Проблемы стоматологии
2025, том 21, № 3 стр. 31-39

DOI: 10.18481/2077-7566-2025-213-31-39

УДК 616.314.-007.2

МНОГОФАКТОРНОСТЬ ДИСТАЛЬНОЙ ОККЛЮЗИИ: РОЛЬ ГЕНЕТИЧЕСКИХ И СРЕДОВЫХ ФАКТОРОВ (ОБЗОР ЛИТЕРАТУРЫ)

Хумгаева Х. Р.[1], Иванов С. Ю.[1, 2], Бопхоев С. В.[1], Кобец К. К.[1]

[1] *Российский университет дружбы народов имени Патриса Лумумбы (РУДН), Москва, Россия*
[2] *Первый Московский государственный медицинский университет им. И.М. Сеченова (Сеченовский университет), Москва, Россия*

Аннотация

Дистальная окклюзия — одна из наиболее распространенных зубочелюстных аномалий, характеризующаяся дистальным расположением нижней челюсти по отношению к верхней. Это состояние сопровождается нарушением жевательной функции, затруднением артикуляции речи и значительными эстетическими проблемами, которые могут влиять на социальную адаптацию и психологическое благополучие.

Целью данного обзора стала систематизация современных знаний о причинах и механизмах развития дистального прикуса и проверка гипотезы о мультифакториальной природе этого состояния, при которой генетическая предрасположенность взаимодействует со средовыми и функциональными факторами.

Методология включала структурированный поиск научных публикаций в базах данных PubMed, Google Scholar и eLIBRARY за последнее десятилетие. Публикации отбирались в соответствии с критериями включения, которые включали анализ этиологических факторов, оценку наследственных факторов, оценку функциональных нарушений и обсуждение особенностей роста краниофациального скелета. В общей сложности 75 источников соответствовали критериям детального анализа, включая клинические исследования, экспериментальные работы и обсервационные исследования.

Результаты обзора подтверждают, что дистальная окклюзия возникает в результате сложного взаимодействия наследственных детерминант, нарушений роста и развития краниофациального скелета и внешних факторов, таких как длительные вредные привычки полости рта, хроническая обструкция носовых ходов, приводящая к ротовому дыханию, и некорректированная преждевременная потеря молочных зубов. Полученные результаты подчеркивают важность раннего выявления факторов риска, междисциплинарных диагностических подходов и своевременного ортодонтического вмешательства. Эти выводы обосновывают необходимость индивидуализированных профилактических и терапевтических стратегий, что повышает эффективность лечения и улучшает долгосрочные результаты.

Ключевые слова: *дистальная окклюзия, аномалия прикуса, патогенез аномалий прикуса, генетика, окружающая среда*

Авторы заявили об отсутствии конфликта интересов

Хадижат Руслановна ХУМГАЕВА *ORCID ID 0009-0004-7848-6554*
врач-ординатор кафедры челюстно-лицевой хирургии и хирургической стоматологии, а также кафедры стоматологии детского возраста и ортодонтии, Российский университет дружбы народов (РУДН), Москва, Россия
kkhumgaeva@mail.ru
Сергей Юрьевич ИВАНОВ *ORCID ID 0000-0001-5458-0192*
д.м.н., профессор, член-корреспондент РАН; Заведующий кафедрой челюстно-лицевой хирургии и хирургической стоматологии Российского университета дружбы народов имени Патриса Лумумбы (РУДН), Москва, Россия; Заведующий кафедрой челюстно-лицевой хирургии, Первый Московский государственный медицинский университет им. И.М. Сеченова (Сеченовский университет), Москва, Россия
syivanov@yandex.ru
Саддам Висингиреевич БОПХОЕВ *ORCID ID 0000-0003-0431-0033*
Аспирант кафедры челюстно-лицевой хирургии и хирургической стоматологии, Российский университет дружбы народов (РУДН), Москва, Россия
bophoevs@gmail.com
Константин Константинович КОБЕЦ *ORCID ID 0000-0002-8141-0460*
Ассистент кафедры челюстно-лицевой хирургии и хирургической стоматологии, Российский университет дружбы народов (РУДН), Москва, Россия
kobetskonstantin@gmail.com

Адрес для корреспонденции: Хадижат Руслановна ХУМГАЕВА
117198, Москва, ул. Миклухо-Маклая, д. 8
+7 (925) 039-73-98
kkhumgaeva@mail.ru

Образец цитирования:
Хумгаева Х. Р., Иванов С. Ю., Бопхоев С. В., Кобец К. К.
МНОГОФАКТОРНОСТЬ ДИСТАЛЬНОЙ ОККЛЮЗИИ: РОЛЬ ГЕНЕТИЧЕСКИХ И СРЕДОВЫХ ФАКТОРОВ (ОБЗОР ЛИТЕРАТУРЫ).
Проблемы стоматологии. 2025; 3: 31-39.

DOI: 10.18481/2077-7566-2025-21-3-2231-39

Поступила 15.09.2025. Принята к печати 12.10.2025

DOI: 10.18481/2077-7566-2025-21-3-31-39

MULTIFACTORIAL NATURE OF DISTAL OCCLUSION: THE ROLE OF GENETIC AND ENVIRONMENTAL FACTORS (LITERATURE REVIEW)

Khumgaeva Kh.R.[1], Ivanov S.Yu.[1, 2], Bopkhoev S.V.[1], Kobets K.K.[1]

[1] *Peoples' Friendship University of Russia named after Patrice Lumumba (RUDN University), Moscow, Russia*
[2] *I.M. Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russia*

Abstract

Distal occlusion is one of the most common dentofacial anomalies, characterized by a distal position of the mandible in relation to the maxilla. This condition is associated with impaired chewing efficiency, difficulties in speech articulation, and significant aesthetic problems that can affect social adaptation and psychological well-being. The purpose of this review was to systematize current knowledge about the causes and mechanisms of distal occlusion development and to test the hypothesis that the condition has a multifactorial nature, in which genetic predisposition interacts with environmental and functional factors.

The methodology included a structured search of scientific publications in PubMed, Google Scholar, and eLibrary databases over the past decade. Publications were selected according to inclusion criteria that required analysis of etiological factors, assessment of hereditary influences, evaluation of functional disturbances, and discussion of craniofacial growth patterns. In total, 75 sources met the criteria for detailed analysis, including clinical studies, experimental works, and observational research.

The results of the review confirm that distal occlusion arises from a complex interaction of hereditary determinants, disturbances in the growth and development of the craniofacial skeleton, and external influences such as prolonged harmful oral habits, chronic nasal obstruction leading to mouth breathing, and uncorrected premature loss of deciduous teeth. The findings highlight the importance of early identification of risk factors, interdisciplinary diagnostic approaches, and timely orthodontic intervention. These conclusions substantiate the need for individualized preventive and therapeutic strategies, thereby improving treatment effectiveness and long-term outcomes.

Keywords: *distal occlusion, malocclusion, malocclusion pathogenesis, genetics, environment*

The authors declare no conflict of interest

Khadizhat R. KHUMGAEVA *ORCID ID 0009-0004-7848-6554*
Resident Doctor, Department of Oral and Maxillofacial Surgery and Surgical Dentistry, and Department of Pediatric Dentistry and Orthodontics, Peoples' Friendship University of Russia (RUDN University), Moscow, Russia
kkhumgaeva@mail.ru
Sergey Yu. IVANOV *ORCID ID 0000-0001-5458-0192*
Grand PhD in Medical sciences, Professor, Corresponding Member of the Russian Academy of Sciences; Head of the Department of Oral and Maxillofacial Surgery and Surgical Dentistry, Peoples' Friendship University of Russia named after Patrice Lumumba (RUDN University), Moscow, Russia; Head of the Department of Oral and Maxillofacial Surgery, I.M. Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russia
syivanov@yandex.ru
Saddam V. BOPKHOEV *ORCID ID 0000-0003-0431-0033*
Postgraduate Student, Department of Oral and Maxillofacial Surgery and Surgical Dentistry, Peoples' Friendship University of Russia (RUDN University), Moscow, Russia
bophoevs@gmail.com
Konstantin K. KOBETS *ORCID ID 0000-0002-8141-0460*
Assistant, Department of Oral and Maxillofacial Surgery and Surgical Dentistry, Peoples' Friendship University of Russia (RUDN University), Moscow, Russia
kobetskonstantin@gmail.com

Correspondence address: Khadizhat R. KHUMGAEVA
8 Miklouho-Maklaya St., Moscow, 117198, Russia
+7 (925) 039-73-98
kkhumgaeva@mail.ru

For citation:
Khumgaeva Kh.R., Ivanov S.Yu., Bopkhoev S.V., Kobets K.K.
MULTIFACTORIAL NATURE OF DISTAL OCCLUSION: THE ROLE OF GENETIC AND ENVIRONMENTAL FACTORS (LITERATURE REVIEW).
Actual problems in dentistry. 2025; 3: 31-39. (In Russ.)

DOI: 10.18481/2077-7566-2025-21-3-31-39

Received 15.09.2025. Accepted 12.10.2025

Introduction

Modern society is facing an increasing number of people with dentoalveolar system problems, among which distal occlusion is common [1]. This type of malocclusion not only affects facial and smile aesthetics but also negatively impacts the functionality of the masticatory system, which may lead to difficulties in digestion and speech [1, 2]. Thus, the identification and understanding of the etiopathogenetic factors contributing to the development of distal occlusion are relevant from both a clinical and a social perspective.

Distal occlusion is characterized by the closing of posterior teeth with the formation of a distal step; as a result of upper incisor protrusion and lower incisor retrusion, anterior teeth may not come into contact, leading to the formation of a sagittal gap. This malocclusion has distinct facial features. Distal occlusion is caused by morphological deviations in the structure of the upper and lower jaw bones, teeth, and dental arches [3].

Distal occlusion is the most common anomaly in the relationship between dental arches, with a population prevalence of more than 30 % of all malocclusions, according to various authors.

According to Angle's classification (classification of malocclusion), distal occlusion belongs to Class II and has two subdivisions:

Subdivision 1 — protrusion of the upper incisors, characterized by a fan-shaped forward inclination and increased overjet.

Subdivision 2 — lingual inclination of the upper anterior teeth, with close contact to the lower teeth and deep overbite.

Clinically, distal occlusion manifests as a convex facial profile, with the chin retruded backward. The lower third of the face is shortened, leading to protrusive inclination of the upper incisors that contact the lower lip, while the upper lip is displaced forward, exposing the upper teeth [1].

Functionally, there is impairment of biting, crushing, and chewing food. The duration of the chewing process increases on average by 30 % [3]. Respiratory and speech functions are also affected — unclear articulation of sounds occurs due to improper tongue positioning. Swallowing is impaired, manifesting as tension in facial muscles, retraction of the mouth corners and lower lip, and a double chin contour due to incorrect tongue posture.

In dentoalveolar anomalies, including distal occlusion, the risk of caries increases due to crowding and misalignment of teeth, which also complicates oral hygiene maintenance [1].

Thus, the high prevalence of distal occlusion, along with its pronounced negative impact on aesthetics, functionality of the masticatory system, and overall health, highlights its important medical and social significance. Understanding the etiopathogenetic factors underlying this malocclusion is essential for the development of effective methods of prevention and treatment.

The aim of this systematic review is to analyze current perspectives on the etiology and pathogenesis of distal occlusion, including genetic, environmental, and biomechanical aspects of its development. The obtained data will provide a deeper understanding of the mechanisms underlying this common malocclusion and contribute to the improvement of timely diagnostic and corrective approaches.

Methods

For the preparation of this literature review, various electronic databases were used, such as PubMed, Google Scholar, and eLibrary. Dissertation research and their recommended sources were also consulted.

he literature search was conducted using keywords and their combinations, including: "pathogenesis of distal occlusion", "prevalence of distal occlusion", "influence of genetic factors on malocclusion", "etiology of disto-occlusion", "types of malocclusion", "causes of malocclusion", "malocclusion types and their prevalence", "genetics and malocclusion".

The selection of articles was based on relevance, methodology, and study results addressing the prevalence of distal occlusion, Angle's classification, as well as exogenous and endogenous.

Results

After removing duplicates, 110 sources were selected for screening and further review. Following the assessment of abstracts and content, 75 studies were evaluated against the inclusion and exclusion criteria. Seventy-five articles were excluded for the following reasons: incomplete data, overlapping information from the same sources, outdated data, and others. A total of 44 sources were included in the final analysis. Description of included studies.

After a detailed review of the 44 selected works, the main etiopathogenetic causes of distal occlusion were identified. These include:

1. Artificial feeding
2. Early childhood diseases
3. Neurohumoral factors disrupting the coordination of masticatory muscles
4. Impaired nasal breathing; mouth breathing
5. Narrowing of the maxilla
6. Harmful oral habits
7. Untimely treatment and extraction of primary teeth without subsequent prosthetic replacement
8. Discrepancy in crown size between upper and lower teeth
9. Heredity

Artificial feeding using bottles with large holes can cause distal occlusion in children, as they do not apply sufficient effort during sucking. This leads to reduced functional load on the muscles, delayed mandibular growth, and persistence of infantile retrognathia. In contrast, breastfeeding activates the mandible, promoting its normal growth and the development of masticatory and facial muscles.

With artificial feeding, the development of prognathism [4] occurs 2–3 times more frequently, and delays in jaw and muscle growth are observed. During breastfeeding, active mandibular movement stimulates its growth, and within approximately six months the correct jaw relationship is established. If the bottle teat has a large diameter, it prevents proper mandibular development due to insufficient effort by the infant [4–7].

Early childhood diseases. Somatic illnesses, rickets, and endocrine disorders can affect the processes of skeletal maturation and cranial bone growth, which also leads to disrupted timing and symmetry of tooth eruption, resulting in tooth dystopia and retention. For example, rickets — a disease caused primarily by vitamin D deficiency and poor absorption of calcium and phosphorus — leads to impaired bone and tooth formation. This condition causes bone softening and deformation, as well as abnormal development and replacement of deciduous teeth, which may result in delays in children's physical development.

Due to rickets, the jaws remain underdeveloped. All subsequent malocclusions are linked to reduced resistance of the jaws to muscle forces. An important aspect is also hypocalcification of tooth enamel and delayed development of permanent tooth buds. This disease leads to changes in all dimensions of the maxilla: reduction of frontal and transverse dimensions, and increase in sagittal length. The anterior part of the maxilla takes on a beak-shaped form, and the palate becomes lyre-shaped. The alveolar processes in the posterior segments diverge, leading to altered tooth positioning and the development of Angle's Class I and II malocclusions, as well as open bite [8].

In addition to the well-established role of vitamin D in bone mineralization and rickets prevention, other nutrients are important for harmonious craniofacial growth. For example, vitamin C is required for collagen synthesis and epigenetically regulates osteoblastogenesis, influencing bone mineralization and craniofacial development [8]. Vitamin K2 activates osteocalcin and matrix Gla protein, ensuring normal bone mineralization; deficiency in children is associated with reduced bone mass, growth delays, and even hypoplasia of facial structures in experimental models [9, 10]. Zinc plays a key role in regulating IGF-I and the activity of growth plates; its deficiency is linked to impaired linear growth and delayed bone development [11]. Furthermore, iron, calcium, and magnesium are necessary for normal bone metabolism, and their deficiency in children is accompanied by a risk of growth and skeletal disproportions [11].

Neurohumoral factors disrupting the coordination of masticatory muscles. Impaired coordination of masticatory muscles may be associated with several neurohumoral factors. Primarily, hyperactivity of muscles that shift the mandible distally can result from alterations in the central nervous system — stress, anxiety, or neurosis may cause excessive muscle tension. Imbalances in neurotransmitters — such as changes in serotonin, dopamine, or gamma-aminobutyric acid levels — can influence muscle tone.

Temporomandibular joint anomalies, including injuries or inflammation, may also disrupt muscle function. In addition, hyperactivity can be triggered by hormonal changes (hormones affecting muscle tone may induce hyperactivity) or by chronic pain syndromes — persistent jaw pain may lead to spasms of the masticatory muscles [13].
Impaired nasal breathing. Mouth breathing is a significant etiological factor in the development of distal occlusion and dentoalveolar anomalies in children. Mechanical obstructions, such as deviated nasal septum, inferior turbinate hypertrophy, and adenoids, interfere with normal breathing and influence craniofacial growth and development.

When nasal obstruction causes a switch to oral breathing, the negative impact becomes more pronounced. The absence of tongue support for the upper dental arch contributes to its narrowing and forward extrusion, leading to vestibular displacement of the maxillary anterior teeth and the formation of a high ("gothic") palate.

Significant mandibular positional changes are observed, including backward and downward displacement, which increases mandibular plane angle and height. These changes predispose to distal and abnormal occlusions, with posterior crossbite particularly prevalent among mouth-breathing children (49 % compared with 26 % in nasal breathers, *P* = 0.006) [8].

Furthermore, anomalies of lip and tongue closure are more common in this group, indicating functional insufficiency. Thus, mouth breathing disrupts the harmony of craniofacial growth, contributing to the development of distal occlusion and other dental anomalies [1, 14, 21].

Additionally, one study [18] found that children with mouth breathing due to grade 4 tonsil hypertrophy developed Class II malocclusion, indicating the interaction of various factors influencing the dentoalveolar system.

In children with chronic nasal obstruction and/or habitual mouth breathing, the tongue drops down and loses contact with the palate, reducing the intraoral "expansive" support of the palatal vaults. As a result, transverse maxillary growth slows, leading to a narrow, high palate, followed by compensatory mandibular retroposition/posterior rotation, increased lower facial height, and a tendency toward Class II malocclusion and open bite. Importantly, the effect of rapid maxillary expansion (RME) on nasal breathing and palatal morphology tends to be more pronounced in children with true obstruction (e.g., adenoidal), whereas in children without marked hypertrophy of nasal structures, the effect is less predictable. Some studies reveal a tendency toward more significant volumetric and aerodynamic improvements after expansion in children with adenoid hypertrophy.

Narrowing of the maxilla is an important factor influencing the formation of distal occlusion. In recent years, evidence has accumulated showing that transverse deficiencies of the maxilla have a complex nature and develop under the influence of genetic, functional, environmental, and osteopathic factors. Genetic predisposition plays a significant role. Twin studies have demonstrated that transverse dimensions of the dental arches, as well as palatal depth and volume, have a high degree of heritability: up to 80–86 % of variation is explained by genetic factors. This indicates that transverse jaw development is largely determined by innate mechanisms, while functional and environmental influences only modulate this potential [29].

At the same time, environmental factors and soft tissue functions can enhance or weaken the effect of the genetic program. Chronic mouth breathing, low tongue posture, as well as harmful oral habits (such as thumb or pacifier sucking), lead to elevation and narrowing of the palatal vault.

Prolonged disruption of the functional balance between the tongue, lips, and cheeks alters the force equilibrium acting on the dental arches, resulting in reduced transverse development of the maxilla and worsening of transverse deficiency [30]. Another important factor is the reduced masticatory load in modern society. The transition to soft, processed food results in insufficient mechanical stimulation of bone tissue and weakened remodeling processes. Under conditions of reduced load, the alveolar processes and the maxillary arch develop less fully, contributing to the formation of a narrow palate and constricted dental arches [31].

An additional layer of understanding is provided by osteopathic and cranio-cervical interactions. Narrowing of the maxilla is accompanied by changes in the spatial positioning of the palatal vault and cranial base, which affects the balance of head and neck muscles. Studies indicate that such cranio-cervical disturbances may exacerbate maxillary growth deficiency and are associated with postural alterations and temporomandibular joint dysfunctions [25, 26].

Thus, narrowing of the maxilla forms at the intersection of congenital and acquired factors: genetic predisposition, respiratory disorders, dietary characteristics, and postural imbalances. This complex mechanism explains why transverse deficiencies act as an independent link in the pathogenesis of distal occlusion: reduced maxillary width leads to mandibular retroposition, disturbance of dental arch relationships, increased sagittal gap, and the formation of characteristic distal occlusion.

Harmful oral habits such as thumb sucking, nail biting, pacifier use, and improper tongue posture exert a significant influence on the formation of distal occlusion. These factors may cause abnormal distribution of masticatory loads and obstruction of normal jaw growth.

Thumb or pacifier sucking often leads to tooth displacement and changes in dental arch shape, which may promote mandibular distalization. Nail biting or habitual jaw clenching can cause masticatory muscle dysfunction and altered occlusion. In addition, improper tongue posture at rest or during swallowing may reduce the necessary pressure on the maxilla, thereby contributing to its narrowing and the development of distal occlusion [1, 8, 21, 23].

Untimely treatment and extraction of primary teeth is one of the most common causes of distal occlusion development. Caries of primary teeth aggravates these issues, as it leads to their premature destruction and extraction. Such destructive processes contribute to pathological changes in occlusion, facilitating or worsening distal and other malocclusions due to the loss of functional load on teeth and altered normal jawbone growth.

Premature loss of certain maxillary primary teeth results in mesial migration of the permanent first molars and disrupted jaw growth, for example, when growth zones in the mandibular condyles are amaged, leading to the formation of mandibular micrognathia. Retention of premolars, displacement of permanent canines, and dentoalveolar elongation of antagonistic teeth are also observed, creating a block for normal mandibular articulation.

Early eruption of the maxillary first molars relative to the mandibular molars in most cases leads to the formation of prognathic occlusion. Early loss of mandibular teeth slows down its normal development. Premature extraction of primary teeth without subsequent prosthetic replacement may cause growth arrest of the mandible and formation of micrognathia. This is especially critical in patients with pre-existing signs of retrognathia, in whom changes in mandibular size and position are observed during treatment.

Discrepancy in crown size between upper and lower teeth, especially molars, plays a key role in the pathogenesis of distal occlusion. A prognathic dental relationship based on dentoalveolar morphology indicates imbalance in crown size, which may result in distal occlusion.

Crown size assessment may be performed using indices developed by H. Gerlach and Tonn, which quantitatively determine the relative position of teeth in occlusion. Crown size discrepancies may be due to several factors, including incomplete molar eruption, which leads to abnormal development of the alveolar process and consequently altered occlusal relationships.

Labial inclination of the upper anterior teeth and vertical positioning of the lower teeth also contribute to distal displacement of the dental arches. This imbalance affects the anterior segment length of the maxillary arch, increasing the severity of distal occlusion in cases of anterior tooth protrusion, while retrusion leads to arch length reduction. Thus, strict proportionality between crown sizes of upper and lower teeth is critically important for maintaining proper function and occlusion [1, 23].

Genetics plays a key role in the development of malocclusions, including distal occlusion [1]. While genetic predisposition was once regarded only as a general risk factor, modern molecular-genetic research has revealed that specific gene mechanisms underlie these abnormalities.

MSX1 (Muscle Segment Homeobox 1 is a key transcriptional regulator of epithelial-mesenchymal interactions during odontogenesis and palatogenesis. Under normal conditions, through its DNA-binding homeodomain, MSX1 coordinates the BMP/SHH/FGF signaling networks and, in particular, enhances BMP4 expression in the dental mesenchyme (in synergy with PAX9). This process is essential for tooth bud progression beyond the bud/cap stage and for normal proliferation of palatal shelf cells [32]. Clinically, MSX1 loss-of-function results in developmental arrest of teeth at early stages and defects in palatal fusion — the mechanistic basis of hypodontia and clefting. A recent protein domain–based review demonstrated a strict correlation between the type/location of variants and the phenotype: structural variants within the homeodomain usually lead to nonsyndromic hypodontia, whereas variants in the intrinsically disordered N-terminal region are more often associated with nonsyndromic orofacial clefts [33].

On a molecular level, amino acid substitutions in the homeodomain reduce MSX1 affinity for regulatory DNA elements and/or disrupt assembly of protein complexes (including interactions with PAX and DLX factors), leading to decreased transcription of key targets such as BMP4 and a halt in dental organogenesis [32]. Functionally validated missense mutations in the MSX1 homeodomain (e. g.,

Arg196Pro, Ala219Thr, Ala221Glu, Leu224Pro) impair DNA binding and stable protein–protein complex formation, blocking normal tooth germ development and most often manifesting clinically as hypodontia, particularly the absence of premolars and third molars [34]. Nonsense variants and deletions in exon 4 result in truncated/nonfunctional proteins lacking the homeodomain, associated with more severe phenotypes — multiple agenesis and cleft lip/palate — with the highest degree of loss of function and clinical severity [33].

An additional regulatory layer has been uncovered in recent years: the N-terminal intrinsically disordered region (IDR) of MSX1 undergoes PRMT1-mediated arginine methylation (at R150, R157), which controls MSX1 phase separation and nuclear condensate formation. Disruption of this process reduces palatal mesenchyme proliferation and leads to clefting — a vertebrate-conserved mechanism demonstrated in model systems and embryonic palatal tissue [35]. Consolidated clinico-genetic data from 2024 further confirmed that the spectrum of MSX1 variants is associated not only with isolated hypodontia but also with a broader set of oro-dental anomalies (including combinations with clefts), underscoring domain-dependent phenotypic expression [36]. Clinical and morphometric studies support the association of hypodontia with Class II anomalies (including Class II/2) and altered mandibular morphology in second premolar agenesis; reduced sagittal dimensions and increased overjet are often observed, reinforcing distal relationships [37–39].

PAX9 is a transcription factor with a paired domain, expressed in the mesenchyme of the developing tooth germ and in maxillary tissues. It is critically important for initiation and subsequent transition of the tooth germ through the bud → cap → bell stages by regulating signaling networks, including interactions with MSX1 and control of BMP4 and other morphogenetic molecules. PAX9 directly or indirectly maintains expression of signaling molecules in the dental mesenchyme and participates in epithelial–mesenchymal interactions required for proper tooth bud differentiation [40].

Multiple variantes have been documented in PAX9, including nonsense, deletions, frameshift, and missense changes affecting different domains. Deleterious (truncating or large deletion) variants result in a classical loss-of-function with haploinsufficiency, leading to severe phenotypes with multiple tooth agenesis. Missense variants — particularly those within the paired domain or affecting structural stability of the DNA-binding domain — reduce the protein's ability to bind promoter/enhancer regions and activate downstream genes (including BMP4), resulting in more variable phenotypes ranging from absence of individual teeth to severe forms. Recent genotype–phenotype analyses confirmed that deletions/translocations are associated with a higher rate of extensive agenesis compared with milder missense variants. Modifiers such as WNT10A have also been shown to exacerbate the phenotype when co-occurring with PAX9 variants [41].

Loss of PAX9 function diminishes transactivation of mesenchymal targets (including the BMP pathway), disrupts paired activation with MSX1 and other factors, and leads to tooth germ arrest at the bud/cap stages. This prevents normal morphogenetic signaling, epithelial invagination, and subsequent dentin/enamel differentiation. At the cellular level, PAX9 loss results in reduced mesenchymal cell proliferation, altered apoptosis, and disrupted epithelial–mesenchymal boundaries [40].

Clinically, agenesis of premolars and/or second molars due to PAX9 variants shortens the dental arch and reduces alveolar growth. Orthodontically, this leads to arch length deficiency, inter-arch imbalance, and inadequate stimulation of alveolar growth mechanisms. Combined with functional, respiratory, or postural factors, this increases the likelihood of sagittal discrepancies, such as excessive overjet or Class II patterns, in certain patients. While population studies show inconsistent associations of hypodontia with Class II/2 and related variations, PAX9 mutations should nonetheless be regarded as significant risk factors for structural dental arch deficiencies [38].

The **FGF signaling pathway** (FGF8, FGF10, and receptors FGFR1/FGFR2) is a critical system regulating survival, proliferation, differentiation, and chemotaxis of cranial neural crest cells, as well as morphogenesis of facial prominences and the palate. FGF8, expressed in the anterior craniofacial epithelium, defines boundaries and chemoattraction of neural crest cells into the first pharyngeal arches, while FGF10 and its receptors act in the mesenchyme to promote proliferation and alveolar development. Dysregulation of this pathway (hypo- or hyperfunction) alters NCC migration/proliferation and cranial base remodeling, directly affecting maxillary size and position [42].

Clinically, this is most evident in pathogenic FGFR2/FGFR1 variants: characteristic missense mutations in FGFR2 lead to craniosynostosis syndromes (Apert, Crouzon, etc.) with premature suture closure, impaired cranial base expansion, and pronounced midface hypoplasia (retrusion). This alters maxillary position and growth, producing severe transverse and sagittal maxillary deficiencies. The result is often marked displacement of the upper arch and/or relative mandibular prognathism — in some cases yielding skeletal Class III of complex origin but always producing severe occlusal disorders requiring comprehensive orthognathic treatment. These findings are well documented in clinical and review studies on FGFR2-related syndromes (Apert, Crouzon) and in broader reviews of FGF signaling in cranial suture development [43, 44].

Discussion

The systematic literature review conducted in this study provided a comprehensive overview of current concepts regarding the etiology and pathogenesis of distal occlusion — one of the most common malocclusions. Analysis of a large body of scientific research confirms that the development of this pathology is multifactorial, involving both genetic and environmental mechanisms. Progression of distal occlusion is accompanied by changes in cephalometric parameters, which can serve as a valuable tool for assessing the severity and dynamics of the condition. Such changes were analyzed in detail in the work of Menshikova E. V. et al. [24].

One of the key findings of this analysis is confirmation of the significant role of hereditary predisposition in the onset

of distal occlusion. Numerous studies demonstrate associations between specific genetic variants and an increased risk of developing this malocclusion. Recent research has shown that mutations in transcription factors (MSX1, PAX9, RUNX2) and key signaling pathways (WNT10A, AXIN2, FGF/FGFR) lead to disturbances in odontogenesis, hypodontia, cleft palate, and craniofacial disproportions. These alterations form the anatomical foundation for sagittal discrepancies of the jaws, including distal occlusion.

The clinical relevance of genetic abnormalities lies in the fact that phenotypes such as shortened dental arches, insufficient alveolar growth, hypoplasia, or multiple tooth agenesis directly influence orthodontic treatment outcomes. For instance, MSX1- or PAX9-associated hypodontia is frequently accompanied by reduced sagittal dimensions and an increased tendency toward overjet. In cases of impaired FGF signaling (e. g., FGFR2 mutations), pronounced maxillary retrusion and severe occlusal disproportions are observed, often requiring complex surgical correction.

It is also important to emphasize that molecular mechanisms exert domain-specific and dose-dependent effects: for example, missense variants within the MSX1 homeodomain are linked to isolated hypodontia, whereas deletions in the C-terminal exons are associated with severe clefts. Such genotype–phenotype correlations open possibilities for predicting clinical course and developing individualized treatment protocols.

At the same time, genetic factors do not act in isolation; they interact with environmental (breathing habits, diet, postural disorders) and epigenetic mechanisms. In some cases, the combination of hypodontia with functional breathing disorders becomes the decisive factor in establishing a pronounced distal jaw relationship.

Thus, the modern perspective on the pathogenesis of distal occlusion is shifting from purely morphological descriptions to a molecularly substantiated model in which key roles are played by genes such as MSX1, PAX9, RUNX2, WNT10A, AXIN2, and FGF/FGFR. This not only broadens our understanding of the biological foundations of malocclusion but also highlights the promise of implementing genetic screening and precision-based approaches in orthodontic prognosis and treatment.

At the same time, the literature review revealed a significant contribution of several environmental factors to the pathogenesis of distal occlusion. These include harmful childhood habits, such as prolonged thumb-sucking or pacifier use, as well as impaired nasal breathing leading to abnormal tongue posture. The surrounding environment also exerts considerable influence on the development of dentoalveolar anomalies. For example, Tikhonov V. E. et al. demonstrated that the prevalence of malocclusions, including distal occlusion, is significantly higher among children living in large industrial cities compared with rural areas. Such external exposures can disrupt the balance between maxillary and mandibular growth, thereby contributing to distal occlusion. Moreover, unfavorable intrauterine conditions and early-life craniofacial trauma may also represent risk factors for this malocclusion.

Its important to note that in the majority of studies reviewed, distal occlusion is considered a condition resulting from the interplay between hereditary and environmental mechanisms. The combination of genetic predisposition and adverse environmental influences during critical periods of dentofacial growth and development creates conditions for the manifestation of distal occlusion. Understanding the complex nature of this etiology is essential for developing effective preventive and therapeutic strategies.

Modern osteopathic approaches view cranial base structures within the context of vertical body chains and overall posture. Postural abnormalities and sphenoid bone inclination alter the spatial position of the maxilla, promoting its constriction and secondary mandibular retrognathia. This further supports the pathogenesis of distal occlusion when considering functional matrices and cranio-cervical biomechanics. The relationship between posture and malocclusion development has been confirmed by recent evidence: a systematic review demonstrated that Class II malocclusions are associated with increased cervical curvature and forward head posture, whereas Class III is linked to a straightened cervical spine [25].

Recent studies also confirm that cranial base angles and soft tissue features exert a significant influence on the development of sagittal anomalies. It has been shown that cranial base angle and soft tissue configuration are directly associated with occlusal type, and changes in these parameters can predispose to distal or mesial jaw relationships [26].

Finally, clinical practice emphasizes that neglecting osteopathic dysfunctions in patients with maxillary constriction may lead to complications such as scoliotic deformities, cranial suture disturbances, and worsening of temporomandibular joint dysfunction. This underscores the necessity of a comprehensive, multidisciplinary approach for managing such patients [27].

Early identification and correction of modifiable risk factors can contribute to reducing the prevalence of distal occlusion in the population. Furthermore, timely orthodontic intervention, with consideration of the patient's individual anatomical features, may correct existing malocclusions and prevent the development of associated dental and systemic complications.

Further investigation of genetic and environmental mechanisms underlying distal occlusion will promote a deeper understanding of its pathogenesis and, consequently, the improvement of prevention and treatment methods for this widespread malocclusion.

Conclusion

The present study highlights the multifaceted etiology and pathogenesis of distal occlusion, emphasizing the combined contribution of both genetic and environmental factors to its development. Based on a systematic literature review, it becomes evident that the interaction between hereditary predisposition and various external influences plays a key role in the manifestation of this malocclusion.

Hereditary factors, such as mutations in genes responsible for jaw growth, create anatomical prerequisites for the onset of distal occlusion. At the same time, environmental fac-

tors, including harmful habits and breathing disorders, may disrupt the harmonious growth of the dentofacial system, thereby exacerbating the predisposition to this pathology.

Early identification and correction of modifiable risk factors, along with an individualized orthodontic approach that considers patient-specific anatomical characteristics, can significantly reduce the prevalence and consequences of distal occlusion. Timely diagnosis and initiation of orthodontic treatment, particularly between the ages of 6 and 8, have demonstrated high effectiveness in managing distal occlusion, as confirmed by the study of Kosyuga S. Yu. and Sirotkina V. S. conducted in 7-year-old children.

Therefore, further research is needed to achieve a deeper understanding of the interplay between genetic and environmental factors. Recognition of the complex nature of this pathology underscores the importance of pre-treatment analysis and the development of multi-level prevention and treatment strategies, which will ultimately help ensure the health and quality of life of patients with distal occlusion.

Conclusions

Distal occlusion is one of the most common dentofacial anomalies and has a multifactorial nature. Its development involves both genetic mechanisms (mutations in genes regulating jaw and tooth growth) and environmental influences (impaired nasal breathing, harmful oral habits, dietary factors, and postural conditions). The interaction of these factors determines the severity of clinical manifestations and the prognosis of the anomaly.

The results of the literature review confirm the need for early identification of predisposing factors and preventive measures in childhood. The effectiveness of treatment largely depends on the timely initiation of orthodontic correction and consideration of individual craniofacial growth characteristics.

A modern approach to distal occlusion should be based on comprehensive interdisciplinary collaboration between dentists, orthodontists, otorhinolaryngologists, and other specialists. The inclusion of genetic analysis and functional diagnostics into clinical practice will not only improve treatment outcomes but also contribute to more accurate preventive strategies.

Thus, distal occlusion is a multifactorial condition, and its successful management requires early diagnosis, individualized therapeutic planning, and integration of modern knowledge about genetic and environmental mechanisms underlying its development.

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