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Perspective

Perspectives on Pathological Crosstalk between Malocclusion and Multi-organ Systems: The Hidden Face of an Iceberg

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ABSTRACT: Malocclusion is a dental disorder that has often been overlooked in physiological studies. It is defined as any malrelationship of dental arches with or without aberration in the teeth developmental disorder, which alters functions like mastication, swallowing, speech, etc. Mounting evidence implies that malocclusion might be associated with adjacent and remote organ dysfunction, albeit the underlying mechanisms are obscure. However, to date, no review has unified the framework correlating malocclusion with oral (mastication, speech) and distant organ pathologies such as ocular, auditory, nasal, cerebral, respiratory, musculoskeletal, cardiovascular, blood-related, renal, and sexual physiologies. Therefore, this perspective provides the first integrated framework correlating malocclusion with multiorgan pathology and outlines a prioritized research agenda to investigate the causality. We have also documented the prevalence of malocclusion types in children as well as adolescents, which has been revealed in Africans, followed by Europeans, Americans, and Asians. Specifically, the impact of occlusal disharmony on brain activity could be attributed to rich neurological connections between the stomatognathic system (jaw, teeth, muscles, joints) and brain regions involved in sensory, autonomic, and emotional regulation. Consequently, chronic orofacial pain and dysfunction related to malocclusion can activate limbic and cortical pathways modulating systemic inflammatory responses and immune regulation, potentially influencing other organ systems through neuroimmune crosstalk and neurobiological circuits. Malocclusion-associated dysfunction might alter neural inputs affecting broader systemic control, thereby impacting bone metabolism, vascular tone, and inflammation. Taken together, we presented our perspective on emerging data implying the possible malocclusion-associated pathological complications. A detailed understanding of these intricate associations between malocclusion and multi-organ system pathologies will offer a new direction for comprehensive intervention strategies to reduce significant mortality and morbidity, resulting in improved quality of life.

Keywords: Malocclusion, Oral, Neurological, Musculoskeletal, Respiratory, Cardiovascular, Renal, Erectile dysfunction

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1. Introduction

Malocclusion has become an extensively distinct oral health disorder in every age group, ranging from children and adolescents to older populations around the globe. This condition can be defined as an abnormal deflection from the average orientation of the mandibular and maxillary arch, forming an anomalous malocclusion [1]. According to Angle's classical classification, occlusion can be categorized into four specific classes, namely normal occlusion, Class I (Neutro-occlusion), Class II (Disto-occlusion), and Class III (Mesio-occlusion) [2]. Identifying and categorizing malocclusions is complex, as the scope and range of abnormalities included are very wide. Based on the extent and pattern of malocclusion, it can be classified as (1) occlusal disorder, which could contribute to difficulties in the operation of the jaw, and (2) teeth-alignment disorder related to physical deformities and abnormal facial aesthetics [3]. According to the World Health Organisation (WHO), malocclusion is the third most observed oral health related disorder, significantly affecting the patient's speech, appearance, confidence, and other daily activities like chewing and swallowing. Malocclusion may mediate extended occlusal disorders associated with mixed and permanent dentitions [4]. Evidence implies that malocclusion may also act as a risk factor for other nearby or distant organ systems that could be chronic and fatal. Therefore, in the next section, we have discussed malocclusion epidemiology and multi-organ pathologic associations.

2. Epidemiology

Over the years, malocclusion has been detected in many ethnicities, races, and ages. Studies have documented that malocclusion is a hereditary disease found in inhabitants of many civilizations, and almost 56% of the world population suffers from malocclusion deformities, mainly from early childhood [4]. Table 1 represents the global, continental (African, European, Asian), and the United States-based higher prevalence of malocclusion.

Table 1. Global, continental (African, European, Asian), and the United States-based higher prevalence of malocclusion. NA: Not available.

Country/ Region	Population type	Overall Prevalence (%)	Class I (%)	Class II (%)	Class III (%)	Other Traits
Global [4, 5]	Adolescents/Children (Mixed/Permanent Dentition)	56	46.3–51.9	19.56–25.0	6.5–7.04	Crowding: ≤84%, Spacing: ≤60%, Posterior Crossbite: 9.39%, Open Bite: ≤10%
Africa [6]	Permanent/Mixed Dentition	81	93 (Mixed) 91 (Permanent)	6.76	3.8	Open Bite: 10% (Mixed) 8% (Permanent),
Europe [5, 6]	Mixed/Permanent Dentition	72	NA	26 (Mixed) 23 (Permanent)	5.92	Deep Overbite: 33.08%, Posterior Crossbite: 15.38%
Asia [5]	Mixed/Permanent Dentition	48	50	14.14	9.63	Deep Bite: 16.3%, Overjet >6 mm: 8.6%,
United States [7, 8]	Adolescents/ Children	20-65	50-55	15	<1	NA

Class I occlusion is highly prevalent in Africans, accounting for 89% of permanent dentition. While Caucasians and Mongoloids exhibit Class II and III occlusions of 23-26% and 9.6%, respectively [5]. In a study on Nepalese adolescents (12-15 years old), approximately 48.5% of children were identified to have

Class I occlusion, while Class III was the least (4.32%), with an immediate need for orthodontic treatment [9]. According to a recent report from the Indian population aged 8-15, males had more cases of malocclusion (36.2%). Facial beauty and appearance are highly affected by the abnormal displacement of the jaw, and enormous implications were observed in young patients, such as low self-confidence, high social anxiety, high consciousness, and psychological apprehensions regarding facial aesthetics [1]. Nearly 49% of the sampled population in the Uttar Pradesh (UP) state of India has shown the occurrence of malocclusion. Class I, Class II, and Class III constituted 34.2%, 11.6%, and 3.2% portions of the sampled populations exhibiting higher percentages of normal overjet, excessive overbite, crowding, and straight profiles [10, 11]. In terms of cross-bite conformations, i.e., anterior and posterior, and functional shifts in cross-bite have been reported with 7.8%, 9%, and 12.2% of the world population by the MINORS tool [6]. In a seminal study, Chaturvedi et al. reviewed the literature on malocclusion prevalence in various countries as well as the different regions within India [12]. These widespread variations in occlusal deformities could be attributed to myriad factors, which have been discussed in the next section.

3. Etiopathology

Initially, malocclusion occurs during the developmental fetal stages [6] and may also be caused by multiple factors such as ethnicity, geographical location, climate, environmental exposures, genetic mutations, nasal obstructions, thumb sucking, mouth breathing, dental caries, and periodontal disorders. Various ethnic groups exhibit variations in facial skeletal structure, mandibular and maxillary bone dimensions, and soft tissue morphology. A systematic review revealed that in mixed and permanent dentitions, Angle Class I malocclusion is greatly prevalent compared to Class II, particularly among Africans [5]. Class III was the least prevalent, however, higher among Mongoloids in mixed dentition. Among Mongoloids, the open bite was highest in mixed dentition, while in Europe, the posterior cross-bite was more prevalent in permanent dentition. Malocclusion may also be affected indirectly by geographical location & climate through oral habits, diet, and environmental pressures. Some studies have advocated that idea, which aligns with evidence on diet-jaw relationships and the climate's dietary influence. Specifically, warmer climate often yields softer and processed diets, which can potentially suppress masticatory stress & jaw size, while colder climates might retain tougher diets [13, 14], contributing to malocclusion. Heat stress may affect oral health as dehydration and suppressed saliva levels enhance the risk of dental caries and soft tissue inflammation [15].

Further, pollutants like lead, cadmium, selenium, and mercury can adversely interfere with bone and cartilage formation [16]. Prenatal exposure may change maxillofacial growth, potentially reduce jaw size, or alter tooth eruption patterns. Excess exposure to heavy metals or mining wastes has been seen as a prevailing cause of occlusal diseases in the inhabitants of mining areas [16]. Heavy metals can disrupt the absorption of minerals like calcium, essential for jaw & tooth development, contributing to malocclusion. Chemicals like Bisphenol A and phthalates mimic hormones and can impact osteogenesis and odontogenesis, leading to smaller jaws and misaligned teeth [17]. Genetic predisposition could also significantly contribute to malocclusion [18], in which traits like jaw size, shape, and tooth size are often inherited through the genetics of dentofacial variation in malocclusion [19]. Hence, malocclusion parents are likely to face similar issues, owing to inherited jaw and tooth size discrepancies. This may occur with certain types of malocclusions, such as class III running in families. Nasal obstruction can lead to mouth opening, altering the normal balance of forces exerted by lips, tongue, and cheeks on dental arches [20]. Malocclusion linked with nasal obstruction can result from deviated nasal septum, adenoid hypertrophy, allergic rhinitis, chronic sinusitis, nasal polyps, and congenital nasal deformities [21]. Reportedly, children with enlarged tonsils and adenoids have higher malocclusion prevalence [22].

Childhood habits like thumb sucking may also be a dental occlusal etiology leading to open bite or overjet by exerting constant pressure on teeth, pushing upper front teeth forward, and potentially retruding lower teeth [23]. Overall, during this pathological process, the physical displacement of teeth is due to prolonged pressure. Evidence indicates linking mouth breathing to malocclusion, particularly class II, open bites, and crowding through altered craniofacial development. Longer duration and early onset may enhance severity [24]. Radiographically, mouth breathers have longer faces and narrower maxillae & retrognathic mandibles compared to nasal breathers [25]. Dental caries and periodontal disorder may engender premature tooth loss and tooth mobility, leading to exacerbated malocclusion [26]. Children breastfed during infancy exhibit less malocclusion in the future compared to children fed with milk powder, as sucking on the nutritional breast milk helps in the healthy development of primary dentition [27]. Other physiological factors, including deficiency of metabolic factors and hormones like calcium and vitamin D, loss of deciduous and permanent teeth at an early age, and facial muscle dysfunction while growing up, are prominent etiologies for developing malocclusion [28]. A brief description of possible etiological factors inducing malocclusion is represented in Figure 1.

Is malocclusion associated with other organs' physiology?

The association between malocclusion and different organ systems is intricate. Most of the patients develop malocclusion and later advance to periodontitis, which is more prominent in mature adults with inflamed gingiva and poor oral health [29]. Some other major issues with dental deformities are swallowing and speaking. Due to jaw displacement, tongue positioning is also deformed in childhood, hindering proper speaking ability. The patient mainly faces issues with regular feeding, as adequate chewing and swallowing channels are displaced from their regular positions. The occlusal deformities bring down confidence and hamper the patient's mental health through these daily life difficulties [30]. Acute malocclusions result in heavy psychological stress among children, while young adults with mild or severe malocclusion have been diagnosed with depression, anxiety, interpersonal sensitivity, compulsive behaviour, and other stress-related diseases. However, these psychological conditions heal away after orthodontic treatment of their malocclusion [31].

Figure 1. Etiopathological factors of malocclusion. PD: Periodontitis. Created in BioRender. Dubey, N. (2025) https://BioRender.com/e99z061.

The facial features deformation related to malocclusion displaces the tongue muscles associated with the trigeminal and oculomotor systems. The vision of patients is henceforth affected by severe Class III malocclusion. Ocular motility and midline deviation are observed in all classes of malocclusion, with occasional cases of convergence defects [32]. Malocclusion may be associated with other complications like erosion of cartilage and bones in different temporomandibular joints (TMJ), resulting in osteoarthritis [33]. Notably, orthodontic treatment doesn't reduce the damage to these joints. A lower heart rate is also observed in patients suffering from malocclusion. Continued malocclusion-related psychological stress leads to the reduction of heart rate, portending the risk of multiple cardiovascular disorders [34]. These impairments are irreversible even after occlusion treatment.

Based on available evidence, we present our viewpoint on possible pathological crosstalk between malocclusion and different organ systems (Fig. 2) to better understand and prevent these comorbidities, which may cause permanent damage to the body.

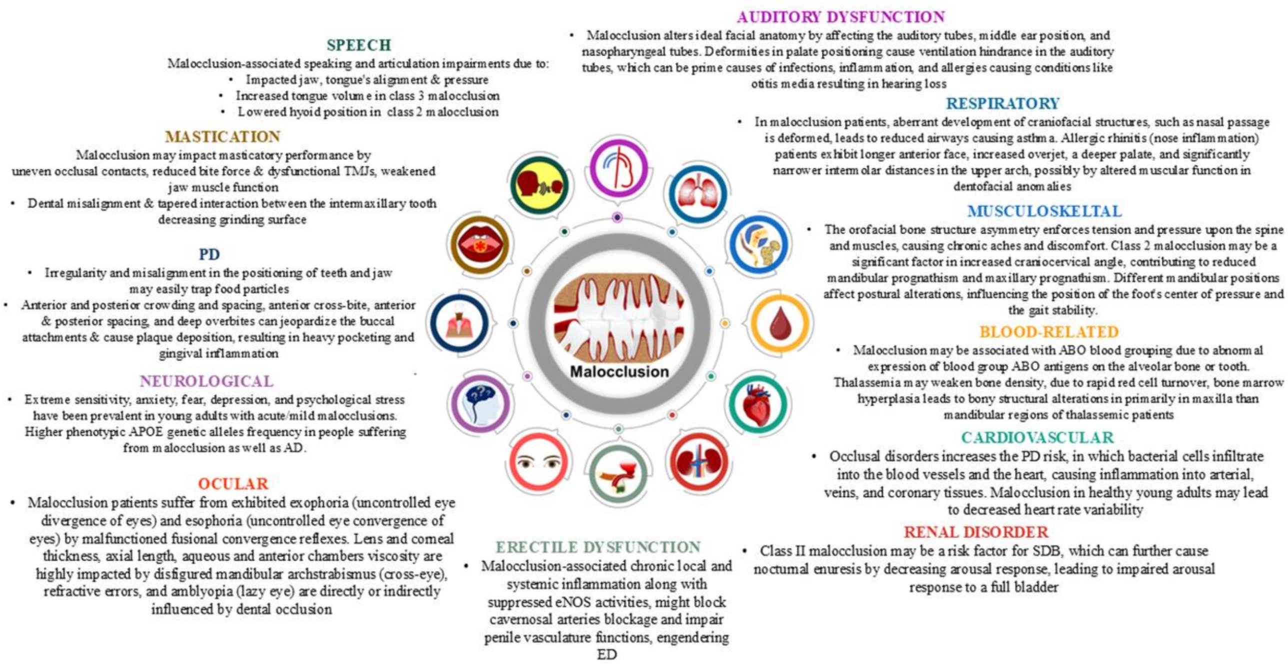

Figure 2. Possible pathologic association between malocclusion and multiple organs. AD: Alzheimer's disease, TMJ: Temporomandibular joint, eNOS: endothelial nitric oxide synthase, BMD: Bone mineral density, SDB: Sleep-disordered breathing, PD: Periodontitis, ED: Erectile dysfunction.

4. Oral

Malocclusions are highly relevant to an individual's physiological and psychological well-being. Orthodontic treatments [35] and malocclusions highly influence the quality of life (QoL) directly and indirectly. This coined the terminology "Oral Health-Related Quality of Life" abbreviated as OHRQoL [36], which is reduced among Malocclusion-affected children and young individuals. Malocclusion leads to an impairment of mastication, speech, swallowing, oral hygiene, and even breathing; however, it prominently induces facial disfigurements, which compels patients to opt for cosmetic surgeries or treatments [36]. The influence of malocclusion on facial aesthetics adversely affects the patient's mental health and psychology to a great extent.

4.1 Speech

The etiology of speech disorders can be genetic, environmental, or physiological. However, in many cases, orofacial myofunctional disorders are the primary reason for speaking and articulation impairments. Malocclusions impact the jaw alignment and hence the tongue's position inside the oral cavity [37], which has been evidenced through the radiographic studies in different populations. Other evaluation methods include speech-language, myofunctional, demographic, and statistical assessments [38]. Children with anterior open-bite and posterior cross-bite are susceptible to developing alterations in the tongue position, which can result in speaking disorders. Males are less prone to developing speech disorders due to malocclusions [30]. The maxillofacial region is highly altered due to Class III malocclusions. An increase in tongue volume is observed mainly in Class III patients, whereas Class II patients exhibit a lowering of the hyoid's position, causing an imbalance in the anatomy [39]. Jaw deformities affect tongue position and the pressure which is reduced in malocclusion patients. However, this could be restored after the orthodontic treatments and surgeries for malocclusion [40].

4.2 Mastication

Even with normal dentition, many people experience difficulty while eating hard and chewy food items. These individuals have poor oral health due to irresponsible oral hygiene practices. Mastication is mostly affected in malocclusion [41], which implies that the dental occlusal pattern plays a vital role in chewing activity. Hence, any dysfunction or misalignment hampers the regular mastication process, reducing OHRQoL. Malocclusion patients exhibit uneven occlusal contacts, reduced bite force, and dysfunctional TMJs. These symptoms influence the masticatory performance drastically [42]. Weakened muscle function in the jaws due to the dental misalignment and tapered interaction between the intermaxillary tooth decreased the grinding surface area. Consequently, malocclusion hampers efficient chewing patterns and leads to degraded masticatory functioning and uneven swallowing threshold. Even after post-orthodontic treatment of malocclusion, abnormal chewing activity had been evident [43].

4.3 Periodontitis (PD)

The etiology of PD involves plaque deposition in the teeth's roots, which harbors pathogenic microbiota, leading to gum inflammation and loss of alveolar bone in the tooth. Any irregularity and misalignment in teeth and jaw positioning promotes bacterial plaque deposition [29], which is an essential factor in PD development. Malocclusion portends the PD risk, as misaligned teeth may easily trap food particles. Food deposition and plaque formation help develop inflammation in the gums due to tissue softening and pocket formation [44]. As per reports, angle Class I occlusion exhibits the highest risk of developing PD, whereas Class II affects the least [45]. Anterior and posterior crowding and spacing, anterior cross-bite, and deep overbites can jeopardize the buccal attachments and cause plaque deposition, resulting in heavy pocketing and gingival inflammation. Since even orthodontic treatments do not guarantee periodontal well-being, the post-orthodontic treatment is essential in cases of severe crowding and plaque accumulation [46].

5. Ocular

The mandibular lateral deviation establishes a possible connecting link between malocclusion and ocular vision. As this axis houses the trigeminal nerve system, controlling both facial and ocular muscle movements and functionalities, it represents an anatomical, physical, neurological, and functional correlation between dental and ocular structures [47]. Any abnormality in the occlusal region engenders motor control dysfunction. Visual coordination, balance, and marginal vision are remotely associated with the motor neurons of the trigeminal system; therefore, the deformities caused by malocclusion distort the smooth functioning of the sensory nervous system and disorganize the symmetric positioning of the eyes, causing asymmetric convergence in vision. Surveys have reported that an open bite enhances the left dominant eye, while a deep bite develops the right dominant eye [48]. In the eyes, convergence disorders (phorias) are observed more in Class II and III malocclusion patients. Among other malocclusion types, Class III patients mainly acquire ocular motility diseases. As malocclusion affects the facial structure, posture, and muscular alignments, the ocular muscles are deranged, causing defects in normal vision and ocular motility [32]. In a report by Caruso et al., 2018 [49], 68% and 17% of the patients exhibited exophoria (uncontrolled eye divergence) and esophoria (uncontrolled eye convergence), respectively, both of which are developed by malfunctioning of the fusional convergence reflexes. Exophoric deviations are more associated with Angel's Class II malocclusion in children. Untreated or undiagnosed deviations in children with ocular errors can result in multiple vision anomalies during adulthood.

The convergence errors also heighten the chances of developing congenital ptosis due to refractive inaccuracies in the eyesight. The lens and corneal thickness, axial length, and viscosity of the aqueous and anterior chambers are highly impacted by disfiguring the mandibular arch, resulting in a ptotic eye in the younger population [50]. Malocclusion directly or indirectly also influences other disorders such as strabismus (cross-eye), refractive errors, and amblyopia (lazy eye). Malocclusion-associated deformities in the craniofacial muscles may adversely impact the development of ocular muscles, resulting in ocular dysfunction [51]. Bruxism (teeth clenching and gnashing), influenced by the disparity in bone anatomy due to malocclusion-induced continuous strain, results in inflammation of craniofacial muscles [52]. This leads to frequent headaches, eye strain and irritation, reduced visual acuity, ptosis, and an inflamed iris. Bruxism is highly detrimental as it enhances muscle sensitivity, rendering it prone to triggered inflammation and hindering other organs' functionality [53]. Apart from these factors, an individual's environment, genetics, and lifestyle also play an important role in maintaining both oral and ocular health. Prolonged stress, faulty diet, and electronic exposure are potential risk factors for compromised visual and dental well-being [54]. Taken together, malocclusion significantly affects the vision of patients of all ages, especially young adults. Therefore, conserving eyesight from malocclusion-induced ocular disorders through continuous diagnosis is essential while receiving orthodontic treatments to prevent incurable vision loss.

6. Auditory

Malocclusion wholly or partially alters the ideal facial anatomy, affecting the auditory tubes, middle ear position, and nasopharyngeal tubes. These deformities may cause multiple infections and disorders related to smooth auditory functioning [55]. The auditory tube (eustachian tube) is essential for the ventilation and drainage of the auditory passage and its safeguarding. The soft palate and associated muscles regulate the opening and closure of the auditory tube. Deformities in the palate positioning cause hindrances in the auditory tube ventilation, which can be prime causes of infections, inflammation, and allergies in the ear [56], leading to severe conditions such as otitis media and hearing loss. This is caused by air pressure disturbance inside the eustachian tube, causing tubal dysfunction and microbial infection inside the middle and inner ear. It has also been observed that children suffering from overbite and cross-bite conditions develop otitis media shortly. The maxillary misalignment may cause constriction in the nasal passage, which is why oral habits like mouth breathing develop. This worsens the malocclusion and might result in enlarged tonsils and adenoids, which open the way for bacterial and viral infections in the nasal chambers. As the eustachian tube is connected to the nasal passage, it also gets infected by microbial invasion into the cochlear region [57]. However, after the treatment of the occlusal position, slow improvements are observed in the cochlear placements, leading to a cure in auditory discrepancies [58].

7. Neurological abnormalities

7.1 Neurological-psychological

Malocclusion can cause a lot of psychological stress in young adults and teenagers. Along with deformities in facial aesthetics, reduced development of the trigeminal nerves results in mental disorders, including anxiety, attention deficit hyperactivity disorder (ADHD), and depression [59]. Patients experience behavioural differences from their surrounding people, such as being often bullied or discriminated against, which can exert immense stress on their psychological well-being. These may contribute to physical symptoms like body fatigue, restlessness, headache, and irritation, which grow over time and might lead to insecurities, a lack of consciousness regarding facial beauty, and low self-confidence in children and young adults [60]. The frequency of individuals who have ADHD with a medical condition of orofacial deformities, like malocclusion, is relatively high. Adolescents diagnosed with various classes of malocclusion are observed to develop psycho-neurological disorders later in adulthood [61]. The malocclusion-associated misalignment in the TMJs results in musculoskeletal disorders in the mandibular and maxillary movements. Bite pressure, bite force, and smooth jaw movement are compromised in malocclusion, causing headaches, muscle pain, jaw pain, mastication issues, and dental decay [62]. Bruxism, musculoskeletal damage, and TMJ disorders induced by malocclusion also adversely impact the myofascial tissues, stimulating pain not only in the occlusal region but also might lead to severe headaches and migraine in patients [63]. Taken together, cerebral illnesses, both physical and psychological, such as ADHD, anxiety, and migraine, are closely associated with malocclusion and oral well-being.

7.2 Neurological-Cognitive

Trigeminal input alters the cognitive brain's functions in acute as well as chronic conditions and plays a vital role in developing neurological disorders [64]. Malocclusion and facial deformity also contribute to the repression of the trigeminal nerve system, affecting multiple neural functions and actions, including mastication, speech, and other motor tasks. A proper masticatory function helps to preserve brain functions, reducing the risk of developing Alzheimer’s disease (AD) and other forms of dementia. Pupil size and occlusal abnormalities are developed due to a compromise in the trigeminal nerves. The unbalanced and unilateral gene expression in the trigeminal system worsens malocclusion conditions [65]. Other ailments, including growth impairments, mandibular retrognathia, hypodontia, psychological disorders, behavioral syndromes, lip and tongue disarrangement, have been observed in patients of critical malocclusion [66]. Though the pathology behind these correlations with acute malocclusion is unclear, the genetic and neuro-developmental mishaps may be attributed. In a study reported by Ekuni et al. on Japanese teenagers, an upsurge in neurological health conditions such as extreme sensitivity, anxiety, fear, depression, and psychological stress was observed in young adults with acute or mild malocclusions [31]. Therefore, patients with severe malocclusion and speech abnormalities should receive particular focus during orthodontic treatment to ascertain the symptoms of possible neurodevelopmental disease at the earliest.

7.2.1 Alzheimer's disease (AD)

Emerging evidence suggests a potential association between malocclusion and the onset of AD through the expression of allele-inducing AD. Malocclusion and other occlusal disorders have been observed to be associated with ε3 and ε4 allelic phenotypes of APOE genes. These genes have a higher phenotypic frequency in people suffering from AD than the other alleles of the APOE genes [67]. Dental disorders such as PD and tooth loss are also precursors of AD in the older population. Malocclusion-associated buccal masticatory deficiency affects oral digestion, leading to the loss of nutrients in the later stages. Continuous loss of important biomolecules and inadequate breakdown of food lead to nutrient deficiency in the cognitive regions of the body. Heavy nutrient loss results in frail physical conditions and neurodegenerative issues in elderly patients above the age of 60, resulting in AD [68]. Cognitive dysfunction further worsens in older people due to poor oral health and practices. In malocclusion patients with reduced OHRQoL, the brain injury and degeneration may be induced, which could further cause confusion and cerebral hemorrhage, ensuing in a condition of delirium [69].

7.2.2 Dementia

Oral health in older people is a great concern, as the continuous oral degenerative aging process could contribute to disorders of multiple organ systems. In correlation to oral health, cognitive disorders such as dementia and delirium are primarily observed in the elderly, which implies the need for special care for oral hygiene. In a home visit survey of people with cognitive decline, the number of teeth, clinical dementia rating, and age were independently associated with periodontal inflamed surface area (PISA) after adjusting for diabetes, biological sex, visual disorder, depression, osteoporosis medication, and collagen disease. It has been hypothesized that PD portends the risk of dementia, possibly through brain infiltration of *P. gingivalis* and lipopolysaccharides through enhanced permeability of the blood-brain barrier. PISA in young adults has been reported to induce mild cognitive impairment onset [70, 71]. Mild or severe cases of malocclusion also tend to develop PD by enhancing food particle accumulation in the unreachable corners of occlusal regions, causing plaque formation, which enhances the risk of dementia and other neurological diseases. Patients with cognitive impairment also suffer from the visuospatial decline of reasoning, which reduces their ability to receive ideal dental care, worsening the ailment. Collectively, malocclusion-associated facial deformation may contribute to dementia through improper nutrition, psychological stress, and deficient neurotransmission [72].

7.2.3 Neurological-Sleep

Sleep is an essential component of well-being in addition to development, learning, and growth [73]. Though the sleep quantity differs by age, the recommended optimal sleep for children (5-16 years) is 10 h/night; therefore, compromised sleep may severely affect health by inducing irritability, snoring, nocturia, learning difficulties, behavioral disorders, and daytime sleepiness. In addition, the risk of comorbidities like metabolic syndromes (diabetes and cardiovascular disorders) also remains elevated [74]. Sleep-disordered breathing (SDB) may be caused primarily by dentocranial changes in the form of severe malocclusion [75]. Studies have shown that compared to neutral occlusion, daytime sleepiness and feelings of extreme tiredness occurred significantly more often in children with severe malocclusion (maxillary inclination)[76].

8. Respiratory

In younger malocclusion patients, the development of craniofacial structures, such as the nasal passage, is deformed, which leads to reduced airways, causing the incidence of respiratory disorders, especially asthma. Mouth breathing, the most common asthma symptom, is worsened by malocclusion, which shelters micro-organisms in the saliva for a prolonged period. Asthmatic patients are observed to suffer from other oral disorders, such as caries, dental erosion, and candidiasis, caused by pathogenic microbiota deposited in the buccopharyngeal region [77]. Class II malocclusion could contribute to anteroposterior disproportion in dentition, and these vertical orofacial deformities alter the progressive formation of the upper nasal passage by narrowing it. Difficulty breathing through a narrow nasopharyngeal tube results in inflammation and may cause the habit of mouth breathing in patients, further displacing the TMJ and mandibular condyle, deforming the malocclusion even more [78]. In a Taiwanese study by Lin et al., patients suffering from acute and chronic sinusitis and allergic rhinitis were observed to develop class I and II malocclusions [79]. Allergic rhinitis (inflammation of the nose) patients had been found to exhibit longer anterior faces, increased overjet, a deeper palate, and significantly narrower intermolar distances in the upper arch [80], possibly by altered muscular function in dentofacial anomalies caused by rhinitis. Therefore, detailed research on this correlation and the awareness of regular check-ups of both disorders is vital to providing efficient treatment to patients [81].

9. Musculoskeletal

9.1 Musculoskeletal-Spine

Malocclusion conditions, such as cross-bite and abnormal mandible, are associated with postural anomalies affecting QoL. The misaligned dental aperture results in severe headaches, migraine, and other oral difficulties. Malocclusion can also cause an imbalance in facial bone symmetry, putting unequal pressure on the collar bones and vertebral column. TMJ disorders trigger conditions such as scoliosis, false scoliosis, herniated discs, paramorphism, lordosis, muscle spasm, and kyphosis due to disturbances in the equilibrium of the spine and columnal anatomy [82]. The orofacial bone structure asymmetry enforces tension and pressure upon the spine and muscles, causing chronic aches and discomfort. At later ages, the alignment of the vertebral column is also affected by poor posture, leading to severe medical conditions like disc dislocation, disc degeneration, muscle spasms, and herniated discs [83]. Therefore, an early diagnosis followed by treatment is needed for malocclusion patients.

Displacement in the dental structure and position also significantly impacts the bone morphology and integrity of the whole body. In malocclusion patients, low bone density is the most commonly observed [84], primarily caused by osteoporosis and aging. Mandibular osteoporosis results in tooth loss in older patients suffering from malocclusion and periodontal disorders [85]. Specifically, the low bone density in the dental stature may promote chronic temporomandibular diseases in malocclusion patients [86]. This is in line with a report in which Class II malocclusion was observed in abundance along with Class I and Class III, with temporomandibular diseases, predominantly in females [87]. Oral hygiene also affects the functionality of bones around arms, limbs, and joints. Poor oral health, malocclusion, and reduced activity enhance microbial growth in the periodontal realm, leading to nutrient loss in the body, which results in a deficiency of essential minerals such as calcium and phosphorus in the bony structure, causing osteoarthritis [88]. Therefore, older patients receiving orthodontic treatment should also be subjected to skeletal radiographic screenings to prevent probable muscle and bone deformities [89].

9.2 Musculoskeletal-postural

Studies have revealed an association between deviations in cervical vertebral morphology and malocclusion, emphasizing a pivotal link between craniofacial dimensions and head posture. The cervical and overall body posture has been correlated with class II malocclusion, which is significantly associated with elevated cervical curvature and forward head inclination [90]. Class II malocclusion also seems to be a significant factor in increased craniocervical angle, contributing to reduced mandibular prognathism and maxillary prognathism [91]. This concluded that increased head extension in relation to the cervical spine might contribute to class II malocclusion.

Interestingly, a recent study observed the relationship between foot posture and dental malocclusions [92]. For the right foot, the Clarke angle and foot postural index (FPI) score were found to be significantly correlated to dental malocclusions as determined by Angle classification. The Clarke angle tends to decrease as the Angle classification increases from Class I to III, whereas the FPI increases with the increase in Angle classification from Class I to III. Evidence also supports that different mandibular positions affect postural alterations, influencing the position of the foot's center of pressure and gait stability [93]. Using a stabilometric platform, it was confirmed that orthodontic plate positioning rebalanced the postural system in patients with cranio-cervical-mandibular disorders [94]. After the treatment, 64% of the patients experienced remission of the pain symptoms. They concluded that this relationship must be studied from a multidisciplinary point of view for an overall therapeutic result.

9.3 Osteoarthritis (OA)

OA is typically characterized by deteriorative changes in the osteochondral unit, consisting of cartilage, meniscus, and subchondral bone [95]. Among musculoskeletal disorders, the OA of the temporomandibular joint could cause discomfort, altered jaw movement, and pain in masticatory muscles and all associated neuromuscular structures, leading to clicking noises and restricted mouth opening [88]. Class II malocclusion and hyper-divergent growth patterns have been associated with increased frequency of TMJ disc displacement (short ramus, posterior facial height, backward position, and rotated mandible) and degenerative disorders [96]. This implies that malocclusion may disrupt TMJ load-bearing capacity, possibly contributing to TMD development. Accumulated plaque and calculus in the occlusal regions also greatly increase dental disease risk [88, 97].

9.4 Osteoporosis

Osteoporosis is a condition affecting the skeletal system, marked by weakened bone strength, making individuals more susceptible to fractures [88, 98]. Studies have shown that in adolescents, malocclusion may influence total bone mineral density (BMD) and head density in males [85]. The abnormal craniofacial bone growth due to vitamin deficiency may also contribute to skeletal and dental abnormalities, resulting in malocclusion. Specifically, vitamin D3 deficiency may influence maxillary development by causing an increased risk of a narrowed upper arch, crowding, and cross-bite [99]. A frequent dehiscence has been observed in Class II and III malocclusions, which could be attributed to elevated loss of vertical alveolar bone and coronal alveolar bone thickness [100]. These studies indicate a modest correlation between BMD and malocclusion. Hence, bone augmentation may be recommended to enhance the alveolar dimension and prevent malocclusion episodes.

10. Cardiovascular-metabolic disorders

Malocclusion has been proven to be associated with many systemic disorders. This dental deformity may significantly impact the circulatory and cardiovascular systems [101], probably by involving oral microorganisms, inflammatory molecules, and stress-induced hormones [102]. The bacterial accumulation in the oral cavities due to occlusal disorders enhances PD risk and consequently leads to inflammation of the gums. PD has been observed as a risk factor for cardiovascular disorders (CVDs) such as high cholesterol, atherosclerosis, and high blood pressure, which makes the patients susceptible to stroke or heart attack [103]. This could be attributable to bacterial cell infiltration into the blood vessels and the heart, causing inflammation in the arteries, veins, and coronary tissue [104]. In this line, a Spanish study on 4224 employed adults, PD with the presence of deep periodontal pockets (≥6 mm) was significantly associated with high CVD risk [systemic coronary risk estimation (SCORE ≥ 5%)][105]. As an immune response against invading oral bacteria, an inflammatory reaction around the local infection is observed along with the secretion of chemokines and cytokines into the bloodstream [106]. However, the production of anti-inflammatory signaling biomolecules is compromised in malocclusion patients due to the pathogenesis of oral bacteria, leading to unchecked chronic inflammation in the oral cavity and systemic organs [107]. Further, myeloperoxidase (MPO), a neutrophil-derived biomarker, may activate proteolytic destructive cascades, leading to subsequent immune-pathological events in malocclusion-induced chronic PD as well as coronary heart disease (CHD) [108]. The stimulated neutrophils represent the principal pathogen-fighting immune cells that stimulate the expression of many proteinases and oxidative enzymes, degrading extracellular matrix components. As per the PAROKRANK study, the salivary matrix metalloproteinase-8 and -9 and MPO have been significantly positive with PD and its relation to CHD [109].

Apart from this, in an eye-tracking survey, various kinds of malocclusion (mid-line diastema, polydiastema, crowding, gummy smile, low smile line) may induce psychosocial stress due to facial unattractiveness [110]. Further, 10 years of study advocated that individuals with physical attractiveness seem to have better biological health with high levels of self-confidence, life satisfaction, and ease of intimate partner finding [111]. However, evidence exists on facial fluctuating asymmetry-based differential endocrine responses in which increased cortisol levels could be correlated to perceived stress and competitiveness [112]. This indicates that due to poorer aesthetic self-perception, malocclusion patients may suffer from societal pressure with reduced oral health-related quality of life (OHRQoL), possibly by the secretion of cortisol (stress hormone), which increases cardiovascular risk [113]. Compared to healthy individuals, higher salivary cortisol levels have also been suggested in patients with temporomandibular disorders, which may be caused by malocclusion [114]. In a seminal study on over 9000 university adolescents, malocclusion was found to be significantly associated with increased rates of arrhythmia [81]. Though a clear relationship between malocclusion and heart diseases is not identified, as chronic stress, malocclusion in healthy young adults may lead to decreased heart rate variability (HRV), a measure of autonomic activity [115]. Hence, malocclusion may likely induce arrhythmia by enhancing sympathetic nerve activity. This aligns with a study revealing alterations in the vertical occlusal dimension affecting heart rate fluctuations in guinea pigs [116]. These data imply that cardiac health is closely impacted by malocclusion, so cohesive monitoring and treating oral and cardiovascular well-being is essential for patients' complete recovery. It is expected that the orthodontic treatment modalities cannot only fix oral aesthetic and functional issues but also improve stress and HRV indices.

11. Blood-related disorders

Interestingly, a Mysuru-based study on 278 people showed a significant correlation between malocclusion and ABO blood grouping [117], in which the blood group 'O' blood group was the commonest and associated with

Angle's Class I malocclusion (71.3%). In blood group 'A', Class II div 1 and 2 malocclusions were common, with a prevalence of 42.68% and 4.9%, respectively. Class III was the most common in the 'B' blood group (6.5%). Therefore, it could be hypothesized that blood group-based development of malocclusion may be associated with abnormal expression of blood group ABO antigens on the alveolar bone or tooth. Another prospective study in Jaipur (an Indian state) revealed the malocclusions prevalence order of blood groups as being highest in B, followed by A, O, and AB [118]. In a cross-sectional study on Saudi adults, blood group A demonstrated a significantly higher prevalence of Class II (34.2%) and 3 (19%) malocclusions [119]. Regarding impacted teeth, blood group AB (48.8%) had the highest occurrence. These differences could be attributed to racial variation and geographical diversity of the population.

Blood-related disorders such as thalassemia may weaken bone density, causing deprivation in the growth and development of the individual [120] due to rapid red cell turnover and bone marrow hyperplasia, leading to bony structural alterations primarily in the maxilla than the mandibular regions of thalassemic patients. Thalassemia has been classified into major, intermediate, and minor, depending on the severity of the symptoms and the etiology of the disease. Thalassemia has been mostly associated with dental disorders, including malocclusion and misalignment of the jawbone and teeth. Bone density loss in the whole body as well as in mandibular and maxillary regions is a significant and chronic symptom in thalassemic patients, which is caused by iron depositions, bone marrow expansion, and reductive growth hormone-insulin-like growth factor-1 axis [121]. The consequences of thalassemia major include deformation in orofacial structures caused by poor OHRQoL, maxillary protrusion, and gingivitis, often leading to Class II malocclusion in patients [121, 122]. In a study by Jeelani et al., about 59% of thalassaemic children were confirmed to suffer from Angel's Class II malocclusion with high severity [123].

Besides, when compared to healthy individuals, a high rate of very severe malocclusion has been observed in patients with sickle cell disease (SCD), an inherited blood disorder characterized by the production of abnormal hemoglobin, leading to the distortion or sickling of red blood cells [124, 125]. The most common malocclusion types were class II molar relationship (due to mandibular retrusion), increased overjet, and anterior open bite. This can be explained by increased bone marrow activity, possibly leading to changes in the trabecular bone associated with bone expansion and with increased overjet between the arches due to maxillary protrusion. Hence, SCD patients should be followed up by dentists to avert a severe impact on the dentition and thus contribute to improving QoL. Overall, these data indicate the association between malocclusion and blood-related disorders.

12. Renal

The Class II malocclusion, a skeletal anteroposterior discrepancy between the maxilla and mandible accompanied by a vertical discrepancy, is a risk factor for sleep-disordered breathing (SDB)[126]. Increasing literature indicates SDB as one of the underlying causative factors of nocturnal enuresis (NE)[127], by decreasing arousal response, leading to impaired arousal response to a full bladder [128]. Globally, about 10% of children suffer from NE or bedwetting influence, which is the second most common health issue in school-aged children after asthma and allergies. SDB leads to excess urine production at night by activating sodium-regulating hormones and altering urodynamics. These reports indicate the indirect association of malocclusion and renal dysfunctions. In a cross-sectional study, the most prevalent malocclusion Class II was identified, where spacing and extrusion were prevalent types of pathologic tooth transfer, mainly impacted by interdental clinical attachment loss and tooth loss due to periodontitis [129]. It has also been reported that the tooth loss due to chronic periodontitis might act as a potential indicator of increased risk for lower urinary tract syndrome (LUTS), specifically in relation to the onset and severity of storage and voiding symptoms present in an overactive bladder. These reports imply that malocclusion-associated PD may enhance the risk of LUTS [130].

13. Erectile dysfunction (ED)

ED is characterized by failure to attain or sustain a penile erection, which severely affects sexual health and activity and adversely influences psychological status, personal relationships, and, hence, the QoL in males [131]. Though the ED etiology is multifactorial (vascular, hormonal, drug-induced, psychological, or combined), vascular is the most common. Among oral disorders, periodontal disease (PD) is a major risk factor for systemic diseases induced by periodontal pathogens and periodontal infection-induced systemic inflammation leading to endothelial dysfunction [132]. In malocclusion, any irregularity and misalignment in teeth and jaw positioning promotes bacterial plaque deposition, portending PD risk [29]. In a recent study on 400 community-dwelling men, poor occlusal support status was independently and significantly associated with ED [133]. In another study including 305 males, 22.9% men had ED, and 4.3% had chronic PD [134]. Chronic PD was significantly more prevalent among men with mild ED and moderate to severe ED when compared to those without ED.

Investigators have recently explored the possible association between chronic PD and ED, which may be mediated by endothelial dysfunction and atherosclerotic plaques [134]. A systematic review and meta-analysis also revealed a significant association between PD and ED with an odds ratio of 2.56, possibly by increasing the expression of proinflammatory cytokines and adhesion molecules, and decreasing systemic inflammatory status and endothelial nitric oxide synthase activity, and nitric oxide synthase in penile cavernous tissues [135]. Therefore, it is plausible that during malocclusion-induced PD, periodontal pathogens, such as Porphyromonas gingivitis, might invade the systemic circulation, followed by arterial wall homing, thereby inducing an inflammatory response. In a randomized controlled trial, periodontal treatment significantly improved periodontal health, International Index of Erectile Function (IIEF) score [136], improved endothelial cell function, and inhibited pro-inflammatory cytokine tumor necrosis factor-α (TNF-α) levels.

In progressive PD patients, TNF-α is associated with various systemic disorders. Besides cytokines, other pro-inflammatory markers, like nitric oxide (NO), increase both in ED and PD [12]. Surprisingly, a nationwide database study in Taiwan revealed that flap surgery or gingivectomy in chronic PD patients exhibited a lower ED prevalence than those without any treatment [137]. Local and systemic inflammation induced by malocclusion-associated chronic PD may increase inflammatory mediators like TNF-α, IL-6, and IL-8, causing atherosclerosis and endothelial dysfunction. During endothelial dysfunction, reactive oxygen species (ROS) are generated, leading to compromised vascular anti-inflammatory responses and disrupted endothelial nitric oxide synthase (eNOS) activities. Thus, atherosclerosis, along with suppressed eNOS activities, might facilitate cavernosal artery blockage and impair the functions of the penile vasculature, engendering ED. This may also be ascribed to testosterone levels [138]. Therefore, men with ED should be encouraged to receive routine dental examinations and appropriate preventive dental measures to maintain oral and periodontal health.

Besides, dental disorders such as anterior tooth trauma or malocclusion negatively affect social acceptance and personal behavior, resulting in lower self-esteem and depression [139]. It may cause ED and, hence, an unsatisfactory sexual life [140]. The negative self-perception effect on sexual behaviour is evident, and sexual dysfunction is further aggravated by the antidepressants (selective serotonin reuptake inhibitors-SSRIs) for treating depression and anxiety [141]. Studies have already reported increased prevalence and ED severity due to anxiety and depression [142, 143]. This implies that the malocclusion-associated psychological disorder may induce ED.

14. Future prospects and challenges

Emerging research into the novel systemic sequelae of malocclusion, including oral and non-oral diseases, needs to be unravelled to determine their prevention and treatment strategies. Specifically, extensive studies should be conducted on malocclusion-associated oral complications like jaw deformities, which can adversely affect tongue alignment and suppress pressure, leading to abnormal speech. Another oral complication, i.e., PD induction, should be investigated for plaque deposition due to crowding, spacing, anterior cross-bite, and deep overbites, resulting in heavy pocketing and gingival inflammation. Mandibular lateral deviation, a possible mediator between malocclusion and ocular vision, should be investigated, as this axis houses the trigeminal nerve system, regulating facial and ocular muscle movements as well as functionalities. Further, the maxillary-auditory axis could be examined, as maxillary misalignment may induce auditory dysfunctions such as otitis media and hearing loss, occurring predominantly due to air pressure disturbance inside the eustachian tube. This may cause constricted nasal passage, leading to tubal dysfunction and microbial infection inside the middle and inner ear. Under the neurological complications, malocclusion-associated PD could enhance the risk of dementia or AD, possibly through brain infiltration of *P. gingivalis* and lipopolysaccharides. Hence, the blood-brain barrier should be examined for enhanced permeability. Respiratory complications, including chronic sinusitis and allergic rhinitis, may develop through vertical orofacial deformities, altering the progressive formation of the narrowed upper nasal passage. Therefore, research should be conducted on cross-sectional associations toward longitudinal, mechanistic, and interventional designs that elucidate causality and guide integrated orthodontic-ENT (ear, nose, throat) management. Poor oral health, malocclusion, and reduced activity could increase microbial growth in the periodontal regions, leading to nutrient loss in the body, which results in a deficiency of essential minerals such as calcium and phosphorus in the bony structures. This implies the plausibility of debilitating conditions like OA and spinal disc degeneration.

Since the deep periodontal pocket in the PD is associated with high CVD risk, periodontal dysbiosis, bacteremia, and microbial strains should be characterized, which are the driving factors for endothelial dysfunction, plaque formation, and plaque instability through various pathways. Similarly, endothelial dysfunction can be examined as a mediator for ED. Tooth loss due to chronic

PD might act as a potential indicator of increased risk for LUTS, specifically in relation to the onset and severity of storage and voiding symptoms present in an overactive bladder. So, how chronic periodontal infection and transient bacteremia allow key pathogens to colonize in the urinary tract should be investigated using 16S sequencing of urine and gingival samples. These reports imply that malocclusion-associated PD may enhance the risk of LUTS. Taken together, the large, prospective, and multi-disciplinary cohorts combining high-quality orthodontic phenotyping with robust systemic outcomes remain the highest research priority in bridging the gap from dental to systemic health. This will require interdisciplinary, mechanistically focused research based on both clinical observation and experimental studies.

15. Conclusion

Malocclusion may negatively impact the QoL by inducing multi-organ pathologies. The malocclusion not only lowers self-esteem and psychological issues but also may trigger various disorders associated with oral, ocular, auditory, nasal, cerebral, respiratory, cardiovascular, renal, metabolic, and sexual physiologies. Hence, understanding the intricate association between these disorders will offer a new direction for comprehensive intervention strategies to improve the QoL, resulting in a decrease in significant mortality and morbidity.

Authorship Contribution Statement

TPC: Conceptualization, Data curation, Formal analysis, Writing – original draft, Visualization, Writing – review & editing. CHC: Data curation, Formal analysis, Writing – original draft, Visualization. PS: Data curation, Formal analysis, Writing – review & editing. NKD: Conceptualization, Data curation, Formal analysis, Visualization, Writing – original draft, Writing – review & editing, Supervision. MCL: Formal Analysis, Visualization, Writing-review & editing, Supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] Balachandran P, Janakiram C (2021). Prevalence of malocclusion among 8-15 years old children, India - A systematic review and meta-analysis. J Oral Biol Craniofac Res, 11:192-199.

[2] Angle EH (1899). Classification of malocclusion. Dent Cosmos, 41:350-357.

[3] Abe M, Mitani A, Yao A, Hoshi K, Yanagimoto S (2022). Systemic Disorders Closely Associated with Malocclusion in Late Adolescence: A Review and Perspective. Int J Environ Res Public Health, 19:3401.

[4] Lombardo G, Vena F, Negri P, Pagano S, Barilotti C, Paglia L, et al. (2020). Worldwide prevalence of malocclusion in the different stages of dentition: A systematic review and meta-analysis. Eur J Paediatr Dent, 21:115-122.

[5] Alhammadi MS, Halboub E, Fayed MS, Labib A, El-Saaidi C (2018). Global distribution of malocclusion traits: A systematic review. Dent Press J Orthod, 23:40.e41-40.e10.

[6] De Ridder L, Aleksieva A, Willems G, Declerck D, Cadenas de Llano-Pérula M (2022). Prevalence of Orthodontic Malocclusions in Healthy Children and Adolescents: A Systematic Review. Int J Environ Res Public Health, 19.

[7] Azami M AS (2023). Prevalence of dental malocclusion and its gender distribution among dental students at Kabul university of medical science. IP Indian J. of Orthod. Dentofac. Res,9:83-89.

[8] Almotairy N, Almutairi F (2022). A Nation-wide Prevalence of Malocclusion Traits in Saudi Arabia: A Systematic Review. J Int Soc Prev Community Dent, 12:1-11.

[9] Singh VP, Sharma A (2014). Epidemiology of Malocclusion and Assessment of Orthodontic Treatment Need for Nepalese Children. Int Sch Res Notices, 2014:768357.

[10] Shukla N, Chaturvedi T (2019). The Prevalence of Malocclusion and the Need for Orthodontic Treatment among Adolescents of the Eastern UP Region of India: An Epidemiological Study. Int J Sci Res, 8:1838-1842

[11] Chaturvedi T, Singh T, Shukla N (2019). The Prevalence of Dentofacial Characteristics and oral habits among Adolescents of Eastern Uttar Pradesh, India: A Survey and Review Report.

[12] Chaturvedi TP SN, Sharma V, Srivastava A, Singh TB (2019). The Prevalence of Dentofacial Characteristics and oral habits among Adolescents of Eastern Uttar Pradesh, India: A Survey and Review Report. Int J Dent Sci Innovat Res, 2:33-51.

[13] Von Cramon-Taubadel N (2011). Global human mandibular variation reflects differences in agricultural and hunter-gatherer subsistence strategies. Proc Natl Acad Sci, 108:19546-19551.

[14] Corruccini RS, Beecher RM (1982). Occlusal variation related to soft diet in a nonhuman primate. Science, 218:74-76.

[15] Hu N (2024). Impacts of Climate Change on Oral Health and Dentistry - Why Should Dentists Care and What Can They Do? Journal of the California Dental Association, 52:2428210.

[16] Todor BI, Scrobota I, Todor L, Lucan AI, Vaida LL (2019). Environmental Factors Associated with Malocclusion in Children Population from Mining

Areas, Western Romania. Int J Environ Res Public Health, 16.
[17] Park SY, Kong SH, Kim KJ, Ahn SH, Hong N, Ha J, et al. (2024). Effects of Endocrine-Disrupting Chemicals on Bone Health. Endocrinol Metab (Seoul), 39:539-551.
[18] Chaturvedi TP, Mishra R, Sharma VK, Aparna AV, Nagvanshi S (2025). Genes to jaws: A systematic review uncovering the role of genetics in malocclusion. Gene Rep, 42:102388.
[19] Moreno Uribe LM, Miller SF (2015). Genetics of the dentofacial variation in human malocclusion. Orthod Craniofac Res, 18 Suppl 1:91-99.
[20] Feştilă D, Ciobotaru CD, Suciu T, Olteanu CD, Ghergie M (2025). Oral Breathing Effects on Malocclusions and Mandibular Posture: Complex Consequences on Dentofacial Development in Pediatric Orthodontics. Children (Basel), 12:72.
[21] Grippaudo C, Paolantonio EG, Antonini G, Saulle R, La Torre G, Deli R (2016). Association between oral habits, mouth breathing and malocclusion. Acta Otorhinolaryngol Ital, 36:386-394.
[22] Souki BQ, Pimenta GB, Souki MQ, Franco LP, Becker HM, Pinto JA (2009). Prevalence of malocclusion among mouth breathing children: do expectations meet reality? Int J Pediatr Otorhinolaryngol, 73:767-773.
[23] Eltager T, Bardissy AE, Abdelgawad F (2025). Cessation of thumb/finger sucking habit in children using electronic habit reminder versus palatal crib: a randomized clinical pilot study. BMC Oral Health, 25:27.
[24] Harari D, Redlich M, Miri S, Hamud T, Gross M (2010). The effect of mouth breathing versus nasal breathing on dentofacial and craniofacial development in orthodontic patients. Laryngoscope, 120:2089-2093.
[25] Zheng W, Zhang X, Dong J, He J (2020). Facial morphological characteristics of mouth breathers vs. nasal breathers: A systematic review and meta-analysis of lateral cephalometric data. Exp Ther Med, 19:3738-3750.
[26] Mundt T, Bernhardt O, Krey K-F, Splieth C, Völzke H, Samietz S, et al. (2025). The impact of malocclusion on tooth loss over a 20-year period: Findings from the Population-Based Study of Health in Pomerania (SHIP). J Dent, 153:105502.
[27] Abate A, Cavagnetto D, Fama A, Maspero C, Farronato G (2020). Relationship between Breastfeeding and Malocclusion: A Systematic Review of the Literature. Nutrients, 12:3688.
[28] Chaturvedi TP. Malocclusion and Genetics, India: Kishor Vidya niketan; 2022.
[29] Javali MA, Betsy J, Al Thobaiti RSS, Alshahrani RA, AlQahtani HAH (2020). Relationship between Malocclusion and Periodontal Disease in Patients Seeking Orthodontic Treatment in Southwestern Saudi Arabia. Saudi J Med Med Sci, 8:133-139.
[30] Görgülü S, Sağdıç D, Akin E, Karaçay S, Bulakbası N (2011). Tongue movements in patients with skeletal Class III malocclusions evaluated with real-time balanced turbo field echo cine magnetic resonance imaging. Am J Orthod Dentofacial Orthop, 139:e405-414.
[31] Ekuni D, Furuta M, Irie K, Azuma T, Tomofuji T, Murakami T, et al. (2011). Relationship between impacts attributed to malocclusion and psychological stress in young Japanese adults. Eur J Orthod, 33:558-563.
[32] Bollero P, Ricchiuti MR, Laganà G, G DIF, Lione R, Cozza P (2017). Correlations between dental malocclusions, ocular motility, and convergence disorders: a cross-sectional study in growing subjects. Oral Implantol (Rome), 10:289-294.
[33] Matías EM, Mecham DK, Black CS, Graf JW, Steel SD, Wilhelm SK, et al. (2016). Malocclusion model of temporomandibular joint osteoarthritis in mice with and without receptor for advanced glycation end products. Arch Oral Biol, 69:47-62.
[34] Drury RL, Simonetti SA (2019). Heart Rate Variability in Dental Science. Front Med (Lausanne), 6:13.
[35] Chaturvedi TP, Singh D, Sharma VK, Priyadarshani P, Turkiya S (2023). Effect of orthodontic retraction force on thick and thin gingival biotypes in different grades of gingival recession and alveolar bone quality: A finite element analysis. J Orthod Sci, 12:22.
[36] Elyaskhil M, Shafai NAA, Mokhtar N (2021). Effect of malocclusion severity on oral health related quality of life in Malay adolescents. Health Qual Life Outcomes, 19:71.
[37] Assaf DDC, Knorst JK, Busanello-Stella AR, Ferrazzo VA, Berwig LC, Ardenghi TM, et al. (2021). Association between malocclusion, tongue position and speech distortion in mixed-dentition schoolchildren: an epidemiological study. J Appl Oral Sci, 29:e20201005.
[38] Verma SK, Tandon P, Agrawal DK, Prabhat KC (2012). A cephalometric evaluation of tongue from the rest position to centric occlusion in the subjects with class II division 1 malocclusion and class I normal occlusion. J Orthod Sci, 1:34-39.
[39] Iwasaki T, Suga H, Yanagisawa-Minami A, Sato H, Sato-Hashiguchi M, Shirazawa Y, et al. (2019). Relationships among tongue volume, hyoid position, airway volume and maxillofacial form in paediatric patients with Class-I, Class-II and Class-III malocclusions. Orthod Craniofac Res, 22:9-15.
[40] Koizumi K, Shintani T, Yoshimi Y, Higaki M, Kunimatsu R, Yoshioka Y, et al. (2022). Impact of Maximum Tongue Pressure in Patients with Jaw Deformities Who Underwent Orthognathic Surgery. Diagnostics (Basel), 12: 404.
[41] Sheiham A, Steele J (2001). Does the condition of the mouth and teeth affect the ability to eat certain foods, nutrient and dietary intake and nutritional status amongst older people? Public Health Nutr, 4:797-803.
[42] Gu M, Yang Y, Shan Z (2018). The Association between Mastication, Malocclusion, and Craniofacial Morphology. Int J Dent Oral Sci, 2018:6-11.
[43] Magalhães IB, Pereira LJ, Marques LS, Gameiro GH (2010). The influence of malocclusion on masticatory performance. A systematic review. Angle Orthod, 80:981-987.

[44] A N. 2012. How Malocclusion can Lead to Periodontal Disease - LA Dental Clinic.
[45] Shen X, Shi J, Xu L, Meng H (2020). Influential factors related to the long-term effect of periodontal-orthodontic treatment in patients with aggressive periodontitis and malocclusion. Zhonghua Kou Qiang Yi Xue Za Zhi, 55:86-92.
[46] Bernhardt O, Krey KF, Daboul A, Voelzke H, Kindler S, Kocher T, et al. (2019). New insights in the link between malocclusion and periodontal disease. J Clin Periodontol, 46:144-159.
[47] Marchili N, Ortu E, Pietropaoli D, Cattaneo R, Monaco A (2016). Dental occlusion and ophthalmology: a literature review. Open Dent J, 10:460.
[48] Silvestrini-Biavati A, Migliorati M, Demarziani E, Tecco S, Silvestrini-Biavati P, Polimeni A, et al. (2013). Clinical association between teeth malocclusions, wrong posture and ocular convergence disorders: an epidemiological investigation on primary school children. BMC pediatrics, 13:1-8.
[49] Caruso S, Gatto R, Capogreco M, Nota A (2018). Association of visual defects and occlusal molar class in children. BioMed Res Int, 2018:7296289.
[50] Liu Y, Chen T, Huang J, Li W, Chen Y, Huo L (2022). Refractive error characteristics and influence on ocular parameters in patients with unilateral congenital ptosis. BMC Ophthalmol, 22:291.
[51] Giuca MR, Pasini M, Giuca G, Mannella EC, Gandini P (2019). Clinical association between dental malocclusion and strabismus in adolescents: a retrospective dental cast analysis. Minerva stomatologica, 68:11-16.
[52] Ribeiro-Lages MB, Martins ML, Magno MB, Masterson Ferreira D, Tavares-Silva CM, Fonseca-Gonçalves A, et al. (2020). Is there association between dental malocclusion and bruxism? A systematic review and meta-analysis. J Oral Rehab, 47:1304-1318.
[53] Michalak M, Wysokińska-Miszczuk J, Wilczak M, Paulo M, Bożyk A, Borowicz J (2012). Correlation between eye and ear symptoms and lack of teeth, bruxism and other parafunctions in a population of 1006 patients in 2003-2008. Arch Med Sci, 8:104-110.
[54] Grippaudo C, Valerio P, Romeo C, Fiasca F, Quinzi V (2020). Bite and Sight: Is There a Correlation? Clinical Association between Dental Malocclusion and Visual Disturbances in Pediatric Patients. Appl Sci, 10:1-11.
[55] Torii K (2019). Ear Symptoms and Malocclusion. Otolaryng Head Neck Surg, 5:1-2.
[56] Spineli E, Studart L, Heimer M, Katz C (2016). Maloclusões e disfunção da tuba auditiva em crianças: uma revisão integrativa. Rev CEFAC, 18:960-964.
[57] Giuca MR, Caputo E, Nastasio S, Pasini M (2011). Correlation between otitis media and dental malocclusion in children. Eur Arch Paediatr Dent, 12:241-244.
[58] Torii K, Chiwata I (2007). Occlusal management for a patient with aural symptoms of unknown etiology: a case report. J Med Case Rep, 1:85.
[59] Roy A, Ferraz Dos Santos B, Rompré P, Nishio C (2020). Dental malocclusion among children with attention deficit hyperactivity disorder. Am J Orthod Dentofacial Orthop, 158:694-699.
[60] Dutra SR, Pretti H, Martins MT, Bendo CB, Vale MP (2018). Impact of malocclusion on the quality of life of children aged 8 to 10 years. Dent Press J Orthod, 23:46-53.
[61] Sabuncuoglu O (2013). Understanding the relationships between breastfeeding, malocclusion, ADHD, sleep-disordered breathing and traumatic dental injuries. Med Hypotheses, 80:315-320.
[62] Poluha RL, Canales GT, Bonjardim LR, Conti PCR (2021). Oral behaviors, bruxism, malocclusion and painful temporomandibular joint clicking: is there an association? Braz Oral Res, 35:e090.
[63] Sindona C, Runci Anastasi M, Chiricosta L, Gugliandolo A, Silvestro S, Bramanti P, et al. (2021). Temporomandibular Disorders Slow Down the Regeneration Process of Masticatory Muscles: Transcriptomic Analysis. Medicina (Kaunas), 57:354.
[64] Tramonti Fantozzi MP, De Cicco V, Argento S, De Cicco D, Barresi M, Cataldo E, et al. (2021). Trigeminal input, pupil size and cognitive performance: From oral to brain matter. Brain Res, 1751:147194.
[65] Tramonti Fantozzi MP, Lazzarini G, De Cicco V, Briganti A, Argento S, De Cicco D, et al. (2021). The path from trigeminal asymmetry to cognitive impairment: a behavioral and molecular study. Sci Rep, 11:4744.
[66] Koskela A, Neittaanmäki A, Rönnberg K, Palotie A, Ripatti S, Palotie T (2021). The relation of severe malocclusion to patients' mental and behavioral disorders, growth, and speech problems. Eur J Orthod, 43:159-164.
[67] Popovac A, Mladenović I, Krunić J, Trifković B, Todorović A, Milašin J, et al. (2020). Apolipoprotein ε4 Allele and Dental Occlusion Deficiency as Risk Factors for Alzheimer's Disease. Journal of Alzheimer's disease : J Alzheimers Dis, 74:797-802.
[68] Tsuneishi M, Yamamoto T, Yamaguchi T, Kodama T, Sato T (2021). Association between number of teeth and Alzheimer’s disease using the National Database of Health Insurance Claims and Specific Health Checkups of Japan. Plos One, 16:e0251056.
[69] Fujinami Y, Hifumi T, Ono Y, Saito M, Okazaki T, Shinohara N, et al. (2021). Malocclusion of Molar Teeth Is Associated with Activities of Daily Living Loss and Delirium in Elderly Critically Ill Older Patients. J Clin Med, 10:2157.
[70] Iwasaki M, Kimura Y, Ogawa H, Yamaga T, Ansai T, Wada T, et al. (2019). Periodontitis, periodontal inflammation, and mild cognitive impairment: A 5-year cohort study. J Periodontal Res, 54:233-240.
[71] Edahiro A, Okamura T, Motohashi Y, Takahashi C, Meguro A, Sugiyama M, et al. (2021). Severity of Dementia Is Associated with Increased Periodontal Inflamed Surface Area: Home Visit Survey of People with Cognitive Decline Living in the Community. Int J Environ Res Public Health, 18.

[72] Nakamura T, Zou K, Shibuya Y, Michikawa M (2021). Oral dysfunctions and cognitive impairment/dementia. J Neurosci Res, 99:518-528.
[73] Kaditis AG, Alonso Alvarez ML, Boudewyns A, Alexopoulos EI, Ersu R, Joosten K, et al. (2016). Obstructive sleep disordered breathing in 2- to 18-year-old children: diagnosis and management. Eur Respir J, 47:69-94.
[74] Fallone G, Owens JA, Deane J (2002). Sleepiness in children and adolescents: clinical implications. Sleep Med Rev, 6:287-306.
[75] Chaturvedi TP, Priyadarshani P, Sharma VK, Shrivastava I, Singh D, Mishra SP, et al. (2024). Evidence in Reaching Consensus in Usage of Mandibular Advancement Device for Pre- and Post-obstructive Sleep Apnea Treatment with Blood and Salivary Inflammatory Biomarkers Profiles. Sleep and Vigilance, 8:329-335.
[76] Bruun SN, Hansen C, Sonnesen L (2024). Sleepiness in children with severe malocclusion compared with in children with neutral occlusion. Am J Orthodont Dentofac Orthop, 165:593-601.
[77] Castañeda-Zetina J, Chuc-Gamboa MG, Aguilar-Pérez FJ, Pinzón-Te AL, Zúñiga-Herrera ID, Esparza-Villalpando V (2022). Malocclusions in Pediatric Patients with Asthma: A Case-Control Study. Healthcare (Basel), 10:1374.
[78] Rathi S, Gilani R, Kamble R, Bhandwalkar S (2022). Temporomandibular Joint Disorder and Airway in Class II Malocclusion: A Review. Cureus, 14:e30515.
[79] Lin SW, Jheng CH, Wang CL, Hsu CW, Lu MC, Koo M (2021). Risk of dental malocclusion in children with upper respiratory tract disorders: A case-control study of a nationwide, population-based health claim database. Int J Pediatr Otorhinolaryngol, 143:110663.
[80] Faria VC, de Oliveira MA, Santos LA, Santoro IL, Fernandes AL (2006). The effects of asthma on dental and facial deformities. J Asthma, 43:307-309.
[81] Abe M, Mitani A, Yao A, Zong L, Hoshi K, Yanagimoto S (2020). Awareness of Malocclusion Is Closely Associated with Allergic Rhinitis, Asthma, and Arrhythmia in Late Adolescents. Healthcare (Basel), 8:209.
[82] Sambataro S, Bocchieri S, Cervino G, La Bruna R, Cicciù A, Innorta M, et al. (2019). Correlations between Malocclusion and Postural Anomalies in Children with Mixed Dentition. J Funct Morphol Kinesiol, 4:45.
[83] Laskowska M, Olczak-Kowalczyk D, Zadurska M, Czubak J, Czubak-Wrzosek M, Walerzak M, et al. (2019). Evaluation of a relationship between malocclusion and idiopathic scoliosis in children and adolescents. J Child Orthop, 13:600-606.
[84] Zong C, Van Dessel J, Vande Velde G, Willems G, Cadenas de Llano-Pérula M (2022). Dynamic changes in tooth displacement and bone morphometry induced by orthodontic force. Sci Rep, 12:13672.
[85] Konstantynowicz J, Sierpinska T, Kaczmarski M, Piotrowska-Jastrzebska J, Golebiewska M (2007). Dental malocclusion is associated with reduced systemic bone mineral density in adolescents. J Clin Densitom, 10:147-152.
[86] Shroff B (2018). Malocclusion as a Cause for Temporomandibular Disorders and Orthodontics as a Treatment. Oral Maxillofac Surg Clin North Am, 30:299-302.
[87] Fichera G, Ronsivalle V, Santonocito S, Aboulazm KS, Isola G, Leonardi R, et al. (2021). Class II Skeletal Malocclusion and Prevalence of Temporomandibular Disorders. An Epidemiological Pilot Study on Growing Subjects. J Funct Morphol Kinesiol, 6;63.
[88] Kelsey JL, Lamster IB (2008). Influence of musculoskeletal conditions on oral health among older adults. Am J Public Health, 98:1177-1183.
[89] Kim JW, Chung MK, Lee J, Kwok SK, Kim WU, Park SH, et al. (2020). Association of periodontitis with radiographic knee osteoarthritis. J Periodontol, 91:369-376.
[90] Różańska-Perlińska D, Potocka-Mitan M, Rydzik Ł, Lipińska P, Perliński J, Javdaneh N, et al. (2024). The Correlation between Malocclusion and Body Posture and Cervical Vertebral, Podal System, and Gait Parameters in Children: A Systematic Review. J Clin Med, 13.
[91] Vukicevic V, Petrovic D (2016). Relationship between head posture and parameters of sagittal position and length of jaws. Med Pregl, 69:288-293.
[92] Marchena-Rodríguez A, Moreno-Morales N, Ramírez-Parga E, Labajo-Manzanares MT, Luque-Suárez A, Gijon-Nogueron G (2018). Relationship between foot posture and dental malocclusions in children aged 6 to 9 years: A cross-sectional study. Medicine (Baltimore), 97:e0701.
[93] Cuccia A, Caradonna C (2009). The relationship between the stomatognathic system and body posture. Clinics (Sao Paulo), 64:61-66.
[94] Chessa G, Capobianco S, Lai V (2002). [Stabilimetry and cranio-cervico-mandibular disorders]. Minerva Stomatol, 51:167-171.
[95] Dubey NK, Wei H-J, Yu S-H, Williams DF, Wang JR, Deng Y-H, et al. (2019). Adipose-derived Stem Cells Attenuates Diabetic Osteoarthritis via Inhibition of Glycation-mediated Inflammatory Cascade. Aging Dis, 10:483-496.
[96] Manfredini D, Segù M, Arveda N, Lombardo L, Siciliani G, Alessandro R, et al. (2016). Temporomandibular Joint Disorders in Patients With Different Facial Morphology. A Systematic Review of the Literature. J Oral Maxillofac Surg, 74:29-46.
[97] Pokrajac-Zirojevic V, Slack-Smith L, Booth D (2002). Arthritis and use of dental services: a population based study. Aust Dent J, 47:208-213.
[98] Jacobs R, Ghyselen J, Koninckx P, van Steenberghe D (1996). Long-term bone mass evaluation of mandible and lumbar spine in a group of women receiving hormone replacement therapy. Eur J Oral Sci, 104:10-16.
[99] Leszczyszyn A, Hnitecka S, Dominiak M (2021). Could Vitamin D3 Deficiency Influence Malocclusion Development? Nutrients, 13:2122.
[100] Wang Z, Ma Z, Yang C (2023). Alveolar bone defects around mandibular anterior teeth in Class I, II, and III

malocclusions: a retrospective CBCT evaluation. Front Oral Maxillofac Med, 5:2.
[101] Abe M, Mitani A, Yao A, Zhang CD, Hoshi K, Yanagimoto S (2021). Close Association between Awareness of Teeth-Alignment Disorder and Systemic Disorders in Late Adolescence. Healthcare (Basel), 9:370.
[102] Sanz M, Marco Del Castillo A, Jepsen S, Gonzalez-Juanatey JR, D'Aiuto F, Bouchard P, et al. (2020). Periodontitis and cardiovascular diseases: Consensus report. J Clin Periodontol, 47:268-288.
[103] Zardawi F, Gul S, Abdulkareem A, Sha A, Yates J (2020). Association Between Periodontal Disease and Atherosclerotic Cardiovascular Diseases: Revisited. Front Cardiovasc Med, 7:625579.
[104] Wang Z, Bao J, Yang Y, Wei Y, Li C, Pan Y, et al. (2025). The Impact of Periodontitis on Cardiovascular Disease: Mechanisms, Evidence, and Therapeutic Implications. International J Dent, 2025:3694736.
[105] Molina A, Martínez M, Montero E, Carasol M, Herrera D, Figuero E, et al. (2025). Association between periodontitis and cardiovascular risk in Spanish employed adults-The Workers' Oral Health study. J Periodontal Res, 60:340-349.
[106] Ramadan DE, Hariyani N, Indrawati R, Ridwan RD, Diyatri I (2020). Cytokines and Chemokines in Periodontitis. Eur J Dent, 14:483-495.
[107] Dhadse P, Gattani D, Mishra R (2010). The link between periodontal disease and cardiovascular disease: How far we have come in last two decades ? J Indian Soc Periodontol, 14:148-154.
[108] Alfakry H, Malle E, Koyani CN, Pussinen PJ, Sorsa T (2016). Neutrophil proteolytic activation cascades: a possible mechanistic link between chronic periodontitis and coronary heart disease. Innate Immun, 22:85-99.
[109] Rathnayake N, Gustafsson A, Norhammar A, Kjellström B, Klinge B, Rydén L, et al. (2015). Salivary Matrix Metalloproteinase-8 and -9 and Myeloperoxidase in Relation to Coronary Heart and Periodontal Diseases: A Subgroup Report from the PAROKRANK Study (Periodontitis and Its Relation to Coronary Artery Disease). Plos One, 10:e0126370.
[110] Zorlu M, Camcı H (2023). The relationship between different levels of facial attractiveness and malocclusion perception: an eye tracking and survey study. Prog Orthod, 24:29.
[111] Bulczak G, Gugushvili A (2023). Physical attractiveness and cardiometabolic risk. Am J Hum Biol, 35:e23895.
[112] Borráz-León JI, Cerda-Molina AL, Mayagoitia-Novales L (2017). Stress and cortisol responses in men: differences according to facial symmetry. Stress, 20:573-579.
[113] Tsai S-Y, Hsu J-Y, Lin C-H, Kuo Y-C, Chen C-H, Chen H-Y, et al. (2024). Association of stress hormones and the risk of cardiovascular diseases systematic review and meta-analysis. Int J Cardiol Cardiovasc Risk Prev, 23:200305.
[114] AlSahman L, AlBagieh H, AlSahman R (2024). Is There a Relationship between Salivary Cortisol and Temporomandibular Disorder: A Systematic Review. Diagnostics, 14:1435.
[115] Drury RL, Simonetti SA (2019). Heart Rate Variability in Dental Science. Front Med, 6: 13.
[116] Taga H, Azuma Y, Maehara K, Nomura S (2012). Effects of changes in vertical occlusal dimension on heart rate fluctuations in guinea pigs. In Vivo, 26:177-182.
[117] Gupta P, Avinash B, Rao RN (2020). Correlation of ABO and Rh Blood Group with Dental Malocclusion in Population of Mysuru. Dent Hypotheses, 11:47-51.
[118] Sharma R PR, Nagarathna C, Navin HK (2015). Association of ABO Blood Groups with Malocclusion in Population of Jaipur, India: A Prospective Study. Int J Sci Stud, 2:45-51.
[119] Almalki SA, Gowdar IM, Arishi FO, Alhumaidani RK, Alhumaidani FK, Gufran K (2024). Association Between ABO Blood Group, Dental Caries, Gingivitis, Impacted Teeth and Malocclusion Among Saudi Adults: A Cross-Sectional Study. Clin Cosmet Investig Dent, 16:371-379.
[120] Namdar P, Shiva A, Etezadi T, Charati J, Karami H, Iri S (2021). Prevalence of Malocclusion in Patients with Thalassemia Major: A Cross-sectional Study. Iranian Journal of Orthodontics, 15.
[121] Gaudio A, Morabito N, Catalano A, Rapisarda R, Xourafa A, Lasco A (2019). Pathogenesis of Thalassemia Major-associated Osteoporosis: A Review with Insights from Clinical Experience. J Clin Res Pediatr Endocrinol, 11:110-117.
[122] Hattab F (2017). Thalassemia major and related maxillofacial complications: Clinical and radiographic overview with reference to dental care. Int J Exp Dent Sci, 6:1-10.
[123] Jeelani W, Sher U, Ahmed M (2020). Nature and severity of dental malocclusion in children suffering from transfusion-dependent (-thalassemia major. Dent Press J Orthod, 25:26e21-26e29.
[124] Lopes CMI, Lira SS, Oliveira JCdS, Luna ACAe, Valença PAdM, Menezes VAd (2021). Occlusal Disorders in Patients with Sickle Cell Disease: Critical Literature Review. J Clin Pediatr Dent, 45:117-122.
[125] Taher M, Aminondin S, Nasir NA, Jasmadi NA, Nizam NIN, Shahrul IS, et al. (2025). Sickle cell disease: understanding pathophysiology, clinical features and advances in gene therapy approaches. Front Pharmacol, 16:1630994.
[126] Kandasamy S, Goonewardene M (2014). Class II malocclusion and sleep-disordered breathing. Semin Orthod, 20:316-323.
[127] Alexopoulos EI, Malakasioti G, Varlami V, Miligkos M, Gourgoulianis K, Kaditis AG (2014). Nocturnal enuresis is associated with moderate-to-severe obstructive sleep apnea in children with snoring. Pediatr Res, 76:555-559.
[128] Bazargani F, Jönson-Ring I, Nevéus T (2015). Rapid maxillary expansion in therapy-resistant enuretic children: An orthodontic perspective. Angle Orthod, 86:481-486.
[129] Zasčiurinskienė E, Rastokaitė L, Lindsten R, Basevičienė N, Šidlauskas A (2023). Malocclusions,

pathologic tooth migration, and the need for orthodontic treatment in subjects with stage III-IV periodontitis. A cross-sectional study. Eur J Orthod, 45:418-429.
[130] Matsuo T, Kakita S, Honda H, Mori S, Araki K, Mitsunari K, et al. (2024). Relationship Between Tooth Loss Due to Chronic Periodontitis and Lower Urinary Tract Symptoms. Medicina (Kaunas), 60:1829.
[131] Lee YC YT, Chen WC, Dubey NK, Chaturvedi H, Huang AC, et al. (2024). Synergistic efficacy of low-intensity extracorporeal shock wave and platelet-rich plasma on erectile dysfunction. Bull RSMU, 6:154-161.
[132] Bui FQ, Almeida-da-Silva CLC, Huynh B, Trinh A, Liu J, Woodward J, et al. (2019). Association between periodontal pathogens and systemic disease. Biomed J, 42:27-35.
[133] Fujita N, Iwane T, Tamura Y, Okamoto T, Yamamoto H, Hatakeyama S, et al. (2024). Associations of remaining teeth number, periodontal disease, and occlusal support status with erectile dysfunction in community-dwelling men. Int J Urol, 31:869-875.
[134] Zadik Y, Bechor R, Galor S, Justo D, Heruti RJ (2009). Erectile dysfunction might be associated with chronic periodontal disease: two ends of the cardiovascular spectrum. J Sex Med, 6:1111-1116.
[135] Farook F, Al Meshrafi A, Mohamed Nizam N, Al Shammari A (2021). The Association Between Periodontitis and Erectile Dysfunction: A Systematic Review and Meta-Analysis. Am J Mens Health, 15:15579883211007277.
[136] Eltas A, Oguz F, Uslu MO, Akdemir E (2013). The effect of periodontal treatment in improving erectile dysfunction: a randomized controlled trial. J Clin Periodontol, 40:148-154.
[137] Keller JJ, Chung S-D, Lin H-C (2012). A nationwide population-based study on the association between chronic periodontitis and erectile dysfunction. J Clin Periodontol, 39:507-512.
[138] Singh BP, Makker A, Tripathi A, Singh MM, Gupta V (2011). Association of testosterone and bone mineral density with tooth loss in men with chronic periodontitis. J Oral Sci, 53:333-339.
[139] Georgina A, Sundar J, Srinivas G. (2023). Psychological and Social Impact of Malocclusion in Children and Young Adults -A Review. J Oral Res Rev, 15:61-64.
[140] Özkent MS, Hamarat MB, Taşkapu HH, Kılınç MT, Göger YE, Sönmez MG (2021). Is erectile dysfunction related to self-esteem and depression? A prospective case-control study. Andrologia, 53:e13910.
[141] Zemishlany Z, Weizman A (2008). The impact of mental illness on sexual dysfunction. Adv Psychosom Med, 29:89-106.
[142] Xiao Y, Xie T, Peng J, Zhou X, Long J, Yang M, et al. (2023). Factors associated with anxiety and depression in patients with erectile dysfunction: a cross-sectional study. BMC Psychol, 11:36.
[143] Saito J, Kumano H, Ghazizadeh M, Shimokawa C, Tanemura H (2023). Relationships Between Erectile Dysfunction, Depression, Anxiety, and Quality of Life in Young Japanese Men: A Cross-Sectional Study. J Psychosexual Health, 5:77-83.