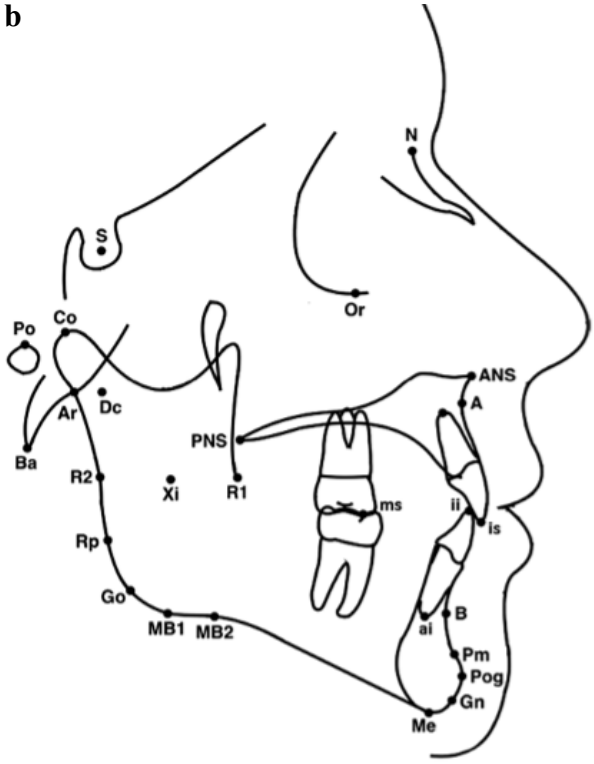
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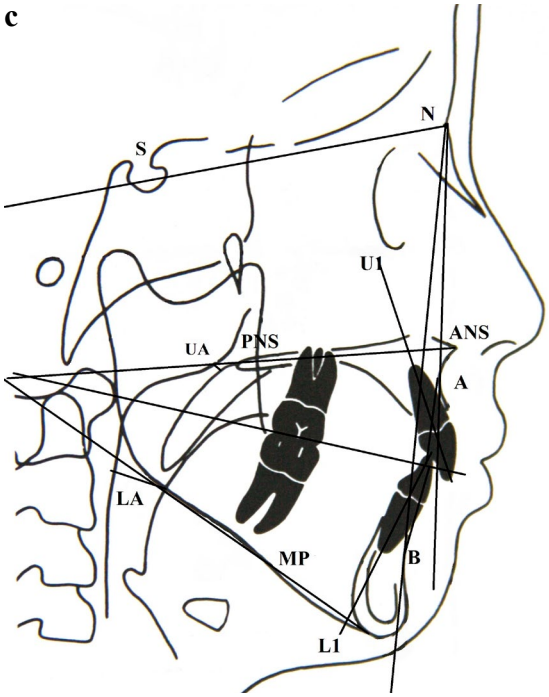


Fig. 2.2.1. *Consolidated list of cephalometric landmarks*

Below is a consolidated list of cephalometric landmarks from the studies provided, ensuring no duplicates: **S (Sella)** – The midpoint of the sella turcica. **N (Nasion)** – The extreme anterior point of the frontonasal suture. **A (Point A)** – The deepest point in the curvature of the maxillary alveolar process. **B (Point B)** – The deepest point in the curvature of the mandibular alveolar process. **ANS (Anterior Nasal Spine)** – The anteriormost point of the anterior nasal spine. **PNS (Posterior Nasal Spine)** – The most posterior point of the hard palate. **Ba (Basion)** – The most anterior-inferior point on the margin of the foramen magnum. **Co (Condylion)** – The most posterior superior point of the condyle. **Ar (Articulare)** – The point at the junction of the posterior border of the ramus and the inferior border of the posterior cranial base. **Go (Gonion)** – The midpoint of the mandibular angle between the ramus and the mandibular corpus. **Me (Menton)** – The lowest point on the anterior border of the mandible. **Gn (Gnathion)** – The midpoint between Pogonion and Menton. **Pog (Pogonion)** – The most anterior point of the chin. **Xi (Xi Point)** – The point located at the geometric center of the ramus. **Rp (Ramus Posterior Point)** – The most prominent postero-superior point at the angle of the mandible on the posterior ramus. **MB1 (Inferior Border Point)** – The most convex point along the inferior border of the ramus. **MB2 (Antegonial Notch)** – The highest point of the notch of the lower border of the body of the mandible. **is (Incision Superior)** – The incisal tip of the most anterior maxillary central incisor. **ii (Incision Inferior)** – The incisal tip of the most anterior mandibular central incisor. **Ms (Molar Superior)** – The tip of the mesial buccal cusp of the mandibular first molar. **Po (Porion)** – The midpoint on the upper contour of the external auditory canal. **Or (Orbitale)** – The deepest point on the infraorbital margin. **Ad1 (Point Ad1)** – The point of intersection of the posterior pharyngeal wall and the line PNS-Ba. **SPPW (Soft Palate Posterior Wall)** – The point of intersection of the poste-

rior pharyngeal wall and the line that extends perpendicularly from the posterior pharyngeal wall to the center of the soft palate. **SPP (Soft Palate Posterior)** – The point of intersection of the posterior margin of the soft palate and the line that extends perpendicularly from the posterior pharyngeal wall to the center of the soft palate. **TPPW (Top Posterior Pharyngeal Wall)** – The point of intersection of the posterior pharyngeal wall and the extension of line B-Go. **LPW (Lower Posterior Pharyngeal Wall)** – The point on the posterior pharyngeal wall from which a perpendicular line will pass through point V. **PCV (Posterior Cervical Vertebra)** – The point of intersection of the posterior pharyngeal wall and an extension of the lower edge of the second cervical vertebra. **U (Uvula)** – The tip of the uvula. **V (Vallecula)** – The point where the epiglottis meets the base of the tongue. **AH (Anterior Hyoid)** – The most anterior and superior point on the body of the hyoid bone. **ai (Apex Inferior)** – The root apex of the most anterior mandibular central incisor. **Pm (Protuberance Mentis)** – The point at which the shape of symphysis mentalis changes from convex to concave. **L1** – Lower incisor axis. **U1** – Upper incisor axis.

Lateral cephalometric radiographs were taken after swallowing. All lateral cephalograms had the same magnification. The radiographs were analyzed using Dolphin Imaging software (v.10.5 and 11.7). Cephalometric variables and definitions used in the study are presented in Table 2.2.1.

Table 2.2.1. *Cephalometric points, linear and angular measurements used in the study*

Measurement	**Definition**
SNA	Angle determined by points S, N and A.
SNB	Angle determined by points S, N, B.
OB	Overbite: distance of vertical overlap of the lower incisors (point ii) by the upper central incisors (point is) in mm.
OJ	Overjet: distance from the tip of the upper central incisor (point is) to the lower incisor (point ii) in mm.
ANB	Angle – the difference between SNA and SNB.
MP-SN	Angle formed by Go-Me plane and SN plane.
U1-ANS/PNS	Inclination of maxillary incisors.
L1-MP	Inclination of mandibular incisors.
UA	The width of the upper airway.
LA	The width of the lower airway.
PNS-Ad1	Distance between PNS and Ad1.
SPPW-SPP	Distance between SPPW and SPP.
U-MPW	Distance between U and MPW.
PPW-TPP	Distance between PPW and TPP.
LPW-V	Distance between LPW and V.
PCV-AH	Distance between PCV and AH.
S-N	Distance between S and N.
N-Me	Distance between N and Me.
S-Go	Distance between S and Go.

Table 2.2.1 cont.

Measurement	Definition
PNS-ANS	Distance between PNS and ANS.
SPL	Soft palate length.
SPW	Soft palate width.
PNS-AH	Distance between PNS and AH.
ANS-AH	Distance between ANS and AH.
ANS-V	Distance between ANS and V.
Go-Gn	Distance between Go and Gn.
Ulip-E	Distance between upper lip anterior border and E line.
Llip-E	Distance between lower lip anterior border and E line.
Wits	Distance between perpendiculars from points A and B onto the occlusal plane in mm.
SNPog	Angle determined by points S, N, and Pog.
NSBa	Angle determined by points N, S, and Ba.
NSAr	Angle determined by points N, S, and Ar.
NAPog	Angle determined by points N, A, and Pog.
SN–GoMe	Angle formed by S–N and Go–Me lines.
ANSPNS–GoMe	Angle formed by ANS–PNS and Go–Me lines.
SN–ArRp	Angle formed by S–N and Ar–Rp lines.
PoOr–GoMe	Angle formed by Po–Or and Go–Me lines.
NGnGo	Angle determined by points N, Gn, and Go.
DcXiPm	Angle formed by Dc, Xi, and Pm points.
ArRp–MB1Me	Angle formed by Ar–Rp and MB1–Me lines.
CoGoMe	Angle determined by points Co, Go, and Me.
ArGoMe	Angle determined by points Ar, Go, and Me.
ai.ii–NB	Angle formed by line ai-ii and N–B lines.
ai.ii–GoMe	Angle formed by line ai-ii and Go–Me lines.
CoA	Distance between points Co and A in mm.
CoGo	Distance between points Co and Go in mm.
CoPog	Distance between points Co and Pog in mm.
CoB	Distance between points Co and B in mm.
ArB	Distance between points Ar and B in mm.
ArA	Distance between points Ar and A in mm.
Pog ⊥ NB	Perpendicular distance from the point Pog to N–B line in mm.
GoGn	Distance between points Go and Gn in mm.
GoPog	Distance between points Go and Pog in mm.
XiPm	Distance between points Xi and Pm in mm.
R1R2	Ramal width at Xi, distance between points R1 and R2 in mm.
NMe	TAFH, total anterior face height, distance between points N and Me in mm.
NANS	UAFH, upper anterior face height, distance between points N and ANS in mm.

Table 2.2.1 cont.

Measurement	Definition
ANSMe	LAFH, lower anterior face height, distance between points ANS and Me in mm.
SGo	TPFH, total posterior face height, distance between points S and Go in mm.
ii ⊥ NB	Perpendicular distance from point ii to N–B line in mm.
ii ⊥ APog	Perpendicular distance from point ii to A-Pog line in mm.
ii ⊥ GoMe	Perpendicular distance from point ii to Go–Me line in mm.
ms ⊥ GoMe	Perpendicular distance from point ms to Go–Me line in mm.
MB2 ⊥ MB1Me	Depth of antegonial notch, perpendicular distance from the line between points MB1 and Me to the point MB2 in mm.

2.3. Assessment of the craniofacial growth and skeletal maturity

The cervical vertebrae maturation (CVM) method, as modified by Baccetti et al., was employed as the preferred approach for evaluating the completion of mandibular growth [105]. This method facilitates the assessment of skeletal age while eliminating the need for additional radiographic imaging, as the vertebrae are already captured in lateral cephalograms. The Baccetti modification relies on visually evaluating the size and shape of a reduced number of cervical vertebrae.

Our studies utilized the CS6 stage, corresponding to active growth completion. Twin participants who had reached CVM stage 6 were included in the study sample. The cervical stage is defined based on concavities along the lower borders of vertebrae C2, C3, and C4 (Fig. 2.3.1 and Fig. 2.3.2). At least one of the vertebral bodies of C3 or C4 must exhibit a rectangular vertical shape. If this condition is not met, the body of the other cervical vertebra should display a squared shape. Notably, the peak mandibular growth phase finishes at least two years before this stage.

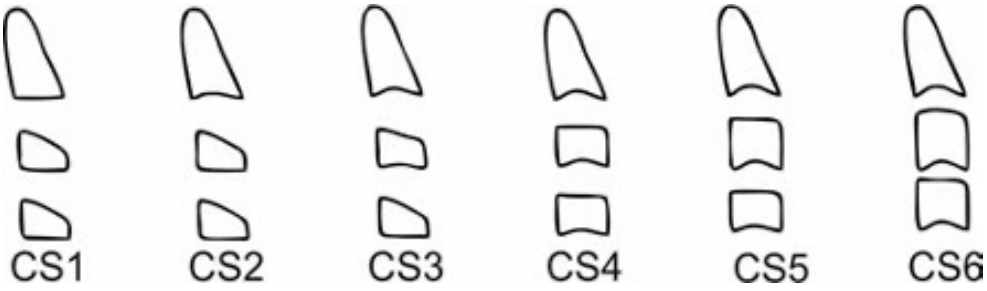


Fig. 2.3.1. *The stages of cervical vertebrae maturation*

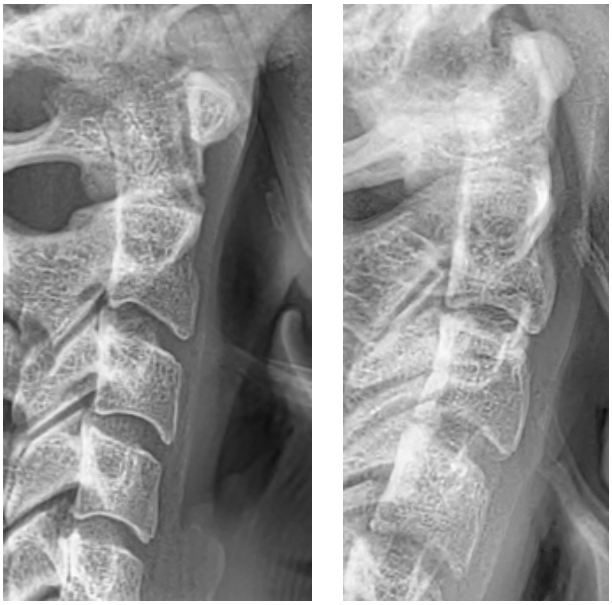


Fig. 2.3.2. *Cervical maturation stage 6 (CS6)*

2.4. Dental arch and palate measurements

In the first study, comprehensive model analysis was conducted focusing on three dimensions. 1. Transverse analysis: This dimension involved diagnosing posterior crossbites, which were identified when at least two teeth exhibited a cross-relationship with antagonists in the posterior dental arch segments. Crossbites were further classified as unilateral or bilateral. 2. Sagittal analysis: Overjet (OJ) measurements were recorded and classified into three categories: normal (1–3 mm), increased (>3 mm), and decreased (<1 mm). 3. Vertical analysis**:** Overbite (OB) was evaluated and similarly categorized as normal (1–3 mm), increased (>3 mm), and decreased (<1 mm). Finally, space analysis assessed the relationship between available and required space for proper dental alignment.

In the fourth study**,** high-precision alginate dental impressions were obtained from study participants. These impressions were digitized using the 3Shape e3 scanner (3Shape, Copenhagen, Denmark), renowned for its accuracy of 7–10 μm (scan time: 18 seconds; resolution: dual 5.0-megapixel cameras). The digital data representing maxillary dental casts and palates were saved in STL format and carefully examined to remove irrelevant or extraneous artifacts. Subsequently, virtual 3D models were analyzed and measured using Blender, a universal software tool for 3D processing and

animation (Fig. 2.4.1). The definitions of the measurements used in the study are presented in Table 2.4.1.

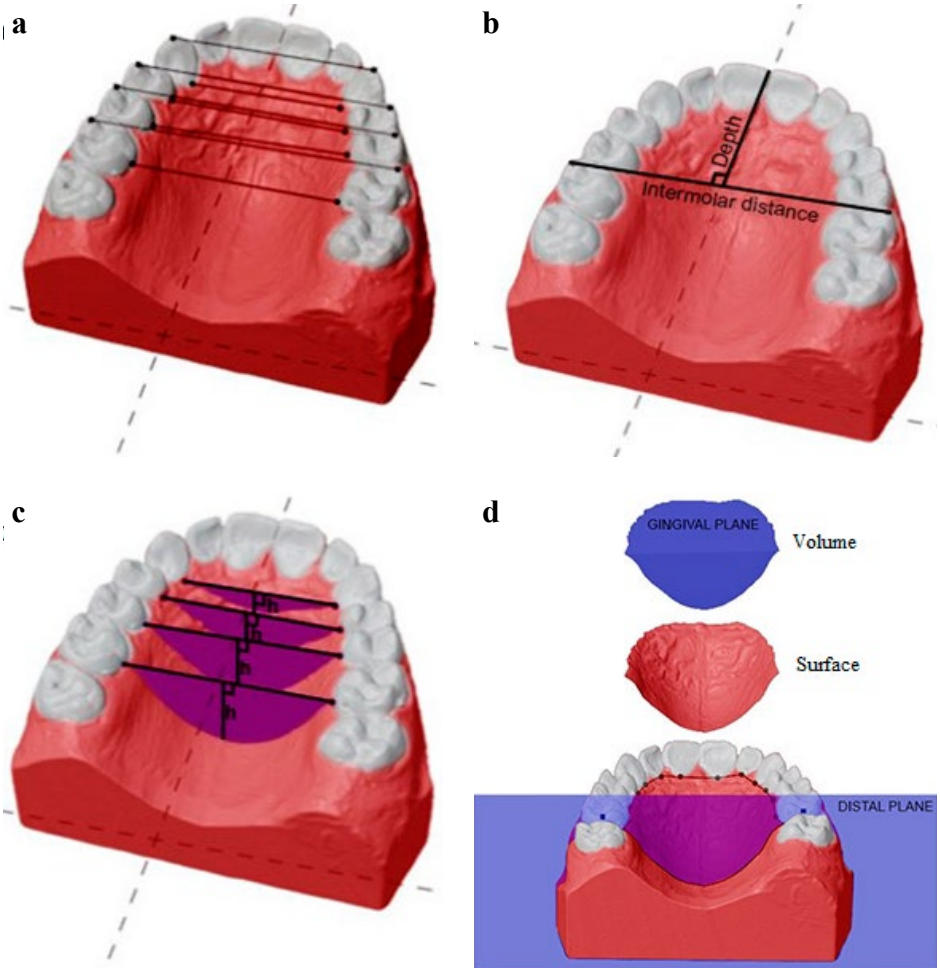


Fig. 2.4.1. *The upper dental arch parameters*

(a) The upper dental arch widths were defined as the distances between the two reference points at the occlusal and dento-gingival junctions. The interdental distances were measured between the cusp tips of the canines, first premolars, second premolars, and first molars at the occlusal plane and between the centers of the dento-gingival junction of the canines, first premolars, second premolars, and first molars at the palatal side. (b) The upper dental arch depth. Distance between a tangent from the incisal edge of the central incisors and a line connecting the contact point between the first molar mesiobuccal cusps. (c) Palate height. Distance between the line connecting the centers of the dento-gingival junctions of second premolars on the palatal side and the highest point of the palatal vault on the midpalatal rafe. (d) Palate surface area is below the gingival plane and limited by the distal plane; palate volume is below the gingival plane and limited by the palate surface and distal plane.

Table 2.4.1. *Definitions of the measurements*

Measurements	Definition
Dental arch widths at occlusal line	
ICW – intercanine width	Distance between cusp tips of the canines on the maxillary occlusal plane.
1IPW – interfirst premolar width	Distance between buccal cusp tips of the first premolars on the maxillary occlusal plane.
2IPW – intersecond premolar width	Distance between buccal cusps tips of the second premolars on the maxillary occlusal plane.
IMW – interfirst molar width	Distance between mesiobuccal cusps tips of the first molars on the maxillary occlusal plane.
Dental arch widths at gingival line	
ICWG – intercanine width at the gum line	Distance connecting the centres of the dentogingival junctions of canines on the palatal side.
1IPWG – interfirst premolar width at the gum line	Distance connecting the centres of the dentogingival junctions of the first premolars on the palatal side.
2IPWG – intersecond premolar width at the gum line	Distance connecting the centres of the dentogingival junctions of the second premolars on the palatal side.
IMWG – interfirst molar distance at the gum line	Distance connecting the centres of the dentogingival junction of the first molars on the palatal side.
Palatal heights	
ICH – intercanine palate height	Distance between the line connecting the centres of the dentogingival junctions of the canines on the palatal side and the highest point of the palatal vault on the midpalatal rafe.
1IPH – interfirst premolar palate height	Distance between the line connecting the centres of the dentogingival junctions of the first premolars on the palatal side and the highest point of the palatal vault on the midpalatal rafe.
2IPH – intersecond premolar palate height	Distance between the line connecting the centres of the dentogingival junctions of the second premolars on the palatal side and the highest point of the palatal vault on the midpalatal rafe.
IMH – interfirst molar palate height	Distance between the line connecting the centres of the dentogingival junctions of the first molars on the palatal side and the highest point of the palatal vault on the midpalatal rafe.
Maxillary arch depth, palate surface area and volume	
MD – maxillary depth	Distance between a tangent from the incisal edge of the central incisors and a line connecting the contact point between the first molar mesiobuccal cusps.

Table 2.4.1 cont.

Measurements	Definition
PSA – palate surface area	Palate surface area below the gingival plane and limited by the distal plane. Gingival plane constructed by connecting the line of the midpoints of the dentogingival junction of all teeth (except second molars). The distal plane constructed perpendicular to the occlusal plane passing from the two most distal points corresponding to the distal surface of the first molars.
PV – palate volume	Volume below the gingival plane and limited by the palate surface and distal plane. Gingival plane constructed by connecting the line of the midpoints of the dentogingival junction of all teeth (except second molars). The distal plane constructed perpendicular to the occlusal plane passing from the two most distal points corresponding to the distal surface of the first molars.

2.5. Zygosity determination of twins

Zygosity was determined through a DNA-based test using the AmpFlSTR® Identifiler® polymerase chain reaction kit (Applied Biosystems, USA), which amplified short tandem repeats and 15 distinct DNA markers (D8S1179, D21S11, D7S820, CSF1PO, D3S1358, TH01, D13S317, D16S539, D2S1338, D19S433, vWA, TROX, D18S51, D5S818, FGA) (Fig.2.5.1). The amelogenin gene fragment was also utilized for genetic profile comparisons, achieving an accuracy rate of 99.9 % [106,107].

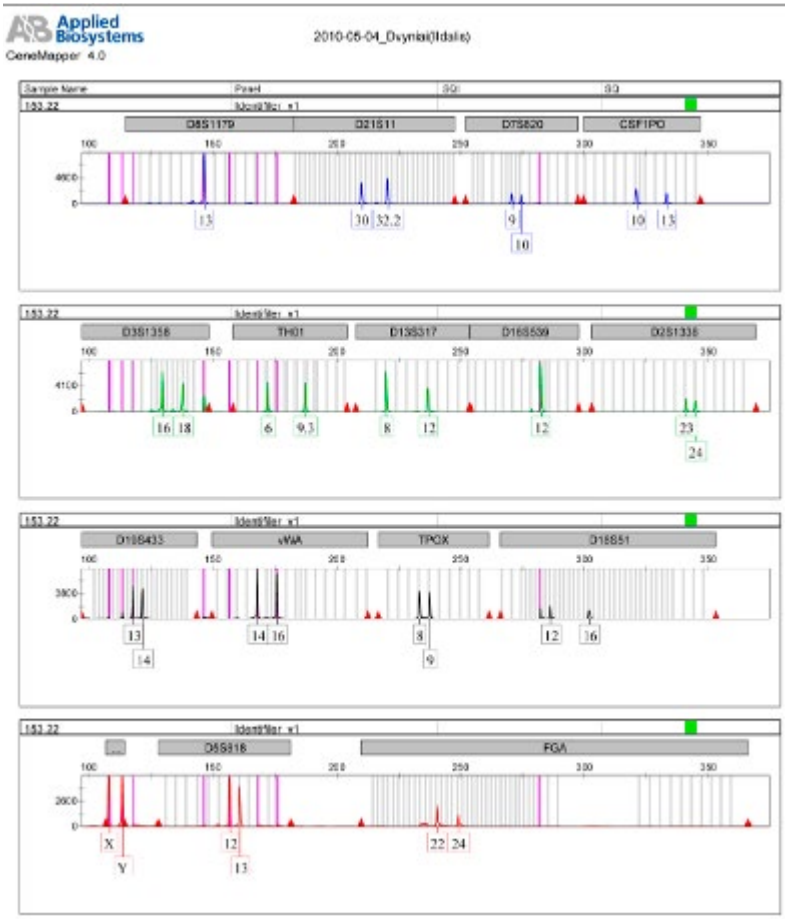


Figure 2.5.1*. Graphic representation of DNA markers used for zygosity determination*

2.6. Otorhinolaryngological examination

Anterior and posterior rhinoscopy and pharyngoscopy were conducted to evaluate the nasal and pharyngeal regions. The following diagnostic criteria were applied: 1. Adenoid hypertrophy (grades 2–3), diagnosed when up to two-thirds of the choanal space was compromised. 2. Palatal tonsil hypertrophy (grades 2–4), defined when <50 % of the space between the tonsillar pillars was obstructed. 3. Nasal septum deviation, identified when the nasal septum failed to align with the center. 4. Allergic rhinitis, diagnosed based on typical allergy symptoms, including nasal congestion, rhinorrhea, sneezing, and watery eyes, corroborated by the results of skin prick tests. Otorhinolaryngological examinations were conducted by expert investigators

(RP). To minimize method error in clinical investigations, the investigator underwent calibration and standardization of their procedures before the study. This involved repeating examinations on 10 patients at two different time points. Inter-rater reliability was assessed using the kappa statistic, with kappa values exceeding 0.8, indicating a high level of agreement.

2.7. Orthopedic examination

The examination was conducted in a quiet classroom, free from external interference. Patients were assessed in a relaxed standing posture, barefoot, and instructed to maintain an upright position without movement. They were asked to look straight ahead with relaxed shoulders and arms resting naturally at their sides to ensure a neutral head and body alignment. A standard routine examination was performed for each patient from the front, side, and back. Since manual orthopedic diagnostics do not allow precise differentiation of severity, findings were categorized as normal or abnormal. Initial assessments were conducted from the side, focusing on evaluating thoracic kyphosis. The posture was classified as kyphotic if increased but adjustable asymptomatic curvature of the thoracic spine was identified. Patients were instructed to stand upright, retract their shoulders to achieve thoracic extension and rule out conditions such as Scheuermann's disease and ankylosing spondylitis. Postural kyphosis was identified when a mobile, regular, increased curvature was observed. Subsequently, patients were examined from the front to assess the position of the shoulders, the symmetry of the waist triangles, and the horizontal alignment of the upper iliac crests. The final assessment was conducted from the back, focusing on the position of the shoulders, scapular height, and the symmetry of the waist triangles, iliac crests, and thoracic rib hump. Differences between the left and right sides were interpreted as asymmetry. To rule out scoliosis, all patients underwent a forward-bend test. They were instructed to bring their chin to their chest, relax their arms, and flex their hips while keeping their knees extended. The examiner observed the presence of a paravertebral muscle roll in the lumbar region or a rib hump in the thoracic region. If a rib prominence hump greater than 1 cm was detected, full-length frontal and lateral spinal radiographs were taken to measure the degree of spinal deformity using Cobb's angle (Fig. 2.7.1). The orthopedic examination was performed by an experienced investigator (EC). To ensure consistency and minimize methodological error, the procedures were standardized prior to the study by conducting repeated clinical assessments on 10 individuals at two different time points. Agreement was evaluated using the kappa coefficient, with values exceeding 0.8, indicating high inter-examination reliability.

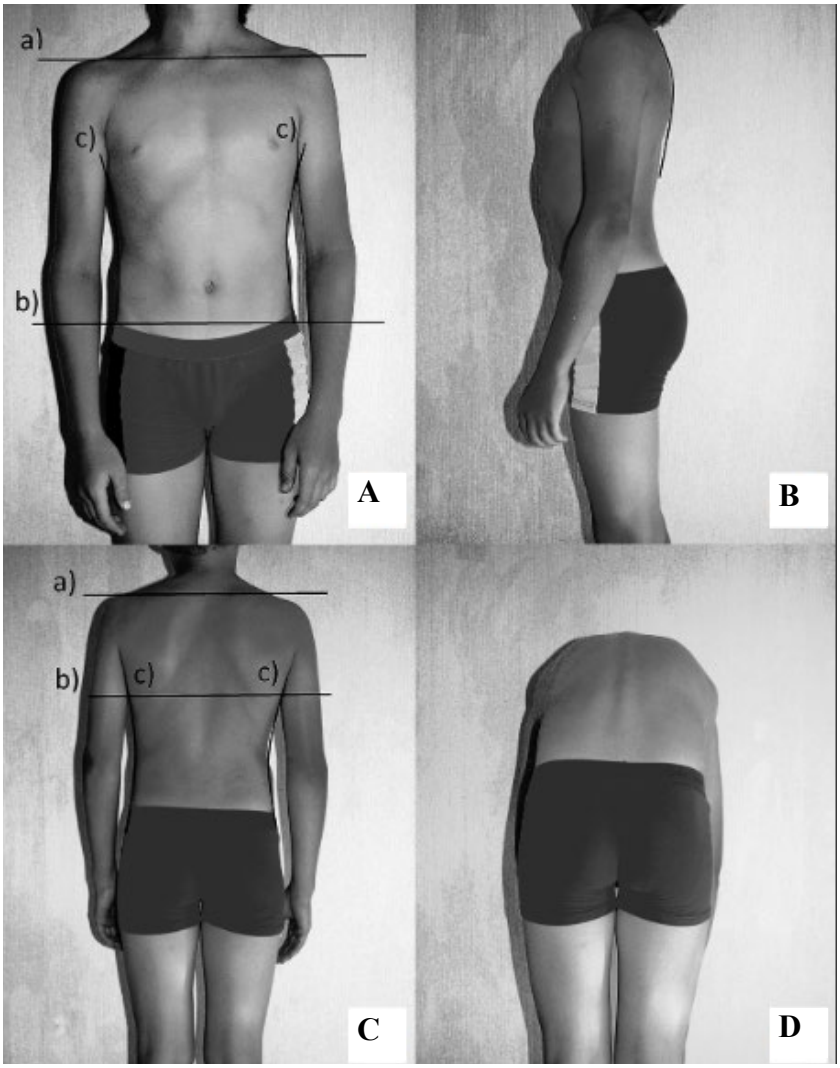


***Fig. 2.7.1**. Orthopedic examination*

A) Evaluation from the front: a) Assess the symmetry of the shoulders. b) Evaluate the symmetry of the waist triangles. c) Examine the horizontal alignment of the upper iliac crests. B) Thoracic kyphosis assessment: Thoracic kyphosis is evaluated from the side view. C) Evaluation from the back: a) Assess the symmetry of the shoulders. b) Examine the height of the scapulae. c) Evaluate the symmetry of the waist triangles. D) Scoliosis assessment: A test is performed to confirm or rule out scoliosis by observing the emergence of a paravertebral muscle roller in the lumbar region and a rib hump in the thoracic region.

2.8. Statistical analysis

In the first, second, and third studies, descriptive statistics, including mean and standard deviation (SD), were used to summarize the data. The normality of data distribution was tested using the Shapiro–Wilk test. For comparisons of quantitative variables between two independent groups, parametric Student's t-tests were applied. Pearson's correlation coefficients were calculated, and the differences between correlation coefficients were statistically evaluated. All statistical analyses were conducted in the R statistical computing environment (R version 3.3.0, http://www.r-project.org). A p-value of <0.05 was considered statistically significant. Pearson's correlation coefficient (r) was used to evaluate the relationship between upper airway dimensions and palatal parameters.

In the fourth study, statistical analyses were conducted using SPSS 20.0 (IBM Corp., Armonk, NY, USA). The Student's t-test compared group means for normally distributed data. Non-normally distributed data were analyzed using the Mann–Whitney U test. Interrelationships among characteristics were evaluated using the chi-square (χ^2) test and Spearman's correlation coefficients (r). Logistic regression analysis and receiver operating characteristic (ROC) curve analysis were applied to identify significant predictors of SNB angle reduction.

Method error

Intraobserver method error was evaluated using the intraclass correlation coefficient (ICC) for reliability and the Bland–Altman method [108]. The estimated random error between repeated measurements was calculated using the Dahlberg formula:

$$SDd = \sqrt{\sum \frac{(d_1 - d_2)^2}{2N}}$$

SD represents the standard deviation of differences, d_1 and d_2 are the first and second measurements, and *N* is the number of samples. Reliability was tested by repeating measurements on lateral cephalograms and models of 20 randomly selected twin pairs at a one-month interval by the same investigator.

Estimation of heritability

Genetic structural equation modeling (GSEM) was conducted using the "OpenMx" package (http://openmx.psyc.virginia.edu) in the R environment [109]. Variance in traits was attributed to additive genetic factors (A), non-additive genetic factors (D), shared environment (C), and unique environment

(E) (Fig. 2.8.1). The sources of genetic and environmental variations considered in the fitted model were: 1. Additive genetic factors (A): genetic factors that cumulatively influence a phenotype. 2. Non-additive genetic factors (D): genetic factors that interact through dominance and epistasis to infuence a phenotype. 3. Shared environmental factors (C): environmental factors shared by twins raised in the same family environment that infuence a phenotype. 4. Non-shared environmental factors (E): environmental factors specifc to each twin that infuence a phenotype. Given the limitations of twins reared together, only ACE or ADE models were tested [110]. The goodness-of-fit for the models was assessed by comparing the Akaike Information Criterion (AIC) and chi-square (χ^2) values. The most parsimonious model with the lowest AIC was selected.

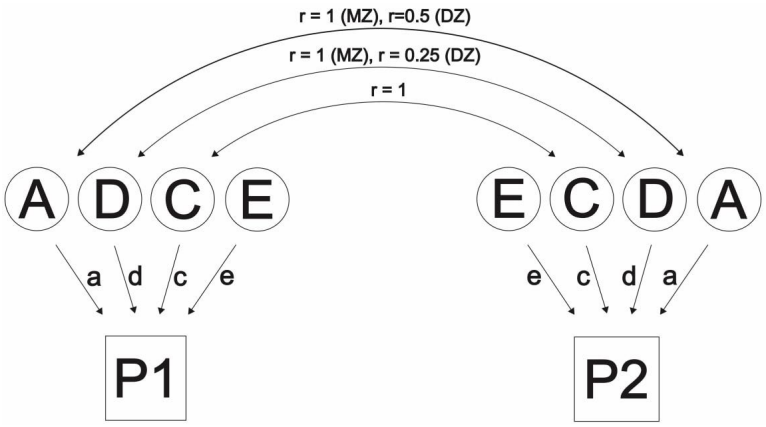


Fig. 2.8.1. *Path diagram for the univariate twin model*

Squares are latent variables (A – additive genetic factors, D – non-additive genetic factors, C – common environmental factors, and E – unique environmental factors) shown with their respective path coefficients (a, d, c, e) indicating the relative importance of each contributing influence. Circles are observed variables, single-headed arrows are one-way (causal) relationships, and double-headed arrows are two-way (covariance).

Principal component analysis

Principal component analysis (PCA) was performed to reduce data dimensionality and explore correlations among cephalometric and palatal variables. The "principal" function from the "Psych package" (Procedures for Psychological, Psychological, Psychometric and Personality research) was used, and varimax rotation was applied to optimize the interpretation of components. Variables with absolute component loadings >0.5 were considered significant contributors.

3. RESULTS

3.1. Relationships between nasopharyngeal obstruction, dental occlusal pathology and body posture

The orthodontic, otorhinolaryngological and orthopaedic characteristics of the patients are presented in Table 3.1.1. Adenoid hypertrophy was present in 54 patients (57.4 %), tonsillar hypertrophy in 85 patients (90.3 %), nasal septum deviation in 51 patients (54.3 %), and allergic rhinitis in 19 patients (20.2 %). Postural disorders were identified in 72 patients (76.6 %).

Table 3.1.1. *Orthodontic, otorhinolaryngological and orthopedic characteristics of the study group*

Characteristic	**Patients n (%)**
Orthodontic characteristics	
Class I (ANB angle 1–3°)	26 (27.7 %)
Class II (ANB angle ≥4°)	60 (63.8 %)
Class III (ANB angle ≤0°)	8 (8.5 %)
Otorhinolaryngological characteristics	
Hypertrophy of adenoids – Grade 1	24 (25.5 %)
Hypertrophy of adenoids – Grade 2	30 (31.9 %)
Hypertrophy of tonsils – Grade 1	46 (48.9 %)
Hypertrophy of tonsils – Grade 2	32 (34 %)
Hypertrophy of tonsils – Grade 3	7 (7.4 %)
Nasal septum deviation	51 (54.3 %)
Allergic rhinitis	19 (20.2 %)
Postural characteristics	
Kyphotic posture	45 (47.9 %)
Asymmetry of shoulder line	23 (24.5 %)
Asymmetry of position of scapulae	23 (24.5 %)
Asymmetry of waist triangles	5 (5.3 %)
Rib hump	48 (51.1 %)

No significant associations were observed between transverse orthopedic pathology and malocclusion or otorhinolaryngologic pathology. There were no relationships between crowding, posterior crossbite, and orthopedic or otorhinolaryngologic parameters (Table 3.1.2).

Table 3.1.3 presents the relationship between malocclusion, sex, and sagittal orthopedic pathologies. A statistically significant correlation was identified between males' kyphotic posture and reduced SNB angle.

Table 3.1.2. *The relationship between orthodontic variables, sex and nasopharyngeal obstruction*

Orthodontic variables	Female n = 50		p	Male n = 44		p	Total n = 94		p
	Nasopharyngeal obstruction			Nasopharyngeal obstruction			Nasopharyngeal obstruction		
	Absent n = 12	Present n = 38		Absent n = 8	Present n = 36		Absent n = 20	Present n = 74	
	Mean, SD	Mean, SD		Mean (SD)	Mean (SD)		Mean (SD)	Mean (SD)	
(SNA°)	81.92±3.55	81.69±3.40	0.85	82.25 (5.01)	81.39 (2.74)	0.5	82.05 (4.07)	81.55 (3.08)	0.56
(SNB°)	79.08±3.80	77.74±3.34	0.25	78.13 (4.26)	77.04 (4.07)	0.5	78.70 (3.91)	77.40 (3.71)	0.17
(ANB°)	2.74±3.30	3.85±2.04	0.17	4.13 (1.64)	4.32 (3.41)	0.88	3.30 (2.79)	4.08 (2.78)	0.48
(MP-SN°)	32.17±3.33	33.93±5.27	0.28	30.85 (6.65)	33.01 (6.32)	0.39	31.64 (4.81)	33.48 (5.79)	0.20
(U1- ANS/PNS)	107.83±9.07	107.29±7.83	0.84	103.38 (12.55)	107.93 (9.26)	0.25	106.05 (10.52)	107.60 (8.50)	0.49
(L1-MP°)	92.67±10.54	92.37±7.71	0.92	93.88 (5.67)	92.78 (7.48)	0.7	93.15 (8.75)	92.57 (7.55)	0.77
Overjet mm	3.08±2.58	3.72±2.09	0.39	4.31 (2.75)	4.46 (3.55)	0.91	3.58 (2.65)	4.08 (2.90)	0.48
Overbite mm	3.21±1.83	4.10±2.35	0.24	4.19 (2.20)	4.57 (2.42)	0.68	3.60 (1.99)	4.33 (2.38)	0.21

Table 3.1.3. *The relationship between orthodontic variables, sex and sagittal orthopaedic parameters (thoracic kyphosis)*

Orthodontic variables	Female		p	Male		p	Total		p
	n=50			n=44			n=94		
	Thoracic kyphosis			Thoracic kyphosis			Thoracic kyphosis		
	Normal	Kyphotic posture		Normal	Kyphotic posture		Normal	Kyphotic posture	
	n=31	n=19		n=18	n=26		n=49	n=45	
	Mean, SD	Mean, SD		Mean (SD)	Mean (SD)		Mean (SD)	Mean (SD)	
(SNA°)	82.03±3.61	81.28±3.08	0.46	82.50, (3.47)	80.88, (2.9)	0.1	82.2, (3.53)	81.05, (2.95)	0.91
(SNB°)	78.58±3.78	77.21±2.76	0.17	79.00, (3.99)	76.02, (3.74)	0.02	78.73, (3.08)	76.52, (3.38)	0.01
(ANB°)	3.35±2.8	3.97±1.58	0.39	3.60, (2.78)	4.75, (3.35)	0.24	3.44, (2.76)	4.42, (2.75)	0.23
(MP-SN°)	32.59±5.02	35.00±4.47	0.92	31.90, (6.60)	33.12, (6.27)	0.54	32.34, (5.59)	33.91, (5.60)	0.18
(U1- ANS/PNS)	107.74±8.41	106.89±7.62	0.72	107.33, (10.8)	106.94, (9.44)	0.9	107.59, (9.29)	106.92, (8.62)	0.72
(L1-MP°)	91.71±9.22	93.63±6.79	0.44	92.36, (8.2)	93.40, (6.44)	0.64	91.95, (8.78)	93.50, (6.51)	0.34
Overjet (mm)	3.37±2.64	3.86±1.2	0.42	3.39, (3.27)	5.15, (3.34)	0.09	3.38, (2.85)	4.62, (2.71)	0.03
Overbite (mm)	3.78±2.39	4.05±2.04	0.67	3.50, (2.35)	5.19, (2.15)	0.02	3.68, (2.36)	4.71, (2.16)	0.03

Kyphotic posture was significantly more prevalent among patients with nasopharyngeal obstruction (54.1 %) than those without obstruction (25 %). Patients with kyphotic posture and nasopharyngeal obstruction exhibited a significant reduction in SNB angle (<77°). Among this group, kyphotic posture was observed in 71.1 % of patients, while normal thoracic kyphosis was seen in 38.8 %.

Regression Analysis: With a significant decrease in the SNB angle in patients with kyphotic posture and nasopharyngeal obstruction, the logistic regression analysis was performed to evaluate the risk of a reduction in the SNB angle. The critical value of the SNB angle was determined using ROC curve analysis (Figure 3.1.1). The threshold of 77° was crucial for the SNB angle (sensitivity 71.1 %; specificity, 69.8 %; p=0.002). Our study indicated that among patients with the SNB angle <77°, kyphotic posture was found in 71.1 % of patients and normal thoracic kyphosis in 38.8 % . Binary logistic regression revealed that kyphotic posture increased the odds of an SNB angle <77° by 3.887 (95 % CI: 1.639–9.218). After adjusting for nasopharyngeal obstruction, the odds ratio increased to 4.037 (95 % CI: 1.652–9.861).

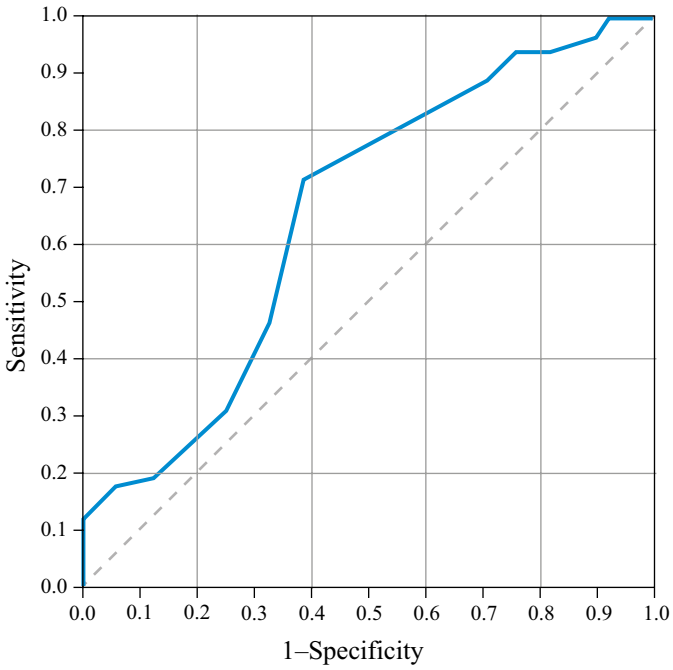


Fig. 3.1.1. *Receiver operating characteristic (ROC) curve analysis for prediction of the critical values of the SNB angle. Area under the receiver operating characteristic curve = 65.2 %*

3.2. Genetic and environmental influences on cephalometric parameters of the airway morphology and related craniofacial structures

The study consisted of 94 twin pairs – mean age 18.85 with standard deviation 4.92. There were no significant differences between the first and second measurements of cephalometric variables. The model-fitting analysis revealed distinct genetic and environmental contributions to craniofacial and airway variables. Table 3.2.1 shows the AIC values for all of the models, and Table 3.2.2 shows the best-fitting models.

Table 3.2.1. *AIC values for all models*

	ACE	**ADE**	**DE**	**AE**	**CE**	**E**
PNS-Ad1	2.48	–1.02	**–3.02**	0.48	10.93	18.99
SPPW-SPP	3.40	3.72	4.74	1.71	4.69	29.32
U-MPW	–5.66	–5.65	–5.83	**–7.64**	–1.88	24.46
PPW-TPP	4.09	4.29	3.30	**2.29**	2.81	15.77
LPW-V	14.57	16.02	15.03	14.02	**12.56**	14.07
PCV-AH	3.71	8.60	11.73	6.60	**1.82**	44.24
S-N	–0.36	–2.16	**–3.90**	–2.36	25.66	54.44
N-Me	–7.86	–1.45	6.41	–3.45	9.48	114.47
S-Go	**2.04**	12.45	21.17	10.49	8.41	115.43
PNS-ANS	–7.19	–7.76	**–9.71**	–9.19	–4.96	3.55
SPW	–10.47	–10.21	–10.65	**–12.21**	–11.55	0.82
SPL	6.84	1.93	**–0.07**	4.84	40.90	64.09
PNS-AH	–8.52	–8.50	–6.41	**–10.5**	33.87	95.01
ANS-AH	–7.51	–7.52	–6.3	**–9.51**	47.11	113.63
ANS-V	–3.02	–2.94	0.2	**–4.94**	28.8	81.16
Go-Gn	**–4.29**	–0.68	3.26	–2.68	–1.08	70.22
SNA	–2.89	–2.89	–3.2	**–4.78**	28.49	94.44
SNB	–2.77	–2.87	–3.66	**–4.77**	28.49	94.44
ANB	3.36	2.44	1.44	**1.35**	32.2	64.97
SN-MP	–0.49	4.54	6.86	2.54	**–2.5**	33.25
Ulip-E	–9.25	9.72	–10.93	**–11.25**	12.09	53.27
Llip-E	–3.00	–4.28	**–6.19**	–5.00	21.44	65.40
WITs	2.52	–1.25	**–3.25**	0.52	22.21	39.98

E – specific environmental factors; CE – common and specific environmental factors; AE – additive genetic factors and specific environmental factors; ACE – additive genetic factors, common environmental factors, and specific environmental factors; ADE – additive genetic factors, dominant genetic factors, and specific environment; DE – dominant genetic factors and specific environmental factors; values in **bold** – best-fitting models (lowest AIC values).

Table 3.2.2. *Best-fitting models for each variable*

	a^2	SE (a^2)	d^2	SE (d^2)	c^2	SE (c^2)	e^2	SE (e^2)
PNS-Ad1 (DE)			0.51	0.08			0.19	0.08
SPPW-SPP (AE)	0.64	0.08					0.24	0.08
U-MPW (AE)	0.50	0.08					0.22	0.07
PPW-TPP (AE)	0.24	0.09					0.38	0.09
LPW-V (CE)					0.20	0.10	0.63	0.10
PCV-AH (CE)					0.47	0.06	0.28	0.06
S-N (DE)			0.77	0.04			0.09	0.04
N-Me (ACE)	0.21	0.02			0.14	0.14	0.05	0.02
S-Go (ACE)	0.89	0.13			0.3	0.12	0.07	0.02
PNS-ANS (DE)			0.48	0.08			0.21	0.08
SPW (AE)	0.46	0.08					0.24	0.08
SPL (DE)			0.81	0.03			0.08	0.03
PNS-AH (AE)	0.9	0.02					0.4	0.02
ANS-AH (AE)	0.92	0.01					0.03	0.01
ANS-V (AE)	0.86	0.02					0.06	0.02
Go-Gn (ACE)	0.05	0.2					0.23	0.04
SNA (AE)	0.78	0.03					0.09	0.03
SNB (AE)	0.84	0.02					0.07	0.02
ANB (AE)	0.8	0.03					0.08	0.03
SN-MP (CE)					0.42	0.69	0.3	0.07
Ulip-E (AE)	0.75	0.04					0.1	0.04
Llip-E (DE)			0.76	0.04			0.1	0.04
WITs (DE)			0.7	0.05			0.12	0.05

a^2 – additive genetic factors; d^2 – dominant genetic factors; c^2 – common environmental factors; e^2 – specific environmental factors; SE – standard error.

Upper airway dimension: Variables such as SPPW-SPP and U-MPW demonstrated moderate to high heritability, with the AE model being the best fit, $a^2 = 0.64$ and 0.5, respectively. PNS-Ad1 exhibited strong dominant genetic determination (DE model, $d^2 = 0.51$).

Soft Palate Dimensions: The soft palate (SPL) length was mainly influenced by dominant genetic factors, while its width (SPW) showed moderate additive genetic influence.

Skeletal Variables: Most skeletal variables demonstrated genetic determination: Maxilla-hyoid relationships showed strong additive genetic influence. Additive genetic and specific environmental influences primarily affected sagittal mandibular positioning (SNA, SNB).

Principal Component Analysis: The data were reduced to five principal components, which jointly explained 36.8 % of the total variance. Figures 3.2.1. and 3.2.2. illustrate the correlation densities and biplot analysis.

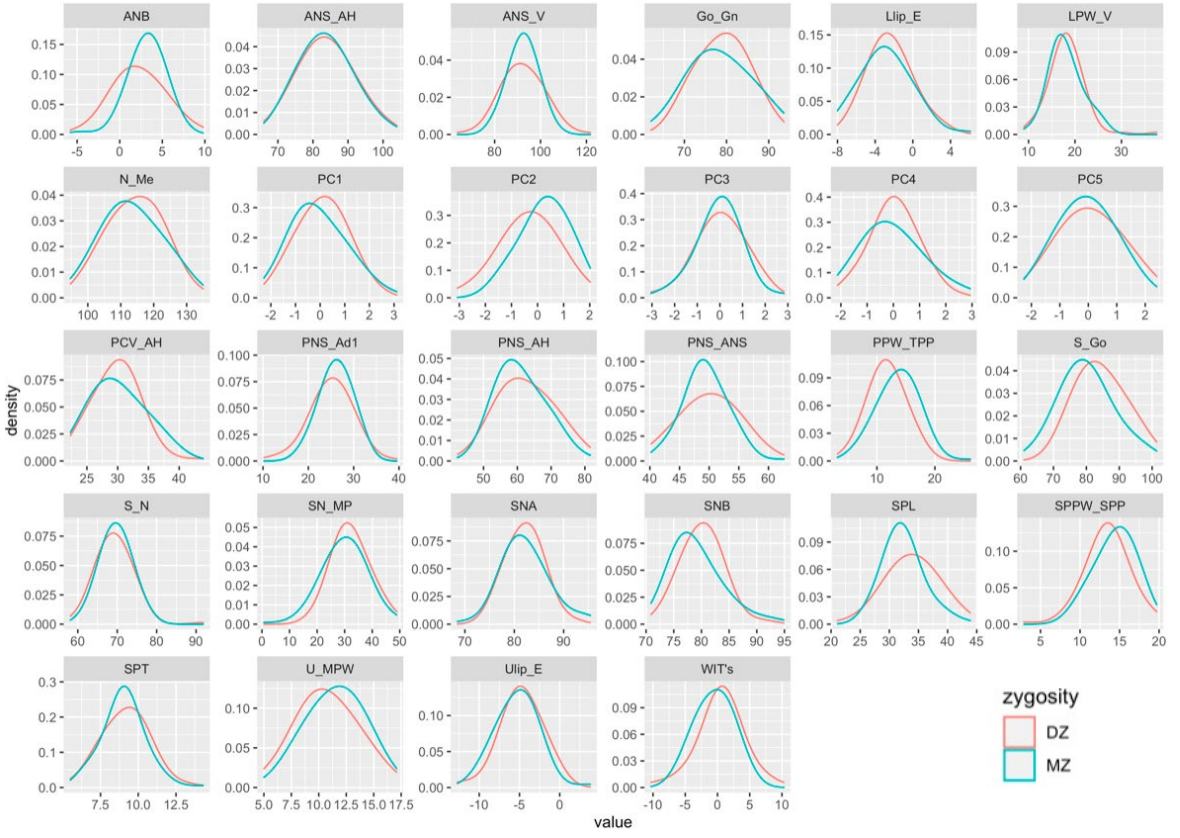


Fig. 3.2.1. *Correlation coefficient densities of airway and craniofacial cephalometric variables*

MZ monozygotic twins, DZ dizygotic twins, ANB-angle formed by SNA and SNB; ANS-AH – distance between ANS and AH; ANS-V – distance between ANS and V; Go-Gn – distance between Go and Gn; Llip-E – distance between lower lip anterior border and E line; LPW-V – distance between LPW and V; N-Me – distance between N and Me; PCV-AH – distance between PCV and AH; PNS-Ad1 – distance between

PNS and Ad1; PNS- AH – distance between PNS and AH; PNS-ANS – distance between PNS and ANS; PPW- TPP – distance between PPW and TPP; S-Go – distance between S and Go; S-N – distance between S and N; SN-MP – angle formed by Go-Me; SNA – angle determined by points S, N and A; SNB – angle determined by points S, N, B; SPL – soft palate length; SPPW-SPP – distance between SPPW and SPP; SPT – soft palate width; U-MPW – distance between U and MPW; Ulip-E – distance between upper lip anterior border and E line; Wits – distance perpendicular to points A and B onto the occlusal plane in mm.

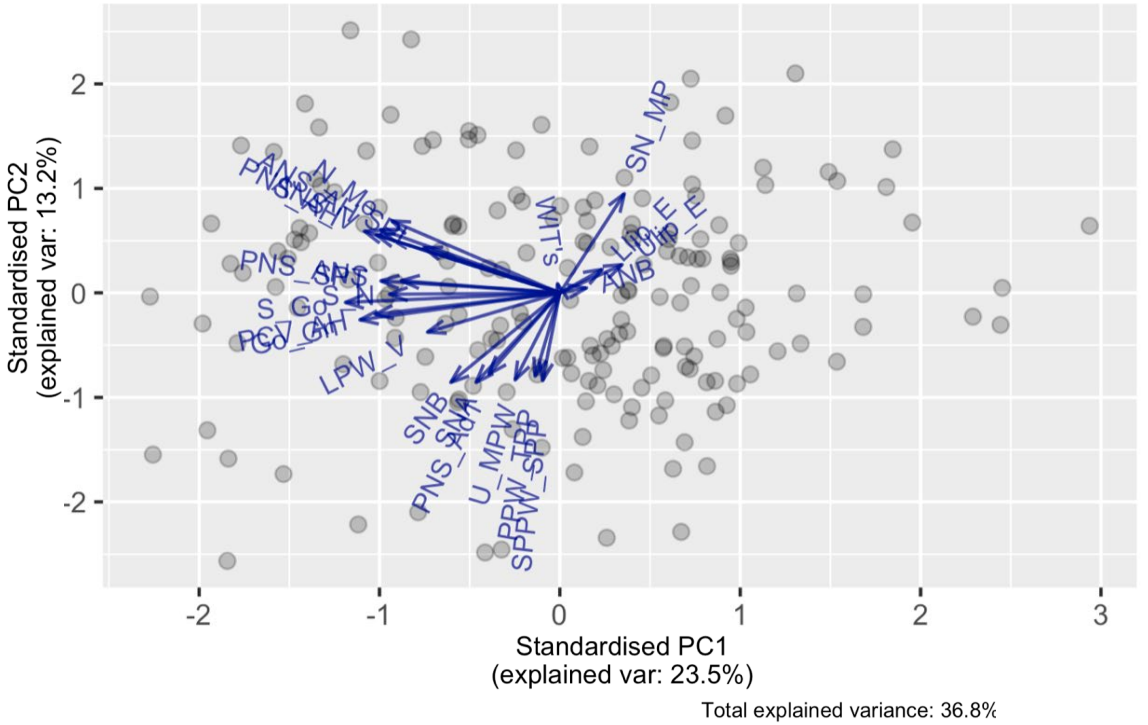


Fig. 3.2.2. *Principal component biplot*

3.3. Genetic and environmental contributions to mandibular morphology and relationship to cranial base and maxilla

The growth and formation of mandible have a major impact on the occlusion and is closely related to and dependent on breathing function and airway morphology. The results of model fitting analysis displaying genetic and environmental impact on mandible morphology cephalometric characteristics are summarized in Tables 3.3.1 and 3.3.2.

Table 3.3.1. *AIC values of all models*

Variable	ACE	ADE	AE	CE	DE	E
SNA (°)	−0.10	−0.10	**−2.10**	10.34	−1.04	87.24
SNB (°)	−6.78	−5.17	**−7.17**	0.81	−2.36	98.61
SNPog (°)	**−6.27**	−3.72	−5.72	−0.82	−0.03	97.55
NSBa (°)	−3.96	−3.96	**−5.96**	12.94	−3.97	91.48
NSAr (°)	−1.72	−2.05	**−3.72**	13.26	−3.64	80.94
NAPog (°)	−4.37	−4.23	**−6.23**	10.38	−2.73	87.50
SN–GoMe (°)	**−10.91**	−7.51	−9.51	−7.55	−2.83	83.45
ANSPNS–GoMe (°)	**−6.14**	−3.23	−5.23	−1.75	0.73	94.60
SN–ArRp (°)	−6.60	−6.70	**−8.60**	9.45	−7.60	79.26
PoOr–GoMe (°)	**−9.16**	−5.19	−7.19	−6.05	−0.16	89.22
NGnGo (°)	−9.38	−8.81	**−10.81**	2.83	−6.32	87.04
DcXiPm (°)	−8.87	−8.45	**−10.45**	−1.09	−6.59	65.49
ArRp–MB1Me (°)	−9.68	−10.36	−11.68	16.13	**−11.89**	88.65
CoGoMe (°)	−10.08	−9.55	**−11.55**	−3.66	−7.95	66.25
ArGoMe (°)	−10.73	−10.83	**−12.73**	6.86	−11.53	77.10
ai.ii–NB (°)	−3.40	−3.41	**−5.40**	5.29	−4.04	58.48
ai.ii–GoMe (°)	−4.11	−3.37	**−5.37**	1.30	−0.97	63.32
CoA (mm)	**−8.09**	−2.24	−4.24	9.05	5.78	157.25
CoGo (mm)	**−8.56**	−1.21	−3.21	−6.51	7.21	95.97
CoPog (mm)	**−7.06**	11.59	9.59	−1.80	24.23	185.25
CoB (mm)	**−8.40**	11.18	9.18	−3.79	23.99	185.22
ArB (mm)	**−11.16**	7.07	5.07	−0.57	19.94	201.11
ArA (mm)	**−6.15**	1.16	−0.84	12.71	10.28	172.45
Pog ⊥ NB (mm)	2.97	3.69	**1.69**	19.03	5.88	126.10
GoGn (mm)	**−9.49**	0.74	−1.26	4.07	10.57	174.38
GoPog (mm)	**−8.75**	3.50	1.50	1.82	14.30	173.61
XiPm (mm)	**−10.28**	4.79	2.79	5.98	16.93	204.94
R1R2 (mm)	**−1.15**	2.92	0.92	2.49	8.39	98.49
NMe (mm)	**−9.74**	7.47	5.47	1.12	19.74	200.72
NANS (mm)	−8.25	4.89	2.89	**−9.43**	13.28	115.68
ANSMe (mm)	**−10.13**	−0.15	−2.15	4.92	9.94	174.85

Table 3.3.1 cont.

Variable	ACE	ADE	AE	CE	DE	E
SGo (mm)	**−10.18**	1.36	−0.64	−7.30	11.92	127.21
ii ⊥ NB (mm)	−0.17	0.02	**−1.98**	21.84	1.44	124.20
ii ⊥ APog (mm)	−4.75	−5.89	−6.75	33.81	**−7.60**	117.77
ii ⊥ GoMe (mm)	**−9.45**	−2.58	−4.58	19.15	7.44	184.65
ms ⊥ GoMe (mm)	−7.84	−0.02	−2.02	**−8.22**	7.82	80.30
OB (mm)	−1.24	−3.39	−3.24	18.46	**−5.36**	56.78
OJ (mm)	−6.33	−3.94	−5.94	**−7.88**	−1.93	31.03
MB2 ⊥ MB1Me (mm)	−3.53	−3.16	**−5.16**	1.62	−1.63	55.71

E – specific environment; CE – common and specific environment; AE – additive genes and specific environment; ACE – additive genes, common and specific environment; ADE – additive genes, dominant genetic factor, specific environment; DE – dominant genetic factor and specific environment; PC – principal component; Values in **bold** – best-fitting model (lowest AIC value).

Table 3.3.2. *Path coefficients of the most parsimonious model for each variable*

		Genetic				Environment			
Variable	**Model**	**a^2**	**SE**	**d^2**	**SE**	**c^2**	**SE**	**e^2**	**SE**
Mandibular relationship to cranial base and maxillary structures									
SNA (°)	AE	0.74	0.04					0.26	0.04
SNB (°)	AE	0.79	0.04					0.21	0.04
SNPog (°)	ACE	0.42	0.18			0.36	0.17	0.22	0.04
NSBa (°)	AE	0.79	0.04					0.21	0.04
NSAr (°)	AE	0.75	0.04					0.25	0.04
NAPog (°)	AE	0.78	0.04					0.22	0.04
SN–GoMe (°)	ACE	0.36	0.19			0.39	0.17	0.24	0.04
ANSPNS–GoMe (°)	ACE	0.39	0.18			0.38	0.17	0.23	0.04
NMe (mm)	ACE	0.24	0.09			0.68	0.09	0.09	0.02
NANS (mm)	CE					0.77	0.03	0.23	0.03
ANSMe (mm)	ACE	0.34	0.12			0.56	0.12	0.10	0.02
CoA (mm)	ACE	0.43	0.14			0.45	0.14	0.12	0.02
ArA (mm)	ACE	0.41	0.13			0.49	0.13	0.10	0.02
SN–ArRp (°)	AE	0.76	0.04					0.24	0.04
PoOr–GoMe (°)	ACE	0.34	0.18			0.42	0.17	0.24	0.04
NGnGo (°)	AE	0.79	0.04					0.21	0.04
SGo (mm)	ACE	0.24	0.13			0.60	0.12	0.17	0.03
Mandibular skeletal variables									
DcXiPm (°)	AE	0.74	0.04					0.26	0.04
CoGoMe (°)	AE	0.73	0.04					0.27	0.04
CoB (mm)	ACE	0.18	0.09			0.71	0.09	0.11	0.02

Table 3.3.2 cont.

		Genetic				Environment			
Variable	**Model**	**a^2**	**SE**	**d^2**	**SE**	**c^2**	**SE**	**e^2**	**SE**
ArB (mm)	ACE	0.23	0.09			0.68	0.09	0.08	0.02
GoGn (mm)	ACE	0.33	0.12			0.57	0.12	0.10	0.02
XiPm (mm)	ACE	0.28	0.10			0.64	0.10	0.08	0.01
R1R2 (mm)	ACE	0.35	0.18			0.42	0.17	0.23	0.04
MB2 ⊥ MB1Me (mm)	AE	0.68	0.05					0.32	0.05
CoPog (mm)	ACE	0.20	0.09			0.70	0.09	0.11	0.02
ArRp–MB1Me (°)	DE			0.81	0.03			0.19	0.03
ArGoMe (°)	AE	0.77	0.04					0.23	0.04
CoGo (mm)	ACE	0.27	0.16			0.50	0.14	0.22	0.04
GoPog (mm)	ACE	0.29	0.11			0.60	0.11	0.11	0.02
Dento-alveolar variables									
Pog ⊥ NB (mm)	AE	0.83	0.03					0.17	0.03
ai.ii–NB (°)	AE	0.69	0.05					0.31	0.05
ii ⊥ NB (mm)	AE	0.84	0.03					0.16	0.03
ii ⊥ APog (mm)	DE			0.85	0.03			0.15	0.03
ii ⊥ GoMe (mm)	ACE	0.46	0.13			0.46	0.13	0.08	0.02
ms ⊥ GoMe (mm)	CE					0.69	0.04	0.31	0.04
OB (mm)	DE			0.74	0.05			0.26	0.05
OJ (mm)	CE					0.50	0.06	0.50	0.06
ai.ii–GoMe (°)	AE	0.71	0.05					0.29	0.05

a^2 – additive genetic factors; d^2 – dominant genetic factors; c^2 – common environment factors; e^2 – specific environment factors; SE – standard error.

The error analysis revealed no statistically significant differences between the initial and repeated measurements.

Sagittal mandibular relationship to cranial base and maxilla. Linear variables (NMe, ANSMe, CoA, ArA, and SGo) showed contributions from additive genetic factors (a^2 = 24–43 %), shared environmental factors (c^2 = 45–68 %), and unique environmental factors (e^2 = 9–17 %). One linear variable, NANS, was influenced solely by environmental factors (c^2 = 77 %, e^2 = 23 %). Angular variables (SNA, SNB, NSBa, NSAr, NAPog, SN–ArRp, and NGnGo) exhibited strong additive genetic determination (a^2 = 74–79 %). Four angular variables (SNPog, SN–GoMe, ANSPNS–GoMe, and PoOr–GoMe) were influenced by both genetic and environmental factors (ACE model).

Mandibular skeletal variables. The ACE model best explained linear variables, except MB2 ⊥ MB1Me, which followed the AE model. Angular variables (DcXiPm, CoGoMe, ArGoMe) demonstrated high additive genetic

determination (a^2 = 73–77 %), while ArRp–MB1Me was best explained by the DE model (d^2 = 81 %).

Mandibular dento-alveolar variables. Angular variables (ai.ii–NB, ai.ii–GoMe) were influenced by the AE model (a^2 = 69–71 %). Linear variables demonstrated diverse influences: AE model: Pog ⊥ NB, ii ⊥ NB (a^2 = 83–84 %) – CE model: ms ⊥ GoMe, OJ. ACE model: ii ⊥ GoMe.

Principal component analysis. Six principal components explained 83 % of the variance: PC1 (linear variables, except Pog ⊥ NB, ii ⊥ NB, ii ⊥ APog, OB, OJ, MB2 ⊥ MB1Me) followed the ACE model. PC2–PC5: Included angular and select linear variables, with high additive genetic determination (a^2 = 76–79 %) and best-fitting AE models. PC6: Comprised of NAPog, OB, and OJ, best explained by the DE model.

3.4. Genetic and environmental determinants of palatal morphology

The error analysis results found no significant differences between the initial and repeated measurements. Males exhibited slightly greater dental arch width at the occlusal plane than females. The most notable difference was observed for 1IPW ($p < 0.01$). Differences in the canine and molar regions were statistically significant but less pronounced ($p < 0.05$). Though not statistically significant, dental arch widths at the gingival line were bigger in males. Palatal height, surface area, and volume were significantly greater in males than in females ($p < 0.01$) (Table 3.4.1).

Table 3.4.1. *Descriptive statistics of the dental arch and palate parameters*

Variables	Males (n = 38)	Females (n = 47)	MZ (n = 50)	DZ (n = 35)	p Males vs. Females	p MZ*vs*DZ
Dental arch widths at occlusal line (mm)						
ICW	34.54 ± 1.93	33.83 ± 2.3	34.27 ± 2.16	33.98 ± 2.17	0.034	0.399
1IPW	41.40 ± 2.47	40.40 ± 2.25	40.98 ± 2.58	40.66 ± 2.15	0.006	0.391
2IPW	46.78 ± 2.81	45.85 ± 2.37	46.3 ± 2.74	46.22 ± 2.43	0.02	0.851
IMW	51.31 ± 3.68	50.35 ± 2.63	50.94 ± 3.36	50.56 ± 2.89	0.049	0.442
Dental arch widths at gingival line (mm)						
ICWG	24.68 ± 1.55	24.97 ± 1.83	25.08 ± 1.78	24.49 ± 1.56	0.276	0.028
1IPWG	27.62 ± 2.39	26.88 ± 2.09	27.19 ± 2.53	27.24 ± 1.79	0.032	0.869
2IPWG	32.62 ± 2.75	32.08 ± 2.7	32.19 ± 2.79	32.51 ± 2.66	0.201	0.454
IMWG	34.75 ± 3.23	34.16 ± 2.47	34.49 ± 3.22	34.33 ± 2.19	0.186	0.709
Palatal heights (mm)						
ICH	5.01 ± 1.39	5.21 ± 1.57	5.22 ± 1.43	4.98 ± 1.33	0.343	0.269
1IPH	11.25 ± 1.83	11.08 ± 1.73	11.22 ± 1.9	11.06 ± 1.56	0.529	0.545
2IPH	15.83 ± 1.81	14.86 ± 1.77	15.24 ± 1..87	15.37 ± 1.84	0.001	0.651
IMH	16.61 ± 2.03	15.17 ± 1.85	15.76 ± 2.02	15.89 ± 2.13	0.001	0.668
Maxillary arch depth (mm), MD	28.12 ± 1.7	27.58 ± 2.22	28.25 ± 1.61	27.2 ± 2.36	0.078	0.124
Palate surface area (mm^2), PSA	1385.81 ± 144.85	1304.72 ± 123.04	1346.38 ± 141.78	1333.24 ± 135.17	0.001	0.545
Palate volume (mm^3), PV	7530.67 ± 1395.93	6944.55 ± 1072.3	7245.99 ± 1332.85	7150.28 ± 1150.09	0.002	0.627

1IPH – interfirst premolar palate height; 1IPWG – interfirst premolar width at the gum line; 2IPH – intersecond premolar palate height; 2IPW – intersecond premolar width; 2IPWG – intersecond premolar width at the gum line; DZ – dizygotic twin; ICH – intercanine palate height; ICW – intercanine width; ICWG – intercanine width at the gum line; IPW – interfirst premolar width; IMH – interfirst molar height; IMW – interfirst molar width; IMWG – interfirst molar distance at the gum line; MD – maxillary depth; MZ – monozygotic twin; PSA – palate surface area; PV – palate volume. All values are presented as mean ± standard deviation.

Genetic analysis: AIC values were calculated (Table 3.4.2). The AE and DE models best fit most variables(Table 3.4.3). Interdental distances (1IPW, 2IPW, IMW) exhibited high genetic determination (AE model, a^2 = 0.76, 0.72, and 0.86, respectively). ICW demonstrated strong dominant genetic determination (DE model, d^2 = 0.59). Palatal gum line distances (ICWG, 1IPWG, 2IPWG) were predominantly influenced by dominant genetic factors (d^2 = 0.50, 0.78, and 0.81, respectively). Genetic factors influenced palatal volume and surface area (a^2 = 0.62). Heritability estimates were high for all widths, maxillary depths, palatal surface, and palatal volume, ranging from 0.48 to 0.8.

Table 3.4.2. *AIC values of all models*

Variables	ACE	ADE	DE	AE	CE	E
Dental arch widths at occlusal line						
ICW	−3.12	−5.53	**−7.54**	−5.12	9.34	30.13
1IPW	−6.53	−6.81	−8.35	**−8.53**	13.26	64.47
2IPW	−7.83	−7.31	−5.98	**−9.31**	3.24	63.78
IMW	−6.41	−6.41	−6.47	**−8.41**	25.47	93.16
Dental arch widths at gingival line						
ICWG	5.97	3.41	**1.41**	3.97	14.7	32.32
1IPWG	2.35	0.48	**−1.52**	0.35	27.37	77.6
2IPWG	1.24	−2.72	**−4.72**	−0.76	36.8	71.27
IMWG	0.2	1.14	2.04	**−0.86**	10.65	86.54
Palatal heights						
ICH	7.25	2.96	**0.96**	5.25	17.13	28.33
1IPH	−5.02	−5.43	**−7.34**	−7.02	2.01	33.3
2IPH	−10.93	−9.42	−6.82	**−11.42**	−5.83	50.04
IMH	−8.65	8.33	−6.45	**−10.33**	9.46	68.81
Maxillary arch depth						
MD	8.32	8.35	8.88	**6.35**	13.27	37.46
Palate surface area and volume						
PSA	−4.14	−3.16	43.84	**−5.26**	−1.57	41.84
PV	−7.44	−6.27	54.52	**−8.28**	−3.11	52.52
Principal component						
PC1	−3.42	−4.01	**−5.83**	−5.42	25.42	84.8
PC2	−9.77	−9.77	−10.52	**−11.77**	−2.44	35.34
PC3	1.67	−1.87	**−3.88**	−0.33	27.92	49.37

ACE – additive genetic factors, common environmental factors, and specific environmental factors; ADE – additive genetic factors, dominant genetic factors, and specific environment; AE – additive genetic factors and specific environmental factors; CE – common and specific

environmental factors; DE – dominant genetic factors and specific environmental factors; E – specific environmental factors; ICH – intercanine palate height; ICW – intercanine width; ICWG – interfirst premolar width; ICWG – intercanine width at the gum line; IMH – interfirst molar height; IMW – interfirst molar width; IMWG – interfirst molar distance at the gum line; 1IPH – interfirst premolar palate height; 2IPH – intersecond premolar palate height; 2IPW – intersecond premolar width; 1IPWG – interfirst premolar width at the gum line; 2IPWG – intersecond premolar width at the gum line; MD – maxillary depth; PSA – palate surface area; PV – palate volume. Notes: Best-fitting models (lowest AIC values) are indicated in **bold**.

Table 3.4.3. *Best-fitting models for each variable*

Variables	a^2	SE (a^2)	d^2	SE (d^2)	c^2	SE (c^2)	e^2	SE (e^2)
Dental arch widths at occlusal line								
ICW (DE)			0.59	0.06			0.17	0.06
1IPW (AE)	0.76	0.04					0.1	0.04
2IPW (AE)	0.72	0.04					0.1	0.04
IMW (AE)	0.86	0.02					0.06	0.02
Dental arch widths at gingival line								
ICWG (DE)			0.5	0.07			0.22	0.07
1IPWG (DE)			0.78	0.03			0.09	0.03
2IPWG (DE)			0.81	0.03			0.08	0.03
IMWG (AE)	0.78	0.03					0.09	0.03
Palatal heights								
ICH (DE)			0.48	0.08			0.22	0. 8
1IPH (DE)			0.56	0.06			0.19	0.06
2IPH (AE)	0.7	0.04					0.13	0.04
IMH (AE)	0.8	0.03					0.08	0.03
Maxillary arch depth								
MD (AE)	0.56	0.07					0.18	0.07
Palate surface area and volume								
PA (AE)	0.61	0.05					0.18	0.05
PV (AE)	0.69	0.04					0.15	0.04
Principal components								
PC1 (DE)			0.82	0.03			0.07	0.03
PC2 (AE)	0.62	0.06					0.16	0.06
PC3 (DE)			0.76	0.04			0.09	0.036

1IPH – interfirst premolar palate height; 1IPWG – interfirst premolar width at the gum line; 2IPH – intersecond premolar palate height; 2IPW – intersecond premolar width; 2IPWG – intersecond premolar width at the gum line; a^2 – additive genetic factors; d^2 – dominant genetic factors; c^2 – common environmental factors; e^2 – specific environmental factors; ICH

– intercanine palate height; ICW – intercanine width; ICWG – intercanine width at the gum line; ICWG – interfirst premolar width; IMH – interfirst molar height; IMW – interfirst molar width; IMWG – interfirst molar distance at the gum line; MD – maxillary depth; PSA – palate surface area; PV – palate volume; SE – standard error.

Principal Component Analysis: Three principal components explained 69.3 % of the total variance (Figure 3.4.1 and Figure 3.4.2).

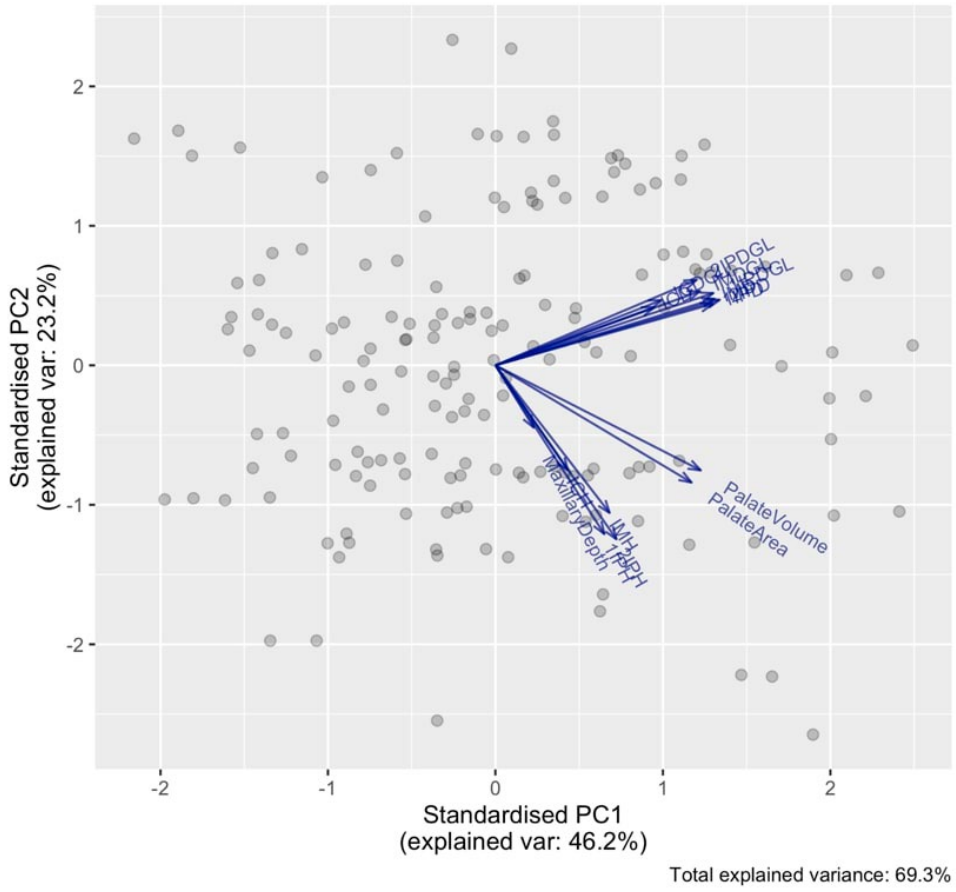


Fig. 3.4.1. *Principal components biplot*

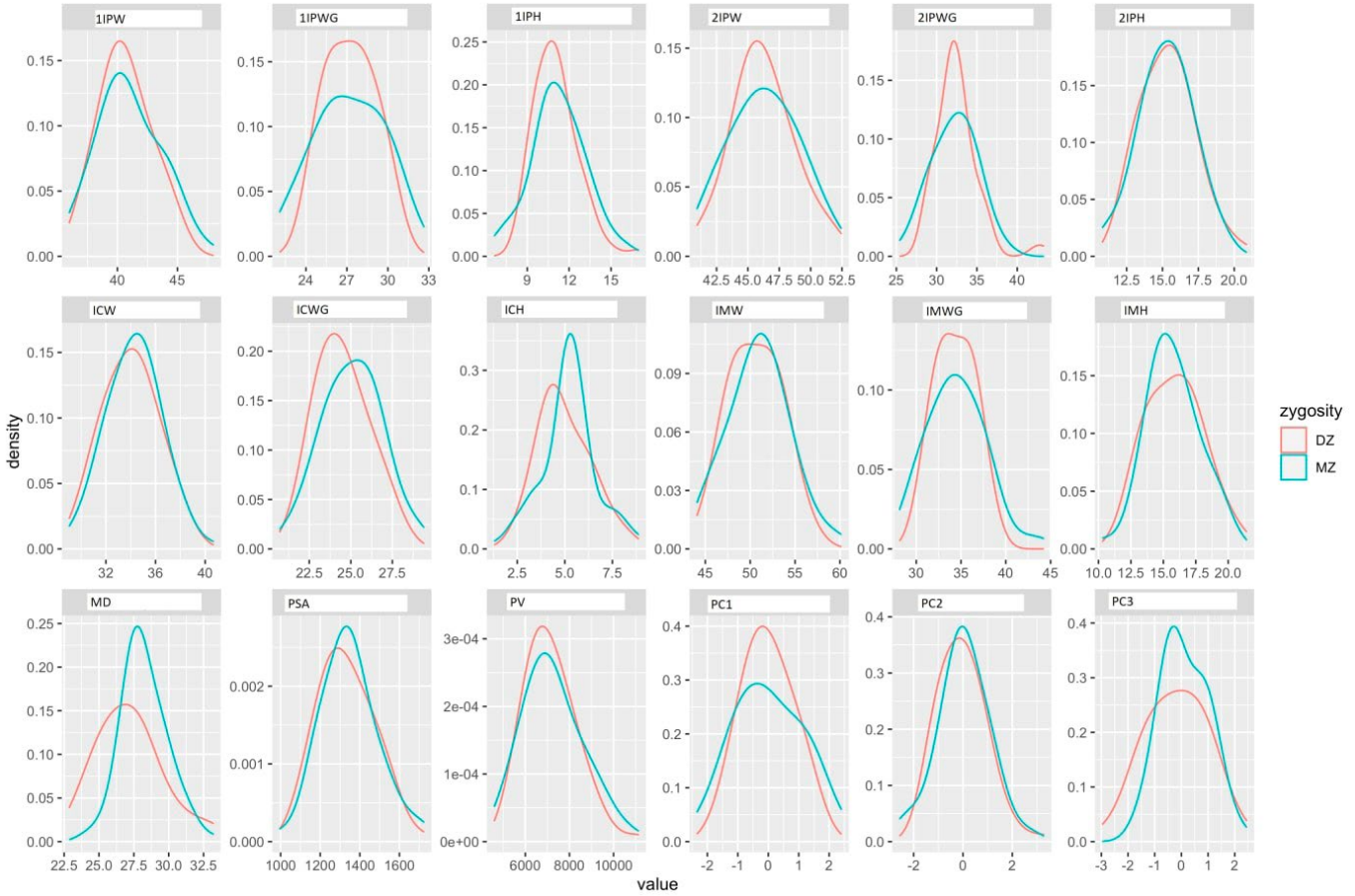


Fig. 3.4.2. *Correlation coefficient densities of palatal variables*

3.5. Relationships between occlusal characteristics, upper dental arche morphology, palate dimensions and upper airway parameters.

The study consisted of 53 twin pairs with a mean age of 17.82 and a standard deviation of 3.05. Table 3.5.1 presents the correlation coefficients (r) and p-values between various palatal dimensions and upper airway parameters. Statistically significant results ($p < 0.05$) are highlighted with an asterisk (*). Figure 3.5.1 demonstrates the correlation heatmap of palatal and upper airway dimensions. Significant correlations were observed between palatal parameters and upper airway dimensions:intercanine distance ((ICD) (GL)) correlated with ANS–AH distance ($r = 0.19$, $p = 0.046$) and ANS–V distance ($r = 0.21$, $p = 0.029$), suggesting a link between arch width and airway space. Intercanine height (ICH) correlated with ANS–AH distance ($r = 0.26$, $p = 0.007$) and ANS–V distance ($r = 0.27$, $p = 0.005$), indicating a vertical influence on airway dimensions. Palate surface area and volume correlated with PCV–AH ($p = 0.002$, $p = 0.003$) and soft palate width (SPW) ($p = 0.047$, $p = 0.035$), reinforcing their importance in airway structure.

Table 3.5.1. *Relationship between palatal dimensions and upper airway parameters*

Palatal Dimension	PNS-AD1	SPPW-SPP	U-MPW	PPW-TPP	LPW-V	PCV-AH	SPT	SPL	PNS-AH	ANS-AH	ANS-V
ICD	-0.08 (0.389)	-0.03 (0.761)	0 (0.98)	0.05 (0.634)	-0.06 (.0.55)	0.16 (0.103)	-0.02 (0.828)	0.06 (0.514)	0.11 (0.256)	-0.01 (0.88)	0.05 (0.622)
ICD (GL)	-0.03 (0.796)	-0.02 (0.802)	-0.13 (0.184)	-0.05 (0.642)	-0.12 (0.229)	0.01 (0.901)	0.06 (0.510)	0.15 (0.128)	0.13 (0.168)	0.19 (0.046) *	0.21 (0.029) *
ICH	-0.06 (0.533)	0.11 (0.248)	0.06 (0.545)	0.03 (0.754)	-0.14 (0.149)	0.00 (0.985)	0.08 (0.423)	-0.06 (0.551)	0.13 (0.182)	0.26 (0.007) *	0.27 (0.005) *
1IPD	-0.01	0.04	0.13	0.17	0.08	0.43	0.19	0.13	0.22	0.04	0.17
	(0.953)	(0.682)	(0.178)	(0.083)	(0.413)	(0.001) *	(0.051)	(0.197)	(0.022) *	(0.656)	(0.077)
1IPD (GL)	0.13 (0.175)	0.09 (0.370)	0.07 (0.473)	0.13 (0.183)	0.07 (0.486)	0.37 (<0.001) *	0.24 (0.015) *	0.11 (0.244)	0.23 (0.019) *	0.07 (0.479)	0.10 (0.333)
1IPH	0.05 (0.596)	0.08 (0.601)	-0.02 (0.892)	-0.04 (0.816)	0.03 (0.890)	0.30 (0.002) *	0.21 (0.047) *	0.14 (0.151)	0.26 (0.007) *	0.19 (0.052)	0.17 (0.080)
2IPD	-0.01	-0.01	0.12	0.08	0.11	0.37	0.19	0.1	0.21	0.04	0.14
	(0.904)	(0.938)	(0.237)	(0.417)	(0.257)	(0.001) *	(0.052)	(0.291)	(0.03) *	(0.688)	(0.159)
2IPD (GL)	0.10 (0.289)	0.03 (0.772)	0.03 (0.797)	0.05 (0.647)	0.09 (0.334)	0.27 (0.005) *	0.10 (0.313)	0.11 (0.281)	0.13 (0.185)	-0.01 (0.935)	0.01 (0.926)
2IPH	0.07 (0.491)	0.06 (0.563)	0.01 (0.926)	-0.02 (0.839)	0.04 (0.676)	0.29 (0.003) *	0.20 (0.035) *	0.11 (0.245)	0.24 (0.015) *	0.12 (0.218)	0.10 (0.325)
IMD	0	0	0.12	0.11	0.09	0.36	0.18	0.07	0.17	0	0.08
	(0.994)	(0.983)	(0.22)	(0.243)	(0.362)	(0.001) *	(0.068)	(0.467)	(0.085)	(0.982)	(0.422)
IMD (GL)	0.07 (0.479)	0.04 (0.671)	0.14 (0.149)	0.12 (0.205)	0.10 (0.319)	0.33 (0.001) *	0.20 (0.043) *	0.09 (0.348)	0.13 (0.196)	-0.04 (0.661)	-0.01 (0.900)
IMH	0.04 (0.697)	-0.08 (0.392)	-0.03 (0.747)	0.10 (0.295)	0.01 (0.916)	0.14 (0.139)	0.09 (0.343)	0.00 (0.965)	-0.02 (0.845)	0.07 (0.477)	0.14 (0.148)
Maxillary depth	0.04	-0.08	-0.03	0.1	0.01	0.14	0.09	0	-0.02	0.07	0.14

Table 3.5.1 cont.

Palatal Dimension	PNS-AD1	SPPW-SPP	U-MPW	PPW-TPP	LPW-V	PCV-AH	SPT	SPL	PNS-AH	ANS-AH	ANS-V
	(0.697)	(0.392)	(0.747)	(0.295)	(0.916)	(0.139)	(0.343)	(0.965)	(0.845)	(0.477)	(0.148)
Palate area	0.05	0.05	-0.01	-0.02	0.01	0.3	0.19	0.14	0.26	0.19	0.17
	(0.596)	(0.601)	(0.892)	(0.816)	(0.89)	(0.002) *	(0.047) *	(0.151)	(0.007) *	(0.052)	(0.08) *
Palate volume	0.07	0.06	0.01	-0.02	0.04	0.29	0.2	0.11	0.24	0.12	0.1
	(0.491)	(0.563)	(0.926)	(0.839)	(0.676)	(0.003) *	(0.035) *	(0.245)	(0.015) *	(0.218)	(0.325)

Coefficients (r) and p-values between palatal dimensions and upper airway parameters. Statistically significant results ($p < 0.05$) are highlighted with an asterisk (*).

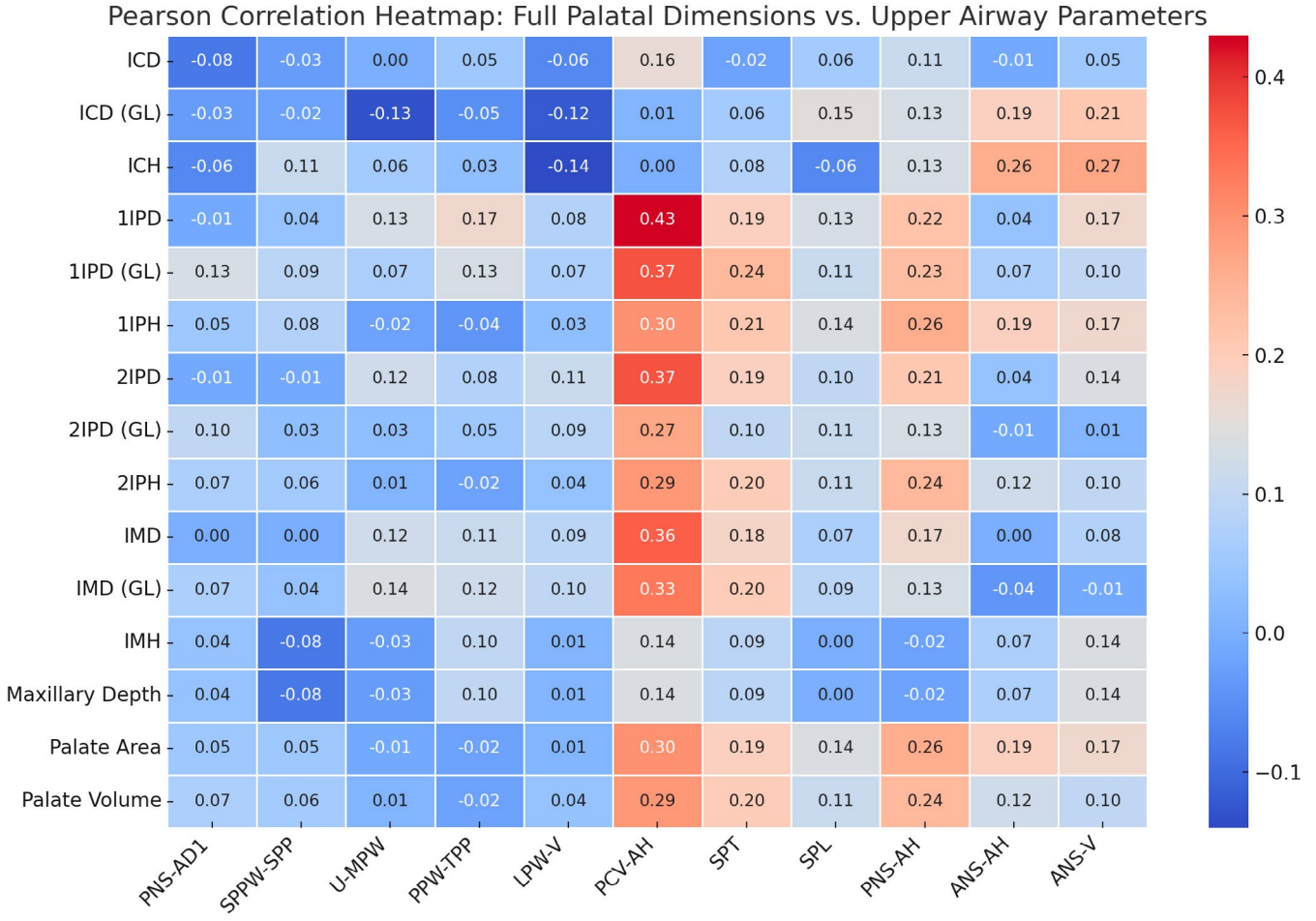


Fig. 3.5.1. *Pearson's correlation heatmap of palatal dimensions and upper airway parameters*

Additionally, significant associations were found between palatal parameters and cephalometric variables. Figure 3.5.2 demonstrates correlation heatmap of palatal dimensions and craniofacial structures. Table 3.5.2. shows correlation between palatal dimensions and craniofacial cephalometric variables. ICD (GL) correlated with ANB ($r = 0.27$, $p = 0.006$) and Wits' appraisal ($r = 0.19$, $p = 0.048$). ICH correlated with SNB ($r = 0.28$, $p = 0.004$) and ANB ($r = 0.23$, $p = 0.018$). Intermolar distance correlated with maxillary length ($r = 0.30$, $p = 0.002$) and Go-Gn distance ($r = 0.26$, $p = 0.007$). Intermolar height was associated with N-Me ($r = 0.29$, $p = 0.003$), S-Go ($r = 0.26$, $p = 0.007$), PNS-ANS ($r = 0.21$, $p = 0.03$), and Go-Gn ($r = 0.21$, $p = 0.03$). Palate area and volume demonstrated relationships with N-Me ($r = 0.37$, $p < 0.001$), S-Go ($r = 0.32$, $p = 0.001$), PNS-ANS ($r = 0.26$, $p = 0.007$), and Go-Gn ($r = 0.28$, $p = 0.004$), reinforcing their role in craniofacial development. Maxillary depth correlated significantly with N-Me ($r = 0.20$, $p = 0.038$) and ANB ($r = 0.14$, $p = 0.139$).

Table 3.5.2. *Correlation between palatal dimensions and craniofacial cephalometric variables*

Parameter	S-N	N-Me	S-Go	PNS-ANS	Go-Gn	SNA	SNB	ANB	SN-MP	Ulip-E	Llip-E	WIT's
ICD	0.02 (0.821)	0.13 (0.2)	0.07 (0.445)	0.09 (0.362)	0.13 (0.192)	0.19 (0.048) *	0.2 (0.04) *	-0.02 (0.829)	0.01 (0.917)	0.18 (0.058) *	0.21 (0.028)8	0.05 (0.627)
ICD (GL)	-0.12 (0.208)	0.09 (0.344)	-0.03 (0.738)	0.04 (0.716)	-0.02 (0.817)	0.11 (0.259)	0.01 (0.907)	0.27 (0.006) *	0.07 (0.445)	0.11 (0.262)	-0.01 (0.947)	0.19 (0.048) *
ICH	0.09 (0.369)	0.18 (0.064)	-0.13 (0.182)	0.09 (0.386)	0.07 (0.471)	-0.17 (0.076)	-0.28 (0.004) *	0.23 (0.018) *	0.16 (0.1)	0.05 (0.583)	-0.08 (0.407)	0.1 (0.301)
1IPD	0.23 (0.016) *	0.27 (0.006) *	0.28 (0.004) *	0.31 (0.001)8	0.4 (0.001) *	0.27 (0.005) *	0.32 (0.001) *	-0.14 (0.139)	-0.12 (0.216)	-0.01 (0.928)	0.03 (0.784)	0.18 (0.07)
1IPD (GL)	0.24 (0.013) *	0.18 (0.058)	0.27 (0.005) *	0.25 (0.011) *	0.35 (0.001) *	0.17 (0.079)	0.2 (0.043) *	-0.11 (0.245)	-0.06 (0.554)	-0.03 (0.744)	-0.07 (0.481)	0.07 (0.467)
1IPH	0.06 (0.518)	0.27 (0.004) *	-0.05 (0.622)	0.09 (0.339)	0.03 (0.746)	-0.28 (0.003) *	-0.38 (0.001) *	0.23 (0.019) *	0.29 (0.003) *	0.13 (0.188)	-0.03 (0.773)	0.17 (0.076)
2IPD	0.24 (0.014) *	0.3 (0.002) *	0.3 (0.002) *	0.3 (0.002) *	0.41 (0.001) *	0.17 (0.078)	0.24 (0.013) *	-0.16 (0.11)	-0.02 (0.83)	-0.09 (0.365)	-0.08 (0.419)	0.21 (0.033) *
2IPD (GL)	0.21 (0.028) *	0.11 (0.249)	0.22 (0.021) *	0.21 (0.03) *	0.28 (0.004) *	0.09 (0.38)	0.12 (0.209)	-0.11 (0.283)	-0.02 (0.852)	-0.08 (0.398)	-0.11 (0.247)	0.05 (0.604)
2IPH	0.09 (0.384)	0.37 (0.001) *	0.13 (0.186)	0.25 (0.011)8	0.16 (0.099)	-0.14 (0.165)	-0.15 (0.124)	0.07 (0.478)	0.22 (0.022) *	0.13 (0.192)	0.05 (0.603)	0.02 (0.815)
IMD	0.22 (0.026) *	0.2 (0.039) *	0.2 (0.038) *	0.26 (0.007) *	0.35 (0.001) *	0.11 (0.276)	0.18 (0.071)	-0.18 (0.058) *	0.0 (1.0)	-0.11 (0.248)	-0.12 (0.237)	0.18 (0.058)
IMD (GL)	0.18 (0.061)	0.09 (0.365)	0.18 (0.065) *	0.24 (0.013) *	0.32 (0.001) *	0.14 (0.149)	0.2 (0.04) *	-0.19 (0.056) *	-0.06 (0.52)	-0.12 (0.236)	-0.17 (0.083)	0.14 (0.147)
IMH	0.09 (0.349)	0.29 (0.003) *	0.21 (0.033) *	0.26 (0.007) *	0.26 (0.008) *	0.09 (0.385)	0.04 (0.692)	0.01 (0.92)	0.04 (0.653)	0.08 (0.393)	0.06 (0.515)	0.06 (0.529)
Maxillary depth	0.0 (0.962)	0.2 (0.038) *	-0.12 (0.238)	0.12 (0.232)	0.13 (0.184)	0.11 (0.274)	-0.01 (0.919)	0.26 (0.006) *	0.08 (0.388)	0.27 (0.005) *	0.3 (0.002) *	0.08 (0.408)

Table 3.5.2 cont.

Parameter	S-N	N-Me	S-Go	PNS-ANS	Go-Gn	SNA	SNB	ANB	SN-MP	Ulip-E	Llip-E	WIT's
Palate area	0.19 (0.048) *	0.37 (0.001) *	0.21 (0.029) *	0.29 (0.002) *	0.28 (0.003) *	0.02 (0.837)	-0.01 (0.897)	0.07 (0.508)	0.09 (0.361)	0.15 (0.119)	0.08 (0.395)	0.07 (0.461)
Palate volume	0.18 (0.065)	0.32 (0.001) *	0.19 (0.05) *	0.27 (0.006) *	0.28 (0.004) *	0.0 (0.992)	-0.02 (0.859)	0.0 (0.975)	0.09 (0.361)	0.09 (0.357)	0.01 (0.924)	0.02 (0.831)

Coefficients (r) and p-values between palatal dimensions and upper airway parameters. Statistically significant results ($p < 0.05$) are highlighted with an asterisk (*).

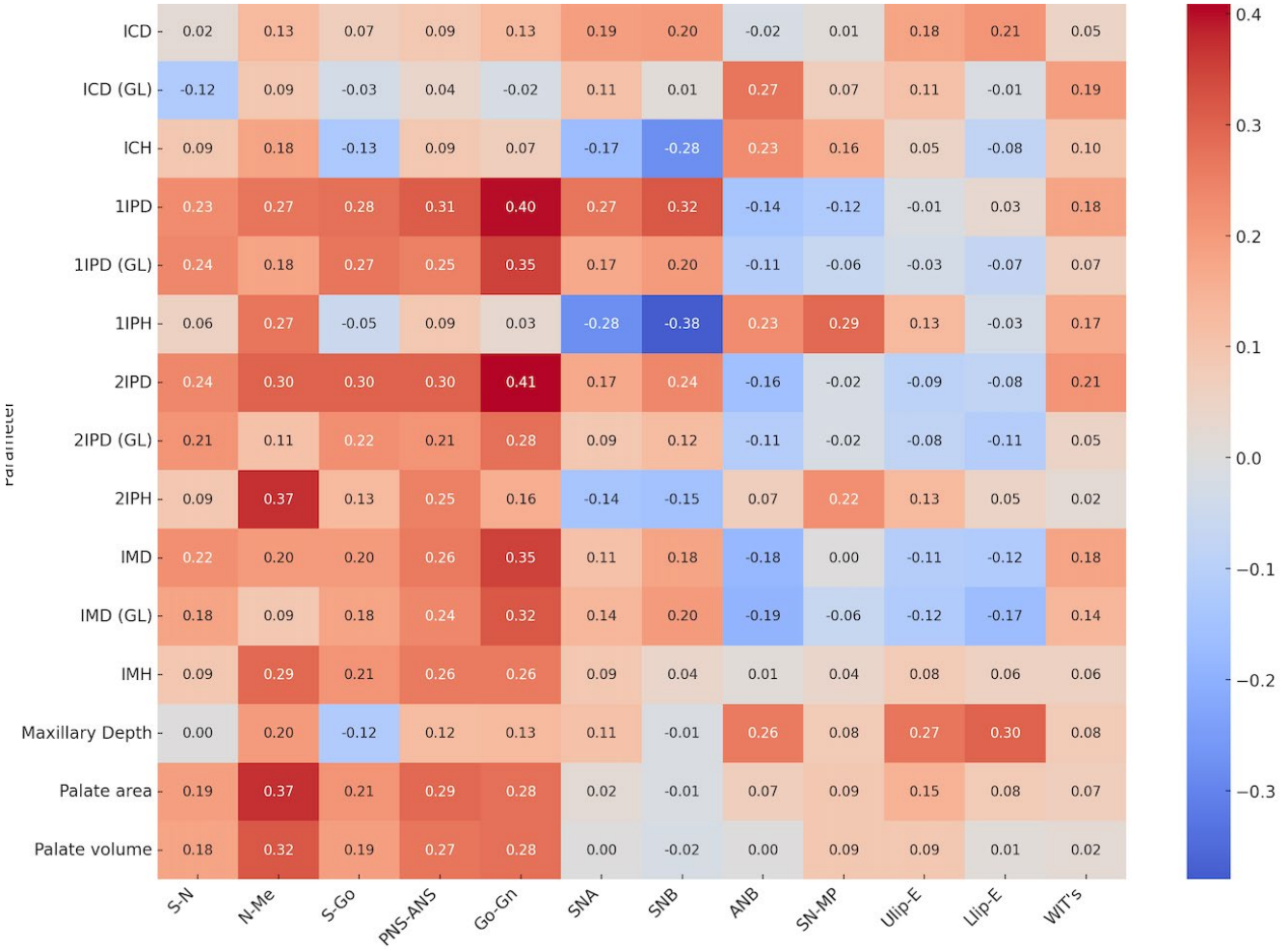


Fig. 3.5.2. *Pearson's correlation heatmap of palatal dimensions and craniofacial parameters*

4. DISCUSSION

This study integrates findings from five key publications to comprehensively understand the interplay between genetic and environmental influences on the upper airway, craniofacial structure, palate, and mandible. By analyzing these interrelationships, this research offers novel insights into the etiology of occlusal and airway pathologies, shedding light on their functional and developmental significance.

4.1. Relationship between malocclusion, nasopharyngeal pathology, and body posture

This study investigated the relationship between craniofacial morphology, nasopharyngeal pathology, and sagittal body posture, in a cohort of orthodontic patients aged 7–14. This developmental period is characterized by the transition from primary to permanent dentition, significant craniofacial growth, and the establishment of spinal curvature. Normal spinal curvature develops by age seven, while peak growth velocity occurs at approximately 12.2 years in females and 13.9 years in males [111]. During this critical phase, postural abnormalities may either self-correct or become more pronounced [111].

Our findings revealed a high prevalence of orthopedic anomalies, with kyphotic posture observed in 47.9 % of participants and thoracic rib hump in 51.1 %. These results are in line with prior studies, such as Lippold et al. [112], who reported orthopedic abnormalities in 52 % of preschool children, and Hagner et al. [113] who found postural defects in 65.71 % of 10-year-olds and 54.29 % of 13-year-olds. Additionally, nasopharyngeal pathology was highly prevalent (78.9 %), consistent with previous findings indicating that adenoid and tonsillar hypertrophy contributes to mouth breathing and affects 40–60 % of children [6,114]. In our sample, adenoid hypertrophy was present in 57.4 % and tonsillar hypertrophy in 90.3 % of patients, a rate possibly influenced by the specific characteristics of our study population.

A significant correlation was observed between sagittal body posture and vertical craniofacial parameters. Patients with kyphotic posture exhibited a reduced SNB angle, suggesting mandibular retrusion. This supports previous studies indicating that mouth breathing affects mandibular growth by promoting a downward and backward rotation pattern [115]. Furthermore, thoracic kyphosis was significantly more common in patients with naso-pharyngeal obstruction, reinforcing findings that postural changes are associated with mouth breathing [136]. Our results also revealed a significant association between kyphotic posture and a reduced SNB angle, which was

primarily observed in male patients. This sex-specific trend may be attributed to the higher prevalence of kyphotic posture among males (59.1 %) compared to females (38 %) ($p = 0.01$). These findings align with Lippold et al. [112], who reported a relationship between mandibular sagittal positioning and thoracic inclination, but no correlation between maxillary position and spinal curvature [117], a conclusion supported by our study. However, unlike Lippold et al. [118], we did not identify a significant relationship between vertical mandibular position and thoracic inclination.

Despite previous studies suggesting an association between craniocervical posture and dental arch narrowing [119–121], our study did not find significant correlations between body posture and transverse malocclusions such as posterior crossbite or dental crowding. Korbmacher et al. [122] reported that children with unilateral crossbites exhibited a higher prevalence of postural asymmetries, including oblique shoulders, oblique pelvis, leg length discrepancies, and scoliosis, compared to those with symmetrical dental arches. However, our study did not establish significant associations between body posture, nasopharyngeal pathology, and posterior crossbite. This aligns with Michelotti et al. [123], who found no significant correlation between posterior crossbite and postural stability or orthopedic asymmetries. Similarly, no association was observed between dental crowding and postural abnormalities, despite previous research by Pachi et al. [124] and Solow [119] suggesting a connection between craniocervical posture and dental crowding.

Differences in study design, sample characteristics, and orthopedic evaluation methodologies may account for these inconsistencies. Similarly, while Silvestrini-Biavati et al. [125] reported a higher prevalence of deep and open bites in children with postural abnormalities, our study did not find statistically significant differences in vertical skeletal parameters between kyphotic and regular posture groups.

The question of causality remains central: do postural and airway changes precede craniofacial adaptations, or are they secondary responses to skeletal and functional imbalances? The functional matrix theory (Moss) posits that craniofacial bone growth is influenced by surrounding soft tissue matrices, including muscles and airway volumes, while Solow's soft tissue stretching hypothesis suggests that airway obstruction leads to compensatory head extension, which in turn affects facial growth patterns [119].

Recent studies have further highlighted the link between craniofacial morphology, postural deviations, and nasopharyngeal obstruction. Saccomanno et al. [126] examined the relationship between malocclusion and scoliosis, emphasizing the importance of a multidisciplinary approach in assessing skeletal and postural anomalies. Similarly, a systematic review by Różańska-Perlińska et al. [12], analyzing data from 24 cross-sectional studies involving

6,199 participants, confirmed significant associations between postural defects, malocclusions, and airway dysfunction. Their findings suggest that nasopharyngeal pathology and poor posture exacerbate craniofacial imbalances, reinforcing the need for early intervention strategies in growing children.

Previous studies have reported that nasopharyngeal obstruction influences mandibular growth by promoting posterior rotation and increasing lower facial height [115,127]. Our results did not support this association. However, kyphotic posture was significantly more common in patients with nasopharyngeal pathology. Interestingly, Neiva et al. [116] did not report a significant increase in thoracic kyphosis among mouth-breathing subjects, suggesting that additional variables, such as individual compensatory mechanisms, may contribute to these discrepancies. While the stomatognathic system likely influences cervical function, its overall impact on body posture remains inconclusive. The absence of definitive scientific evidence linking occlusion, nasopharyngeal pathology, and postural abnormalities underscores the need for further well-designed longitudinal studies to elucidate these complex interactions.

4.2. Genetic and environmental influences on craniofacial and airway morphology

Understanding upper airway morphology, heritability, and growth patterns in a healthy population is essential for identifying individuals at risk of breathing disorders such as snoring, obstructive sleep apnea (OSA), and mouth breathing. Heritability analysis in this study revealed that 19 out of 23 cephalometric parameters exhibit strong genetic determination, while the remaining parameters are influenced by environmental influences or a combination of both. Upper airway dimensions, particularly SPPW-SPP and U-MPW, showed moderate to high heritability, with additive genetic factors accounting for 50–64 % of the variance. These findings align with Billing et al. [43], who reported that pharyngeal space dimensions, posterior nasopharyngeal wall thickness, and nasopharyngeal airway size are predominantly genetically determined. Similarly, Kang et al. [72] confirmed genetic control over airway features using lateral cephalograms of adult twins. Our findings further support this idea. The nasopharyngeal airway parameter (PNS-Ad1) demonstrated significant genetic influence ($a^2 = 0.51$), likely due to its anatomical positioning within the sphenoid and occipital bones and the atlas vertebra – highly heritable structures. However, given its functional interaction with the oropharynx and soft palate, environmental influences

also contribute to their variability [54]. The relatively low environmental influence on PNS-Ad1 ($e^2 = 0.19$) reinforces this observation.

Obesity is known to affect upper airway dimensions [56]. While environmental factors contribute to obesity, familial BMI correlations and twin studies suggest a strong genetic component in its development. In our study, the oropharyngeal airway space (U-MPW) exhibited moderate heritability ($a^2 = 0.5$), suggesting a genetic basis. However, this contrasts with previous research emphasizing the role of environmental influences such as posture and muscle function [73]. Our study also found an environmental contribution to U-MPW ($e^2 = 0.22$), likely due to its anatomical interaction with the tongue, hyoid bone, and cervical vertebrae, which are susceptible to environmental stimuli [16]. Lower airway dimensions, including LPW-V and PCV-AH, were predominantly determined by shared and unique environmental influences, highlighting the complex interplay between genetic predisposition and environmental exposures.

Orthodontic treatments have been associated with upper airway modifications, including rapid maxillary expansion (RME) and functional appliances (e.g., Herbst, Twin Block). Studies indicate that RME enhances oropharyngeal airway volume and nasal airflow [38], though some reports have found no significant post-treatment changes compared to control groups [128]. Functional appliances, including the Twin Block and Herbst devices, have been linked to increased airway volume and reduced airflow resistance [96–99]. While they induce skeletal and soft tissue adaptations, our findings confirm that oropharyngeal airway development results from genetic and environmental influences.

The relationship between upper airway morphology and craniofacial structures remains debated. Some studies suggest that airway size correlates with malocclusion type and craniofacial morphology [101] while others, including Di Carlo et al. [129], report no significant association between sagittal skeletal patterns and upper airway volume. Our findings did not establish a direct correlation, indicating that additional factors may contribute to these variations. Environmental factors predominantly influence hypopharyngeal dimensions, consistent with the studies linking pharyngeal space reduction to obesity [130]. Kim et al. [131] reported that OSA patients exhibit increased tongue volume and fat deposition, impairing tongue function as an airway dilator, supporting our findings on environmental contributions to hypopharyngeal morphology. However, Kang et al. [72] reported high heritability for hypopharyngeal structures, contrasting our results. This discrepancy may stem from measurement variability, as the valleculae can collect saliva, affecting assessments. Factors such as head posture, cervical spine positioning, and craniofacial angulation also contribute

to inconsistencies in hypopharyngeal measurements. Da Costa et al. [132] noted that cephalometric analysis of the hyoid bone position is particularly challenging due to minor deviations leading to substantial measurement variations. These findings emphasize the need for a multidisciplinary approach to airway assessment, integrating genetic, environmental, and functional considerations to optimize orthodontic and orthopedic interventions.

4.3. Heritability of mandibular cephalometric variables

Several key determinants, including the position of the mandibular fossa, cranial base length, and overall growth pattern shape the sagittal position of the mandible. The location of the mandibular fossa, which is governed by cranial base morphology, can be described using the saddle angle (NSBa). In our study, NSBa demonstrated strong genetic determination (a^2 = 79 %). However, previous research presents conflicting results:studies involving twins over 16 years of age report high heritability, whereas younger twin cohorts indicate minimal or no genetic influence [34]. Longitudinal parent-offspring analyses suggest that the heritability of the saddle angle increases with age, a trend supported by our data [133]. Additional angular variables representing the sagittal relationship between the mandible and cranial base, such as SN–ArRp and SNB, also exhibited substantial genetic control (a^2 = 76 % and 79 %, respectively), corroborating findings from previous studies [102].

Linear cephalometric measurements describing the vertical and horizontal positioning of the mandible relative to the cranial base and maxilla (e.g., ANS-Me, N-Me, S-Go, Co-A, and Ar-A) were found to have low-to-moderate heritability, with most variables fitting the ACE model. An exception was N-ANS, which demonstrated strong environmental determination (CE model). Our analysis revealed a notable distinction between the genetic influences on horizontal versus vertical mandibular positioning. Genetic factors more strongly determined horizontal variables than vertical ones, contrasting with some studies that report higher heritability estimates for vertical measurements [34,134–136]. These discrepancies may stem from differences in measurement techniques, as our study utilized actual lengths rather than projected lengths, which may not fully reflect the relationship between horizontal and vertical dimensions. Our findings suggest that genetic control is more pronounced in the sagittal positioning of the mandible than in the vertical positioning. Furthermore, anterior facial height (TAFH, LAFH) exhibited higher heritability than posterior facial height (TPFH), reinforcing the importance of genetic influences on vertical facial dimensions.

Key morphological features of the mandible such as angles ArGoM and DcXiPm are critical in determining skeletal form. Our findings indicate high heritability for the ArGoMe (a^2 = 77 %) and DcXiPm, (a^2 = 74 %). However, linear parameters such as mandibular body length (Go-Pog, Go-Gn), ramus width (R1-R2), and ramus height (Co-Go) demonstrated lower genetic determination. These linear measurements were explained by ACE model. This suggests that while the mandibular angles are primarily governed by genetic factors, mandibular length and ramus height are more susceptible to environmental influences, particularly during the pubertal growth spurt. Previous studies indicate that genetic control over mandibular length is more substantial in younger cohorts, whereas environmental influences become more prominent with age [34,102]. Dudas and Sassouni [137] also reported an increasing environmental contribution to linear cephalometric measurements, aligning with our findings.

Dentoalveolar to skeletal parameters appear to be predominantly influenced by environmental rather than genetic factors. This observation aligns with previous studies demonstrating lower heritability estimates for dentoalveolar traits than craniofacial variables [138-140]. Clinical research has established that environmental factors significantly shape occlusal development, including tongue posture, lip pressure, oral musculature, and functional habits such as breathing and mastication [40]. Our findings further support these clinical observations, suggesting that dentoalveolar height is more susceptible to environmental modulation. However, sagittal positioning of the lower incisors and chin protrusion (ai.ii–NB, ii ⊥ NB, ii ⊥ APog, and Pog ⊥ NB) exhibited very high heritability, indicating that specific components of the dentofacial complex operate within a genetically determined equilibrium. In contrast, to individuals with genetically stable traits, others adapt more readily to environmental stimuli [102].

Comparing twin study findings is inherently challenging due to variations in sample characteristics, zygosity determination, statistical methodologies, and skeletal maturity stages. Earlier twin studies often employed traditional path analysis and Dahlberg quotient calculations. In contrast, contemporary research employs model-fitting techniques to statistically test the goodness-of-fit of various genetic and environmental models [34,135]. The principal component analysis in our study identified six components that explain 83 % of the total variance. In contrast, Carels et al. [34] found five components accounting for 81 % of variance, and Nakata et al. [141] identified nine independent components. Differences in eigenvalue criteria likely account for these variations across studies.

From a clinical perspective, our results indicate that mandibular skeletal morphology – particularly gonial angle and mandibular arc angles – is more

genetically determined than mandibular length. Consequently, orthodontic and orthopedic interventions may be more effective in modifying mandibular size rather than its inherent form. However, it is essential to recognize that heritability is a population-level concept and does not necessarily predict treatment outcomes for individual patients. While traits with low heritability are generally considered more amenable to intervention, treatment success remains case-specific and cannot be determined solely based on genetic predisposition.

An intriguing aspect of our findings is the identification of a specific lateral facial region delineated by highly heritable angles, including SNB (a^2 = 79 %), NSAr (a^2 = 75 %), and ArGoMe (a^2 = 77 %). By analogy with the 'triangle of facial similarity' defined by Na, Go, and Gn landmarks, we propose designating this strongly genetically determined region as the 'polygon of facial profile similarity' [88]. This area may contribute to the striking resemblance observed among twins, underscoring the role of genetic factors in defining facial aesthetics.

4.4. Heritability in the palatal dimension

Numerous twin studies have explored the genetic and environmental influences on upper arch morphology and palatal characteristics. However, comparing these studies is challenging due to variations in sample size, population characteristics, and zygosity classification. The statistical method of model-fitting analysis provides a robust means of distinguishing the sources of variation affecting dental arch and palate dimensions. Our study implemented this analytical approach to enhance accuracy. Our findings revealed significant sexual dimorphism in palatal parameters. Males demonstrated slightly wider dental arches than females, and the palatal surface area and volume were significantly larger ($p < 0.01$). This is consistent with previous research [18,35]. However, a longitudinal study by Chaaban et al. [79] on monozygotic and dizygotic twins reported a weaker genetic influence on transverse palatal dimensions, indicating a more substantial environmental impact. It is worth noting that Chaaban et al. [79] relied on the Pearson's correlation coefficient and Falconer's heritability test to estimate genetic contributions retrospectively, which may account for differences in findings. Lione et al. [142] suggested that tongue pressure largely shapes maxillary arch form.

Our study found that the AE (additive genetic and unique environmental) and DE (dominant genetic and unique ecological) models best explained the variance in palatal dimensions. The DE model primarily influenced interdental distances at the gingival plane, except IMWG. This suggests that genetic

factors and specific non-shared environmental influences mainly drive palatal variability in individuals with complete maxillary growth. Furthermore, dominant genetic effects predominantly determined distances at the gingival plane. The higher correlation of all parameters in monozygotic twins compared to dizygotic twins supports the substantial genetic contribution to dental arch width and palatal morphology, including depth, height, and volume.

While the dental arch influences palate morphology, our study did not find significant environmental effects on palatal area or volume variation. Since we did not assess mouth breathing in our twin cohort, it was not possible to determine the influence of tongue positioning on dental arch and palate morphology. However, our results strongly indicate that genetic factors play a dominant role in palatal variability. Genetic influence on inter canine width was lower ($a^2 = 0.59$), suggesting that environmental factors play a more significant role in shaping this transverse dimension. The influence of genetic factors on palatal and dental arch width in the canine region was also reduced (ICW $d^2 = 0.59$, ICWG $d^2 = 0.5$, ICH $d^2 = 0.48$). These findings align with previous research by King et al. [48] and Cassidy et al. [143], who reported heritability estimates of 0.53 and 0.56 for intercanine width, respectively. This region's more substantial environmental influence may be attributed to functional factors such as tongue posture, swallowing habits, and mouth breathing. These parafunctional habits can contribute to a flatter, narrower palate and maxillary anterior teeth protrusion [142].

In patients with completed maxillary growth, the midpalatal suture ossifies around the age of 13 [143], meaning that conventional rapid maxillary expansion (RME) may only lead to buccal tipping of the posterior teeth, increasing the risk of relapse. Surgical expansion or miniscrew-assisted RME (MARPE) may be necessary. Palatal suture ossification has been reported as early as 11, making chronological age an unreliable predictor of suture maturation [143]. According to our results, palatal surface area ($a^2 = 0.61$), palate volume ($a^2 = 0.69$), and maxillary arch depth ($a^2 = 0.56$) are predominantly influenced by genetic factors. These findings suggest that for patients older than 11 years, MARPE may provide more stable maxillary expansion than conventional RME. However, even with MARPE, long-term stability remains uncertain, as both dental and skeletal relapse can occur over time [70]. Our study also revealed that heritability estimates for intermolar width ($a^2 = 0.86$) were the highest among all parameters. This is particularly relevant since RME appliances are typically anchored on the first molars, and the strong genetic influence on intermolar width may contribute to relapse following expansion. Similar findings were reported by Eguchi et al. [76] ($a^2 = 0.82$) and Hughes et al. [77] ($a^2 = 0.87$), further supporting the idea of the genetic dominance in this region.

Our results may have implications for predicting patient responses to orthodontic interventions, particularly maxillary expansion. Traits with strong genetic determination may exhibit less responsiveness to corrective procedures whereas those with more significant environmental influence may be more adaptable and exhibit greater post-treatment stability. A key clinical takeaway from this study is that orthodontic interventions modifying dental arch and palate dimensions should respect biological limits. Maintaining equilibrium among skeletal, dental, and muscular structures is essential, as excessive deviation from an individual's genetically determined arch form may increase the likelihood of post-treatment relapse toward the genetic norm.

4.5. Relationship between upper airway and palatal parameters

The relationship between palatal dimensions and upper airway morphology has been extensively studied due to its implications for orthodontics, sleep-disordered breathing, and craniofacial development. Pearson's correlation analysis provides novel insights into how palatal width and height influence airway patency, emphasizing the clinical significance of maxillary constriction in airway-related conditions. Our study's findings reveal significant correlations between transverse palatal dimensions and airway morphology. Specifically, 1IPD ($r = 0.43$, $p < 0.05$) and 1IPD (GL) ($r = 0.37$, $p < 0.05$) demonstrated notable associations with PCV-AH, suggesting that a narrower palate may contribute to a reduced lower airway space. This aligns with prior research indicating that maxillary constriction is linked to pharyngeal airway narrowing and increased respiratory resistance [117]. Additionally, IMD ($r = 0.36$, $p < 0.05$) exhibited a moderate correlation with PCV-AH, reinforcing the role of posterior palatal width in airway structure. These findings suggest that a wider interdental width correlates with a more anterior tongue and hyoid bone position, further supporting the idea of the interplay between palatal dimensions and airway morphology.

Palatal height also demonstrated significant correlations with airway parameters. Measurements such as 1IPH ($r = 0.30$, $p < 0.05$) and 2IPH ($r = 0.29$, $p < 0.05$) showed positive relationships with airway variables, supporting the hypothesis that increased palatal height may contribute to airway restriction by altering the posterior pharyngeal space [144]. However, maxillary depth and overall palate volume exhibited weak or negligible correlations, suggesting that these parameters alone do not strongly determine upper airway morphology. Interestingly, lower airway dimensions such as LPW-V did not correlate strongly with palatal morphology. This highlights the more significant influence of environmental and functional factors, such as tongue posture, head position, and hyoid bone movement hypopharyngeal

airway development. This underscores the complex interplay between skeletal structures and soft tissue adaptations in airway formation.

Our results align with Ciavarella et al. [145], who found a negative correlation between palatal height, palatal area, maxillary sagittal and transverse dimensions. These findings suggest that specific craniofacial characteristics may be anatomical markers for increased OSA severity in individuals with dental malocclusions, facilitating early diagnosis and intervention. Similarly, Oliveira et al. [146] demonstrated that craniofacial structures, including maxillary length, occlusal plane inclination, dental angulation, soft palate dimensions, tongue size, and hyoid bone position, are significantly correlated with sagittal pharyngeal airway parameters.

Orthodontic interventions such as rapid maxillary expansion (RME) or miniscrew-assisted RME (MARPE) may benefit patients with compromised airway dimensions, particularly those with narrow palatal widths impacting upper airway space. An important clinical consideration is the definition of a "narrow maxilla." While a posterior crossbite is a clear indicator, not all individuals with a narrow palate exhibit this feature, emphasizing the need for standardized reference parameters to establish normative functional and aesthetic values. Additionally, the observed correlation between palatal morphology and upper airway dimensions reinforces the importance of a multidisciplinary treatment approach, integrating orthodontic, otolaryngologic, and myofunctional therapy to optimize patient outcomes in airway-related conditions [146].

4.6. Summary of studies

This study provides novel insights into craniofacial morphology's genetic and environmental determinants, upper airway structure, and their interplay with postural and functional factors. The findings highlight the critical role of genetic influences in determining upper airway, palatal, and mandibular morphology, with angular cephalometric parameters demonstrating particularly strong heritability. However, environmental influences such as breathing patterns, tongue posture, and body alignment were also found to significantly modulate these inherited traits, influencing airway patency and craniofacial development.

A strong association was observed between kyphotic posture, reduced SNB angles, and nasopharyngeal obstruction. Patients with kyphotic alignment exhibited mandibular retrusion and increased vertical facial dimensions, indicating a compensatory mechanism in response to airway obstruction. These findings align with the functional matrix theory, which posits that craniofacial structures adapt to surrounding functional and

postural influences. This study's integration of postural assessments with cephalometric and otorhinolaryngological evaluations underscores the need for a multidisciplinary approach to managing malocclusions and airway disorders.

Heritability analysis confirmed that upper airway dimensions are predominantly under genetic control. However, the interplay between genetic predisposition and environmental influences remains crucial. Our findings demonstrated significant correlations between palatal dimensions and upper airway morphology, emphasizing the impact of maxillary constriction on respiratory function. Specifically, interdental and palatal height measurements were significantly associated with the PCV-AH distance, suggesting that narrow palates may contribute to reduced airway dimensions. This underscores the importance of orthodontic interventions such as rapid maxillary expansion (RME) in managing airway-related concerns.

CLINICAL IMPLICATIONS AND FUTURE DIRECTIONS

Future studies should focus on longitudinal investigations that integrate genetic analysis, advanced imaging techniques, like CBTC, and multidisciplinary treatment strategies to enhance treatment protocols and further validate these findings. For example, they should evaluate long-term occlusal changes in twins to determine the stability of orthodontic treatment over time.

The findings of this study are clinically relevant to orthodontic treatment planning and early intervention strategies for patients with airway dysfunction and postural imbalances. The strong genetic component of upper airway morphology suggests that certain specific facial structures may exhibit limited adaptability to mechanical correction. In contrast, more significant traits under environmental influence may respond more favorably to intervention. Additionally, identifying significant associations between airway morphology, posture, and malocclusion highlights the importance of early screening and multidisciplinary management to optimize treatment outcomes.

Despite these insights, limitations such as the cross-sectional study design and population homogeneity necessitate further research. Future studies should employ longitudinal designs, incorporate three-dimensional imaging modalities such as CBCT, and investigate the role of soft tissue adaptations in craniofacial growth and airway function. Additionally, expanding the study population to include diverse ethnic groups would enhance the generalizability of these findings. The major limitation of twin studies is that they do not represent the whole society as a general unit.

In conclusion, this study underscores the complex interplay between genetic and environmental determinants in craniofacial and airway morphology. The findings support the integration of orthodontic, otolaryngologic, and postural assessments in clinical practice to improve diagnostic precision and treatment efficacy in managing airway-related disorders.

CONCLUSIONS

1. Nasopharyngeal obstruction is associated with kyphotic posture and craniofacial alterations – a statistically significantly reduced anteroposterior position of the mandible relative to the cranial base, indicating mandibular retrusion. The presence of kyphotic posture was twice as common in patients with nasopharyngeal obstruction than in those with normal airway morphology ($p < 0.05$).

2. a. The upper airway dimensions are strongly controlled by additive genetics (AE model, with a^2 ranging from 0.5 to 0.64) and dominant determination (DE model, d^2 at the level of 0.5). Airway dimensions in the hypopharyngeal region were predominantly influenced by shared and specific environmental influences.

   b. The cephalometric parameters of the facial bony structures have a high heritability coefficient (h^2). There is a strong additive genetic influence on cephalometric variables defining the form and sagittal position of the mandible (a^2 = 74–79 %). The environment significantly contributes to the variance of facial height and mandibular skeletal linear cephalometric variables (c^2 = 45–68 %).

3. The palate and maxillary dental arch morphology were under strong genetic control. High additive genetic impact was found for palate height (a^2 =0.86), palate surface area (a^2 =0.61), and palate volume (a^2 =0.69). Moderate genetic dominance was recorded for dental arch width in the canine and premolar regions (d^2 =0.5 and d^2=0.78 – 0.81, respectively). The reduced genetic influence on the dental arch width and palatal variables in the canine region (e.g., a^2 = 0.59 for arch width; d^2 = 0.59 for ICW, d^2 = 0.50 for ICWG, d^2 = 0.48 for ICH) suggests that environmental impact plays a more prominent role in shaping these transverse dimensions.

4. This study revealed significant correlations between palatal dimensions and upper airway parameters. Specifically, intercanine distance was associated with the distance between the anterior nasal spine and the hyoid bone, and the distance between the anterior nasal spine and the vallecula, while intercanine height showed stronger associations with these same distances. Palate area and volume demonstrated significant correlations with the distance between the posterior pharyngeal wall and the hyoid bone, and with the width of the soft palate. These results emphasize the functional interdependence between transverse and vertical palatal development and the upper airway morphology.

PRACTICAL RECOMMENDATIONS

Based on the findings of this study, the following clinical recommendations are proposed:

1. Orthodontists should collaborate with otolaryngologists and physiotherapists to address underlying functional issues contributing to airway obstruction.
2. Orthodontic treatment plans should account for both genetic predisposition and environmental influences, as twin studies reveal variations in occlusal traits due to external influences.
3. Palatal expansion techniques should be considered to enhance airway volume in patients with constricted maxillary arches.
4. Functional appliances, such as the Twin Block or Herbst, should improve occlusion and respiratory function in growing patients with airway-related skeletal imbalances.
5. Clinicians should evaluate and manage parafunctional habits (e.g., tongue thrusting, mouth breathing, and atypical swallowing) as they can impact craniofacial growth and orthodontic stability.
6. Orthodontic patients should have their head and cervical spine posture assessed, as poor posture may contribute to airway constriction and malocclusion.

SANTRAUKA

PAGRINDINĖS SANTRUMPOS

C2 – antrasis kaklo slankstelis
C3 – trečiasis kaklo slankstelis
C4 – ketvirtasis kaklo slankstelis
DNR – deoksiribonukleorūgštis
DZ – dizigotinis
MZ – monozigotinis
NS – nereikšmingas skirtumas
OMA – obstrukcinė miego apnėja
SN – standartinis nuokrypis

ĮVADAS

Ortodontijoje idealus sąkandis apibrėžiamas kaip taisyklingas dantų išsidėstymas ir kontaktai, užtikrinantys efektyvią kramtymo funkciją, apatinio žandikaulio sąnario sveikatą, ilgalaikį stabilumą ir estetiką [1]. Sąkandis yra glaudžiai susijęs su svarbiausia žmogaus funkcija – kvėpavimu. Kvėpavimo takų sąsaja su veido augimu ir vystymusi tampa vis aktualesne tema dėl didėjančio kvėpavimo sutrikimų paplitimo [2–8]. Tyrimai rodo, kad 11–56 proc. vaikų vyraujantis kvėpavimo būdas yra per burną [6], o 21–27 proc. vaikų reikalingas ortodontinis gydymas [8,9]. Malvinos Moss funkcinės užpildo teorija – aplinkiniai minkštieji audiniai daro įtaką kaulinių struktūrų formavimuisi [10,11]. Tačiau veido ir žandikaulių sistemos vystymasis nėra izoliuotas procesas, nes jį veikia kaulų ir raumenų sistema, jungianti galvą su kūnu [12]. Tyrimai rodo, kad kvėpavimo būdas ir kūno laikysena turi didelę įtaką sąkandžio patologijų vystymuisi [12]. Šios sąsajos dar labiau pabrėžia ortodontinio gydymo reikšmę ne tik dantų išlyginimui, bet ir kvėpavimo takų funkcijai bei bendram organizmo sveikatos gerinimui. Sveikos populiacijos viršutinių kvėpavimo takų morfologijos, paveldimumo įvertinimas ir augimo modelių nustatymas yra esminiai veiksniai nustatant asmenis, kuriems kyla kvėpavimo sutrikimų, įskaitant knarkimą, obstrukcinę miego apnėją (OMA) ir kvėpavimą per burną. Supratus, kaip genetiniai ir aplinkos veiksniai veikia kvėpavimo takų morfologiją, gali pagerinti ankstyvąją diagnostiką ir pasirinkti teisingą gydymo strategiją [27].

Dvynių tyrimai yra svarbus metodas siekiant atskirti genetinius ir aplinkos veiksnius. Monozigotiniai dvyniai (MZ) turi identišką genetinę informaci-

ją ir augimo aplinką, o dizigotiniai dvyniai (DZ) dalijasi 50 proc. vienodų genų ir jų fenotipiniai skirtumai nulemti tiek adityviojo genų, tiek ir aplinkos poveikio [26]. Tokie tyrimai leidžia tiksliau įvertinti genetikos ir aplinkos įtaką sąkandžio patologijoms. Genetiškai nulemtos sąkandžio patologijos yra mažiau jautrios gydymui, o aplinkos veiksnių sukelti sąkandžio pokyčiai dažniau sėkmingai koreguojami [29]. Tyrimai rodo, kad kietojo gomurio plotis ir apatinio žandikaulio padėtis labiausiai veikia kvėpavimo takus [31,33]. Daug dėmesio ortodontijoje skiriama gomurio plėtimui, tačiau ilgalaikiai tyrimai rodo, kad šio metodo poveikis gali būti kintamas [38]. Be to, apatinio žandikaulio padėties koregavimas gali pagerinti kvėpavimą, todėl tai svarbu planuojant kompleksinį ortodontinį gydymą [94,95]. Aplinkos veiksniai, pvz., žalingi įpročiai (infantilus rijimas, daiktų kramtymas), taip pat prisideda prie sąkandžio patologijų vystymosi [24]. Tačiau šiuo metu vis dar trūksta tyrimų, kurie patvirtintų aiškią šių įpročių sąsają su veido ir žandikaulių sistema. Pastebėta, kad vaikai, kvėpuojantys per burną, dažniausiai turi siauresnį gomurį, didesnį veido kampą ir labiau susigrūdusius dantis, susiaurėjusi burnos ertmė dar labiau sunkina normalų kvėpavimą[33,37,43,69]. Svarbu nustatyti, ar kvėpavimas per burną tiesiogiai susijęs su kvėpavimo takų pločiu, bei identifikuoti šį ryšį lemiančius veiksnius. Dvynių tyrimai suteikia unikalią galimybę analizuoti šių veiksnių įtaką. Nors didėja mokslinis susidomėjimas kvėpavimo funkcija, veido ir žandikaulių vystymusi ir ortodontiniu gydymu, tačiau trūksta išsamių tyrimų, nagrinėjančių genetinių ir aplinkos veiksnių bendrą poveikį kvėpavimo takų obstrukcijai ir sąkandžio patologijoms. Šis tyrimas siekia atsakyti į minėtus klausimus analizuodamas šių veiksnių sąveiką ir įvertindamas ortodontinio gydymo svarbą gerinant kvėpavimą per nosį ir vaikų kvėpavimo takų vystymąsi.

Tyrimo tikslas

Įvertinti genetinių ir aplinkos veiksnių įtaką viršutinių kvėpavimo takų morfologijai ir su ja susijusioms kaukolės struktūroms, taip pat nustatyti šių struktūrų tarpusavio sąsajas.

Tyrimo uždaviniai

1. Įvertinti tarpusavio ryšius tarp viršutinių kvėpavimo takų obstrukcijos, sąkandžio patologijos ir kūno laikysenos.
2. Išanalizuoti genetinių ir aplinkos veiksnių įtaką kvėpavimo takų ir su jais susijusių kaukolės struktūrų cefalometriniams parametrams.
3. Nustatyti genetinių ir aplinkos veiksnių įtaką gomurio morfologijai pasibaigus viršutinio žandikaulio augimui.

4. Įvertinti gomurio matmenų ir viršutinių kvėpavimo takų parametrų tarpusavio sąsajas.

Mokslinio darbo naujumas ir praktinė reikšmė

1. Pirmą kartą tarpdalykiniu požiūriu analizuojami viršutinių kvėpavimo takų obstrukcijos, sąkandžio patologijos ir kūno laikysenos ryšiai.
2. Tai yra pirmasis tyrimas, nagrinėjantis genetinius ir aplinkos veiksnius, lemiančius kvėpavimo takų morfologiją, naudojant DNR testą, pagrįstą 15 specifinių genų žymenų.
3. Atliekama genetinė analizė po aktyvaus augimo laikotarpio, todėl gaunami tikslesni genetiniai duomenys. Ankstesniuose tyrimuose buvo sunku atskirti genetinius veiksnius nuo aktyvių augimo procesų. Todėl šiame tyrime pasirinkus jau nebeaugančius tiriamuosius, genetiniai žandikaulių morfologijos veiksniai vertinami be aktyvaus augimo įtakos.
4. Pirmą kartą dvynių tyrimuose vertinami ne tik linijiniai gomurio matmenys, bet ir jo paviršiaus plotas bei tūris.
5. Nagrinėjama viršutinių kvėpavimo takų ir gomurio parametrų tarpusavio sąsaja – iki šiol mažai tirta mokslo tema.

MEDŽIAGA IR METODAI

Tyrimo medžiaga

Šio tyrimo protokolus patvirtino Regioninė biomedicininių tyrimų etikos komisija (Nr. BE-2-41 ir BE-2-48). Gautas informuoto asmens sutikimas, o jaunesniems nei 18 metų dalyviams – jų tėvų sutikimas. Visi dalyviai dalyvavo klinikinėse konsultacijose. Šiame tyrime dalyvavę dvyniai buvo atrinkti iš Lietuvos sveikatos mokslų universiteto Dvynių centro.

Tyrimo metodai

Tiriamųjų įtraukimo ir atmetimo kriterijai yra 1 lentelėje. Tiriamųjų imtis ir amžius – 2 lentelėje.

1 lentelė. *Tiriamieji: įtraukimo ir atmetimo kriterijai*

Tyrimo uždaviniai	**Įtraukimo kriterijai**	**Atmetimo kriterijai**
Nustatyti sąsajas tarp nosiaryklės obstrukcijos, sąkandžio ypatumų ir kūno laikysenos	7–14 metų vaikai	Žandikaulių traumos ar operacijos, sindromai, ankstesnis ortodontinis gydymas, stuburo ar dubens traumos
Įvertinti genetinių ir aplinkos veiksnių įtaką kvėpavimo takų morfologijos ir su ja susijusių kaukolės struktūrų cefalometriniams parametrams	Europidinės kilmės dvyniai, CVM (kaklo slankstelių brendimo stadija) – 6, aukštos kokybės šoninės galvos cefalogramos	Ankstesnis ortodontinis gydymas, pastoviųjų dantų šalinimas, veido ar dantų traumos, sisteminės ligos
Išanalizuoti genetinių ir aplinkos veiksnių įtaką viršutinio žandikaulio dantų lanko ir gomurio morfologijai, pasibaigus viršutinio žandikaulio augimui	Europidinės kilmės dvyniai, pasibaigęs viršutinio žandikaulio augimas (amžius > 13 metų), visi pastovieji dantys (išskyrus trečiuosius krūminius dantis)	Ankstesnis ortodontinis gydymas, pastoviųjų dantų šalinimas, restauracijos, trukdančios atlikti matavimus, didelis dantų nusidėvėjimas, nekokybiški dantų lankų ir gomurio modeliai, veido ar dantų traumos, sisteminės ligos
Įvertinti ryšius tarp viršutinių dantų lankų morfologijos, gomurio matmenų ir viršutinių kvėpavimo takų parametrų	Europidinės kilmės dvyniai, pacientams atlikta tiek šoninė galvos cefalograma, tiek turimi dantų modeliai	Ankstesnis ortodontinis gydymas, pastoviųjų dantų šalinimas, veido ar dantų traumos, sisteminės ligos

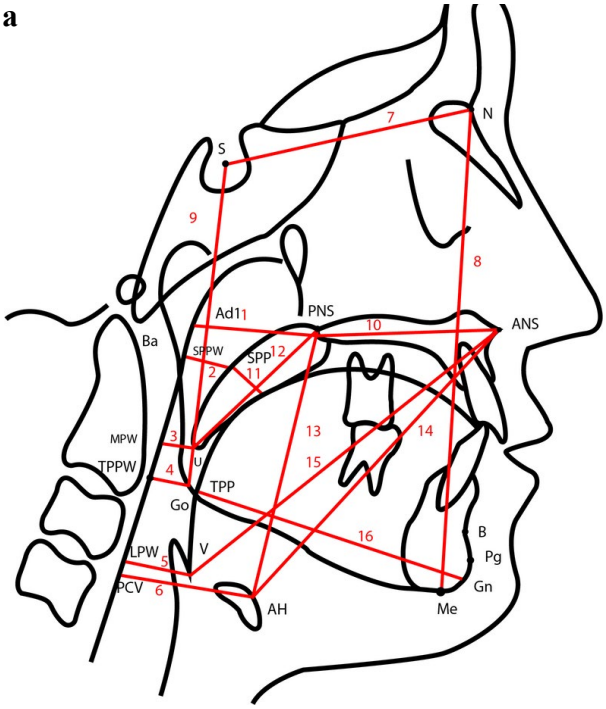
***2 lentelė**. Tiriamųjų imtis ir amžius*

Tyrimo uždavinys ir grupė	N (asmenų)	Vidutinis amžius (metai)	Standartinis nuokrypis (metai)
Nustatyti sąsajas tarp nosiaryklės obstrukcijos, sąkandžio ypatumų ir kūno laikysenos	**94**	**11,90**	**2,10**
Įvertinti genetinių ir aplinkos veiksnių įtaką kvėpavimo takų morfologijos ir su ja susijusių kaukolės struktūrų cefalometriniams parametrams (dvynių poros)	**94**	**18,85**	**4,92**
Monozigotiniai (MZ) dvyniai	50	-	-
Dizigotiniai (DZ) dvyniai	44	-	-
Susijusių kaukolės struktūrų vertinimas (dvynių poros)	**141**	**21,73**	**5,24**
Monozigotiniai (MZ) dvyniai	90	-	-
Dizigotiniai (DZ) dvyniai	51	-	-
Išanalizuoti genetinių ir aplinkos veiksnių įtaką viršutinio žandikaulio dantų lanko ir gomurio morfologijai, pasibaigus viršutinio žandikaulio augimui (dvynių poros)	**85**	**17,95**	**2,83**
Monozigotiniai (MZ) dvyniai	50	-	-
Dizigotiniai (DZ) dvyniai	35	-	-
Įvertinti ryšius tarp viršutinių dantų lankų morfologijos, gomurio matmenų ir viršutinių kvėpavimo takų parametrų (dvynių poros)	**53**	**17,82**	**3,05**
Monozigotiniai (MZ) dvyniai	27	-	-
Dizigotiniai (DZ) dvyniai	26	-	-

Cefalometrinė analizė

Cefalometrinė analizė buvo naudojama vertinant kvėpavimo takus, galvos griaučių parametrus ir apatinio žandikaulio morfologiją. Rentgenogramos buvo atliekamos naudojant Kodak 8000C skaitmeninę rentgeno įrangą, laikantis ALARA (As Low as Reasonably Achievable) principo, siekiant kuo mažesnio radiacijos poveikio. Rentgenogramos buvo analizuojamos naudojant Dolphin Imaging programinę įrangą (v.10.5 ir 11.7).

a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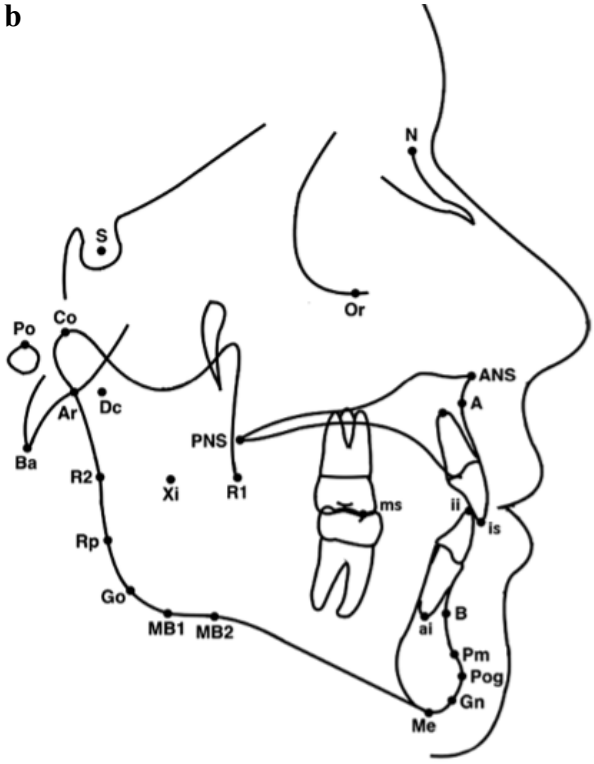
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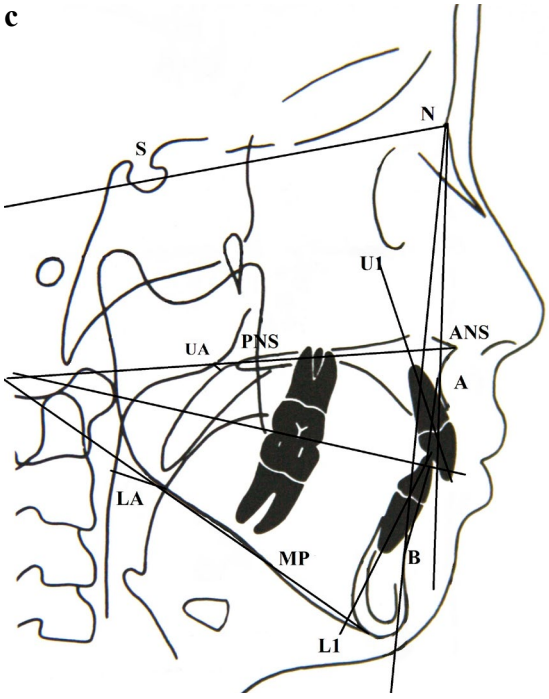


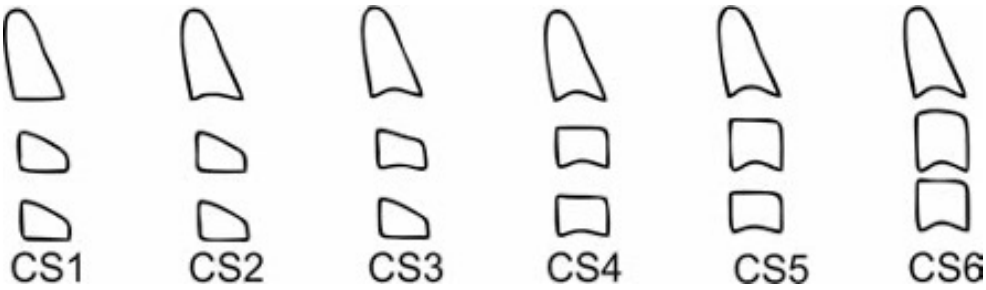
1 pav. *Cefalometriniai taškai ir linijiniai bei kampiniai parametrai,v artoti tyrime*

S – vidurio taškas turkiškojo balno srityje. **N** – priekinis taškas frontonazalinėje siūlėje. **A**– giliausias išgaubtos kreivės taškas viršutinio žandikaulio alveolinėje ataugoje. **B** – giliausias išgaubtos kreivės taškas apatinio žandikaulio alveolinėje ataugoje. **ANS** – priekiniausias priekinio nosies spyglio taškas. **PNS** – užpakalinis taškas kietajame gomuryje. **Ba** – priekinis-apatinis taškas ant didžiosios angos krašto. **Co** – užpakalinis-viršutinis žandikaulio sąnarinės galvos taškas. **Ar** – taškas ties užpakalinio žandikaulio šakos krašto ir užpakalinės kaukolės pamato apatinio krašto susikirtimu. **Go** – apatinio žandikaulio kampo vidurio taškas tarp šakos ir kūno. **Me** – žemiausias priekinis apatinio žandikaulio krašto taškas. **Gn** – vidurio taškas tarp Pg ir Me. **Pog** – priekiniausias smakro taškas. **Xi** – geometrinis žandikaulio šakos centras. **Rp** – išsikišęs užpakalinis-viršutinis taškas žandikaulio kampo užpakalinėje šakoje. **MB1** – išgaubčiausias taškas palei žandikaulio šakos apatinį kraštą. **MB2** – aukščiausias įdubos taškas apatinio žandikaulio kūno apatiniame krašte. **is** – priekinio viršutinio centrinio kandžio incizinis taškas. **ii** – priekinio apatinio centrinio kandžio incizinis taškas. **ms** – apatinio pirmojo krūminio mezialinio bukalinio gumburo viršūnė. **Po** – vidurio taškas išoriniame klausos kanalo viršutiniame kontūre. **Or** – giliausias taškas infraorbitaliniame krašte. **Ad1** – užpakalinės ryklės sienelės ir linijos PNS-Ba susikirtimo taškas. **SPPW** – užpakalinės ryklės sienelės ir linijos, kuri eina statmenai užpakalinės ryklės sienelės–minkštojo gomurio centro susikirtimo taškui. **SPP** – užpakalinės ryklės sienelės ir linijos, kuri eina statmenai užpakalinės ryklės sienelės–minkštojo gomurio centro susikirtimo taškui. **TPPW** – užpakalinės ryklės sienelės ir linijos B-Go susikirtimo taškas. **LPW** – užpakalinės ryklės sienelės taškas, nuo kurio statmena linija kerta tašką V.**PCV** – užpakalinės ryklės sienelės ir antrojo kaklo slankstelio apatinio krašto susikirtimo taškas. **U** – liežuvėlio (uvulos) viršūnė.

V – taškas, kuriame entgerklis susijungia su liežuvio pagrindu. **AH** – priekinis ir viršutinis poliežuvinio kaulo taškas. **ai** –apatinio centrinio kandžio šaknies viršūnė. **Pm** – taškas, kuriame pasikeičia simfizės metu forma iš išgaubtos į įgaubtą. **L1** – apatinio centrinio kandžio kryptis. **U1** – viršutinio centrinio kandžio kryptis.

Veido ir žandikaulių augimo brandos vertinimas

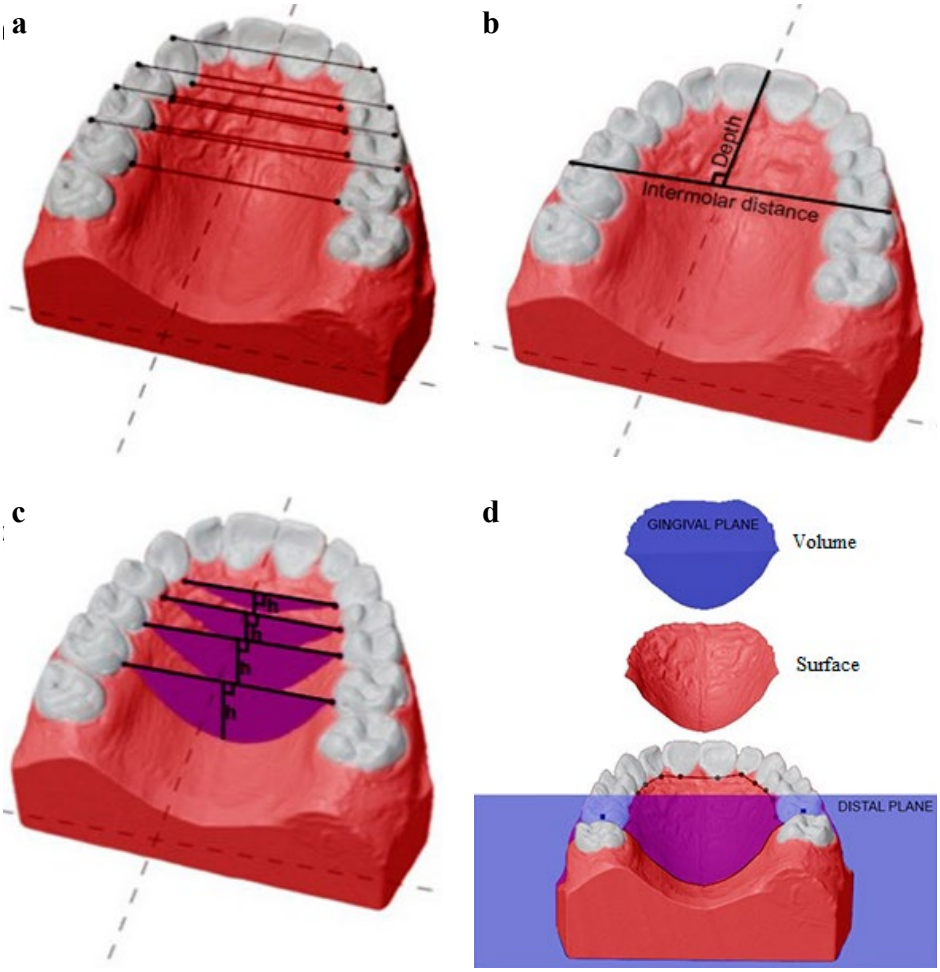
Griaučių brandai vertinti buvo taikomas kaklelio slankstelių brandos stadijos (CVM) metodas – pagal Baccetti modifikaciją [105]. Šis metodas leidžia nustatyti tiriamojo griačių brandos amžių šoninėje galvos rentgenogramoje. Vertinimas buvo atliekamas pagal antrojo (C2), trečiojo (C3) ir ketvirtojo C4 slankstelių formos įvertinimą ir dydį. Dvyniai, pasiekę CVM 6 stadiją, buvo įtraukti į tyrimą. Kaklo slankstelių brandos stadijos parodytos 2 paveiksle.



2 pav. *Kaklo slankstelių brandos stadijos*

Viršutinio žandikaulio ir gomurio matmenys

Tyrimo dalyvių gipsiniai dantų modeliai buvo skaitmeninami naudojant 3Shape e3 skenerį (Kopenhaga, Danija) (3 pav.). Matavimai atlikti trimatėje (3D) aplinkoje, naudojant Blender programinę įrangą. Buvo apskaičiuoti šie gomurio parametrai: gomurio plotis (tarp iltinių dantų, pirmųjų ir antrųjų kaplių bei pirmųjų krūminių dantų), gomurio aukštis, gomurio paviršiaus plotas ir tūris.



***3 pav**. Gomurio parametrų matavimas*

***3 lentelė.** Gomurio parametrų apibūdinimas*

Matavimas	Apibrėžtis
Dantų lankų plotis okliuzinėje linijoje	
ICW – tarpiltinių dantų plotis	Nuotolis tarp iltinių dantų viršūnių viršutinio žandikaulio okliuzinėje plokštumoje
1IPW – dantų plotis tarp pirmųjų kaplių	Nuotolis tarp pirmųjų kaplių skruostinių viršūnių viršutinio žandikaulio okliuzinėje plokštumoje
2IPW – dantų plotis tarp antrųjų kaplių	Nuotolis tarp antrųjų kaplių skruostinių viršūnių viršutinio žandikaulio okliuzinėje plokštumoje
IMW – krūminių dantų plotis tarp pirmųjų krūminių dantų	Nuotolis tarp pirmųjų krūminių dantų artimesnių vidurio linijai skruostinių viršūnių viršutinio žandikaulio okliuzinėje plokštumoje

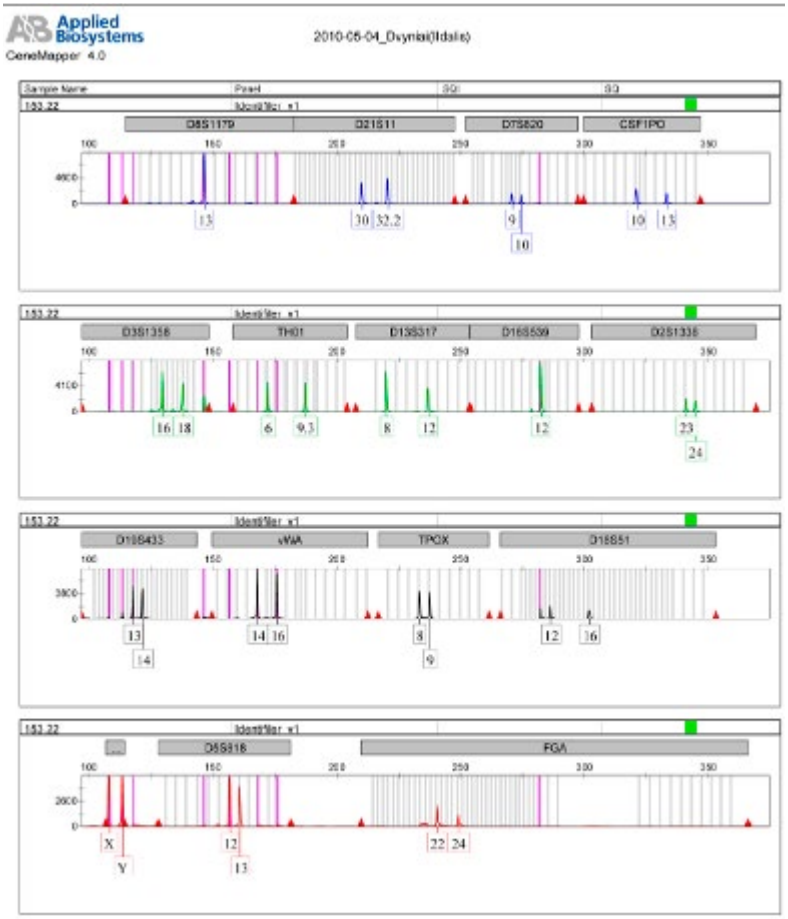
3 lentelės tęsinys

Matavimas	Apibrėžtis
Dantų lankų plotis dantenų linijoje	
ICWG – tarpiltinių dantų plotis dantenų linijoje	Nuotolis tarp iltinių dantų dantenų linijos centrų gomurinėje pusėje
1IPWG – dantų plotis tarp pirmųjų kaplų dantenų linijoje	Nuotolis tarp pirmųjų kaplių dantenų linijos centrų gomurinėje pusėje
2IPWG – dantų plotis tarp antrųjų kaplių dantenų linijoje	Nuotolis tarp antrųjų kaplių dantenų linijos centrų gomurinėje pusėje
IMWG – dantų plotis tarp pirmųjų krūminių dantenų linijoje	Nuotolis tarp pirmųjų krūminių dantų dantenų linijos centrų gomurinėje pusėje
Gomurio aukštis	
ICH – tarpiltinis gomurio aukštis	Nuotolis tarp iltinių dantų dantenų linijos centrų gomurinėje pusėje ir aukščiausio taško gomurio skliaute
1IPH – gomurio aukštis tarp pirmųjų kaplių	Nuotolis tarp pirmųjų kaplių dantenų linijos centrų gomurinėje pusėje ir aukščiausio taško gomurio skliaute
2IPH – gomurio aukštis tarp antrųjų kaplių	Nuotolis tarp antrųjų kaplių dantenų linijos centrų gomurinė pusėje ir aukščiausio taško gomurio skliaute
IMH – gomurio aukštis tarp pirmųjų krūminių dantų	Nuotolis tarp pirmųjų krūminių dantų dantenų linijos centrų gomurinėje pusėje ir aukščiausio taško gomurio skliaute
Viršutinio žandikaulio lankas, gomurio paviršiaus plotas ir tūris	
MD – viršutinio žandikaulio gylis	Nuotolis tarp susijungiančios linijos nuo centrinių kandžių kandamųjų kraštų ir linijos, jungiančios pirmųjų krūminių dantų artimesnių vidurio linijai skruostinių viršūnių kontaktinio taško
PSA – gomurio paviršiaus plotas	Gomurio paviršiaus plotas žemiau dantenų plokštumos, ribotas galine plokštuma
PV – gomurio tūris	Tūris po dantenų plokštuma, ribojamas gomurio paviršiaus ir galinės plokštumos

Dvynių zigotiškumo nustatymas

Dvynių zigotiškumas buvo nustatytas DNR tyrimu, naudojant AmpFlSTR® Identifiler® polimerazinės grandininės reakcijos rinkinį (Applied Biosystems, JAV). Trumpų tandemiškai pasikartojančių (TTP) polimorfinių DNR nukleotidų sekos padauginimas, naudojant polimerazinės grandininės reakcijos reagentų rinkinį AmpFlSTR® Identifiler® (*Applied bio-systems*, JAV). Rinkinys AmpFlSTR® Identifiler® – amplifikuoja 15 TTP lokusų (D8S1179, D21S11, D7S820, CSF1PO, D3S1358, TH01, D13S317, D16S539, D2S1338, D19S433, vWA, TROX, D18S51, D5S818, FGA). Papildomai buvo naudo-

jamas amelogenino geno fragmentas genetiniams profiliams palyginti, pasiekiant 99,9 proc. tikslumo.



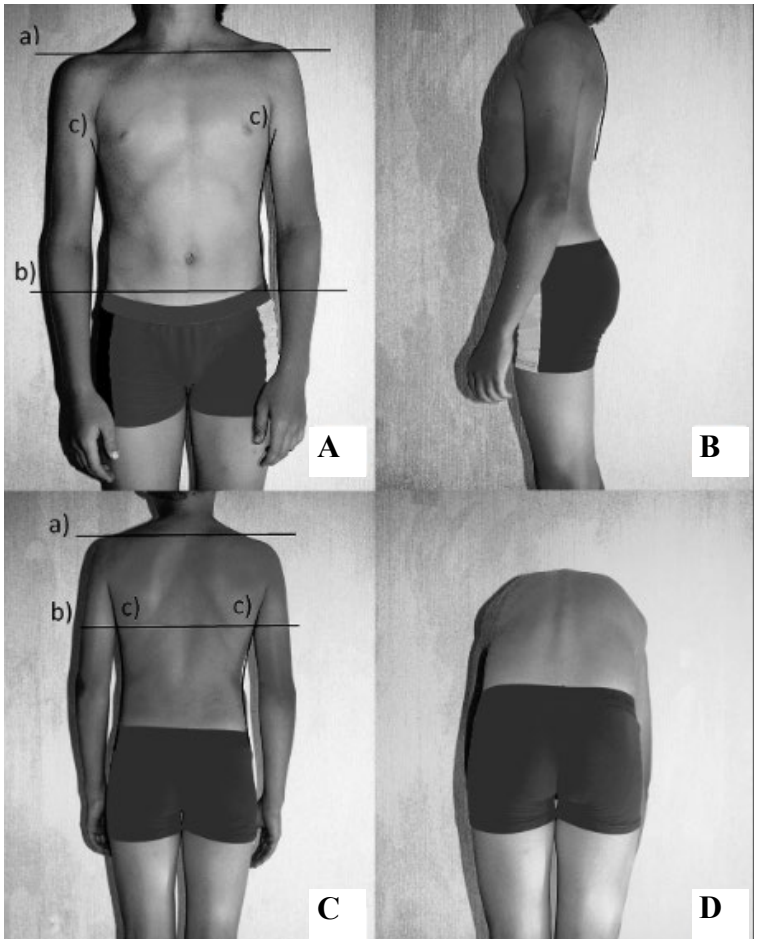
4 ***pav****. DNR sritys, naudotos dvynių zigotiškumui nustatyti*

Otorinolaringologinis vertinimas

Buvo atlikta priekinė ir užpakalinė rinoskopija bei faringoskopija. Diagnozės vertinti buvo naudojami šie kriterijai: adenoidų hipertrofija (2–3 laipsnių: jei uždengta ≥ ⅔ užpakalinė nosies etrmės erdvės); gomurinės migdolų hipertrofija (2–4 laipsnių: jei uždengta > 50proc. tarp migdolų arkų; nosies pertvaros kreivumas; alerginis rinitas (diagnozuotas pagal klinikinius požymius ir odos dūrio testus).

Ortopedinis vertinimas

Sąkandžio patologija suskirstyta pagal sąkandžio tipus esant vertikaliai, horizontaliai ir strėlinei padėtims. Ortopedinis vertinimas atliktas pacientui ramiai stovint (kifozės, lordozės, skoliozės diagnostika) – iš priekio, šono ir nugaros. Rezultatai buvo vertinami kaip atitinkantys normą arba ne. Atliktas kifozinės laikysenos, pečių linijos, menčių, klubų asimetrijos vertinimas (5 pav.).



5 pav. *Ortopedinis tyrimas*

A) vertinimas iš priekio: a) pečių simetrija; b) juosmens simetrija; c) viršutinių klubakaulių keterų horizontalus išsidėstymas. B) krūtinės kifozės vertinimas: krūtinės kifozės vertinimas atliekamas stebint pacientą iš šonino. C) vertinimas iš nugaros: a) pečių simetrija; b) menčių aukštis; c) juosmens simetrija. D) skoliozės vertinimas: norint patvirtinti arba paneigti skoliozę, atliekamas testas, kurio metu stebimas paravertebralinio raumens volelio atsiradimas juosmens srityje ir šonkaulinės kupros susiformavimas krūtinės ląstos srityje.

Statistinė analizė

Tyrimo metu buvo taikomos šios statistinės analizės: dviejų nepriklausomų grupių kiekybiniams dydžiams palyginti taikytas Stjudento *t* kriterijus, jei kintamojo skirstinys atitiko skirstinio normalumo sąlygą. Jei kintamieji netitiko skirstinio normalumo sąlygų, reikšmingumo lygmuo buvo tikrinamas neparametriniu Mann-Whitney metodu. Cefalometrinių matavimų paklaida nustatyta Bland ir Altman metodu. Pearsono koreliacijos koeficientas (r) (vertinant ryšius tarp matmenų); tiesinė kintamųjų priklausomybė vertinta apskaičiuojant monozigotinių (rMZ) ir dizigotinių (rDZ) dvynių Pearsono koreliacijos koeficientą (r). Genetinės struktūrinės lygtys (GSEM) – genetinės ir aplinkos įtakos kvėpavimo takų morfologijai modeliavimui (naudojant paketą „OpenMx“). Kintamumo šaltiniai buvo priskirti prie adityvių genetinių veiksnių (A), dominantinių genetinių veiksnių (D), bendrųjų aplinkos veiksnių (C) ir specifinių (unikalių) aplinkos veiksnių (E). Tyrime dalyvavo kartu augę dvyniai, todėl buvo taikomi tik ACE arba ADE modeliai. Modelių tinkamumas buvo vertinamas lyginant Akaike informacijos kriterijų (AIC) ir chi kvadrato (χ^2) reikšmes. Pasirinktas mažiausią AIC reikšmę turintis modelis. Lyties įtaka cefalometrinių parametrų koreliacijai buvo įvertinta prieš apskaičiuojant adityviosios genų ir modelis įtakos koeficientus. Rezultatai vertinti kaip statistiškai reikšmingi, reikšmingumo lygmuo $p < 0,05$. Pagrindinių komponentų analizė (PCA): sumažinti duomenų dimensiją ir nustatyti ryšius tarp cefalometrinių ir gomurio parametrų. Statistinė analizė atlikta naudojant R statistikos aplinką (versija 3.3.0) ir SPSS 20.0 (IBM Corp., Armonk, NY, JAV).

4 lentelė. *Genetinių struktūrinių lygčių modeliai*

Modelio santrumpa	Modelis	Paaiškinimas
E	Specifiniai aplinkos veiksniai	Modelis, kurio skirtumus lemia tik saviti aplinkos veiksniai – nėra atsižvelgiama į genetinius ar bendruosius aplinkos poveikius.
CE	Bendriieji ir specifiniai aplinkos veiksniai	Modelis, kurio skirtumus lemia bendrieji aplinkos veiksniai ir individualūs aplinkos veiksniai – genetinė įtaka neįtraukiama.
AE	Adityvieji genetiniai veiksniai ir specifiniai aplinkos veiksniai	Modelis, kurio skirtumus lemia adityvieji (suminiai) genetiniai veiksniai ir individualūs aplinkos veiksniai – bendros aplinkos poveikio nenumatyta.
ACE	Adityvieji genetiniai, bendrieji aplinkos ir specifiniai aplinkos veiksniai	Modelis, kurio skirtumus lemia trys komponentai: adityvieji genetiniai veiksniai, bendrieji aplinkos veiksniai ir individualūs aplinkos veiksniai.

4 lentelės tęsinys

Modelio santrumpa	Modelis	Paaiškinimas
ADE	Adityvieji genetiniai, dominantiniai genetiniai ir specifiniai aplinkos veiksniai	Modelis, kurio skirtumus lemia adityvieji genetiniai veiksniai, dominantiniai (neadityvūs) genetiniai veiksniai ir individualūs aplinkos veiksniai – bendros aplinkos įtaka neįtraukiama.
DE	Dominantiniai genetiniai ir specifiniai aplinkos veiksniai	Modelis, kurio skirtumus lemia tik dominantiniai genetiniai veiksniai ir individualūs aplinkos veiksniai – adityviosios genetinės ir bendros aplinkos įtakos nenumatyta.

REZULTATAI IR JŲ APŽVALGA

Sąsajos tarp nosiaryklės obstrukcijos, sąkandžio ypatumų ir kūno laikysenos

Tyrimu nustatyta, kad kifozinė laikysena buvo statistiškai reikšmingai susijusi su sumažėjusiu berniukų SNB kampu. Nebuvo nustatyta reikšmingų sąsajų tarp skersinių ortopedinių patologijų ir sąkandžio ar otorinolaringologinių sutrikimų. Kifozinė laikysena buvo dažnesnė tarp pacientų, turinčių nosiaryklės obstrukciją (54,1 proc.), palyginti su tais, kurie jos neturėjo (25 proc.). Pacientams, turintiems nosiaryklės obstrukciją ir kifozinę laikyseną, nustatytas reikšmingai sumažėjęs SNB kampas (apatinio žandikaulio padėties kampas kaukolės pagrindo atžvilgiu) (< 77°).

Genetinių ir aplinkos veiksnių įtaka kvėpavimo takų morfologijos ir su ja susijusių kaukolės struktūrų cefalometriniams parametrams

Modelių pritaikymo analizė atskleidė skirtingus genetinius ir aplinkos veiksnius, lemiančius kraniofacialinius ir kvėpavimo takų kintamuosius: viršutinių kvėpavimo takų matmenys – linijiniams parametrams, pvz., SPPW-SPP ir U-MPW, nustatyta vidutinė ar didelė įtaka paveldimumui, AE modelis buvo tinkamiausias. PNS-Ad1 nustatyta stipri vyraujanti genetinė determinacija (DE modelis, $d^2 = 0,51$). Nosiaryklės kvėpavimo takų matmuo (PNS-Ad1) pasižymėjo reikšminga genetine įtaka ($a^2 = 0,51$). Tai gali būti susiję su anatominėmis šio atstumo ypatybėmis, kuris jungia struktūras, tokias kaip pleištakaulis, pakaušio kaulas ir atlaso slankstelis. PNS-AD1 funkciškai sąveikauja su burnine ryklės dalimi ir minkštuoju gomuriu, todėl aplinkos veiksniai taip pat turi įtakos šio atstumo variacijoms. Nutukimas gali būti siejamas su sumažėjusiais viršutinių kvėpavimo takų matmenimis [44]. Aplinkos veiksniai prisideda prie nutukimo, tačiau paveldimieji KMI koreliacijos tyrimai ir dvynių tyrimai rodo stiprų genetinį komponentą. Mūsų tyrime bur-

ninei ryklės daliai (U-MPW) nustatyta didelė genetinė įtaka. Mūsų tyrime burninė ryklės dalis (U-MPW) turėjo didelę įtaką paveldimumui ($a^2 = 0,5$), tai rodo genetinę įtaką. Mūsų išvados taip pat atskleidė aplinkos įtaką U-MPW ($e^2 = 0,22$).

Minkštojo gomurio ilgis (SPL) buvo labiausiai veikiamas vyraujančių genetinių veiksnių, o minkštojo gomurio plotis (SPW) turėjo vidutinį adityvųjį genetinį poveikį. Apatinių kvėpavimo takų matmenys: parametrai, įskaitant PPW-TPP, LPW-V ir PCV-AH, daugiausia buvo nulemti aplinkos veiksnių (bendrų ir specifinių). Dauguma griaučių kintamųjų turėjo genetinę determinaciją: santykiai tarp viršutinio žandikaulio ir poliežuvinio kaulo rodė stiprų adityvųjį genetinį poveikį. Strėlinė apatinio žandikaulio padėtis (SNA, SNB) buvo daugiausia veikiama adityviųjų genetinių ir specifinių aplinkos veiksnių. SN-MP kampą lėmė specifiniai ir bendri aplinkos veiksniai.

Šiame tyrime nustatyta, kad 19 iš 23 cefalometrinių parametrų būdinga didelė genetinė determinacija, o kiti parametrai priklauso nuo aplinkos veiksnių arba jų derinio.

Strėlinis apatinio žandikaulio santykis su kaukolės pamatu ir viršutiniu žandikauliu

Linijiniams kintamiesiems (NMe, ANSMe, CoA, ArA ir SGo) buvo svarbūs genetiniai ($a^2 = 24–43$ proc.), bendri aplinkos ($c^2 = 45–68$ proc.) ir unikalūs aplinkos ($e^2 = 9–17$proc.) veiksniai ir jų įtaka. Vienas linijinis kintamasis, N-ANS, buvo veikiamas tik aplinkos veiksnių ($c^2 = 77$ proc., $e^2 = 23$ proc.). Kampiniams kintamiesiams (SNA, SNB, NSBa, NSAr, NAPog, SN–ArRp ir NGnGo) būdingas stiprus genetinis paveldimumas ($a^2 = 74–79$ proc.). Keturi kampiniai kintamieji (SNPog, SN–GoMe, ANSPNS–GoMe ir PoOr–GoMe) buvo paveikti tiek genetinių, tiek aplinkos veiksnių (ACE modelis).

Linijiniai kintamieji geriausiai atitiko ACE modelį, išskyrus MB2 ⊥ MB1Me, kuris buvo paaiškinamas AE modeliu. Kampiniams kintamiesiems (DcXiPm, CoGoMe, ArGoMe) būdingas didelis genetinis paveldimumas ($a^2 = 73–77$ proc.). ArRp–MB1Me geriausiai atitiko DE modelį ($d^2 = 81$proc.). Apatinio žandikaulio dantų ir atraminių jų struktūrų (dantoalveolinių) kintamieji: kampiniai kintamieji (ai.ii–NB, ai.ii–GoMe) buvo veikiami AE modelio ($a^2 = 69–71$ proc.). Linijiniai kintamieji turėjo tam tikras įtakas: AE modelis – Pog ⊥ NB, ii ⊥ NB ($a^2 = 83–84$ proc.). DE modelis: ii ⊥ APog, OB ($d^2 = 85–74$ proc.). CE modelis: ms ⊥ GoMe, OJ. ACE modelis: ii ⊥ GoMe.

Šeši pagrindiniai komponentai paaiškino 83 proc. bendros variacijos: PC1 (linijiniai kintamieji, išskyrus Pog ⊥ NB, ii ⊥ NB, ii ⊥ APog, OB, OJ, MB2 ⊥ MB1Me) atitiko ACE modelį. PC2–PC5: apėmė kampinius ir tam tikrus linijinius kintamuosius, turėjo didelį genetinį paveldimumą ($a^2 = 76–79$ proc.) ir

geriausiai atitiko AE modelį. PC6: Sudarė NAPog, OB ir OJ, kurie geriausiai buvo paaiškinami DE modeliu.

Genetiniai ir aplinkos veiksniai, lemiantys gomurio morfologiją

Aprašomoji statistika: vyrų dantų lankų plotis buvo šiek tiek didesnis nei moterų. Ryškiausias skirtumas nustatytas ties pirmaisiais kapliais ($p < 0,01$). Skirtumai ties iltimi ir krūminiais dantimis buvo statistiškai reikšmingi, tačiau mažiau ryškūs ($p < 0,05$). Vyrų dantų lankų plotis dantenų linijoje buvo didesnis, tačiau statistiškai nereikšmingas. Vyrų gomurio aukštis, paviršiaus plotas ir tūris buvo daug didesni nei moterų ($p < 0,01$). Matavimo patikimumo analize nustatytas didelis pakartotinių matavimų patikimuma (ICC = 0,90–0,96, $p < 0,01$). Dahlbergo formulė patvirtino, kad atsitiktinės paklaidos buvo mažesnės nei 1,0 mm linijinių matavimų, 15 mm^2 paviršiaus ploto ir 40 mm^3 tūrio.

Genetinė analizė: AE ir DE modeliai geriausiai atitiko daugumą kintamųjų. Dantų nuotoliai tarp kaplių (1IPW, 2IPW, IMW) rodė didelę genetinę determinaciją (AE modelis, $a^2 = 0,76$, 0,72 ir 0,86, atitinkamai). ICW nustatyta stipri vyraujanti genetinė determinacija (DE modelis, $d^2 = 0,59$). Gomurio dantenų linijų nuotoliai (ICWG, 1IPWG, 2IPWG) buvo daugiausia veikiami vyraujančių genetinių veiksnių ($d^2 = 0,50$, 0,78 ir 0,81, atitinkamai). Adityvieji genetiniai veiksniai turėjo įtakos tokiems kintamiesiems kaip gomurio tūris ir paviršiaus plotas ($a^2 = 0,62$).

Santykis tarp viršutinio dantų lanko morfologijos ir viršutinių kvėpavimo takų

Šiame tyrime dalyvavo 53 dvynių poros (27 monozigotinės ir 26 dizigotinės), kurių vidutinis amžius buvo 17,82 metų. Nustatyti reikšmingi ryšiai tarp gomurio parametrų ir viršutinių kvėpavimo takų matmenų: tarpiltinis nuotolis (ICD) (GL) koreliavo su ANS-AH nuololiu ($r = 0,19$, $p = 0,046$) ir ANS-V atstumu ($r = 0,21$, $p = 0,029$), nurodydamas ryšį tarp lanko pločio ir kvėpavimo takų erdvės. Tarpiltinis aukštis (ICH) parodė koreliaciją su ANS-AH nuotoliu ($r = 0,26$, $p = 0,007$) ir ANS-V nuotoliu ($r = 0,27$, $p = 0,005$). Gomurio paviršiaus plotas ir tūris koreliavo su PCV-AH ($p = 0,002$, $p = 0,003$) ir minkštojo gomurio pločiu (SPW) ($p = 0,047$, $p = 0,035$).

IŠVADOS

Ši disertacija nagrinėjo sudėtingą viršutinių kvėpavimo takų morfologijos ir kaukolės ir žandikaulio vystymosi ryšį, pabrėžiant genetinius ir aplinkos veiksnius, darančius įtaką šioms struktūroms. Analizuojant dvynių tyrimus, cefalometrinius parametrus ir tarpdisciplininius vertinimus, pateiktos naujos įžvalgos apie kvėpavimo takų matmenų paveldimumą ir ortodontinio gydymo poveikį kvėpavimo takų funkcijai.

1. Kifozinė laikysena buvo du kartus dažnesnė turintiems nosiaryklės obstrukcija pacientams, palyginti obstrukcijos neturinčiais pacientais (54,1 proc. ir 25 proc., atitinkamai, p = 0,02). Pacientams, turintiems kifozinę laikyseną, buvo statistiškai reikšmingai sumažėjęs kampas apatinio žandikaulio padėties ir kaukolės pagrindo.

2. Genetiniai veiksniai daro lemiamą įtaką kvėpavimo takų ir veido kaulinių struktūrų formavimuisi.

   a)Viršutinių kvėpavimo takų matmenis labai lemia adityvioji genetika (AE modelis, a^2 0,5–0,64) ir vyraujantis paveldimumas (DE modelis, d^2 – 0,5). Aplinkos veiksniai turi įtakos kvėpavimo takų apatinės ryklės dalies parametrams;

   b) veido kaulinių struktūrų cefalometriniai parametrai turi didelį paveldimumo koeficientą (h^2). Stebima stipri adityvioji genetinė įtaka cefalometriniams rodikliams, apibūdinantiems apatinio žandikaulio formą ir sagitalinę padėtį (a^2 = 0,74–79). Aplinkos veiksniai reikšmingai prisideda prie veido aukščio ir apatinio žandikaulio kaulinių linijinių cefalometrinių parametrų variacijos (c^2 = 0,45–0,68).

3. Gomurio ir viršutinio žandikaulio dantų lanko morfologiją labai lemia genetika. Didžiausias genetinis poveikis nustatytas gomurio aukščiui (a^2 = 0,86), gomurio paviršiaus plotui (a^2 = 0,61) ir tūriui (a^2 = 0,69). Mažesnis genetinis poveikis – dantų lanko pločiui ir gomurio kintamiesiems iltinių dantų srityje (d^2 = 0,48–0,59) – rodo, kad aplinkos veiksniai čia daro stipresnę įtaką formuojantis šiai gomurio zonai.

4. Nustatyta reikšmingų koreliacijų tarp gomurio matmenų ir viršutinių kvėpavimo takų parametrų. Tarpiltinis nuotolis ir aukštis koreliavo su nuotoliu tarp priekinio nosies keteros taško ir poliežuvinio kaulo ir nuotoliu tarp priekinio nosies keteros taško ir antgerklio. Gomurio plotas ir tūris reikšmingai koreliavo su nuotoliu tarp užpakalinės ryklės sienelės ir poliežuvinio kaulo ir minkštojo gomurio pločio. Tai rodo tarpusavio priklausomybę tarp gomurio skersinio ir vertikalaus vystymosi bei viršutinių kvėpavimo takų morfologijos.

DARBO TĘSTINUMAS IR KLINIKINĖ REIKŠMĖ

Ilgalaikiai tyrimai: būsimi tyrimai turėtų būti orientuoti į ilgalaikius stebėjimus, apimančius: genetinę analizę, CBCT ir kitus pažangius metodus,

Klinikinė reikšmė: aplinkos veiksniams jautresnės struktūros gali geriau reaguoti į ortodoninį gydymą. Ankstyva patikra ir tarpdisciplininis požiūris didina ortodontinio gydymo veiksmingumą ir stabilumą.

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LIST OF AUTHOR'S PUBLICATIONS

Publications related to the results of this dissertation

1. **Šidlauskienė, M.,** Papievis, V., Šidlauskas, A., Šidlauskas, M., Juzėnas, S., and Lopatienė, K.. (2024). Genetic and environmental impact on variation in the palatal dimensions in permanent dentition: a twin study. Scientific Reports, 14(1), 1-12. https://doi.org/10.1038/s41598-024-70985-4 [S1] [M.kr.: M002, N004] [Citav. rodiklis: 3.8, bendr. cit. rod.: 5.68, kvartilis: Q1 (2023. InCites JCR SCIE)]
2. **Šidlauskienė, M.,** Šidlauskas, M., Šidlauskas, A., Juzėnas, S., and Lopatienė, K.. (2023). Heritability of cephalometric variables of airway morphology in twins with completed active growth. BMC Oral Health. London : BioMed Central, 2023, Vol. 23, No. 1., 1-9. https://doi.org/10.1186/s12903-023-02919-x [S1a] [M.kr.: M002, N010] [Citav. rodiklis: 2.6, bendr. cit. rod.: 2.359, kvartilis: Q1 (2023. InCites JCR SCIE)]
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Abstracts related to the results of this dissertation at scientific conferences

1. Oral presentation "How the orthodontic palatal expansion affects the upper airway". **Šidlauskienė Monika**, 2nd International Scientific-Practical Conference "Digital or Conventional? What is more effective?" 18 January 2025, Kaunas, Lithuania.

2. Conference paper “How do environmental and genetic factors determine the anatomy of the palate. The relationship between the palate and upper airway”**. Šidlauskienė Monika**, et al. Stomatologija. Baltic Dental and Maxillofacial Journal: 2nd International Scientific-Practical Conference “Digital or Conventional? What is more effective?” 17-18 January 2025, vol. 26, no. 2, p. 5-5. Kaunas, Lithuania.
3. Poster presentation “Heritability of palatal area surface and volume in twins”. **Šidlauskienė Monika** et al. International conference “Surpassing the Limits in Orthodontics”, 16-17 November 2024, Vilnius, Lithuania.
4. Oral presentation “Heritability of maxillary, mandibular, airway dimensions cephalometric variables in twins with completed active growth”. **Šidlauskienė Monika** et al., International Health Sciences Conference for all 2024, March 26, Kaunas, Lithuania.
5. Oral presentation “Heritability of the upper airway dimensions using twin method”. **Šidlauskienė Monika**, International Congress, Baltic Days of Dentistry 2023, October 28, Vilnius, Lithuania.
6. Poster presentation “Impact of genetics on the position of hyoid bone”. **Šidlauskienė Monika**, et al. 98th Annual Congress of the European Orthodontic Society, 2023 11 -15 June, Oslo, Norway.
7. Poster presentation “Heritability of the upper airway dimensions using twin method”. **Šidlauskienė Monika** et al. 98th Annual Congress of the European Orthodontic Society, 2023 11- 15 June, Oslo, Norway.
8. Poster presentation “Mouth breathing habit correction. Interdisciplinary literature review” **Šidlauskienė Monika** et al. 95th European Orthodontic Society Congress, 2019 June 17-22, Nice, France.

Other abstacts at scientific conferences

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Relationships between Malocclusion, Body Posture, and Nasopharyngeal Pathology in Pre-Orthodontic Children

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Background: Malocclusion, body posture, and breathing pattern may be correlated, but this issue is still controversial. The aim of the study was to examine the relationship between the type of malocclusion, body posture, and nasopharyngeal obstruction in children aged 7–14 years.

Material/Methods: The study group comprised 94 patients aged 7–14 years (mean±SD: 11.9±2.1 years); 44 (46.8%) males and 50 (53.2%) females. All patients passed an examination performed by the same orthodontist (study model and cephalometric radiograph analysis), orthopedic surgeon (body posture examined from the front, side, and back), and otorhinolaryngologist (anterior and posterior rhinoscopy and pharyngoscopy) in a blind manner.

Results: Postural disorders were observed in 72 (76.6%) patients. Hypertrophy of the adenoids was diagnosed in 54 (57.4%) patients, hypertrophy of the tonsils in 85 (90.3%), nasal septum deviation in 51 (54.3%), and allergic rhinitis in 19 (20.2%) patients. There was a statistically significant correlation between presence of kyphotic posture and a reduction in the SNB angle, representing sagittal position of the mandible. Also, there was a statistically significant association between kyphotic posture and nasopharyngeal obstruction (54.1% of patients with nasopharyngeal obstruction were kyphotic, compared with 25% of patients with no nasopharyngeal obstruction; p=0.02). Kyphotic posture and reduced SNB angle were more common among males.

Conclusions: We concluded that: 1) there was a significant association between the sagittal position of the mandible (SNB angle) and a kyphotic posture; 2) kyphotic posture was significantly more common among patients with nasopharyngeal obstruction.

MeSH Keywords: Malocclusion • Nasopharyngeal Diseases • Posture

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Background

The stomatognathic system, an integral component of the upper body, may play an important role in postural control. Thus, changes in body posture may affect craniofacial development. Several studies suggest that spatial relationships between the jaws may influence the distal musculature and induce body postural adaptations [1,2]. However, Perinetti et al. concluded that mandibular position, asymmetric occlusion, and temporomandibular disorders do not appear to correlate with body sway or muscle activity in other parts of the body, including those responsible for maintaining posture, at a clinically relevant level [3,4].

Several studies have examined the relationship between malocclusion and parameters of body posture in the sagittal and frontal planes; the results identified a correlation between structural orthopaedic diseases and occlusal morphology [6,5]. Segatto et al. found that children with various spinal deformities have a high number of malocclusions [7], and Ben-Bassat et al. found that patients with idiopathic scoliosis showed more asymmetric features characteristic of malocclusion than a random control group [8]. Also, children with congenital hip dislocation are more predisposed to the development of a lateral cross-bite [9]. However, the results from studies looking at the correlation between poor body posture and dental occlusion are conflicting. For example, Lippold et al. examined 59 pre-school children and found statistically significant correlations between weak body posture and Class II malocclusion [6]. Also, Lippold et al. used rasterstereography to examine the sagittal profile of the spine in 53 adults with skeletal Class II and Class III malocclusions, and found a correlation between the vertical and sagittal position of the lower jaw and thoracic, lordotic, and pelvic inclination [10], and between the vertical and sagittal position of the lower jaw and pelvic rotation [11]. Thus, 2 different models of back shape were devised based on of the results on these studies: 1) a more distal and vertical craniofacial pattern is associated with an increase in the upper thoracic, lumbar-lordotic, and pelvic angles; and 2) a more mesial and horizontal craniofacial pattern is associated with smaller upper thoracic, lumbar-lordotic, and pelvic angles. Sinko et al. compared body posture in 29 Class II and Class III patients, and found that the apex of the thoracic kyphosis was more cranial in Class III patients than in Class II patients or healthy controls [12]. However, these studies are based on small samples. When Perillo et al. examined 703 children, they found no association between body posture and clinically assessed dental occlusion [13]. Silvestrini-Biavati et al. investigated association between malocclusion, poor posture, and ocular convergence disorders. They observed that about 14% of all patients had a pathological gait; among them, children demonstrated a higher prevalence of vertical occlusion anomalies [14]. Contradictory results of studies can arise because there was a large diversity among the studies with regard to the protocols used; some studies assessed body posture by physical examination while other studies used body photographs and rasterstereography.

There is also a correlation between body posture and breathing pattern. Enlarged tonsils and adenoids, allergic rhinitis, and chronic respiratory problems cause a mouth breathing syndrome, resulting in adaptive head and body postures [15], which also affects the development of the facial skeleton. It is generally accepted that anterior tilting of the head is the main postural change in such subjects, who push their heads forward and extend their neck to facilitate air flow through the mouth. An altered neck posture was observed in 80.0% of mouth-breathing children [15]. The forward position of the head causes protraction and rotation of the shoulders, elevation and abduction of the scapulae, depression of the thoracic anterior region, and forward displacement of the whole body. Unlike in nasal-breathing children, these postural changes in mouth-breathing children do not improve spontaneously once they are older (>8 years-of-age) [16]. Milanesi et al. demonstrated that adults who were mouth-breathers during childhood had a more anterior head posture and a larger lumbar lordosis angle than individuals in a control group [17].

To date, no study has examined the association between malocclusion, body posture, and breathing pattern. The assessment of correlations between orthopedic, otorhinolaryngologic, and orthodontic findings derived from interdisciplinary studies appears to be of practical importance in diagnosis and prevention. Therefore, the aim of the present study was to examine the relationship between the type of malocclusion, body posture, and nasopharyngeal obstruction in children aged 7–14 years. The tested null hypotheses were that: 1) sagittal craniofacial skeletal morphology depends on the nasopharyngeal obstruction and body posture, and 2) vertical craniofacial skeletal morphology depends on the nasopharyngeal obstruction and body posture.

Material and Methods

The study sample was obtained from consecutive patients attending for orthodontic treatment at the Department of Orthodontics who agreed to participate in the study from September 2013 through May 2014. A full explanation of the study aims and procedures was provided to the parents of each patient and signed consent forms were obtained. The study was approved by the Regional Biomedical Research Ethics Committee (no. BE-2-48).

The study group comprised 94 patients aged 7–14 years (mean ±SD: 11.9±2.1 years). Forty-four were male (46.8%) and 50 were

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female (53.2%). All patients passed an examination performed by the same clinical team in a blinded manner. Power analysis was used to determine the sample size. Performing a power calculation, we anticipated changes in SNB angle by 2° (SD=2), α=0.05. In such circumstances, this study aimed to investigate 90 patients (n1=45, n2=45) to achieve 0.99 power. After investigation we concluded the study needed a power 0.802 (n1=49, n2=45; α=0.05; change in SNB angle 2.21) (SD=3.77).

The inclusion criteria into the study were as follows: age 7–14 years; no history of maxillofacial trauma or surgery, syndromes, clefts, or orthodontic treatment; no previous treatment for orthopedic disorders; and no previous injury to the pelvis, spine, or long bones.

Orthodontic examination

The orthodontic examination consisted of the study model and cephalometric radiograph analysis. The study model examination consisted of a transverse examination in which a posterior cross-bite was confirmed (at least 2 teeth showed a cross-relationship with the opposite teeth in the posterior segments of the dental arches. The cross-bite was categorized as unilateral or bilateral, and we performed a space analysis in which the difference between the available space and the necessary space in the dental arch was calculated. Crowding was categorized as mild (lack of space: 2–4 mm), moderate (5–9 mm), or severe (>9 mm). A standardized lateral cephalometric radiograph was taken for each patient (Kodak 8000C; enlargement factor 1.15; exposure: 12 mAs, 76–80 kV) and analyzed using Dolphin software (version 10.5). The sagittal position of the maxilla (SNA) and the mandible (SNB), the sagittal jaw relationship (ANB), the mandibular plane angle (MP-SN), and the inclination of the maxillary incisors and mandibular incisors (U1-ANS/PNS and L1-MP, respectively) were used to analyze the facial skull parameters. All measurements are shown in Figure 1.

The error margins for the study models and lateral cephalometric analysis were determined by repeatedly measuring the 6 variables on 10 randomly selected models and radiographs at 2-week intervals. Measurements were made by the same operator (MS). Parametric data were subjected to a paired-samples t-test and non-parametric Wilcoxon signed ranks test, which showed that there was no significant difference between the data sets.

Orthopedic examination

The examination was performed in a quiet classroom without external interference. The patient was examined in a relaxed standing posture: subjects were asked to stand in an upright position, barefoot, without moving, looking straight ahead,

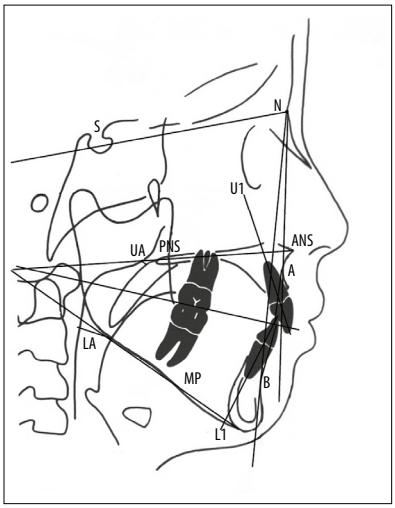

Figure 1. References and points used for this study. The sagittal position of the maxilla (SNA) and the mandible (SNB), the sagittal jaw relationship (ANB), the mandibular plane angle (MP-SN), the inclination of the maxillary incisors and mandibular incisors (U1-ANS/PNS and L1-MP).

with relaxed shoulders and arms resting at their sides for a natural head and body position. A standard routine examination from the front, side, and back was performed for each patient. Degrees of severity cannot be differentiated with adequate precision by manual orthopedic diagnostics; therefore, the findings were graded either as normal or abnormal. Patients were first examined from the side and the thoracic kyphosis was evaluated. If an increased, but adjustable, asymptomatic curvature of the thoracic spine was observed, the posture was classed as kyphotic. All patients underwent tests to rule out Scheuermann's disease and ankylosing spondylitis; briefly, each patient was asked to stand upright and pull back the shoulders to induce thoracic extension. In cases of postural kyphosis, an increased curvature, which is regular and mobile, was found. Next, patients were examined from the front, and the position of shoulders, the symmetry of the waist triangles, and the horizontal alignment of the upper iliac crests were noted. Finally, patients were examined from the back, and the position of the shoulders, the scapular height, and the symmetry of the waist triangles, iliac crests, and thoracic rib hump were noted. Differences between the left and right sides were interpreted as asymmetry. All the patients underwent testing

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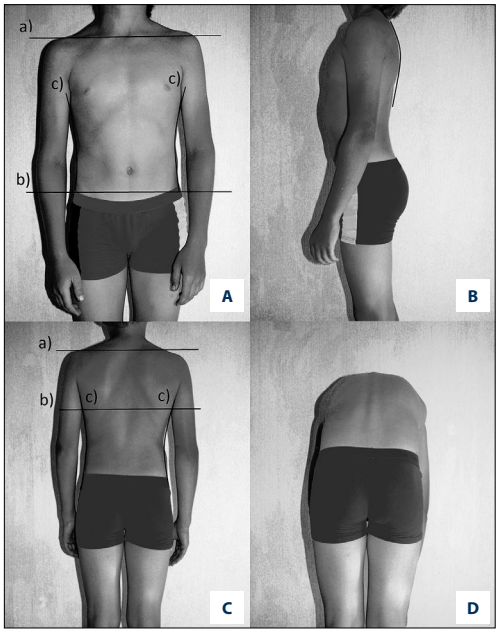

Figure 2. Orthopedic examination: (**A**) Evaluation from the front: a) symmetry of the shoulders; b) symmetry of the waist triangles; c) horizontality of frontal upper iliac crests. (**B**) Thoracic kyphosis has to be evaluated from the side. (**C**) Evaluation from the back: a) symmetry of the shoulders; b) the scapular height; c) symmetry of the waist triangles. (**D**) Test to confirm or rule out scoliosis. It has to be observed if the paravertebral muscle roller emerges in the lumbar region and the rib hump in the thoracic region.

to rule out scoliosis. Briefly, patients were asked to bring their chin to their chest, relax the hands, and flex the hips with the knees extended. The examiner then looked for the emergence of a paravertebral muscle roller in the lumbar region or a rib hump in the thoracic region. If a rib prominence hump was present (>1 cm), then full-length frontal and lateral spinal radiographs were obtained to evaluate the degree of spinal deformation (by measuring the Cobb's angle) (Figure 2).

Otorhinolaryngological examination

Anterior and posterior rhinoscopy and pharyngoscopy were performed to assess nasal and pharyngeal status. The following diagnoses were made based on the findings: hypertrophy of the adenoids (Grade 2–3) was diagnosed when up to 2/3 of the choana was compromised; hypertrophy of the palatal tonsils (Grade 2–4) was diagnosed when there was <50% of normal space between tonsillar pillars; nasal septum deviation was diagnosed when the nasal septum was severely shifted away from the midline; and allergic rhinitis was diagnosed when the patient showed typical allergy symptoms (nasal congestion, runny nose, sneezing, and watery eyes) and skin-prick test results were positive. Nasopharyngeal obstruction was determined when hypertrophy of the adenoids (2nd degree or higher) and/or hypertrophy of the tonsils (2nd degree or higher), and/or nasal septum deviation and/or allergic rhinitis was diagnosed for the patient.

The orthopedic and otorhinolaryngological examination was performed by expert investigators (EC and RP). To assess the method error of clinical investigation, prior to the survey, the investigators calibrated and standardized their procedures by repeating examinations of 10 patients at 2 different times (measuring agreement was calculated by kappa; kappa values were >0.8).

Statistical analysis

All statistical analyses were performed using the statistical software package SPSS 20.0 for Windows. To compare the mean values, the Student's t test was used if the distribution of data was normal. In case of non-normal data, the Mann-Whitney U test was used. Hypotheses of interrelations between characteristics were verified using the χ^2 criterion method and Spearman correlation coefficients (r). The most specific predictors of the

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Table 1. The orthodontic, orthopedic, and otorhinolaryngological characteristics of the study group.

Characteristic		Patients n (%)	
Orthodontic characteristics:			
Skeletal sagittal relationship	Class I (ANB angle 1–3°)	26	(27.7%)
	Class II (ANB angle ≥4°)	60	(63.8%)
	Class III (ANB angle ≤0°)	8	(8.5%)
Postural characteristics			
Kyphotic posture		45	(47.9%)
Asymmetry of shoulder line		23	(24.5%)
Asymmetry of position of scapulae		23	(24.5%)
Asymmetry of waist triangles		5	(5.3%)
Rib hump		48	(51.1%)
Otorhinolaryngological characteristics			
Hypertrophy of adenoids	Grade 1	24	(25.5%)
	Grade 2	30	(31.9%)
Hypertrophy of tonsils	Grade 1	46	(48.9%)
	Grade 2	32	(34%)
	Grade 3	7	(7.4%)
Nasal septum deviation		51	(54.3%)
Allergic rhinitis		19	(20.2%)

decrease in the SNB angle were assessed using logistic regression analysis and receiver operating characteristic (ROC) curve analysis. A p-value of <0.05 was considered statistically significant.

Results

The orthodontic, orthopedic, and otorhinolaryngological characteristics of the patients are described in Table 1.

Postural disorders were observed in 72 (76.6%) patients. Structural orthopedic anomaly (scoliosis) was observed in 1 patient. Kyphotic posture was more common among males (26; 59.1%) than females (19; 38%) (p=0.01). There was no statistically significant association between sex and the occurrence of transverse orthopedic pathology. The relationships between malocclusion, sex, and sagittal orthopaedic pathology are presented in Table 2.

There was a statistically significant correlation between presence of kyphotic posture and a reduction in the SNB angle (statistically significant in males but not significant in females).

Table 3 shows the relationship between orthodontic anomalies, sex, and nasopharyngeal obstruction.

There was no significant association between the presence of transverse orthopedic pathology and orthodontic or otorhinolaryngologic pathology. Also, there was no relationship between crowding, posterior cross-bite, and orthopedic or otorhinolaryngologic parameters.

The findings evaluating the relationship between nasopharyngeal obstruction and sagittal orthopedic pathology indicated that kyphotic posture was significantly more common among patients with nasopharyngeal obstruction – 54.1% patients with nasopharyngeal obstruction were kyphotic, compared with 25% patients with no nasopharyngeal obstruction (Spearman's correlation coefficient=0.24; p=0.02).

Because we identified a significant decrease in the SNB angle in patients with kyphotic posture and nasopharyngeal obstruction, we performed logistic regression analysis to evaluate the risk of a decrease in the SNB angle. The critical value of the SNB angle was determined using ROC curve analysis (Figure 3).

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Table 2. The relationship between orthodontic variables, sex, and sagittal orthopaedic parameters (thoracic kyphosis).

Orthodontic variables	Female		p	Male		p	Total		p
	n=50			n=44			n=94		
	Thoracic kyphosis			Thoracic kyphosis			Thoracic kyphosis		
	Normal	Kyphotic posture		Normal	Kyphotic posture		Normal	Kyphotic posture	
	n=31	n=19		n=18	n=26		n=49	n=45	
	Mean, SD	Mean, SD		Mean, SD	Mean, SD		Mean, SD	Mean, SD	
Sagittal position of the maxilla (SNA°)	82.03±3.61	81.28±3.08	0.46	82.50±3.47	80.88±2.9	0.1	82.2±3.53	81.05±2.95	0.91
Sagittal position of the mandible (SNB°)	78.58±3.78	77.21±2.76	0.17	79.00±3.99	76.02±3.74	0.02*	78.73±3.08	76.52±3.38	0.01*
Sagittal jaw relationship (ANB°)	3.35±2.8	3.97±1.58	0.39	3.60±2.78	4.75±3.35	0.24	3.44±2.76	4.42±2.75	0.23
Mandibular plane angle (MP-SN°)	32.59±5.02	35.00±4.47	0.92	31.90±6.60	33.12±6.27	0.54	32.34±5.59	33.91±5.60	0.18
Inclination of maxillary incisors (U1-ANS/PNS)	107.74±8.41	106.89±7.62	0.72	107.33±10.8	106.94±9.44	0.9	107.59±9.29	106.92±8.62	0.72
Inclination of mandibular incisors (L1-MP°)	91.71±9.22	93.63±6.79	0.44	92.36±8.2	93.40±6.44	0.64	91.95±8.78	93.50±6.51	0.34
Overjet (mm)	3.37±2.64	3.86±1.2	0.42	3.39±3.27	5.15±3.34	0.09	3.38±2.85	4.62±2.71	0.03*
Overbite (mm)	3.78±2.39	4.05±2.04	0.67	3.50±2.35	5.19±2.15	0.02*	3.68±2.36	4.71±2.16	0.03*

The threshold of 77° was crucial for the SNB angle (sensitivity 71.1%; specificity, 69.8%; p=0,002). We found that among patients with SNB angle <77°, kyphotic posture was found in 71.1% of patients and normal thoracic kyphosis was found in 38.8%.

Therefore, we performed binary logistic regression analysis, which revealed that kyphotic posture increases odds ratio of the SNB<77° angle by 3.887 (95% CI; 1.639–9.218). This calculation adjusted with nasopharyngeal obstruction indicated odds ratio of the SNB<77° angle by 4.037 (95% CI; 1.652–9.861).

Discussion

Malocclusion has a multifactorial etiology; several of these factors, including oral habits and breathing mode, play an important role in pathogenesis. Changes in body posture may also influence craniofacial development. An improved understanding of the mechanism underlying normal craniofacial development is needed for the accurate diagnosis and appropriate treatment of malocclusion. The present study was based on the hypothesis that body posture, breathing pattern, and the type of malocclusion are inter-dependent.

The study group comprised consecutive orthodontic patients aged 7–14 years (the age during which transition from primary to permanent dentition occurs). This age range of patients was also selected on the basis of growth peculiarities. A healthy child assumes a normal spinal curvature at around 7 years of age. The rate of spinal growth is not constant – there is a period of accelerated growth between 10.5 and 15.5 years of age, and peak height velocity occurs at an average of 12.2 years in

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Table 3. The relationship between orthodontic variables, sex, and nasopharyngeal obstruction.

Orthodontic variables	Female		p	Male		p	Total		p
	n=50			n=44			n=94		
	Nasopharyngeal obstruction			Nasopharyngeal obstruction			Nasopharyngeal obstruction		
	Absent	Present		Absent	Present		Absent	Present	
	n=12	n=38		n=8	n=36		n=20	n=74	
	Mean, SD	Mean, SD		Mean, SD	Mean, SD		Mean, SD	Mean, SD	
Sagittal position of the maxilla (SNA°)	81.92±3.55	81.69±3.40	0.85	82.25±5.01	81.39±2.74	0.5	82.05±4.07	81.55±3.08	0.56
Sagittal position of the mandible (SNB°)	79.08±3.80	77.74±3.34	0.25	78.13±4.26	77.04±4.07	0.5	78.70±3.91	77.40±3.71	0.17
Sagittal jaw relationship (ANB°)	2.74±3.30	3.85±2.04	0.17	4.13±1.64	4.32±3.41	0.88	3.30±2.79	4.08±2.78	0.48
Mandibular plane angle (MP-SN°)	32.17±3.33	33.93±5.27	0.28	30.85±6.65	33.01±6.32	0.39	31.64±4.81	33.48±5.79	0.2
Inclination of maxillary incisors (U1-ANS/PNS)	107.83±9.07	107.29±7.83	0.84	103.38±12.55	107.93±9.26	0.25	106.05±10.52	107.60±8.50	0.49
Inclination of mandibular incisors (L1-MP°)	92.67±10.54	92.37±7.71	0.92	93.88±5.67	92.78±7.48	0.7	93.15±8.75	92.57±7.55	0.77
Overjet (mm)	3.08±2.58	3.72±2.09	0.39	4.31±2.75	4.46±3.55	0.91	3.58±2.65	4.08±2.90	0.48
Overbite (mm)	3.21±1.83	4.10±2.35	0.24	4.19±2.20	4.57±2.42	0.68	3.60±1.99	4.33±2.38	0.21

girls and 13.9 years in boys [18]. During this period, any postural defects may be either spontaneously corrected or become worse [19]. We detected a high prevalence of orthopedic anomalies in the study group, the most common being kyphotic posture (47.9%) and a thoracic rib hump (51.1%). This is in agreement with the findings of other studies. For example, Lippold et al. reported orthopedic pathological findings in 52% of preschool children [6], and Hagner et al. identified poor body posture in 65.71% of 10-year-old and 54.29% of 13-year-old non-orthodontic children [19]. Nasopharyngeal pathology also was a common finding in the present study. According to the literature, hypertrophy of the adenoids and tonsils, which causes mouth breathing, is common in children (varying from 40% to 60%) [20]. The present study identified hypertrophy of the adenoids in 57.4% and of the tonsils in 90.3% of subjects; these high levels may be due to the selection of the specific group of patients.

Overall, the results showed that sagittal body posture was related to sagittal craniofacial parameters. Patients with a kyphotic posture had an increased overjet and lower SNB angle. This was significant in males, but was only a tendency in females. Such a difference could occur because kyphotic posture was more common among males (59.1%) than females (38%) (p=0.01). This is in agreement with the results of Lippold et al., who identified correlations between the sagittal position of the lower jaw and thoracic inclination [10]. Lippold et al. also reported that the position of the maxilla does not correlate with spinal curvature [10,11], which also agrees with our results. However, we found no relationship of the vertical position of the lower jaw and thoracic inclination, which is in contrast to the results of Lippold et al. [10]. The results of our study show that the facial angle (MP-SN) tended to be increased in patients with a kyphotic posture; however, this

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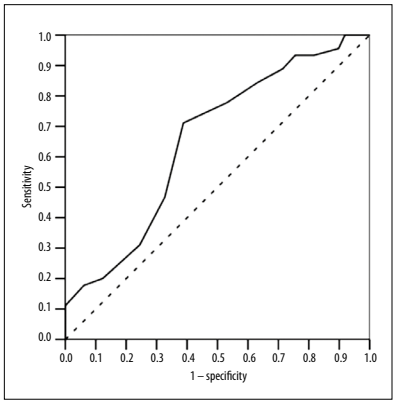

Figure 3. Receiver operating characteristic (ROC) curve analysis for prediction of the critical values of the SNB angle. Area under the receiver operating characteristic curve=65.2%.

difference was not significant. Silvestrini-Biavati et al. reported that about 13% of children 8.5±2.3 years old showed a pathological gait, and among them there was a higher prevalence of patients with a deep bite and open bite. The authors also suggested that vertical malocclusions are correlated to the dominant eye [14]. In our study we found that dental overjet and overbite were statistically significantly greater in patients with a kyphotic posture; however, skeletal vertical parameters (angle MP-SN) did not differ in groups with normal or kyphotic posture.

According to our results, craniofacial parameters were not associated with nasopharyngeal pathology. Previous studies showed that nasopharyngeal pathology causes changes in the growth of the mandible (which rotates downward and backward), and an increase in the height of the lower face [21,22]. We also found that a kyphotic posture was statistically significantly more common among patients with nasopharyngeal pathology; however, Neiva et al. did not find an increase in thoracic kyphosis in mouth-breathing subjects [23].

When we evaluated body posture in the transverse plane, we identified any association between asymmetric posture and orthodontic parameters. The malocclusion most likely to be related to asymmetric orthopaedic anomalies should be a posterior cross-bite. Korbmacher et al. examined 55 children referred to an orthopedic center and found that those with a unilateral cross-bite were more likely to have an oblique shoulder, oblique pelvis, functional leg length differences, and scoliosis than children with dental symmetry [24]. Mouth breathing is also associated with narrowing of the upper dental arch and a posterior cross-bite. However, we did not find any relationship between body posture, nasopharyngeal pathology, and a posterior cross-bite. Michelotti et al. also failed to demonstrate a significant association between a posterior cross-bite and postural stability or transverse orthopedic pathology [25]. Here, we found no relationship between crowding of the dental arches and body posture or nasopharyngeal pathology. This is in contrast to the findings of Pachi et al. and Solow and Sonnesen, who reported that crowding was associated with craniocervical posture [26,27]. The discrepancy between the results reported herein and those of others can be explained, at least in part, by differences in study design (e.g., type of orthopedic evaluation), specific patient groups (e.g., orthodontic/non-orthodontic patients), different age groups, and different sample sizes.

In summary, the results of the present study suggest that there is a significant association between a decrease in the SNB angle, kyphotic posture, and nasopharyngeal pathology. The presence of kyphotic posture, especially together with a nasopharyngeal obstruction, increases the possibility of the mandibular retrusion. The null hypotheses were tested: 1) sagittal craniofacial skeletal morphology depended on the nasopharyngeal obstruction and body posture; and 2) vertical craniofacial skeletal morphology did not depend on the nasopharyngeal obstruction and body posture. However, the question of causality remains. Which of these morphologic changes are primary and which are consequential? To answer this question, we looked at a few studies that evaluated changes in body posture after the correction of malocclusion. Lippold et al. conducted a randomized clinical trial in a juvenile population with a unilateral posterior cross-bite and found that early orthodontic treatment had no effect on postural parameters [28]. Sinko et al. found that there was no significant difference between body posture before orthognathic surgery and at 1 year after surgery [12]. Tecco et al. suggest that improvements in nasopharyngeal airway adequacy after rapid maxillary expansion were only mildly associated with changes in the craniocervical angle and tipping of the head [29], and a review by Michelotti et al. concluded that even if there is an association between occlusal factors and postural alterations, there is not enough scientific evidence to support a cause-effect relationship [30]. Therefore, although it is reasonable to suppose that the stomatognathic system can affect cervical region function, its overall relevance to body posture is still unclear. This lack of scientific evidence in the literature of a cause-effect relationship between occlusion, nasopharyngeal pathology, and postural disorders makes this question difficult to answer. Further studies with correct methods are needed to clarify these cause-effect relationships.

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Conclusions

The present study has 2 main findings: 1) there was a significant association between the sagittal position of the mandible (SNB angle) and a kyphotic posture; and 2) based on study results, kyphotic posture was significantly more common among patients with nasopharyngeal obstruction.

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RESEARCH Open Access

Heritability of cephalometric variables of airway morphology in twins with completed active growth

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Abstract

Background The interplay between genetic and environmental impacts on dental and facial morphology has been widely analyzed, but little is known about their relative contributions to airway morphology. The aim of this study was to evaluate the genetic and environmental influences on the cephalometric variables of airway morphology in a group of postpubertal twins with completed craniofacial growth.

Materials and methods The materials comprised lateral head cephalograms of 94 pairs of twins (50 monozygotic, 44 dizygotic) with completed craniofacial growth. Zygosity was determined using 15 specific DNA markers. The computerized cephalometric analysis included 22 craniofacial, hyoideal, pharyngeal structural linear and angular variables. Genetic analysis and heritability estimation were performed using maximum likelihood genetic structural equation modeling (GSEM). Principal component analysis (PCA) was used to assess the correlations between cephalometric measurement variables.

Results Upper airway dimensions showed moderate to high genetic determination (SPPW-SPP and U-MPW: $a^2 = 0.64$ and 0.5, respectively). Lower airway parameters showed only common and specific environmental determination (PPW-TPP $a^2 = 0.24$, $e^2 = 0.38$; LPW-V $c^2 = 0.2$, $e^2 = 0.63$; PCV-AH $c^2 = 0.47$, $e^2 = 0.28$). The relationship between the maxilla and the hyoid bone (for variables PNS-AH, ANS-AH $d^2 = 0.9$, 0.92, respectively) showed very strong additive genetic determination. The size of the soft palate was affected by additive and dominant genes. Its length (SPL) was strongly influenced by dominant genes, while its width (SPW) showed a moderate additive genetic influence. Owing to correlations in the behavior of variables, the data could be expressed in 5 principal components that jointly explained 36.8% of the total variance.

Conclusions The dimensions of the upper airway are strongly determined by genes, while the parameters of the lower airway depend mainly on environmental factors.

Trial registration The protocol has been approved by the Kaunas Regional Ethical Committee (No. BE – 2–41., May 13, 2020).

Keywords Twin study, Upper airway, Cephalometrics, Genetics, Orthodontics

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Introduction

The airway, mode of breathing, and craniofacial formation are very closely interrelated during growth and development [1]. It is known that dysfunction of the human airway and breathing can cause malocclusion and skeletal deformation. [2]. An open bite, a hyperdivergent growth pattern, proclined upper incisors, increased lower facial height, steepening of the mandibular plane angle, lowering of the chin and increase in the gonial angle are among these features [3, 4].

Nasal breathing abnormalities may develop due to a variety of conditions, such as adenoid and tonsil hypertrophy, mandibular or maxillary retrognathism, a short mandibular body, and backward and downward rotation of the mandible, which may lead to upper airway stenosis, reduction of the pharyngeal airway space and even the development of obstructive sleep apnea (OSA) [5, 6]. Obesity increases any present airway obstruction by enlarging the tongue, uvula and throat tissues [7, 8]. All of these conditions, as well as facial phenotype and dental and skeletal morphology, are influenced by genes and the environment. The interplay between genetic and environmental impacts on dental and facial morphology has been widely analyzed, but little is known about their relative contributions to airway morphology [9–11].

The prognosis of the success for orthodontic and dentofacial orthopaedic correction of malocclusion is determined by the extent to which a particular malocclusion can be influenced by therapeutic environmental intervention. Generally, malocclusions with a genetic cause are thought to be less amenable to treatment than those with an environmental cause. The same is truth for the success of airway morphology improvement by means of corrective orthodontics and orthopaedics [12]. Therefore, knowledge of genetic and environmental impact on airway structures, is of primary interest for orthodontic research and clinical practice [13].

Although the use of comprehensive phenotype analysis in combination with large-scale genome-wide association studies maximizes the efficiency with which clinically relevant phenotype–genotype correlations can be detected, only a few correlations of this type have been discovered. Significant genetic contributions to variables such as the timing of dental maturation, incisor and canine crown diameters, missing or supernumerary teeth, arch dimensions and Class III malocclusion development have been established [14]. However, data concerning genetic and environmental influences on airway morphology are scarce and mainly related to sleep apnea cases [15, 16]. Determining the degree of influence exerted by genetics and by environmental factors, such as orthodontic treatment, in the development of airway obstruction can help shed light on the role of orthodontists in addressing this health issue.

Twin studies combined with advanced statistical methods provide an opportunity to determine the relative contributions of genetics and environment to dentofacial development [10, 11, 14].

The aim of this study was to evaluate the genetic and environmental influences on the cephalometric variables of airway morphology in a group of postpubertal twins with completed craniofacial growth.

Materials and methods

The study was undertaken in the Department of Orthodontics, Lithuanian University of Health Sciences (LSMU). The sample consisted of 94 pairs of same-gender twins (50 monozygotic, 44 dizygotic) selected from the register of the Twin Centre at LSMU. The protocol was approved by Kaunas Regional Ethical Committee (No. BE – 2–41). All twins had clinical consultations, and lateral cephalograms necessary for this study were performed. The CVM method was used to assess the completion of skeletal maturation [17].

Inclusion criteria: twins of European origin, cervical vertebral maturation (CVM) stage 6 (active growth completed), high-quality cephalometric data available from both twins in the database.

Exclusion criteria: previous orthodontic treatment, permanent tooth extractions, dental or facial trauma, systemic diseases or syndroms.

Zygosity determination

All participating twins underwent DNA tests to determine their zygosity [18].

Zygosity determination was carried out using a DNA test. The polymerase chain reaction set AmpFLSTR Identifiler (Applied Biosystems, USA) was used to amplify short tandem repeats, and 15 specific DNA markers (D8S1179, D21S11, D7S820, CSF1PO, D3S1358, TH01, D13S317, D16S539, D2S1338, D19S433, vWA, TROX, D18S51, D5S818, FGA) and the Amel fragment of the amelogenin gene were used for comparison of genetic profiles. Zygosity determination using this molecular genetic technique has 99.9% accuracy [18, 19].

Cephalometric analysis

The cephalometric analysis was used to measure airway and skeletal dimensions. The cephalograms were taken in centric occlusion under standard conditions using digital X-ray equipment. For standardized positioning, a cephalostat was used to stabilize the subject's head in a constant position relative to the sensor. Lateral cephalometric (LC) radiographs were taken after swallowing. All lateral cephalograms had the same magnification. The radiographs were analyzed by using Dolphin Imaging v.11.7.

Definitions of cephalometric landmarks, reference lines, and cephalometric measurements are presented in Fig. 1.

Cephalometric points: *S, sella* – the midpoint of the hypophyseal fossa; *N, nasion* – the anterior point at the frontonasal suture; *A, point A* – the deepest point in the curvature of the maxillary alveolar process; *B, point B* – the deepest point in the curvature of the mandibular alveolar process; *ANS, point ANS* – the anteriormost point of the anterior nasal spine; *PNS, point PNS* – the posteriormost point of the hard palate; *Ad1, point Ad1* – the point of intersection of the posterior pharyngeal wall and line PNS-Ba; *SPPW, point SPPW* – the point of intersection of the posterior pharyngeal wall and the line that extends perpendicularly from the posterior pharyngeal wall to the center of the soft palate; *SPP, point SPP* – the point of intersection of the posterior margin of the soft palate and the line that extends perpendicularly from the posterior pharyngeal wall to the center of the soft palate; *MPW, point MPW* – the middle pharyngeal wall, located at the intersection of the posterior pharyngeal wall and the line extending perpendicularly from that surface to U; *TPPW, point TPPW* – the point of intersection of the posterior pharyngeal wall and the extension of line B-Go; *LPW, point LPW* – the point on the posterior pharyngeal wall from which a perpendicular line will pass through point V; *PCV, point PCV* – the point of intersection of the posterior pharyngeal wall and an extension of the lower edge of the second cervical vertebra; *U – uvula*, tip of the uvula; *V, vallecula* – the point where the epiglottis meets the base of the tongue; *AH, anterior hyoid* – the most anterior and superior point on the body of the

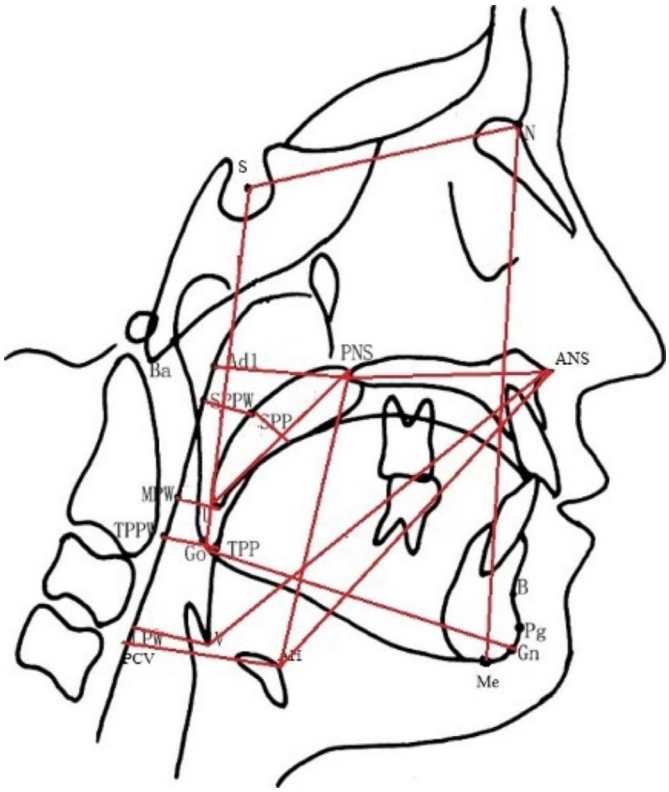

Fig. 1 Definitions of cephalometric landmarks used in the study

hyoid bone, representing the inferior part of tongue; *Gn, gnathion* – the midpoint between Pogonion and Menton; *Go, gonion* – the mid-plane point at the gonial located by bisecting the posterior border lines of the mandible; *Me, menton* – the lowest mandible anterior point.

Cephalometric variables: *PNS-Ad1* – distance between PNS and Ad1; *SPPW-SPP* – distance between SPPW and SPP; *U-MPW* – distance between U and MPW; *PPW-TPP* – distance between PPW and TPP; *LPW-V* – distance between LPW and V; *PCV-AH* – distance between PCV and AH; *S-N* – distance between S and N; *N-Me* – distance between N and Me; *S-Go* – distance between S and Go; *PNS-ANS* – distance between PNS and ANS; *SPL* – soft palate length; *SPW* – soft palate width; *PNS-AH* – distance between PNS and AH; *ANS-AH* – distance between ANS and AH; *ANS-V* – distance between ANS and V; *Go-Gn* – distance between Go and Gn; *Ulip-E* – distance between upper lip anterior border and E line; *Llip-E* – distance between lower lip anterior border and E line; *Wits* – distance perpendicular to points A and B onto the occlusal plane in mm; *SNA* – angle determined by points S, N and A; *SNB* – angle determined by points S, N, B; *SN-MP* – angle formed by Go-Me.

Table 1 Method error determined by a Bland–Altman plot for repeatability of the cephalometric measurements, with statistical significance calculations

Variable	SE	p
PNS-Ad1	0.24	N.S.
SPPW-SPP	0.43	N.S.
U-MPW	0.30	N.S.
PPW-TPP	0.23	N.S.
LPW-V	0.48	N.S.
PCV-AH	0.41	N.S.
S-N	0.50	N.S.
N-Me	0.81	N.S.
S-Go	0.65	N.S.
PNS-ANS	0.47	N.S.
SPW	0.60	N.S.
SPL	0.21	N.S.
PNS-AH	0.22	N.S.
ANS-AH	1.15	N.S.
ANS-V	1.16	N.S.
Go-Gn	0.28	N.S.
SNA	0.41	N.S.
SNB	0.26	N.S.
ANB	0.45	N.S.
SN-MP	0.65	N.S.
Ulip-E	0.35	N.S.
Llip-E	0.16	N.S.
WITs	0.09	N.S.

SE – error of method, expressed as standard error; p – probability that the means of the first and second measurements differed as assessed by the Wilcoxon signed-rank test; NS – not significant

Method error

Intraobserver method error was checked on 20 randomly selected patients' cephalograms with the method offered by Bland and Altman [20]. Cephalograms were traced twice after a one-month interval.

Estimation of heritability

Genetic structural equation modeling (GSEM) was performed using the "OpenX" package [21]. Classical univariate ACE and ADE twin models were fitted to the gender-adjusted cephalometric measurement data. The models were used to estimate the significance of the different components of total phenotypic variance (P), which is equal to the sum of the following variance components: the additive genetic factor (A), the shared environment (C), the nonadditive genetic factor (D), and the unique environment (E). The goodness of fit of the complete and reduced ACE and ADE models relative to a perfectly fitted (saturated) model was measured by the Akaike information criterion (AIC) [22]. The model of each cephalometric variable with the lowest AIC value was selected as the best fitting model.

Principal component analysis

Principal component analysis (PCA) was used to reduce the dimensionality of cephalometric measurement data and to check the correlations between variables. PCA was performed using the "principal" function from the "psych" package (Procedures for Psychological, Psychometric and Personality Research: https://cran.r-project.org/web/packages/nFactors/index.html). The principal components were rotated using varimax rotation. The number of components was determined using the "nScree()" function from the "nFactors" package according to the optimal coordinates index. A variable belonged to a component if the absolute value of the component loading was larger than 0.5.

Statistical analysis

Statistical analyses were performed in the statistical computing environment R (version 3.3.0). P values below 0.05 were considered statistically significant.

Results

Method error

The results of error analysis found no significant differences between the initial and repeated measurements (Table 1).

Estimation of heritability

The AIC was calculated for each parameter, and the AIC values of each model were analyzed. Only the lowest values were chosen and considered to be the most suitable model for further analysis. The contribution of factors

(a^2, c^2, d^2, e^2) of the best-fitting model for each parameter was counted. The results of the model-fitting analysis are presented in Tables 2 and 3.

Variables representing upper airway dimensions (SPPW-SPP, U-MPW) showed moderate to high genetic determination (AE model), with a^2=0.64 and 0.5, respectively; PNS-Ad1 had strong dominant determination (DE), with d^2=0.51. Lower airway parameters were mostly determined by environmental factors. PPW-TPP, LPW-V, and PCV-AH showed only common and specific environmental dependency.

Skeletal variables were all dependent on genetics to some extent. Maxilla length and had high dominant genetic determination, and Go-Gn and S-Go showed additive genetic, common environmental, and specific environmental influences. N-Me length was affected by additive genetic factors and by common and specific environmental influences.

The size of the soft palate was determined by additive and dominant genetic factors. Its length (SPL) was strongly influenced by dominant genetic factors, while its width (SPW) showed a moderate additive genetic influence.

Variables reflecting the relationship between the maxilla and the hyoid bone (PNS-AH, ANS-AH) showed very strong additive genetic determination, with d^2=0.9 and 0.92, respectively.

The parameters representing the sagittal position of the mandible and its relationship with the cranial base and lip position were all strongly influenced by genetics. Angles SNA and SNB fit best to the model determined by additive genes and specific environment. Angle SN-MP was determined by specific and common environmental factors, angle Ulip-E was determined by dominant genetic factors, and Llip-E was determined by additive genetic factors.

Principal components

According to the correlations in the behavior of the variables, the data were reduced to 5 principal components, which jointly explained 36.8% of the total variance (Table 4). The first component (PC1) showed correlations with the Go-Gn, LPW-V, N-Me, PCV-AH, PNS-ANS, S-Go, S-N, and SPW and explained 23.5% of the total variance. This component represented linear variables describing dimensions of the face and was highly influenced by genetics. The second principal component (PC2) showed strong correlations with angles PNS-Ad1, PPW-TPP, SPPW-SPP, and U-MPW, which explained 13.2% % of total variance and showed high genetic determination. The third component (PC3) showed

Table 2 AIC values of all the models

	ACE	ADE	DE	AE	CE	E
PNS-Ad1	2.48	-1.02	**-3.02**	0.48	10.93	18.99
SPPW-SPP	3.40	3.72	4.74	1.71	4.69	29.32
U-MPW	-5.66	-5.65	-5.83	**-7.64**	-1.88	24.46
PPW-TPP	4.09	4.29	3.30	**2.29**	2.81	15.77
LPW-V	14.57	16.02	15.03	14.02	**12.56**	14.07
PCV-AH	3.71	8.60	11.73	6.60	**1.82**	44.24
S-N	-0.36	-2.16	**-3.90**	-2.36	25.66	54.44
N-Me	**-7.86**	-1.45	6.41	-3.45	9.48	114.47
S-Go	**2.04**	12.45	21.17	10.49	8.41	115.43
PNS-ANS	-7.19	-7.76	**-9.71**	-9.19	-4.96	3.55
SPW	-10.47	-10.21	-10.65	**-12.21**	-11.55	0.82
SPL	6.84	1.93	**-0.07**	4.84	40.90	64.09
PNS-AH	-8.52	-8.50	-6.41	**-10.5**	33.87	95.01
ANS-AH	-7.51	-7.52	-6.3	**-9.51**	47.11	113.63
ANS-V	-3.02	-2.94	0.2	**-4.94**	28.8	81.16
Go-Gn	**-4.29**	-0.68	3.26	-2.68	-1.08	70.22
SNA	-2.89	-2.89	-3.2	**-4.78**	28.49	94.44
SNB	-2.77	-2.87	-3.66	**-4.77**	28.49	94.44
ANB	3.36	2.44	1.44	**1.35**	32.2	64.97
SN-MP	-0.49	4.54	6.86	2.54	**-2.5**	33.25
Ulip-E	-9.25	9.72	-10.93	**-11.25**	12.09	53.27
Llip-E	-3.00	-4.28	**-6.19**	-5.00	21.44	65.40
WITs	2.52	-1.25	**-3.25**	0.52	22.21	39.98

E – specific environmental factors; CE – common and specific environmental factors; AE – additive genetic factors and specific environmental factors; ACE – additive genetic factors, common environmental factors, and specific environmental factors; ADE – additive genetic factors, dominant genetic factors, and specific environment; DE – dominant genetic factors and specific environmental factors; values in **bold** – best-fitting models (lowest AIC values)

Table 3 Best-fitting models for each variable

	a^2	SE (a^2)	d^2	SE (d^2)	c^2	SE (c^2)	e^2	SE (e^2)
PNS-Ad1 (DE)			0.51	0.08			0.19	0.08
SPPW-SPP (AE)	0.64	0.08					0.24	0.08
U-MPW (AE)	0.50	0.08					0.22	0.07
PPW-TPP (AE)	0.24	0.09					0.38	0.09
LPW-V (CE)					0.20	0.10	0.63	0.10
PCV-AH (CE)					0.47	0.06	0.28	0.06
S-N (DE)			0.77	0.04			0.09	0.04
N-Me (ACE)	0.21	0.02			0.14	0.14	0.05	0.02
S-Go (ACE)	0.89	0.13			0.3	0.12	0.07	0.02
PNS-ANS (DE)			0.48	0.08			0.21	0.08
SPW (AE)	0.46	0.08					0.24	0.08
SPL (DE)			0.81	0.03			0.08	0.03
PNS-AH (AE)	0.9	0.02					0.4	0.02
ANS-AH (AE)	0.92	0.01					0.03	0.01
ANS-V (AE)	0.86	0.02					0.06	0.02
Go-Gn (ACE)	0.05	0.2					0.23	0.04
SNA (AE)	0.78	0.03					0.09	0.03
SNB (AE)	0.84	0.02					0.07	0.02
ANB (AE)	0.8	0.03					0.08	0.03
SN-MP (CE)					0.42	0.69	0.3	0.07
Ulip-E (AE)	0.75	0.04					0.1	0.04
Llip-E (DE)			0.76	0.04			0.1	0.04
WITs (DE)			0.7	0.05			0.12	0.05

a^2 – additive genetic factors; d^2 – dominant genetic factors; c^2 – common environmental factors; e^2 – specific environmental factors; SE – standard error.

Table 4 Factor loadings after varimax rotation

	PC1	PC2	PC3	PC4	PC5
ANB	-0.13	0.19	**0.71**	0.01	0.12
ANS_AH	0.25	0.11	0.13	-0.12	**0.85**
ANS_V	0.34	0.08	0.14	-0.11	**0.76**
Go_Gn	**0.72**	0.13	-0.24	0.14	0.14
Llip_E	0.03	0.01	**0.77**	-0.15	-0.10
LPW_V	**0.51**	0.24	0.01	0.14	0.03
N_Me	**0.67**	-0.06	-0.01	-0.46	0.32
PCV_AH	**0.71**	0.12	-0.09	0.10	0.11
PNS_Ad1	0.01	**0.62**	-0.10	0.30	0.19
PNS_AH	0.37	-0.08	0.05	-0.01	**0.76**
PNS_ANS	**0.61**	-0.04	0.10	0.03	0.18
PPW_TPP	0.29	**0.61**	0.09	-0.01	-0.35
S_Go	**0.58**	-0.05	-0.19	0.35	0.41
S_N	**0.53**	0.14	-0.15	0.01	0.28
SN_MP	0.03	-0.23	0.17	**-0.78**	-0.09
SNA	0.26	0.08	0.33	**0.80**	-0.06
SNB	0.35	-0.06	-0.07	**0.83**	-0.10
SPL	0.17	-0.18	-0.09	0.13	**0.6**
SPPW_SPP	-0.11	**0.85**	-0.01	0.07	0.05
SPW	**0.65**	-0.13	-0.01	0.11	0.22
U_MPW	0.22	**0.83**	0.08	-0.05	-0.15
Ulip_E	-0.10	-0.06	**0.88**	-0.05	-0.04
WITs	-0.04	-0.06	0.39	0.13	0.12

Values in bold: factor loadings that are significant at $p > 0.05$

correlation of 3 variables ANB, Ulip-E, Llip-E that represent lips position and sagittal jaw position relationship. PC4 showed correlation with SN-MP, SNA, SNB and this component describes jaws relationship with cranial base. PC5 showed correlation ANS-AH, ANS-V, PNS-AH, SPL.

Discussion

Understand upper airway morphology, assessing its heritability and knowing characteristics of its growth in a healthy population could help doctors identify persons at risk of breathing problems, such as snoring, OSA or mouth breathing, and even improve the treatments available to patients [23–25].

Heritability was analyzed to understand how upper airway morphology was influenced by genetic factors. The results of our study showed that 19 of 23 cephalometric parameters were strongly determined by genetics, while the remaining parameters were strongly influenced by environmental factors or both genetic and environmental factors. The considerable influence of genetic factors on pharyngeal space variations has been studied by Billing et al. [26]. The study participants were 19 monozygotic and 23 dizygotic twin pairs. The results of that study showed that the size of the pharyngeal space, the thickness of the posterior nasopharyngeal wall and the nasopharyngeal airway are strongly influenced by genetic factors. J. H. Kang et al. measured pharyngeal parameters using lateral

cephalograms of adult monozygotic and dizygotic twins. They also found that airway structures were under strong genetic control [27].

These findings are in agreement with the results of our study: the nasopharyngeal airway measurement (PNS-Ad1) was influenced by genetic factors (a^2=0.51). This might be explained by the fact that the nasopharyngeal area is surrounded by the body of the sphenoid bone, the basilar part of the occipital bone and the arch of the atlas on the posterior and superior sides; the morphology of these bony structures are strongly determined by genetic predisposition. On the other hand, the nasopharynx communicates with the oropharynx on the inferior side and the soft palate on the superior side, and these airways are necessary for speech, breathing and swallowing [28]. This could explain the weak environmental determination of the linear parameter PNS-Ad1 (e^2=0.19).

There is research showing that obesity is also related to reduced upper airway dimensions [9]. Although the environment plays a role in the development of obesity, body mass index (BMI) is correlated within families, but never the less, twin studies demonstrate an important role of genetics in the development of obesity [29].

The oropharyngeal airway space (U-MPW) was determined by additive genetic factors (a^2=0.5). The high heritability of this trait means that the oropharyngeal airway space is strongly influenced by genetic factors. This is in contrast to the results of previous studies, which have suggested that the oropharynx is more likely to be related to environmental factors, such as posture, than to genetic factors and that surrounding soft tissues are more influenced by environmental factors [30].

The oropharynx has an important role in orthodontic treatment planning. It has been reported that rapid maxillary expansion (RME) causes not only an increase in dental width but also changes in the oropharyngeal airway space [31]. After orthodontic treatment with the RME/Hyrax appliance, the volume of the oropharyngeal airway increased, and the results persisted in the long term after controlling for growth. Other investigations showed that the oropharyngeal airway volume did not change after orthodontic treatment with RME compared to that of the control group [32]. These contradictory results may be due to the use of different methods, an insufficient sample size or inaccuracies in measurement. Orthodontic treatment with fixed orthodontic appliances and the use of functional appliances such as the Herbst appliance increase airway volume and reduce resistance to airflow [33–36]. However, the oropharyngeal airway space (U-MPW) was also affected by environmental influences (e^2=0.22), which, although statistically non-significant in the overall sample, can also be crucial for some individuals. This might be because the oropharynx is surrounded by the tongue and the hyoid bone on the anterior side and the cervical vertebrae on the posterior side; these structures can change their positions [37].

The upper airway space has been studied by orthodontists for its close relation to the jaws and the craniofacial morphology. Some studies have revealed that the respiratory system is related not only to upper airway size but also to malocclusion type or craniofacial structures [38]. In the present study, we did not find any significant correlation between the sagittal spatial relationships of skeletal structures and the upper airway dimensions. This correlation is still controversial among researchers. Di Carlo G et al. reported that there are no significant relationships between the sagittal jaw structure and the upper airway volume [39].

Our results showed that hypopharyngeal structures are under environmental influence. It is known that there is a direct correlation between pharyngeal space and obesity [40]. According to Andrew M. Kim et al., tongue volume and tongue fat are increased in patients with OSA. These researchers claim that fat deposition not only influences tongue size but may also decrease tongue force and hinder the tongue from properly functioning as an upper airway dilator muscle. These findings coincide with those of our study, which showed that hypopharynx dimensions are affected by environmental factors [41].

Contrary to the environmental influence hypothesis, J. H. Kang showed that the structure of the hypopharynx has high heritability. This contradiction of our findings and the findings of J. H. Kang et al. could be due to inaccuracy of measurement because the vallecula can collect saliva, preventing initiation of the swallowing reflex. These measurements can also be influenced by head posture, cervical spine position and craniofacial angulation. Da Costa et al. stated that exact measurements of hyoid bone position through cephalometric analysis are difficult because even small deviations may generate apparent variation in the location of the hyoid [42].

Some of the limitations that we encountered in this study are common for research of this nature. The most common limitation in twin studies is sample size [43]. It is well known that twin births account for only a small proportion of births; for example, the twin birth rate in Lithuania was 11.7 per 1,000 births (Medical Data of Births 2014). In the present study, participants were required to meet certain conditions. Additionally, participation in this research was voluntary, which also reduced the sample size of twins.

Since most studies use two-dimensional cephalometry for orthodontic diagnosis and treatment planning, it is not surprising that some difficulties are encountered. The main problems that orthodontists face are difficulties in evaluating three-dimensional structures of the upper respiratory tract with two-dimensional cephalometric analysis, difficulties in identifying the landmarks,

and overprojection [18, 44]. The hyoid triangle method, despite being used as a standard method for assessing hyoid bone position in lateral cephalometric images, is not applicable to 3D image analysis [45]. In comparison with cone-beam computed tomography (CBCT), lateral cephalometric (LC) imaging is a preferable tool to measure linear and angular parameters and is a valuable instrument in the screening process [46]. Despite certain limitations, studies with twins are informative and a useful method to evaluate genetic and environmental influences on phenotype [47]. The findings from the present study could help orthodontists, otolaryngologists, speech-language pathologists and pediatricians better understand what role heredity and environment plays in airway width. These findings might also be useful for diagnosing and planning treatment. Further research using CBCT or MRI and investigating larger sample sizes would be relevant and helpful.

Conclusions

The dimensions of the upper airway are strongly determined by genes, while the parameters of the lower airway are mainly affected by environmental factors.

Abbreviations

CVM	cervical vertebral maturation
CBCT	cone-beam computed tomography
DNA	deoxyribonucleic acid
GSEM	genetic structural equation modeling
LC	lateral cephalometric (imaging)
LSMU	Lithuanian University of Health Sciences
OSA	obstructive sleep apnea
RME	rapid maxillary expansion

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Author Contribution
Monika Šidlauskienė: conceptualization, funding acquisition, data collection, methodology, cephalometric analysis, formal analysis, visualization, writing—original draft, and writing—review and editing.
Mantas Šidlauskas: data collection, formal analysis, writing—original draft, and writing—review.
Antanas Šidlauskas: supervision, formal analysis, writing—original draft, and writing—review and editing.
Simonas Juzėnas: statistical analysis and formal analysis.
Kristina Lopatienė: formal analysis, funding acquisition, supervision, and writing—review and editing.
All authors read and approved the manuscript.

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Data Availability
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study was approved by the Kaunas Regional Ethical Committee No. BE – 2–41. We declare that free and informed consent was obtained from all subjects. All experiments were performed in accordance with relevant guidelines and regulations (such as the Declaration of Helsinki) along with statements regarding approval of the study and informed consent of the participants. Informed consent was obtained from the legal guardians and/or parents of all participants below the age of 16 years.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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Original Article

Heritability of mandibular cephalometric variables in twins with completed craniofacial growth

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Summary

Objectives: To determine genetic and environmental impact on mandibular morphology using lateral cephalometric analysis of twins with completed mandibular growth and deoxyribonucleic acid (DNA) based zygosity determination.
Materials and methods: The 39 cephalometric variables of 141 same gender adult pair of twins were analysed. Zygosity was determined using 15 specific DNA markers and cervical vertebral maturation method was used to assess completion of the mandibular growth. A genetic analysis was performed using maximum likelihood genetic structural equation modelling (GSEM).
Results: The genetic heritability estimates of angular variables describing horizontal mandibular position in relationship to cranial base and maxilla were considerably higher than in those describing vertical position. The mandibular skeletal cephalometric variables also showed high heritability estimates with angular measurements being considerably higher than linear ones. Results of this study indicate that the angular measurements representing mandibular skeletal morphology (mandibular form) have greater genetic determination than the linear measurements (mandibular size).
Conclusions: The shape and sagittal position of the mandible is under stronger genetic control, than is its size and vertical relationship to cranial base.

Introduction

The mandibular growth modification is based on the knowledge that genetic and environmental factors are both responsible for its size and form (1). Nevertheless, the data concerning genetic determination of malocclusion and mandibular morphology are inconsistent. The genetic mechanisms, specific genes leading to a particular skeletal variability are not completely understood and clear (2). Technological advances have now made association analysis possible on a genome-wide level, but usually before starting to look for a quantitative trait loci for complex traits, it is critical to know that there is a significant component of genetic variation present (3). The classical twin study model provides a powerful tool to confirm the presence of this genetic effect (4). Therefore, twin studies can shed some light on the role of genes and environment on mandibular phenotypic variation (5).

A basic problem with previous twin studies is the reliability of the twin zygosity diagnostics. For many years, zygosity determination was based on assessment of anthropological similarity including tooth anatomy (5). Although comparison of physical appearance can provide a reasonably reliable means of determining zygosity, errors can occur up to 15–20% with this methodology (6). The use

of blood group determination, as well as serum and enzyme polymorphism analysis, improved the ability to assign zygosities to twins (4). More recently, the use of highly polymorphic regions of deoxyribonucleic acid (DNA) derived from blood or buccal cells has proved to accurately measure zygosity in up to 90–95% of cases (7). The more precise determination requires an increased number of highly polymorphic regions of DNA.

The second problem with twin studies relevant to mandibular morphology is maturity of the study sample. The vast majority of studies analyse data from growing subjects (1, 8–11), twins who have just passed their peak of pubertal growth spurts (12) or use age-adjusted measurements to simulate completed growth of the mandible (13). The results of such studies on mandibular morphology heritability estimates should be interpreted with caution, because complete genetic predisposition of mandibular morphology can be detected only if mandible growth is completely finished.

The third problem lies within the statistical methods used to analyse the twin data. The path analysis and Dahlberg quotient used in the 1980s are not appropriate for today's studies and model fitting methods should be used to get more accurate data.

The purpose of this study was to determine genetic and environmental impact on mandibular morphology using model fitting statistical analysis of lateral cephalometric variables of twins with completed mandibular growth and zygosity determination based on 15 highly polymorphic DNA regions and Amel fragment of amelogenin gene.

Materials and methods

Study sample

The twins participated in this study were from the Twin centre of Lithuanian university of health sciences. This ongoing register already covers more than 600 twin pairs voluntary registered and willing participate in different medical and genetic studies. All twins of this register were offered free of charge medical consultations including dental and orthodontic consultations. As part of dental and orthodontic examination lateral head cephalograms were taken. The study sample consisted of lateral cephalograms of 141 same gender pair of twins. All twins were Europeans, had no previous orthodontic treatment or permanent dental extractions and had not suffered any facial trauma. The protocol of the studies has been approved by the Regional Ethical Committee and informed consent was given by the twins and their parents.

The cervical vertebral maturation (CVM) method was used to assess the completion of the mandibular growth (14). Only twins which had attained the CVM stage 6 (active growth completed) were included in the study sample.

Zygosity determination was carried out using DNA test. The polymerase chain reaction set AmpFlSTR® Identifiler® (Applied Biosystems) was used to amplify short tandem repeats and 15 specific DNA markers (D8S1179, D21S11, D7S820, CSF1PO, D3S1358, TH01, D13S317, D16S539, D2S1338, D19S433, vWA, TROX, D18S51, D5S818, and FGA) and Amel fragment of amelogenin gene were used for comparison of genetic profiles. The sample's age, gender, and zygosity characteristics are shown in Table 1.

Cephalometric measurements

The cephalograms were taken in centric occlusion and cephalostat was used to maintain the subject's head in constant relationship to the sensor. To minimize radiation doze digital panoramic systems were used and ALARA radiation safety principle was followed. All radiographs were analysed by the same investigator (MS) using commercially available software (Dolphin Imaging 11.7 Premium). Cephalometric landmarks presented in the Figure 1 and cephalometric variables in the Table 2.

Table 1. Study sample: age (years), zygosity, and gender of twin pairs.

		Age			
Twins	*n*	Mean	SD	Min	Max
MZ	90	22.45	5.81	15.3	39.6
Male	29	22.1	4.82	15.8	36.4
Female	61	22.62	6.25	15.3	39.6
DZ	51	20.47	3.78	15.4	37.8
Male	20	21.2	3.36	15.4	29.3
Female	31	20.0	4.01	15.5	37.8
Total	141	21.73	5.24	15.3	39.6

Statistical analysis

Statistical analyses were performed with the R.v.3.1.2 software environment (http://www.r-project.org). Probabilities below 0.05 were considered statistically significant. All the analyses were calculated on gender adjusted cephalometric measurements (15).

Method error

Intra-observer method error was assessed using coefficient of reliability and a method suggested by Bland and Altman (16). The reliability of the method was tested by tracing and measuring 20 randomly selected lateral cephalograms twice with a 1-month time interval.

Estimation of heritability

Heritability is usually defined as the proportion of phenotypic variation that is due to genetic differences. Two types of heritability can be distinguished: 'narrow-sense heritability' refers to the contribution of additive genetic variance to observed phenotypic variance, whereas 'broad-sense' heritability refers to total contribution of genetic factors (additive and non-additive) to observed variation (4). The genetic analysis by model fitting was done with OpenMx package (http://openmx.psyc.virginia.edu) and performed using maximum likelihood genetic structural equation modelling (GSEM) (17). This analysis allows estimation of the significance of the different components of variance: the additive genetic factor (A), the shared environment (C), or the non-additive genetic factor (D), and the unique environment (E). Univariate ACE/ADE models were executed with standardized path coefficients and expected variance and covariance matrices. The goodness of fit of the full and reduced ACE/ADE models was compared with a univariate saturated twin model imposing equal means and variance restriction across twins and zygosity to maximize information. It should be noted that the power of the sample was sufficient to detect additive genetic influence (narrow-sense heritability), but might to low to detect dominance or shared environment, unless the effect was large.

The Akaike information criterion (AIC) statistics (18) and the difference in the chi-square (χ^2) value relative to the change in degrees of freedom provided an indication of the models' goodness of fit. The most parsimonious model (lowest AIC value) to explain the observed variance was selected.

Principal component analysis

Principal components analysis (PCA) was performed using 'Psych package' (Procedures for Psychological, Psychometric and

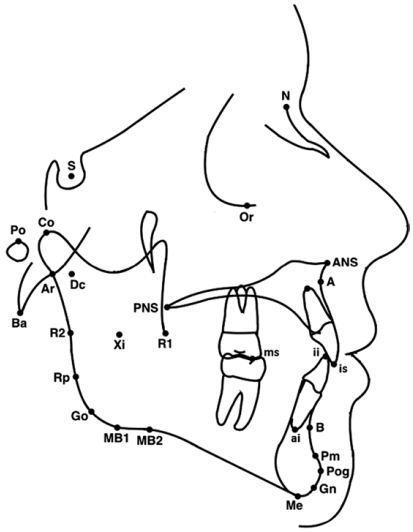

Figure 1. Cephalometric landmarks used in the study. S, Sella - the midpoint of sella turcica; N, Nasion - the extreme anterior point of the frontonasal suture; Ba, Basion - the most anterior-inferior point on the margin of the foramen magnum; A, point A - the deepest point in the curvature of the maxillary alveolar process; B, point B - the deepest point in the curvature of the mandibular alveolar process; ANS, point ANS - the tip of the anterior nasal spine; PNS, point PNS - the tip of the posterior nasal spine; Co, Condylion - the most posterior superior point of the condyle; Ar, Articulare - the point at the junction of the posterior border of the ramus and the inferior border of the posterior cranial base; Rp, ramus posterior point - the most prominent postero-superior point at the angle of the mandible on the posterior ramus; R1, ramus point 1 - the most concave point on the interior of the ramus; R2, ramus point 2 - the most convex point on the exterior border of the ramus along the vertical; Pog, Pogonion - the most anterior point of the chin; Me, Menton - the most inferior point of the chin; Go, Gonion - the midpoint of the mandibular angle between ramus and the mandibular corpus; MB1, inferior border point - the most convex point along the inferior border of the ramus; MB2, antegonial notch: the highest point of the notch of the lower border of the body of the mandible; Gn, Gnathion - the midpoint between Pog and Me on the bony chin; Xi, Xi point - the point located at the geometrical center of the ramus; Dc, Dc point - the point representing the center of the neck of the condyle on the Ba-N line; Pm, protuberance menti - the point at which the shape of symphysis mentalis changes from convex to concave; ai, apex inferior - the root apex of the most anterior mandibular central incisor; is, incision superior - the incisal tip of the most anterior maxillary central incisor; ii, incision inferior - the incisal tip of the most anterior mandibular central incisor; ms, molar superior - tip of the mesial buccal cusp of the mandibular first molar; Po, Porion - midpoint on upper contour of external auditory canal; Or, Orbitale - deepest point on infraorbital margin.

Personality research: http://cran.r-project.org/web/packages/psych/index.html) on 39 cephalometric measurements in order to establish whether they could be reduced to a smaller number of components. The number of components was determined by selecting all components with an eigenvalue larger than 2. A variable belonged to a component if the absolute value of the component loading was larger than 0.5. Principal components were rotated using varimax rotation.

Table 2. Cepahlometric variables and definitions used in the study.

Variables	Definitions
Angular	
SNA	Angle determined by points S, N, and A.
SNB	Angle determined by points S, N, and B.
SNPog	Angle determined by points S, N, and Pog.
NSBa	Angle determined by points N, S, and Ba.
NSAr	Angle determined by points N, S, and Ar.
NAPog	Angle determined by points N, A, and Pog.
SN–GoMe	Angle formed by S–N and Go–Me lines.
ANSPNS–GoMe	Angle formed by ANS–PNS and Go–Me lines.
SN–ArRp	Angle formed by S–N and Ar–Rp lines.
PoOr–GoMe	Angle formed by Po–Or and Go–Me lines.
NGnGo	Angle determined by points N, Gn, and Go.
DcXiPm	Angle formed by Dc, Xi, and Pm points.
ArRp–MB1Me	Angle formed by Ar–Rp and MB1–Me lines.
CoGoMe	Angle determined by points Co, Go, and Me.
ArGoMe	Angle determined by points Ar, Go, and Me.
ai.ii–NB	Angle formed by line ai-ii and N–B lines.
ai.ii–GoMe	Angle formed by line ai-ii and Go–Me lines.
Linear	
CoA	Distance between points Co and A in mm.
CoGo	Distance between points Co and Go in mm.
CoPog	Distance between points Co and Pog in mm.
CoB	Distance between points Co and B in mm.
ArB	Distance between points Ar and B in mm.
ArA	Distance between points Ar and A in mm.
Pog ⊥ NB	Perpendicular distance from the point Pog to N–B line in mm.
GoGn	Distance between points Go and Gn in mm.
GoPog	Distance between points Go and Pog in mm.
XiPm	Distance between points Xi and Pm in mm.
R1R2	Ramal width at Xi, distance between points R1 and R2 in mm.
NMe	TAFH, total anterior face height, distance between points N and Me in mm.
NANS	UAFH, upper anterior face height, distance between points N and ANS in mm.
ANSMe	LAFH, lower anterior face height, distance between points ANS and Me in mm.
SGo	TPFH, total posterior face height, distance between points S and Go in mm.
ii ⊥ NB	Perpendicular distance from point ii to N–B line in mm.
ii ⊥ APog	Perpendicular distance from point ii to A-Pog line in mm.
ii ⊥ GoMe	Perpendicular distance from point ii to Go–Me line in mm.
ms ⊥ GoMe	Perpendicular distance from point ms to Go–Me line in mm.
OB	Overbite: distance of vertical overlap of the lower incisors (point ii) by the upper central incisors (point is) in mm
OJ	Overjet: distance from the tip of the upper central incisor (point is) to the lower incisor (point ii) in mm.
MB2 ⊥ MB1Me	Depth of antegonial notch, perpendicular distance from the line between points MB1 and Me to the point MB2 in mm.

Results

Method error

There were no significant differences between the first and the second measurements of cephalometric variables, except for Xi-Pm and OB (Table 3).

Table 3. Method error by Bland–Altman for repeatability of the cephalometric measurements and its statistical significance.

Cephalometric variables	SE	*P*
Mandibular relationship to cranial base and maxillary structures		
SNA (°)	0.60	NS
SNB (°)	0.40	NS
SNPog (°)	0.40	NS
NSBa (°)	1.14	NS
NSAr (°)	1.14	NS
NAPog (°)	0.89	NS
SN–GoMe (°)	0.88	NS
ANSPNS–GoMe (°)	0.91	NS
NMe (mm), TAFH	0.76	NS
NANS (mm), UAFH	0.68	NS
ANSMe (mm), LAFH	0.78	NS
CoA (mm)	1.24	NS
ArA (mm)	0.56	NS
SNArRp (°)	0.93	NS
PoOrGoMe (°)	1.20	NS
NGnGo (°)	0.54	NS
SGo (mm), TPFH	0.83	NS
Mandibular skeletal variables		
DcXiPm (°)	1.93	NS
CoGoMe (°)	1.49	NS
CoB (mm)	1.73	NS
ArB (mm)	0.99	NS
GoGn (mm)	0.84	NS
XiPm (mm)	0.59	0.01
R1R2 (mm)	0.68	NS
MB2 ⊥ MB1Me (mm)	0.32	NS
CoPog (mm)	1.41	NS
ArRp–MB1Me (°)	0.71	NS
ArGoMe (°)	1.30	NS
CoGo (mm)	1.55	NS
GoPog (mm)	0.78	NS
Dento-alveolar variables		
Pog ⊥ NB (mm)	0.38	NS
ai.ii–NB (°)	1.64	NS
ii ⊥ NB (mm)	0.38	NS
ii ⊥ APog (mm)	0.31	NS
ii ⊥ GoMe (mm)	0.38	NS
ms ⊥ GoMe (mm)	0.69	NS
OB (mm)	0.32	0.01
OJ (mm)	0.27	NS
ai.ii–GoMe (°)	1.71	NS

SE, error of method; *P*, probability of means of first and second measurement to be different assessed by Exact Wilcoxon signed rank test; NS, not significant.

Estimation of heritability

The AIC values for each model were calculated and the most parsimonious models with the lowest values were chosen. Only the results of the best-fitting model have been taken into account. Variables with best fitting-model and contribution of factors (a^2, c^2, d^2, e^2) were counted. The results of model-fitting analyses are summarized in Tables 4 and 5.

Sagittal mandibular relationship to cranial base and maxilla

This group of variables were divided into linear and angular subgroups. Linear variables (NMe, ANSMe, CoA, ArA, and SGo) showed dependence of additive genetic factors a^2 (24–43%), shared environment c^2 (45–68%) and unique environment e^2 (9–17%). One linear variable (NANS) showed dependency only of environment effects c^2 = 77% and e^2 = 23%. Angular variables (SNA, SNB, NSBa, NSAr, NAPog, SN–ArRp, and NGnGo) showed highly additive genetic determination a^2 (74–79%), except four variables (SNPog, SN–GoMe, ANSPNS–GoMe, and PoOr–GoMe) which showed dependency of additive genetic and common/unique environment factors (ACE model).

Mandibular skeletal variables

The best fitting model for all linear variables was ACE, except one variable (MB2 ⊥ MB1Me) which was best explained by an AE model. Angular variables showed high genetic determination: AE model for DcXiPm, CoGoMe, ArGoMe a^2 (73–77%) and DE model for ArRp–MB1Me (d^2 = 81%).

Mandibular dento-alveolar variables

Both angular variables (ai.ii–NB, ai.ii–GoMe) were determined by AE model (a^2 = 69% and a^2 = 71%, respectively). Linear variables belonged to variety of models: AE was the best-fitting model for Pog ⊥ NB, ii ⊥ NB variables and showed high additive genetic determination a^2 (83% and 84%), DE model for ii ⊥ APog and OB d^2 (85% and 74%), CE for ms ⊥ GoMe and OJ variables and ACE was the best-fitting model for ii ⊥ GoMe.

Principal components

Six principal components were determined by principal components analysis explaining 83% of total variance (Table 6). First component PC1 consisted of all linear variables except Pog ⊥ NB, ii ⊥ NB, ii ⊥ APog, OB, OJ, MB2 ⊥ MB1Me and the best-fitting model was ACE. All angular and three linear variables (Pog ⊥ NB, ii ⊥ NB, and ii ⊥ APog) were determined to PC2, PC3, PC4, and PC5 groups. These components show high additive genetic determination a^2 (76–79%) with best-fitting model AE. NaPog, OB, and OJ formed PC6 with best fitting model DE. Three variables (NAPog, SN–GoMe, and ai.ii–GoMe) were included in two different components.

Discussion

The reproducibility of the measurements was good except for the Xi-Pm and OB measurements. These 2 of 39 variables showed small, but significant differences between the first and second measurement. The inaccuracy of determining the anatomical landmarks for some variables is a well-known problem in the clinical cephalometrics. It is difficult and often nearly impossible to distinguish between left–right sides and it complicates landmark definitions due to over-projecting structures in lateral head radiograms. This problem is especially true for the deepest point of the mandible and maxilla concavity (19).

Heritability assessment is usually a first step in genetic studies, because it provides an estimate of how much phenotypic variation is attributable to genetic influence (12). Model-fitting is a method used to calculate the proportion of the total variance explained by additive/dominant genes and common/specific environment (4, 13, 20). The studies of craniofacial growth from 4 to 20 years demonstrated increasing heritability estimates of cephalometric variables with the age (21). Therefore, comparison of hereditary characteristics is more valid in the post-adolescent period when the growth is completed, as it is the case in our study. It is well known that skeletal facial maturity develops in females between 12 and 14 years and 2 years of age later for males. Nevertheless, the chronological age is not a reliable and accurate maturity indicator. Therefore, in this study, cervical maturation method was used to select a sample with completed facial skeletal growth. Although there is study reporting lifelong mandibular size/shape changes, but the remaining skeletal growth of

Table 4. AIC values of all the models.

Variable	ACE	ADE	AE	CE	DE	E
SNA (°)	−0.10	−0.10	**−2.10**	10.34	−1.04	87.24
SNB (°)	−6.78	−5.17	**−7.17**	0.81	−2.36	98.61
SNPog (°)	**−6.27**	−3.72	−5.72	−0.82	−0.03	97.55
NSBa (°)	−3.96	−3.96	**−5.96**	12.94	−3.97	91.48
NSAr (°)	−1.72	−2.05	**−3.72**	13.26	−3.64	80.94
NAPog (°)	−4.37	−4.23	**−6.23**	10.38	−2.73	87.50
SN–GoMe (°)	**−10.91**	−7.51	−9.51	−7.55	−2.83	83.45
ANSPNS–GoMe (°)	**−6.14**	−3.23	−5.23	−1.75	0.73	94.60
SN–ArRp (°)	−6.60	−6.70	**−8.60**	9.45	−7.60	79.26
PoOr–GoMe (°)	**−9.16**	−5.19	−7.19	−6.05	−0.16	89.22
NGnGo (°)	−9.38	−8.81	**−10.81**	2.83	−6.32	87.04
DcXiPm (°)	−8.87	−8.45	**−10.45**	−1.09	−6.59	65.49
ArRp–MB1Me (°)	−9.68	−10.36	−11.68	16.13	**−11.89**	88.65
CoGoMe (°)	−10.08	−9.55	**−11.55**	−3.66	−7.95	66.25
ArGoMe (°)	−10.73	−10.83	**−12.73**	6.86	−11.53	77.10
ai.ii–NB (°)	−3.40	−3.41	**−5.40**	5.29	−4.04	58.48
ai.ii–GoMe (°)	−4.11	−3.37	**−5.37**	1.30	−0.97	63.32
CoA (mm)	**−8.09**	−2.24	−4.24	9.05	5.78	157.25
CoGo (mm)	**−8.56**	−1.21	−3.21	−6.51	7.21	95.97
CoPog (mm)	**−7.06**	11.59	9.59	−1.80	24.23	185.25
CoB (mm)	**−8.40**	11.18	9.18	−3.79	23.99	185.22
ArB (mm)	**−11.16**	7.07	5.07	−0.57	19.94	201.11
ArA (mm)	**−6.15**	1.16	−0.84	12.71	10.28	172.45
Pog ⊥ NB (mm)	2.97	3.69	**1.69**	19.03	5.88	126.10
GoGn (mm)	**−9.49**	0.74	−1.26	4.07	10.57	174.38
GoPog (mm)	**−8.75**	3.50	1.50	1.82	14.30	173.61
XiPm (mm)	**−10.28**	4.79	2.79	5.98	16.93	204.94
R1R2 (mm)	**−1.15**	2.92	0.92	2.49	8.39	98.49
NMe (mm)	**−9.74**	7.47	5.47	1.12	19.74	200.72
NANS (mm)	−8.25	4.89	2.89	**−9.43**	13.28	115.68
ANSMe (mm)	**−10.13**	−0.15	−2.15	4.92	9.94	174.85
SGo (mm)	**−10.18**	1.36	−0.64	−7.30	11.92	127.21
ii ⊥ NB (mm)	−0.17	0.02	**−1.98**	21.84	1.44	124.20
ii ⊥ APog (mm)	−4.75	−5.89	−6.75	33.81	**−7.60**	117.77
ii ⊥ GoMe (mm)	**−9.45**	−2.58	−4.58	19.15	7.44	184.65
ms ⊥ GoMe (mm)	−7.84	−0.02	−2.02	**−8.22**	7.82	80.30
OB (mm)	−1.24	−3.39	−3.24	18.46	**−5.36**	56.78
OJ (mm)	−6.33	−3.94	−5.94	**−7.88**	−1.93	31.03
MB2 ⊥ MB1Me (mm)	−3.53	−3.16	**−5.16**	1.62	−1.63	55.71
PC1	**−10.30**	25.29	23.29	−4.03	41.76	257.01
PC2	−10.71	−9.99	**−11.99**	−0.62	−7.61	83.68
PC3	−7.59	−7.28	**−9.28**	3.50	−6.08	88.07
PC4	−4.54	−4.48	**−6.48**	11.26	−3.54	91.96
PC5	−1.65	−1.55	**−3.55**	10.78	0.03	74.23
PC6	−7.73	−8.48	−9.73	11.18	**−10.12**	69.11

E, specific environment; CE, common and specific environment; AE, additive genes and specific environment; ACE, additive genes, common and specific environment; ADE, additive genes, dominant genetic factor, specific environment; DE, dominant genetic factor and specific environment; PC, principal component; Values in **bold**—best fitting model (lowest AIC value).

the mandible 2 years after the pre-adoslescent growth spurt completion is negligible from the clinical and theoretical stand-point and therefore, individuals with cervical maturation stage 6 were considered as adults (22).

Our attempt to summarize and compare own results with the previous twin studies of genetic influence on mandible morphology and its position in the craniofacial skeleton is presented in the Table 7.

Sagittal position of the mandible in the craniofacial complex depends on many determinants, the most important being: position of mandibular fossa, cranial base length and growth pattern. Sagittal localization of mandibular fossa is determined by morphology of cranial base and can be described by saddle angle (NSBa). We found its high genetic determination (a^2 = 79%) but results of the previous reports are contradictory. Studies with the twin age over 16 years found high genetic influence, whereas younger twins demonstrated low or no heritability estimate for the saddle angle (9, 12, 13, 25). As demonstrated in the study of heritability between parents and their offspring, heritability of saddle angle increases with age: our data support this statement (26). Other angular measurements representing sagittal position of the mandible to cranial base (SN–ArRp, SNB) also were found to be under strong genetic influence a^2 = 76% and 79%, respectively. Considering genetic control of SNB angle our results are consistent with the results of the latest studies (12).

Table 5. Path coefficients of the most parsimonious model for each variable.

		Genetic				Environment			
Variable	Model	a^2	SE	d^2	SE	c^2	SE	e^2	SE
Mandibular relationship to cranial base and maxillary structures									
SNA (°)	AE	0.74	0.04					0.26	0.04
SNB (°)	AE	0.79	0.04					0.21	0.04
SNPog (°)	ACE	0.42	0.18			0.36	0.17	0.22	0.04
NSBa (°)	AE	0.79	0.04					0.21	0.04
NSAr (°)	AE	0.75	0.04					0.25	0.04
NAPog (°)	AE	0.78	0.04					0.22	0.04
SN–GoMe (°)	ACE	0.36	0.19			0.39	0.17	0.24	0.04
ANSPNS–GoMe (°)	ACE	0.39	0.18			0.38	0.17	0.23	0.04
NMe (mm)	ACE	0.24	0.09			0.68	0.09	0.09	0.02
NANS (mm)	CE					0.77	0.03	0.23	0.03
ANSMe (mm)	ACE	0.34	0.12			0.56	0.12	0.10	0.02
CoA (mm)	ACE	0.43	0.14			0.45	0.14	0.12	0.02
ArA (mm)	ACE	0.41	0.13			0.49	0.13	0.10	0.02
SN–ArRp (°)	AE	0.76	0.04					0.24	0.04
PoOr–GoMe (°)	ACE	0.34	0.18			0.42	0.17	0.24	0.04
NGnGo (°)	AE	0.79	0.04					0.21	0.04
SGo (mm)	ACE	0.24	0.13			0.60	0.12	0.17	0.03
Mandibular skeletal variables									
DcXiPm (°)	AE	0.74	0.04					0.26	0.04
CoGoMe (°)	AE	0.73	0.04					0.27	0.04
CoB (mm)	ACE	0.18	0.09			0.71	0.09	0.11	0.02
ArB (mm)	ACE	0.23	0.09			0.68	0.09	0.08	0.02
GoGn (mm)	ACE	0.33	0.12			0.57	0.12	0.10	0.02
XiPm (mm)	ACE	0.28	0.10			0.64	0.10	0.08	0.01
R1R2 (mm)	ACE	0.35	0.18			0.42	0.17	0.23	0.04
MB2 ⊥ MB1Me (mm)	AE	0.68	0.05					0.32	0.05
CoPog (mm)	ACE	0.20	0.09			0.70	0.09	0.11	0.02
ArRp–MB1Me (°)	DE			0.81	0.03			0.19	0.03
ArGoMe (°)	AE	0.77	0.04					0.23	0.04
CoGo (mm)	ACE	0.27	0.16			0.50	0.14	0.22	0.04
GoPog (mm)	ACE	0.29	0.11			0.60	0.11	0.11	0.02
Dento-alveolar variables									
Pog ⊥ NB (mm)	AE	0.83	0.03					0.17	0.03
ai.ii–NB (°)	AE	0.69	0.05					0.31	0.05
ii ⊥ NB (mm)	AE	0.84	0.03					0.16	0.03
ii ⊥ APog (mm)	DE			0.85	0.03			0.15	0.03
ii ⊥ GoMe (mm)	ACE	0.46	0.13			0.46	0.13	0.08	0.02
ms ⊥ GoMe (mm)	CE					0.69	0.04	0.31	0.04
OB (mm)	DE			0.74	0.05			0.26	0.05
OJ (mm)	CE					0.50	0.06	0.50	0.06
ai.ii–GoMe (°)	AE	0.71	0.05					0.29	0.05
Principal components									
PC1	ACE	0.12	0.06			0.82	0.05	0.06	0.01
PC2	AE	0.78	0.04					0.22	0.04
PC3	AE	0.77	0.04					0.23	0.04
PC4	AE	0.79	0.04					0.21	0.04
PC5	AE	0.76	0.04					0.24	0.04
PC6	DE			0.76	0.04			0.25	0.04

a^2, additive genetic factors; d^2, dominant genetic factors; c^2, common environment factors; e^2, specific environment factors; SE, standard error.

Linear variables representing vertical and horizontal mandibular position to cranial base and maxilla (ANSMe, NMe, SGo, CoA, and ArA), and angles describing vertical relationship of mandible (SN–GoMe, PoOr–GoMe, and ANSPNS–GoMe) to upwards-located skeletal structures demonstrated low to moderate genetic influence and were determined by the ACE model, except NANS, which shows strong environment determination (CE model). We also noticed some differences for heritability estimates between horizontal and vertical linear measurements describing positions of the mandible in relation to the cranial base. We found that horizontal linear variables are more determined by genetic factors, than vertical variables. This is in contrast to the results of some previous studies reporting higher heritability estimates for many vertical linear measurements compared with horizontal ones (5, 13, 20, 27). This may be due to methodological differences (we used actual lengths, while many other studies used projected lengths) and different study sample maturation

Table 6. Factor loadings after varimax rotation.

Variables	PC1	PC2	PC3	PC4	PC5	PC6
SNA (°)	0.16	−0.06	**−0.76**	0.20	0.36	0.29
SNB (°)	0.21	−0.13	**−0.88**	−0.15	0.27	−0.10
SNPog (°)	0.20	−0.21	**−0.84**	−0.26	0.27	−0.11
NSBa (°)	−0.09	0.07	0.28	0.12	**−0.86**	−0.03
NSAr (°)	0.00	−0.06	0.31	0.07	**−0.86**	−0.07
NAPog (°)	−0.07	0.23	0.17	**0.66**	0.10	**0.57**
SN–GoMe (°)	−0.05	**0.82**	**0.51**	0.16	−0.07	−0.03
ANSPNS–GoMe (°)	0.02	**0.82**	0.35	0.14	0.12	−0.09
SN–ArRp (°)	0.03	−0.19	**0.84**	0.03	0.04	0.12
PoOr–GoMe (°)	0.06	**0.87**	0.33	0.15	0.14	−0.03
NGnGo (°)	−0.11	**−0.88**	0.02	0.03	−0.14	0.15
DcXiPm (°)	−0.02	**−0.83**	−0.02	−0.21	0.01	−0.08
ArRp–MB1Me (°)	−0.07	**0.91**	−0.19	0.13	−0.09	−0.12
CoGoMe (°)	−0.04	**0.92**	−0.10	0.07	−0.10	−0.10
ArGoMe (°)	−0.08	**0.91**	−0.17	0.08	−0.11	−0.14
ai.ii–NB (°)	−0.05	0.05	0.07	**0.91**	−0.05	−0.08
ai.ii–GoMe (°)	−0.11	**−0.60**	0.08	**0.70**	−0.12	0.01
CoA (mm)	**0.89**	−0.04	−0.23	0.09	−0.09	0.25
CoGo (mm)	**0.73**	−0.38	−0.12	−0.04	0.18	−0.27
CoPog (mm)	**0.94**	0.10	−0.18	−0.11	0.07	−0.16
CoB (mm)	**0.94**	0.13	−0.22	−0.06	0.04	−0.11
ArB (mm)	**0.92**	0.07	−0.29	−0.04	−0.06	−0.14
ArA (mm)	**0.88**	−0.12	−0.23	0.12	−0.16	0.22
Pog ⊥ NB (mm)	0.12	−0.39	0.09	**−0.57**	0.12	−0.10
GoGn (mm)	**0.87**	−0.04	−0.06	−0.25	0.00	0.02
GoPog (mm)	**0.88**	−0.07	−0.09	−0.23	−0.04	0.03
XiPm (mm)	**0.90**	0.06	−0.24	−0.20	0.04	−0.11
R1R2 (mm)	**0.66**	−0.27	0.02	0.03	−0.25	0.23
NMe (mm)	**0.84**	0.27	0.36	0.05	0.19	−0.16
NANS (mm)	**0.72**	0.04	0.31	−0.07	0.06	0.09
ANSMe (mm)	**0.73**	0.36	0.32	0.17	0.23	−0.21
SGo (mm)	**0.77**	−0.39	−0.07	−0.04	0.31	−0.21
ii ⊥ NB (mm)	0.06	0.31	0.14	**0.88**	0.04	−0.09
ii ⊥ APog (mm)	0.05	0.35	−0.01	**0.71**	−0.07	−0.46
ii ⊥ GoMe (mm)	**0.81**	0.23	0.19	0.31	0.22	−0.08
ms ⊥ GoMe (mm)	**0.76**	−0.20	0.23	0.31	0.21	−0.18
OB (mm)	−0.01	−0.31	−0.06	−0.17	−0.02	**0.74**
OJ (mm)	−0.13	−0.10	0.10	−0.01	0.08	**0.72**
MB2 ⊥ MB1Me (mm)	0.34	0.06	0.18	0.13	0.30	0.07

Values in bold: factor loadings greater than 0.50 are significant.

(5, 13, 20). The projected lengths may not reflect the actual ratio between horizontal and vertical measurements. The results of our study indicate that genetic control is more attributable to mandible sagittal than vertical position. The anterior face height (TAFH, LAFH) demonstrated higher genetic determination compared with posterior face height (TPFH).

The most important characteristics of mandible skeletal morphology are gonial angle, mandibular body length, and ramus width. The present study showed high heritability values for the gonial angle (ArGoMe, a^2 = 77%) and mandibular arc angle (DcXiPm, a^2 = 74%). For the linear measurements such as mandibular body length (GoPog, GoGn), ramus width (R1R2), and ramus height (CoGo) the best-fitting model was ACE, indicating low genetic determination. The gonial angle and mandibular arc angle are under stronger genetic control compare to the mandibular length or ramus height at the time close to pubertal growth spurt, while strong genetic determination of mandibular body length was more dominant in the younger study sample (12, 13, 23). As demonstrated by Dudas and Sassouni (24), there is increasing influence of the environment on linear distances during facial growth with age.

The results of our study showed that alveolar height depends more on the environmental, than on genetic influence. This is in agreement with previous studies demonstrating that heritability estimates for dentoalveolar traits were considerably lower than skeletal variables (28–30). It is known from clinical research, that environmental factors like lips, tongue and cheeks, oral muscles, and certain functions (breathing and mastication) or even body posture play an important part in the development of occlusion (31–34). Our results support these clinical observations related to dentoalveolar height. However, variables describing sagittal position of lower incisors and chin protrusion (ai-ii–NB, ii ⊥ NB, ii ⊥ APog, and Pog ⊥ NB) showed very high heritability. This indicates an existence of an integrated balance between morphologic units in the dentofacial complex which are under strong genetic control, and units that may accommodate more to environmental factors for final establishment of the variety of occlusion (12).

It is worth to notice, that results of twin studies are difficult to compare and inconsistence or similarity should be interpreted with caution, because of the differences in zygosity determination, sample size, maturity stage, and statistical methods used. The modern model-fitting methods that allow the goodness-of-fit of various

Table 7. Comparison of the heritability estimates of cephalometric variables of twin studies.

Study authors	Sample size (number of twin pairs)	Sample age range (years)	Face height				Mandibular relationship to cranial base and maxillary structures				Mandibular skeletal variables		
			UAFH	LAFH	TAFH	TPFH	Saddle angle	SNB	SN–MP	PP–MP	Gonial angle	Mandibular body length	Ramus height
Model fitting analysis			Best fitting model and a^2 (or d^2) values										
Sidlauskas et al. (current study)	90MZ	15.3–39.6	CE	ACE	ACE	ACE	AE	AE	ACE	ACE	AE	ACE	ACE
	51DZ		—	0.34	0.24	0.24	0.79	0.79	0.36	0.39	0.77	0.33	0.27
Carels *et al.* (13)	33MZ	9.0–16.0	AE	—	AE	AE	CE	CE	—	—	AE	DE	AE
	46DZ		0.675		f = 0.685, m = 0.912	0.735	—	—			0.453	0.791*	0.682
Savoye *et al.* (20)	33MZ	9.0–16.0	UAFH/LAFH										
	46DZ		AE 0.71										
Classical correlation analysis			Heritability estimates h^2										
Amini and Borzabadi-Farahani (12)	25MZ	13.4–20.1	0.18	1.08	1.08	0.18	1.00	0.98	1.22	1.22	1.62	0.26	0.50
	25DZ												
Manfredi *et al.* (9)	10MZ	10.0–13.0	–0.36	1.56	1.5	0.32	0.04	—	—	2.23	1.16	—	0.52
	10DZ												
Lundström and McWilliam (5)	28MZ	13.0–20.0	0.16	0.86	0.86	0.26	—	—	—	—	—	—	—
	27DZ												
Lobb (8)	30MZ	12.0–21.0	UAFH/LAFH		—	—	0.66	0.21	—	0.36	0.41	—	—
	30DZ		0.52										
Nakata *et al.* (23)	67MZ	Average 12.2	0.63	—	0.77	0.59	0.51	—	0.59	—	0.57	0.61	0.27
	29DZ												
Variance analysis			*F*-ratios										
Dudas and Sassouni (24)	12MZ	Early:4.4–13.2	5.62**	4.71**	6.41**	—	—	—	2.71	—	1.99	4.26**	2.63
	10DZ	Late:13.1–21.8	2.55	3.92**	5.17**				2.80		2.39	0.80	0.87
Sreedevi *et al.* (25)	12MZ	14.0–25.0	2.76	13.81***	9.06***	4.43**	2.70	—	1.59	3.60**	1.99	2.91	0.96
	7DZ												

TAFH, total anterior face height; UAFH, upper anterior face height; LAFH, lower anterior face height; TPFH, total posterior face height; MP, mandibular plane; PP, palatal plane; f, female; m, male; *, d^2; For *F*-ratios: significance < 0.05. **significant at 5% level; ***significant at 1% level.

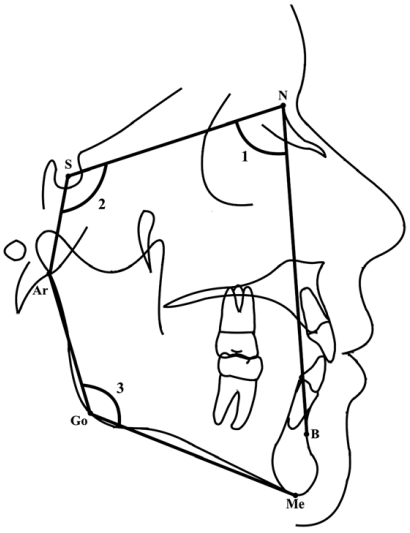

Figure 2. 'Polygon of the facial profile similarity'—the craniofacial area determined by angles with high heritability estimates: 1, SNB; 2, NSAr; 3, ArGoMe.

genetic and environmental models to be tested statistically are not comparable with path analysis and Dahlberg quotient used in the 1980s. Only a few studies used model fitting analysis for cephalometric twin studies (13, 20, 23). Principal components analysis showed six components explaining 83% of variance in our study. Whereas Carels *et al*. (13) found five independent factors explaining 81% of variance in a similar study. However, Nakata *et al*. (23) found at least nine independent significant components. All the differences of results among the studies are potentialy driven by usage of different criterion (i.e. eigenvalue) for determining the number of factors. The detailed comparison of the results using model fitting analysis presented in the Table 7.

Concerning the clinical relevance of our results it could be concluded that form of the mandible determined by the gonial and mandibular arc angles seems to be more under genetic control than its length, therefore orthodontic and/or orthopedic treatment procedures are expected to act more on mandibular size then form modification. However, it should be remembered that heritability is a population concept and is irrelevant to the individual. It would be misleading to suggest that structures with low heritability and highly influenced by the environment are always more amenable to prevention or treatment at the individual level. Therefore, using the present findings it is difficult to predict success of orthodontic treatment procedures with high degree of certainty for every clinical case.

A specific area on the lateral view of the face delimitated by the angles with high heritability estimates (SNB, a^2 = 79%; NSAr, a^2 = 75%; ArGoMe, a^2 = 77%) attracted our attention (Figure 2). By analogy with 'triangle of face-similarity' formed by Na, Go, and Gn points, we propose to name this strongly genetically determined area as 'polygon of the facial profile similarity' (9). This area presumably could be responsible for inherited facial profile similarity between twins.

Conclusions

The shape and sagittal position of the mandible is under stronger genetic control than is its size and vertical relationship to the cranial base.

Polygon of the 'face-similarity' is under strong genetic control and may explain facial profile resemblance between twins.

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Genetic and environmental impact on variation in the palatal dimensions in permanent dentition: a twin study

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The objective of this study was to assess the relative contributions of genetic and environmental factors to variation in palatal parameters in twins with completed maxillary growth. The subjects of this study comprised digital dental casts of 50 monozygotic and 35 dizygotic twin pairs. The subjects' average age was 17.95 ± 2.83 years. Zygosity determination was carried out using 15 specific DNA markers and an amel fragment of the amelogenin gene. The interdental distances were measured between selected dental landmarks at the occlusal and gingival planes. The palatal height, surface area and volume were measured between the gingival plane and the midpalate suture. High heritability estimates were observed for all transverse intra-arch measurements. The palate height ($a^2 = 0.8$), dental arch width in the molar area ($a^2 = 0.86$), palatal surface area ($a^2 = 0.61$) and palate volume ($a^2 = 0.69$) were under strong additive genetic control. Moderate genetic dominance was observed for dental arch widths at the gingival line in the canine ($d^2 = 0.5$) and premolar regions ($d^2 = 0.78–0.81$). Sexual dimorphism was shown, with males exhibiting a greater arch width, palate surface area and volume than females ($p < 0.01$). The majority of palate parameters variation in twins was controlled by genetic effects, and most were highly heritable.

Keywords Twin study, Palatal parameters, Heritability, Orthodontics

The size, shape and transverse dimension of the upper jaw are among the most important factors determining orthodontic treatment options for malocclusions, such as crossbite, dental crowding, lower anterior dentition irregularities and distal lower jaw position[1,2]. The palate form and volume are closely related to the width of the maxillary dental arch and have an impact on the position of the tongue and breathing function. Understanding facial skeletal and functional pattern changes throughout life and their control mechanisms is crucial for orthodontic treatment planning and subsequent stability[3,4]. There is ongoing discussion about the importance of genetic and environmental factors on maxillary dental arch and palatal morphology[5].

A recent systematic literature review and meta-analysis demonstrated that maxillary arch dimensions have high heritability estimates [6]. For the maxillary arch length heritability estimates were above moderate ranging from 0.42 to 0.92 [7–9]. Heritability for the palatal depth was estimated at 0.56 (95% CI range 0.22–0.90)[6]. The heritability of maxillary transversal dimensions such as intercanine and intermolar widths also have high estimates. Eugushi et al. [7] found these estimates equal 0.86 and 0.82 respectively. Similar estimates reported by Hughes et al.[9] (0.84 and 0.87), Lapter et al.[10] (0.69 and 0.58).

In contrast, there are studies showing that environmental factors have a greater influence on the formation of dental arches than previously thought[11,12]. Moreover, there is no doubt that soft tissue imbalance, including mouth breathing, irregular tongue position, irregular posture and other parafunctions, has a major impact on the upper dental arch and palatal formation. Studies have shown that mouth breathers have significantly smaller intermolar widths and palatal volumes and greater palatal heights[13]. A narrower and longer palate forms because of the short lingual frenulum, and these individuals have narrower arches in transverse dimensions and triangular arch shapes because of frontal tooth proclination [14]. Tongue posture is also related to palatal width.

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Fatima and Fida reported significant differences in maxillary intercanine and intermolar widths at the cusp and gingival levels in patients with different resting tongue postures[15]. The combination of direct pressure on the teeth and an alteration in the pattern of resting cheek and lip pressures can change the tooth position and dental arch shape[16]. Mouth breathing allows the tongue to rest on the lower part of the oral cavity. This changes the equilibrium of the forces between the cheeks and the tongue, leading to the development of a narrow maxilla and increased palatal height[17].

The similarity of twins within pair sources from shared genes and shared family environment. MZ twins share genetic effects and family environment to the full extent. DZ twins share 50% of additive genetic effects, 25% of non-additive genetic effects and 100% of family environment. MZ twins differ because of person-specific environment, DZ twins—because of unique environment and genes. Due to the underlying genetic and environmental similarities in related individuals, twin studies play a crucial role in understanding the aetiology of malocclusion by enabling the separation of genetic and environmental influences on dental arches and occlusion[18].

Structural equation modelling (SEM) is a set of methods which allows checking the hypothesis about the structure of relationship between observed and unobserved (latent variables). The model is usually represented by path diagram which include variables and linear relationship between them (Fig. 1). The combination of twin method and SEM allows precise estimation of the role of genes and environment on the phenotype trait. Even in the postgenomic era, estimation of heritability from twin and sibling studies is foundational for investigating the genes involved in complex traits[19].

However, the basic problems with the majority of previous twin studies are the reliability of the twin zygosity determination, the statistical methods used to analyse the twin data and the growth stage of the study sample. Regarding the first problem, for many years, zygosity determination was based on assessments of anthropological similarity, including tooth anatomy[20]. Although a comparison of physical appearance can provide a reasonably reliable means of determining zygosity, errors can occur in up to 15–20% of cases with this methodology[21]. The use of blood group determination, as well as serum and enzyme polymorphism analysis, improved the ability to assign zygosities to twins[22]. More recently, the use of highly polymorphic regions of DNA derived from blood or buccal cells has been shown to accurately measure zygosity in up to 90–95% of cases[23]. A more precise determination requires an increased number of highly polymorphic regions of DNA[24].

The second problem lies in the statistical methods used to analyse the twin data. In twin studies performed 20–30 years ago, the heritability coefficient was calculated using the classical correlation approach. The essential limitation of the heritability coefficient is that it does not estimate the influence of the shared environment, and consequently, the calculated heritability coefficient could be inflated[25]. The path analysis and Dahlberg quotient used in the 1980s are also not appropriate for today's studies, and model-fitting methods should be used to obtain more accurate data[6].

The third problem with twin studies relevant to maxillary dental arch and palate morphology is the maturity of the study sample. Many studies have assessed the maxilla in the intensive growth process of growing children[11,26,27]. The results of such studies on the heritability of maxillary dental arch and palate final parameters should be interpreted with caution because complete genetic predisposition to maxillary morphology can be detected only if growth is complete.

The aim of this study was to determine the genetic and environmental impacts on the maxillary arch and palatal morphology of twins with completed maxillary growth using structural equation modelling (SEM) and precise zygosity determination.

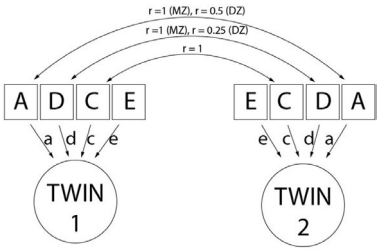

Fig. 1. Path diagram for the univariate twin model. Squares are latent variables (A—additive genetic factors, D—non-additive genetic factors, C—common environmental factors and E—unique environmental factors) shown with their respective path coefficients (a, d, c, e) indicating the relative importance of each of the contributing influences. Circles are observed variables, single-headed arrows are one-way (causal) relationships, and double-headed arrows are two way relationships (covariance).

Results

Descriptive statistics

The results of the descriptive statistics are shown in Table 1. Compared with females, males had slightly greater increases in all parameters of dental arch width at the occlusal plane. The most notable difference at the occlusal plane was registered for 1IPW ($p < 0.01$), while at the canine and molar regions males had wider dental arches, but with lower statistical significance ($p < 0.05$). Dental arch widths of males at the gingival line also demonstrated higher values, but the differences had no statistical significance. The palate height at the second premolar and molar region, the palatal surface area and the palate volume in males were significantly greater than those in females ($p < 0.01$).

Measurement reliability analysis

The results of the measurement error analysis revealed no significant differences between the first and second measurements on the models. The ICCs showed high intrarater reliability for all measurements (0.90–0.96, $p < 0.01$). Dahlberg's formula showed a random error of less than 1.0 mm for all linear measurements, 15 mm^2 for the palate surface area and 40 mm^3 for the palate volume.

Genetic analysis

The AIC values for each model were calculated (Table 2). The most parsimonious model and the lowest values were chosen. The AE and DE models were found to be the most parsimonious for variables. Variables with the best-fitting model of the contribution of factors (a^2, c^2, d^2, e^2) were counted. The results of the model-fitting analysis are summarized in Table 3. Variables representing interdental distances between cusp tips of teeth 1IPW, 2IPW and IMW showed high genetic determination (AE model), with $a^2 = 0.76$, 0.72 and 0.86, respectively, and ICW had a strong dominant determination (DE), with $d^2 = 0.59$.

The variables representing interdental distances at the palatal gum lines ICWG, 1IPWG, and 2IPWG had strongly dominant values of $d^2 = 0.5$, 0.78, and 0.81, respectively, while IMWGL had an additive genetic factor of $a^2 = 0.78$.

Variables showing interdental height 2IPH and IMH were affected by additive genetics ($a^2 = 0.7$ and 0.8, respectively), while 1IPH and ICH were determined by dominant genetic factors.

The parameters representing the maxillary depth, palatal area and palatal volume were affected by additive genetic factors.

A model with specific environmental factors (e^2) and common environmental factors (c^2) was rejected. The AE and DE models were adequate for all variables. Heritability estimates were high for all widths, maxillary depths, palatal surface areas and palatal volumes, ranging from 0.48 to 0.8.

Variables	Males (n = 38)	Females (n = 47)	MZ (n = 50)	DZ (n = 35)	P Males vs. females	P MZ vs DZ
Dental arch widths at occlusal line (mm)						
ICW	34.54 ± 1.93	33.83 ± 2.3	34.27 ± 2.16	33.98 ± 2.17	0.034	0.399
1IPW	41.40 ± 2.47	40.40 ± 2.25	40.98 ± 2.58	40.66 ± 2.15	0.006	0.391
2IPW	46.78 ± 2.81	45.85 ± 2.37	46.3 ± 2.74	46.22 ± 2.43	0.02	0.851
IMW	51.31 ± 3.68	50.35 ± 2.63	50.94 ± 3.36	50.56 ± 2.89	0.049	0.442
Dental arch widths at gingival line (mm)						
ICWG	24.68 ± 1.55	24.97 ± 1.83	25.08 ± 1.78	24.49 ± 1.56	0.276	0.028
1IPWG	27.62 ± 2.39	26.88 ± 2.09	27.19 ± 2.53	27.24 ± 1.79	0.032	0.869
2IPWG	32.62 ± 2.75	32.08 ± 2.7	32.19 ± 2.79	32.51 ± 2.66	0.201	0.454
IMWG	34.75 ± 3.23	34.16 ± 2.47	34.49 ± 3.22	34.33 ± 2.19	0.186	0.709
Palatal heights (mm)						
ICH	5.01 ± 1.39	5.21 ± 1.57	5.22 ± 1.43	4.98 ± 1.33	0.343	0.269
1IPH	11.25 ± 1.83	11.08 ± 1.73	11.22 ± 1.9	11.06 ± 1.56	0.529	0.545
2IPH	15.83 ± 1.81	14.86 ± 1.77	15.24 ± 1..87	15.37 ± 1.84	0.001	0.651
IMH	16.61 ± 2.03	15.17 ± 1.85	15.76 ± 2.02	15.89 ± 2.13	0.001	0.668
Maxillary arch depth (mm), MD	28.12 ± 1.7	27.58 ± 2.22	28.25 ± 1.61	27.2 ± 2.36	0.078	0.124
Palate surface area (mm^2), PSA	1385.81 ± 144.85	1304.72 ± 123.04	1346.38 ± 141.78	1333.24 ± 135.17	0.001	0.545

Table 1. Descriptive statistics of the dental arch and palate variables. *1IPH* interfirst premolar palate height; *1IPWG* interfirst premolar width at the gum line, *2IPH* intersecond premolar palate height, *2IPW* intersecond premolar width, *2IPWG* intersecond premolar width at the gum line, *DZ* dizygotic twin, *ICH* intercanine palate height, *ICW* intercanine width, *ICWG* intercanine width at the gum line, *IPW* interfirst premolar width, *IMH* interfirst molar height, *IMW* interfirst molar width, *IMWG* interfirst molar distance at the gum line, *MD* maxillary depth, *MZ* monozygotic twin, *PSA* palate surface area, *PV* palate volume. All values are provided in mean ± standard deviation.

Variables	ACE	ADE	DE	AE	CE	E
Dental arch widths at occlusal line						
ICW	−3.12	−5.53	**−7.54**	−5.12	9.34	30.13
1IPW	−6.53	−6.81	−8.35	**−8.53**	13.26	64.47
2IPW	−7.83	−7.31	−5.98	**−9.31**	3.24	63.78
IMW	−6.41	−6.41	−6.47	**−8.41**	25.47	93.16
Dental arch widths at gingival line						
ICWG	5.97	3.41	**1.41**	3.97	14.7	32.32
1IPWG	2.35	0.48	**−1.52**	0.35	27.37	77.6
2IPWG	1.24	−2.72	**−4.72**	−0.76	36.8	71.27
IMWG	0.2	1.14	2.04	**−0.86**	10.65	86.54
Palatal heights						
ICH	7.25	2.96	**0.96**	5.25	17.13	28.33
1IPH	−5.02	−5.43	**−7.34**	−7.02	2.01	33.3
2IPH	−10.93	−9.42	−6.82	**−11.42**	−5.83	50.04
IMH	−8.65	8.33	−6.45	**−10.33**	9.46	68.81
Maxillary arch depth						
MD	8.32	8.35	8.88	**6.35**	13.27	37.46
Palate surface area and volume						
PSA	−4.14	−3.16	43.84	**−5.26**	−1.57	41.84
PV	−7.44	−6.27	54.52	**−8.28**	−3.11	52.52
Principal component						
PC1	−3.42	−4.01	**−5.83**	−5.42	25.42	84.8
PC2	−9.77	−9.77	−10.52	**−11.77**	−2.44	35.34
PC3	1.67	−1.87	**−3.88**	−0.33	27.92	49.37

Table 2. AIC values of all the models. *ACE* additive genetic factors, common environmental factors, and specific environmental factors; *ADE* additive genetic factors, dominant genetic factors, and specific environment; *AE* additive genetic factors and specific environmental factors; *CE* common and specific environmental factors; *DE* dominant genetic factors and specific environmental factors; *E* specific environmental factors; *ICH* intercanine palate height; *ICW* intercanine width; *ICWG* interfirst premolar width; *ICWG* intercanine width at the gum line; *IMH* interfirst molar height; *IMW* interfirst molar width; *IMWG* interfirst molar distance at the gum line; *1IPH* interfirst premolar palate height; *2IPH* intersecond premolar palate height; *2IPW* intersecond premolar width; *1IPWG* interfirst premolar width at the gum line; *2IPWG* intersecond premolar width at the gum line; *MD* maxillary depth; *PSA* palate surface area; *PV* palate volume. Best-fitting models (lowest AIC values) are indicated in bold.

Principal components

Principal component analysis revealed that three principal components explained 69.3% of the total variance. The first component consisted of 1IPW, 1IPWG, 2IPW, 2IPWG, ICWG, IMW, and IMWG and explained 46.2% of the total variance, and the best-fitting model was DE. The palatal surface area and volume (IMW) were determined for the PC2 group, which showed an additive genetic determination of $a^2 = 0.62$ with the best-fitting model AE. PC2 explained 23.2% of the total variance. The third component showed a correlation between two variables, ICW and maxillary depth, and these components showed strong genetic dominance (Table 4, Figs. 2 and 3).

Discussion

There are many twin studies assessing genetic and environmental contributions to the upper arch form and palate parameters. However, it is challenging to compare different twin studies due to differences in the sample size, population, zygosity, and statistical methods used. The use of a model-fitting analysis allows the most accurate differentiation of sources of variation affecting the dental arch and palate form and size. This statistical method was used in our study.

Our results showed sexual dimorphism in palatal parameters. Compared with females, males exhibited slightly greater dental arch widths, whereas the palatal surface area and palate volume in males were significantly greater ($p < 0.01$).

According to our findings, the AE and DE models best explained the variance in the palatal parameters. Interdental distances at the gingival plane are mostly affected by the DE model, except for the IMWG. This means that palatal variances for patients with complete maxillary growth were due to additive genetic factors and specific non shared environmental factors. Distances at the gingival planes are mainly defined by dominant genetic factors.

The correlations for all parameters in the MZ twin analysis were greater than those in the DZ, which is likely due to genetic influences. The variance in the dental arch width and palatal morphology (depth, height, and volume area) had a high genetic contribution. Recent research in twin studies of palatal parameters confirms

Variables	a^2	SE (a^2)	d^2	SE (d^2)	c^2	SE (c^2)	e^2	SE (e^2)
Dental arch widths at occlusal line								
ICW (DE)			0.59	0.06			0.17	0.06
1IPW (AE)	0.76	0.04					0.1	0.04
2IPW (AE)	0.72	0.04					0.1	0.04
IMW (AE)	0.86	0.02					0.06	0.02
Dental arch widths at gingival line								
ICWG (DE)			0.5	0.07			0.22	0.07
1IPWG (DE)			0.78	0.03			0.09	0.03
2IPWG (DE)			0.81	0.03			0.08	0.03
IMWG (AE)	0.78	0.03					0.09	0.03
Palatal heights								
ICH (DE)			0.48	0.08			0.22	0. 8
1IPH (DE)			0.56	0.06			0.19	0.06
2IPH (AE)	0.7	0.04					0.13	0.04
IMH (AE)	0.8	0.03					0.08	0.03
Maxillary arch depth								
MD (AE)	0.56	0.07					0.18	0.07
Palate surface area and volume								
PA (AE)	0.61	0.05					0.18	0.05
PV (AE)	0.69	0.04					0.15	0.04
Principal components								
PC1 (DE)			0.82	0.03			0.07	0.03
PC2 (AE)	0.62	0.06					0.16	0.06
PC3 (DE)			0.76	0.04			0.09	0.036

Table 3. Best-fitting models for each variable. *1IPH* interfirst premolar palate height, *1IPWG* interfirst premolar width at the gum line, *2IPH* intersecond premolar palate height, *2IPW* intersecond premolar width, *2IPWG* intersecond premolar width at the gum line, a^2 additive genetic factors, d^2 dominant genetic factors, c^2 common environmental factors, e^2 specific environmental factors, *ICH* intercanine palate height, *ICW* intercanine width, *ICWG* intercanine width at the gum line, *ICWG* interfirst premolar width, *IMH* interfirst molar height, *IMW* interfirst molar width, *IMWG* interfirst molar distance at the gum line, *MD* maxillary depth, *PSA* palate surface area, *PV* palate volume, *SE* standard error.

this finding[18,26]. In contrast, a longitudinal study with identical and fraternal twins performed by Chaaban et al.[11] showed that heritability had a weak influence on palatal transverse variables and was more strongly affected by environmental factors. However, in the Chaaban et al.[11] study, heritability patterns were retrospectively obtained from the Pearson correlation coefficient and Falconer's heritability test.

Lione et al.[27] reported that the maxillary arch form is determined by tongue pressure. The dental arch usually has an impact on palate form, but we did not find a remarkable environmental influence on the palatal area or volume variability. We did not examine whether the twins in our study were mouth breathers, so it was difficult to evaluate the tongue position and possible impact on the dental arch palate. Our results showed that genetic contributions have a remarkable impact on the variability of palatal parameters.

For patients with complete maxillary growth, the suture of the maxilla is ossified after approximately 13 years[28], and treatment with conventional RME possibly causes only buccal inclination of the teeth, which can lead to relapse. To expand the palate, surgery and miniscrew-assisted RME may be needed. Palatal suture ossification may occur even at eleven years of age, and chronological age is not reliable for determining suture development[29]. According to our findings, the palatal surface area ($a^2 = 0.61$), palate volume ($a^2 = 0.69$), and maxillary arch depth ($a^2 = 0.56$) are mostly affected by additive genetic factors. These findings suggest that miniscrew-assisted RME should be considered a better choice than conventional RME for maxillary expansion in patients older than 11 years for expansion stability. Although it has been proven that even with MARPE treatment, long-term stability is not reliable, dental and skeletal relapse are still observed over time[30]. The heritability estimates in the area of the first molars ($a^2 = 0.86$) were the highest of all the parameters. These are teeth where the RME appliance is bonded, and due to the strong genetic influence on the width of the dental arch between the first molars, relapse is more likely to occur. The high heritability estimates maxillary intermolar width was reported by Eguchi et al.[7] (0.82) and Hughes et al.[9] (0.87).

The genetic influence on the dental arch width in the canine region is lower ($a^2 = 0.59$), and possibly, environmental factors are more responsible for this transverse dimension. The genetic influence on the dental arch and palatal variables in the canine region showed reduced genetic dominance (ICW $d^2 = 0.59$, ICWG $d^2 = 0.5$, ICH $d^2 = 0.48$). This is in agreement with findings of King et al. [31] and Cassidy et al. [32] reporting estimates of ICW at 0.53 and 0.56 respectively. This can be explained by the stronger environmental influence in this area, such as the position of the tongue, swallowing parafunction and mouth breathing. These abnormal functions can lead to a flatter and narrower palate and maxillary anterior tooth protrusion[33].

Variable	PC1	PC2	PC3
Dental arch widths at occlusal line			
ICW	0.5	− 0.01	**0.66**
1IPW	**0.83**	0.13	0.36
2IPW	**0.91**	0.15	0.13
IMW	**0.92**	0.16	− 0.03
Dental arch widths at gingival line			
ICWG	**0.65**	0.01	0.47
1IPWG	**0.91**	0.13	0.04
2IPWG	**0.91**	0.05	− 0.11
IMWG	**0.91**	0.11	− 0.17
Palatal heights			
ICH	0.08	**0.52**	− 0.42
1IPH	0.01	**0.92**	− 0.13
2IPH	− 0.01	**0.93**	0.16
IMH	0.01	**0.8**	0.28
Maxillary arch depth			
MD	− 0.13	0.25	**0.72**
Palate surface area and volume			
PSA	0.36	**0.83**	0.29
PV	0.45	**0.82**	0.1

Table 4. Factor loadings after varimax rotation. *1IPH* interfirst premolar palate height, *1IPWG* interfirst premolar width at the gum line, *2IPH* intersecond premolar palate height, *2IPW* intersecond premolar width, *2IPWG* intersecond premolar width at the gum line, *ICH* intercanine palate height, *ICW* intercanine width, *ICWG* intercanine width at the gum line, *ICWG* interfirst premolar width, *IMH* interfirst molar height, *IMW* interfirst molar width, *IMWG* interfirst molar distance at the gum line, *MD* maxillary depth, *PSA* palate surface area, *PV* palate volume. Factor loadings greater than 0.50 are significant and indicated in bold.

The results of our study may have some clinical relevance and may be useful in predicting the response of different parts of the dental arch to various orthodontic interventions, especially maxillary dental arch expansion. The occlusal variables that are more influenced by genetic factors may be less receptive to corrective procedures; in contrast, traits that are more influenced by environmental factors may be more prone to respond positively and demonstrate a greater level of stability after orthodontic treatment. The most important finding from this study regarding orthotreatment planning is that changes in the dimensions of the dental arch and palate should not surpass the biological limits. The balance between bone, dental, and muscular structures should be maintained, as deviations from the original shape of the dental arch may increase the likelihood of treatment relapse to a genetic norm.

The present study has several strengths, including DNA-based zygosity determination and the use of a model-fitting analysis that allowed for a more accurate partitioning of different sources of variation affecting the palate parameters. This study also has some limitations. The complete dental and medical records were not available for all twins, and a questionnaire was used to determine whether previous orthodontic treatment was undertaken, which may have led to bias. Additionally, this study involved a sample of Lithuanian twins, and thus the generalizability of the findings to other populations may be limited.

Conclusion

Palatal dimensions have high heritability. The majority of dental arch widths at the occlusal line, palate height, palatal surface area, palate volume and maxillary arch depth were found to be under strong-to-moderate additive genetic control. Maxillary dental arch inter-canine width and widths at gingival line in premolar regions demonstrated dominant genetic determination. Sexual dimorphism was shown, with males exhibiting greater arch width, palate surface area and volume than females.

Methods

Study sample

The present study sample consisted of dental casts of 50 monozygotic (19 males and 31 females) and 35 dizygotic (19 males and 16 females) twin pairs of the same sex. Twins were selected from the Twin Centre of the Lithuanian University of Health Sciences (LSMU). All twins were of European ancestry. Their mean age was 17.95 ± 2.83 years. The protocol of the study was approved by the Regional Ethical Committee No. BE-2-41, and informed consent was given by the twins and their parents of any participant younger than 18 years. The study was conducted in accordance with relevant guidelines and regulations.

The following inclusion criteria were applied: (1) full adult dentition not including the third molars and (2) maxillary growth largely completed (defined as age > 15). The twins were excluded on the basis of the following

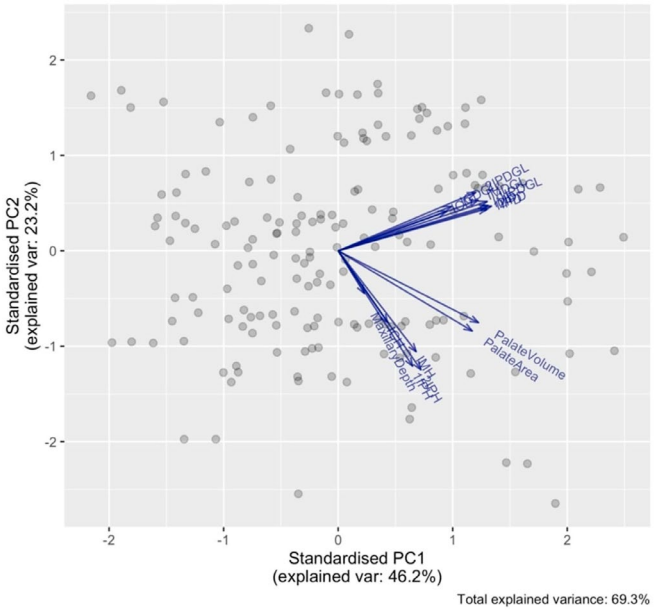

Fig. 2. Principal component biplot.

criteria: (1) existing restorations involving landmarks on the cusps and incisal regions, (2) previous orthodontic treatment, (3) poor quality or damaged models, (4) excessive wear of the teeth, or (5) dental anomalies such as supernumerary or missing teeth.

Dental arch and palate measurements

Alginate dental impressions were obtained from the study participants. A three-dimensional 3Shape scanner (3Shape e3, Copenhagen, Denmark) with a reported accuracy of 7/10 µm was used. (Scan time 18 s, Resolution 2 cameras 5.0 megapixels) was used to obtain 3D data from dental casts (format STL) of maxillary dentition and palate.

The definitions of the measurements used in the study are presented in Table 5. Linear measurements were calculated utilizing the selected dental landmarks as well as the maxillary occlusal plane as a plane of reference (Fig. 4). The maxillary occlusal plane was defined as the midpoint between a line connecting the central point of the incisal edges of the two maxillary central incisors and the mesiobuccal cusp tips of the maxillary first molars (Fig. 4a). The widths at the gingival level were measured connecting the appropriate points at the dentogingival junctions of the teeth on the palatal side (Fig. 4a). The gingival plane and distal plane were used as margins for the palate. The gingival plane was obtained by connecting the midpoints of the dentogingival junction of all permanent teeth on the palatal side (Fig. 4a). The distal plane was created through two points at the distal aspect of the first molars perpendicular to the gingival plane (Fig. 4b). Palate height was measured as the distance between the line connecting the centres of the dentogingival junctions of the canines, first and second premolars, and first molars on the palatal side and the highest point of the palatal vault on the midpalatal rafe (Fig. 4c). The measurements of the palate surface area and palate volume are presented in Fig. 4d and were performed according to the methods proposed by Kecik[34] and Primožič et al.[35].

All linear landmark-based dimensions were calculated using the open-source universal 3D processing and animation software Blender 3.4.1 with the "3D Print Toolbox". The digitization of the landmarks was conducted by a single investigator (VP). Prior to data collection, the investigator (VP) was calibrated in the use of the software.

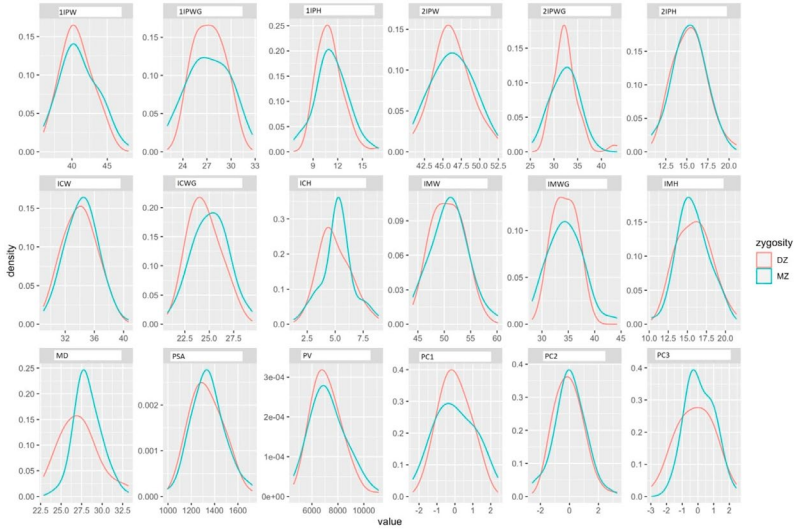

Fig. 3. Correlation coefficient densities of palatal variables. *MZ* monozygotic twins, *DZ* dizygotic twins, *ICW* intercanine width, *ICWG* interfirst premolar width, *2IPW* intersecond premolar width, *IMW* interfirst molar width, *ICWG* intercanine width at the gum line, *1IPWG* interfirst premolar width at the gum line, *2IPWG* intersecond premolar width at the gum line, *IMWG* interfirst molar distance at the gum line, *ICH* intercanine palate height, *1IPH* interfirst premolar palate height, *2IPH* intersecond premolar palate height, *IMH* interfirst molar height, *MD* maxillary depth, *PSA* palate surface area, *PV* palate volume.

Measurement error

Measurements were performed twice on the digital models by the same investigator, with a 1-month time interval on both members of 20 randomly selected twin pairs to determine measurement error. Intraobserver method error was assessed using the intraclass correlation coefficient (ICC) of reliability and the method suggested by Bland and Altman[36]. The estimated random error between the measurements was calculated using the Dahlberg formula:

$$SDd = \sqrt{\sum (d_1 - d_2)^2 \Big/ (2N)}$$

Zygosity determination

Zygosity determination was carried out using a DNA test. The polymerase chain reaction set AmpFlSTR® Identifiler® (Applied Biosystems, USA) was used to amplify short tandem repeats, and 15 specific DNA markers (D8S1179, D21S11, D7S820, CSF1PO, D3S1358, TH01, D13S317, D16S539, D2S1338, D19S433, vWA, TROX, D18S51, D5S818, FGA) and an amel fragment of the amelogenin gene were used for comparison of genetic profiles. Zygosity determination using this molecular genetic technique reached 99.9% accuracy[21].

Heritability estimation

Heritability was estimated by structural equation modelling (SEM) with the OpenMx software package (http://openmx.psyc.virginia.edu) and R code examples provided at https://github.com/OpenMx/OpenMx. The variance of a trait was estimated by evaluating the contributions of three factors: the additive genetic factor (A), the shared environment (C), the nonadditive genetic factor (D), and the unique environment (E)[37]. As the C and D components cannot be estimated simultaneously in twins reared together, only the ACE (or ADE) models with two degrees of freedom were tested [38]. Univariate ACE/ADE models were constructed with standardized path coefficients and expected variance and covariance matrices. The goodness of fit of the full and reduced ACE/ADE

Measurements	Definition
Dental arch widths at occlusal line	
ICW—intercanine width	Distance between cusp tips of the canines on the maxillary occlusal plane
1IPW—interfirst premolar width	Distance between buccal cusp tips of the first premolars on the maxillary occlusal plane
2IPW—intersecond premolar width	Distance between buccal cusps tips of the second premolars on the maxillary occlusal plane
IMW—interfirst molar width	Distance between mesiobuccal cusps tips of the first molars on the maxillary occlusal plane
Dental arch widths at gingival line	
ICWG—intercanine width at the gum line	Distance connecting the centres of the dentogingival junctions of canines on the palatal side
1IPWG—interfirst premolar width at the gum line	Distance connecting the centres of the dentogingival junctions of the first premolars on the palatal side
2IPWG—intersecond premolar width at the gum line	Distance connecting the centres of the dentogingival junctions of the second premolars on the palatal side
IMWG—interfirst molar distance at the gum line	Distance connecting the centres of the dentogingival junction of the first molars on the palatal side
Palatal heights	
ICH—intercanine palate height	Distance between the line connecting the centres of the dentogingival junctions of the canines on the palatal side and the highest point of the palatal vault on the midpalatal rafe
1IPH—interfirst premolar palate height	Distance between the line connecting the centres of the dentogingival junctions of the first premolars on the palatal side and the highest point of the palatal vault on the midpalatal rafe
2IPH—intersecond premolar palate height	Distance between the line connecting the centres of the dentogingival junctions of the second premolars on the palatal side and the highest point of the palatal vault on the midpalatal rafe
IMH—interfirst molar palate height	Distance between the line connecting the centres of the dentogingival junctions of the first molars on the palatal side and the highest point of the palatal vault on the midpalatal rafe
Maxillary arch depth, palate surface area and volume	
MD—maxillary depth	Distance between a tangent from the incisal edge of the central incisors and a line connecting the contact point between the first molar mesiobuccal cusps
PSA—palate surface area	Palate surface area below the gingival plane and limited by the distal plane. Gingival plane constructed by connecting the line of the midpoints of the dentogingival junction of all teeth (except second molars). The distal plane constructed perpendicular to the occlusal plane passing from the two most distal points corresponding to the distal surface of the first molars
PV—palate volume	Volume below the gingival plane and limited by the palate surface and distal plane. Gingival plane constructed by connecting the line of the midpoints of the dentogingival junction of all teeth (except second molars). The distal plane constructed perpendicular to the occlusal plane passing from the two most distal points corresponding to the distal surface of the first molars

Table 5. Definitions of the measurements.

models were compared with a univariate saturated twin model imposing equal means and variance restriction across twins and zygosity to maximize information.

The Akaike information criterion (AIC) statistic and the difference in the chi-square (χ^2) value relative to the chance in degrees of freedom provided an indication of the models' goodness of fit. The most parsimonious model (lowest AIC value) to explain the observed variance was selected [39].

Principal component analysis

Principal component analysis (PCA) of the palatal measurements was performed using the "Psych package" (Procedures of Psychological, Psychometric and Personality Research) to reduce dimensionality and to assess correlations between variables. The principal components were rotated using varimax rotation. A variable was considered a component if the absolute value of the component loading was greater than 0.5.

Statistical analysis

Descriptive statistics included the mean and standard deviation. The normality of the data distribution was tested with the Shapiro–Wilk test. Parametric Student's t tests were applied for comparisons of quantitative variables between two independent groups. Pearson's correlation coefficient was calculated, and the difference between the two correlation coefficients was computed. Statistical analyses were performed in the statistical computing environment R (version 4.3.3). P values less than 0.05 were considered to indicate statistical significance.

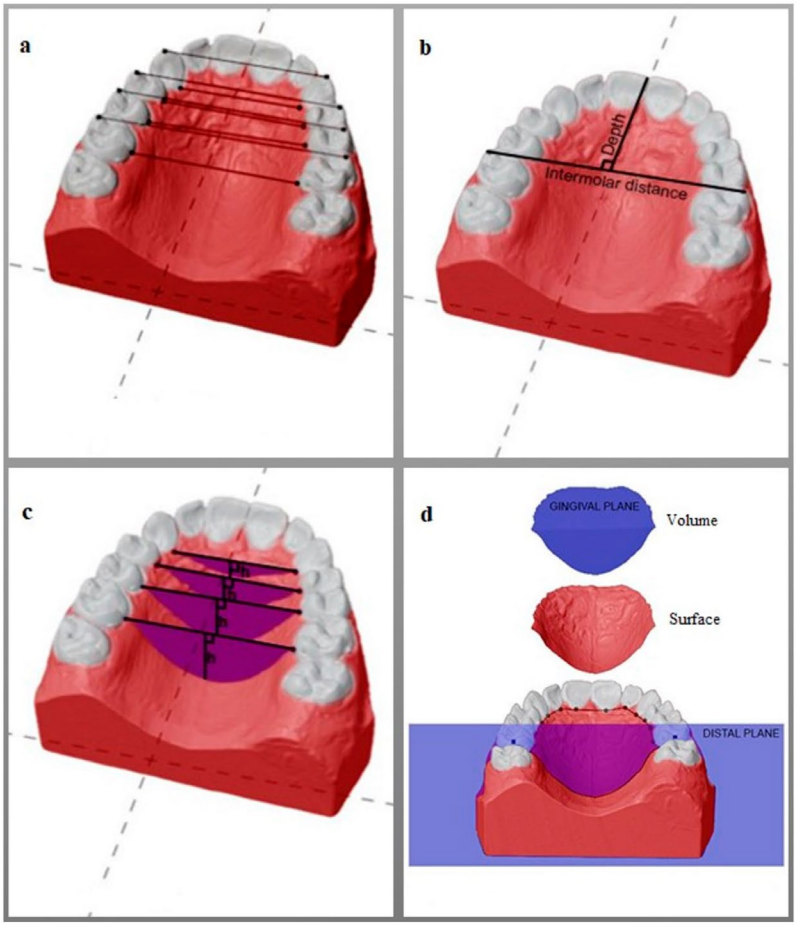

Fig. 4. The upper dental arch parameters. (**a**) The upper dental arch widths were defined as the distances between the two reference points at the occlusal and dento-gingival junctions. The interdental distances were measured between the cusp tips of the canines, first premolars, second premolars, and first molars at the occlusal plane and between the centers of the dento-gingival junction of the canines, first premolars, second premolars and first molars at the palatal side. (**b**) The upper dental arch depth. Distance between a tangent from the incisal edge of the central incisors and a line connecting the contact point between the first molar mesiobucal cusps. (**c**) Palate height. Distance between the line connecting the centers of the dento-gingival junctions of second premolars on the palatal side and the highest point of the palatal vault on the midpalatal rafe. (**d**) Palate surface area—area below the gingival plane and limited by the distal plane; palate volume—volume below the gingival plane and limited by the palate surface and distal plane.

Data availability

The data underlying this article will be shared upon reasonable request to the corresponding author.

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Author contributions
M.Š.—conceptualization, data curation, formal analysis, investigation, methodology, visualization, writing of the original draft, review and editing.V.P. – data curation, methodology. M.Š. – data collection, formal analysis. A.Š. – supervision, formal analysis, writing, review and editing, project administration, data collection, funding acquisition. S.J. – statistical analysis and formal analysis. K.L. – formal analysis, funding acquisition, supervision, writing, review and editing, project administration. All authors reviewed the manuscript.

Competing interests
The authors declare no competing interests.

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