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Genetics In Orthodontics-A Comprehensive Review

[1]Ouma Maguesvary S, [2]Mohamed Arafath M[*] , [3]Mohamed Shamsudeen A I, [3]Nanthini G, [3]Pavithra P

[1]Postgraduate,[2]Professor,[3]Postgraduate
Department of orthodontics & Dentofacial Orthopedics,
Government Dental College and Hospital,Cuddalore Dt, Chidambaram, Tamilnadu-608002

***Corresponding Author:**
Dr. Mohamed Arafath M
Professor, Department of orthodontics & Dentofacial Orthopedics, Government Dental College and Hospital,Cuddalore Dt, Chidambaram, Tamilnadu-608002

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Abstract

Genetics play a major role in craniofacial development and orthodontic conditions such as malocclusion, tooth eruption abnormalities, skeletal discrepancies, impacted canines, and root resorption. Advances in molecular biology and genetic research have improved understanding of how hereditary and environmental factors together influence orthodontic problems. Recent studies focus on identifying genetic markers that may help predict growth patterns, treatment outcomes, and possible complications, enabling more personalized and biologically compatible treatment plans. The development of genomics also supports early diagnosis and preventive orthodontics. Knowledge of orthodontic genetics improves clinical decision-making, treatment outcomes, and long-term stability, with future advances expected to further enhance personalized and evidence-based orthodontic care**.**

Keywords: Genetics, Orthodontics, Craniofacial growth, Gene polymorphism, Genetic markers

Introduction

Facial deformity and malocclusion variation within the population is largely due to genetic factors. It is important to note, however, that genetics does not have a deterministic view with a single gene causing malocclusions. Malocclusion and other human disease conditions are only modelled by a few monogenic diseases, and there are a number of other traits such as height, weight, blood sugar, blood pressure, intelligence, behavior, and sexual orientation which are only modelled by a few monogenic traits. Most human diseases, congenital defects and traits are complex or multifactorial, meaning that they are polygenetic and can be modified by the environment[1].

Numerous countries have been able to find estimates of malocclusions; in general, they are quite substantial, about 33% of the population will need treatment[2]. Malocclusion is not considered a disease but a condition which consists of a number of irregularities which in some cases can affect the quality of one's life. Although there is no clear evidence that orthodontic care improves the health or function of the mouth, the reason to seek orthodontic care is that a change in appearance may improve the social and psychological functioning of the person[3].

The topic of malocclusions development is of great interest, and a lot of researchers investigate this question by developing mechanistic hypothesis. While defining growth trajectories can help us to understand a trajectory, it does not uncover why it happens. The study of individual susceptibility to malocclusion, of why some people have more variations in their craniofacial development[1].

Malocclusions have multifactorial inheritance

As many of the family members were affected, it was believed the condition was inherited autosomal dominantly, which means one of the family genes is responsible for the condition.[4] In a Research with North American families of Hispanic descent, the pattern of autosomal dominant mandibular prognathism was found. Five loci were identified as being linked to mandibular prognathism due to maxillary deficiency: 1p22.1, 3q26.2, 11q22, 12q13.13, and 12q23 19. The regions of the chromosomes which were identified to be associated with MYO1H were located in 12q23 in North Americans[5]. This was also observed in other patients in Brazil and in individuals from the midwestern areas of the United States, a non-conventional myosin. A mutation in the MYO1H protein could be a functional variant in humans and the existence of orthologs in the zebrafish indicates that it has a function in mandibular development[6]. The evidence suggests that MYO1H may have predictive value for prognathism, and the test might be useful to guide treatment decision making of patients who would benefit most[6].

Facial Asymmetry

The symmetry of the face is a factor which can add to its attractiveness and balance, and disturbances can cause the face to become asymmetrical, which can impact on appearance and self-esteem. During development, the body is symmetrical, and some lefty proteins could be responsible for this and how left-sided cleft lip occurs. Asymmetry is very common, usually on the left side and can be in the form of mandibular body, ramus, or atypical. Polymorphisms in the genes ENPP1 and ESR1 have been linked to craniofacial asymmetry. Research also indicates that there is a close relationship between facial asymmetry and temporomandibular joint disorders (TMJD), and there are patients who experience a worsening of their joint dysfunction following orthognathic surgery. [7-10]

Chung et al. divided asymmetry into four types: mandibular body asymmetry, ramus asymmetry, atypical asymmetry, and C-shaped asymmetry.

Orthodontic tooth movement

The genes activated by orthodontic forces are related to inflammation, angiogenesis, bone remodeling and tissue repair. Osteopontin is a protein that is involved in bone remodeling which could serve as a biomarker to predict treatment outcomes. The risk of teeth shifting in the temporomandibular joint (TMJ) and external root resorption are among the many factors that can be influenced by genetic and epigenetic factors, which in turn can affect individual responses to orthodontic treatment. The orthodontist can better tailor the treatment to each individual with fewer problems if he or she knows about these differences.[11]

Types of genetic effects and type of inheritance

A trait is an individual phenotype feature or characteristic. Those with a genetic component to their characteristics are usually divided into three categories: monogenic, polygenic, and multifactorial. Useful in an understanding of the patterns of inheritance, but these are taken to be simplified representations of genetic effects[12].

Monogenic Traits

Monogenic traits are associated with a single gene locus and are typically qualitative or discrete traits, which may be either yes/no or categorical traits. They can be expressed through dominant, recessive or intermediate alleles. The person can be homozygous (both alleles are the same) or heterozygous (alleles are different).[13]

Autosomal Dominant Traits and Penetrance

The difference between an autosomal recessive and an autosomal dominant trait is that the dominant traits are expressed by only one allele, while the recessive traits are expressed by only two alleles. Pedigrees are used to analyze these patterns of inheritance. Autosomal dominant inheritance is generally passed from generation to generation, is observed in males and females at the same rate and each child of an affected parent has a 50% risk of inheriting it. Non-penetrance is when a person has the gene, but does not express the trait.[14]

Variable Expressivity

Penetrance is the likelihood that a genetic trait will occur, but the severity of the trait may differ among individuals. In the same family, disorders like osteogenesis imperfecta manifest different ways. In non-penetrance, a person may have a genetic mutation but not experience the symptoms, making diagnosis more difficult. Craniosynostosis syndromes are

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characterized by premature fusion of cranial sutures, resulting in craniofacial abnormalities.[15,16]

Complex (polygenic/multifactorial) traits

Polygenic traits are complex traits that are influenced by the combined effect of many genes. These traits can be passed on to the next generation, as they are hereditary. Polygenic traits are characterised by a wide phenotypic distribution in a population, while monogenic traits are determined by a single gene.[18]

Polygenic traits are influenced by many genes and environmental factors such as diet and lifestyle. Examples are IQ and height. Cleft lip-palate and neural tube defects are multifactorial traits resulting from the combined effect of genetic and environmental factors.[17]

Role Of Epigenetic In Malocclusion

Epigenetics

Epigenetics explains how genes can be expressed differently without changing the sequence of the DNA. It provides insight into how genomes work, how genes are controlled, and how diseases develop, going beyond just the structure and function of DNA.[19]

Epigenetics concerns modifications in gene regulation without alterations in the DNA sequence. It discusses the interaction of genes with environment and development to produce phenotype. The term was coined by Conrad Waddington, who described epigenetics as the interaction between genes and their products during development. Later definitions highlighted heritable changes in gene function that are not due to changes in DNA sequence. In 2008, a broad definition of epigenetics was adopted as "a stably heritable phenotype resulting from changes in a chromosome without alteration of the DNA sequence.[20]

Epigenetic changes are complicated and include DNA methylation, histone modification and gene regulation by non-coding RNAs. These changes are also reversible and temporary. Several environmental factors can affect these mechanisms. Finally, epigenetic modifications regulate gene expression and modify different gene functions[21].

Environmental and epigenetic factors:

Many environmental factors such as diet, smoking, inflammation, stimuli, and age may impact gene regulation leading to epigenetic modification in the genome. Mechanisms of epigenetic modification are DNA methylation, histone modification and gene regulation by non- coding RNAs. These processes regulate gene expression and influence the functions of many genes.

Role Of Epigenetic In Malocclusion

The development of malocclusion has been suggested to involve the basic participation of epigenetic regulation of the whole masticatory musculoskeletal complex[22].Understanding epigenetic factors and processes that regulate gene expression is important to understand the impact of genetic factors on growth and on the diversity of facial characteristics. Homeobox genes are considered the key genes of the head and face, among the genes that may be involved in the growth development through influencing the patterns of embryonic development [23].

Transcription factors like Hox, Msx1, Msx2, Dlx, Otx, Gsc, and Shh drive gene expression and play a big role in how the face and jaw develop and take shape. Growth factors and bone morphogenetic proteins also impact how the jaw grows, how big teeth get, and the shape of the dental arch. Basically, both genetics and the environment shape craniofacial features and influence whether someone develops malocclusion. Things like poor oral posture or changes in muscle function can mess with bone growth and how teeth line up. So, variations in bite and jaw structure really come from a mix of genes and outside influences. Still, there's not much solid evidence that environmental factors are the main culprit. Genetics do most of the heavy lifting[24,25].

A study by Manel Esteller Fraga and colleagues on monozygotic twins showed that young twins were epigenetically similar, whereas older twins exhibited significant differences in DNA methylation and histone modification due to environmental influences and lifestyle differences. These epigenetic changes affected gene expression and may explain how different craniofacial phenotypes, such as skeletal Class II and Class III malocclusions, can arise from the same genotype. Disturbances in the interaction between genetic and environmental factors may also

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contribute to craniofacial anomalies such as cleft lip, palate, and facial asymmetry.[21]

Clinical applications

Initial research suggests that orthodontic treatment may help manage pediatric Obstructive Sleep Apnea and reduce its occurrence in adulthood. Orthodontic therapy can modify dentofacial growth and correct skeletal jaw discrepancies, but treatment success depends on the interaction between genetic and environmental factors. Severe skeletal malocclusions, particularly mandibular prognathism with strong genetic influence, often show limited response to orthodontic treatment and may require orthognathic surgery. Understanding the genes involved in jaw discrepancies and their interaction with environmental factors is essential for developing more effective and personalized treatment approaches.[20]

Genetic Effects On Skeletal And Individual Tooth Variation And Malocclusion

Skeletal variation

Malocclusion represents a notable departure from an optimal or typical occlusion[13]. Malocclusion may present as either skeletal or dental, characterized by variations in jaw size, tooth size, shape, crowding, or spacing. This condition is a result of genetic factors and environmental influences that impact the development of the craniofacial complex. Determining whether malocclusions are primarily influenced by genetics, environment, or a combination of both can be challenging[25].

The etiology of the majority of skeletal and dentoalveolar-based malocclusions is primarily multifactorial, as various contributing factors come together to result in the final presentation[26]

Several studies have investigated the role of genetic variation in influencing the occlusal and skeletal differences observed among family members[27].

Harris (1975) conducted comprehensive cephalometric studies that proposed the idea of polygenic inheritance in Class II division 1 malocclusion. The research demonstrated that the craniofacial skeletal patterns observed in children with class II malocclusions are genetically influenced and exhibit a significant similarity to the skeletal patterns found in their siblings with normal occlusion[28].

Several published reports have documented the occurrence of Class II division 2 within families, including studies involving twins and triplets as well as family pedigrees. The findings from twin studies revealed that identical twins exhibited complete agreement, or 100% concordance, for Class II division 2 malocclusion. This suggests a significant genetic influence in the development of deep bite malocclusion associated with Class II Division 2[29-32]

Individual tooth variation

Genetic components regulate the size, shape, quantity, placement, and heredity of teeth, as indicated in multiple studies involving twins[33,34].

HOX genes are a conserved subset of the homeobox superfamily that play essential roles in development by controlling various processes such as receptor signaling, differentiation, motility, and angiogenesis. Dysregulation of their expression has been linked to abnormal development and cancer[35].

Genetic variation for mesiodistal and buccolingual crown dimensions of the permanent 28 teeth (excluding third molars) accounted for between 56% and 92% of the observed phenotypic variation[36].

Dental agenesis

Dental agenesis is a congenital condition characterized by the absence of one or more teeth due to disruptions during the early stages of tooth development[36]. It is the prevailing developmental abnormality observed in humans, displaying genetic and phenotypic heterogeneity[37].

According to the existing understanding of genes and the processes that contribute to tooth development and formation, it is believed that various physic different genes that interact with distinct molecular pathways. This not only accounts for the diverse range of agenesis patterns but also explains the connections between dental agenesis and other oral abnormalities. Over 200 genes have been discovered thus far that are active during tooth development, and mutations in some of these genes have been found to hinder tooth growth in mice[38].

Hypodontia can often be familial, but it may also manifest without any family history. It can be associated with a syndrome, particularly ectodermal dysplasia, although it commonly occurs in isolation. Despite being isolated, hypodontia can still have a hereditary component. Patients with hypodontia typically have relatively small mesiodistal size crowns

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when multiple teeth are missing. Conversely, cases with supernumerary teeth tend to have large mesiodistal size crowns for permanent maxillary incisors and canines[36]

The maxillary lateral incisors are frequently affected by hypodontia, which is a common pattern excluding the third molars. This condition can be inherited as an autosomal dominant trait with incomplete penetrance and variable expressivity. It is interesting to note that the phenotype of hypodontia sometimes skips generations and can manifest as a peg-shaped lateral incisor instead of complete agenesis. Additionally, it can affect either one or both sides of the maxillary arch[37,38].

Primary failure of eruption

Tooth eruption is a complex process that is an essential part of the overall tooth development process[39]. It is understood that during tooth eruption, the tooth follicle interacts with both osteoblasts and osteoclasts[40]. However, the exact mechanism of eruption and the factors that control it are not fully understood. Eruption disorders can be classified based on their causes, such as obstruction (cysts, ankylosis, lateral tongue pressure, impaction, etc.), or genetic factors (e.g., primary failure of eruption (PFE); cleidocranial dysplasia, Hunter's disease, and osteopetrosis). PFE is a common diagnostic distinction and is an example of a non-syndromic eruption disorder. PFE, as described by Proffit and Vig (1981), is a condition where non- ankylosed teeth fail to fully erupt. These teeth may partially erupt and then stop, becoming partially submerged without being ankylosed[48.] PFE also affects posterior teeth, leading to a posterior open bite. Accurate diagnosis of PFE is crucial to avoid the complications that can arise from using a continuous archwire.[41-44]

Differentiating eruption failure involves evaluating dental history, clinical features, radiographs, and genetic analysis. Primary Failure of Eruption is characterized by poor response to orthodontic treatment, ankylosis, and possible intrusion of adjacent teeth. It may occur unilaterally or bilaterally, affecting one or more posterior quadrants. Mutations in the PTH1R gene, inherited in an autosomal dominant pattern, are strongly associated with PFE. Genetic analysis of the PTH1R gene helps in early and accurate diagnosis, even in the absence of a positive family history.[45,46]

GENETIC FACTORS INFLUENCE OF DENTAL ARCH FORMATION

The initial phases of human organ development rely on inductive interactions between epithelium and adjacent mesenchymal tissue, from the beginning to the final differentiation stage[47].

Dental arch and tooth development require complex molecular and cellular interactions at multiple levels, leading to specific outcomes. Disruptions in the communication between ectodermal and neural crest-derived mesenchymal cells can lead to abnormalities in teeth and variations in the shape and size of the dental arch[48]

Genetic Markers and Mutation Associated with Dental Arch Variation

Additional genetic studies are necessary to complement heritability studies in order to establish a link between genetic variation and specific phenotypic outcomes. Numerous studies have been conducted to investigate the genetic factors influencing the horizontal growth of the jaws, which form the foundation of the dental arch[16].

Fontoura et al. (2015) conducted a study to explore the association between facial skeletal variation and skeletal malocclusion types. Their findings revealed the presence of a gene (TWIST1 rs2189000) that is associated with variations in mandibular body length, ranging from short to long. Inactivation of this gene during the mandibular curve neural peak leads to mandibular shortening and irregular ramus development. Furthermore, this gene has also been linked to mandibular solidification and the arrangement of molar cusps.

Christiane Cruz et al. (2008) discovered that a polymorphism in the Myosin 1H gene (MYO1H rs10850110 A<G) is associated with mandibular prognathism and horizontal maxillomandibular discrepancies[49].Weaver et al. (2017) proposed that there is a correlation between genotype and phenotype in relation to the asymmetric components of dentoalveolar dental arch variation. This correlation is associated with genes such as TBX1, AJUBA, SNAI3, SATB2, TP63, and 1p22.1[50].

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The homeobox gene MSX1, which regulates cell proliferation and differentiation, is among the candidate genes implicated in tooth agenesis. In addition to MSX1, several other genes, including PAX9, WNT10A, AXIN2, and EDA, have been identified as causative factors for congenitally missing teeth[52].Recent research has definitively linked the MSX1 gene to malocclusion, as it affects nasal cycles, maxilla, and mandible advancement. Previous studies have established a significant association between the MSX1 gene and Class I and II malocclusions[51].

Genetic Variation In Muscle And Its Influence On Malocclusion

Sciote et al. (2013) and their colleagues conducted a research study that revealed the association between variations in masseter muscle fiber type, gene expression in masseter muscle, and epigenetic changes that alter gene expression with certain dental conditions. These conditions include anterior open versus deep bites, mandibular retrognathism versus prognathism, and mandibular asymmetry[52]. Skeletal muscle cells play a crucial role in producing various proteins that define the unique characteristics and function of the muscle fiber tissue. Interestingly, differences in muscle fiber composition have been observed in the masseter muscle tissue of patients with mandibular asymmetry[53] The study found significant increases in type II muscle fiber area and frequency on the same side as the deviation, compared to muscle fibers on the opposite side. However, no significant differences were noted when comparing the muscle composition on the right and left sides of symmetrical patients[54,55].

Genetic Factors And External Apical Root Resorption

External Apical Root Resorption is the shortening of the tooth root apex visible on radiographs, often associated with orthodontic tooth movement. Orthodontic forces can cause resorption lacunae on the cementum surface, which may progress to EARR if repair is insufficient. Maxillary incisors are the teeth most commonly affected during orthodontic treatment. Occlusal forces and genetic factors are believed to contribute significantly to EARR, with studies suggesting a hereditary influence. Root resorption greater than 3 mm occurs in over one-third of orthodontic patients, while severe resorption (>5 mm) affects about 2%–5% of individuals[56]

Interleukin Family

The Interleukin 1 Family plays an important role in inflammation and bone remodeling during orthodontic treatment. IL-1β promotes bone and root resorption and has been strongly associated with External Apical Root Resorption through various gene polymorphisms, particularly IL-1B (+3954). IL-1 receptor antagonist (IL-1ra) may reduce root resorption by inhibiting osteoclast activity. Polymorphisms in IRAK1, IL-6, IL-17A, and P2RX7 genes have also been linked to EARR, influencing inflammatory response, bone remodeling, and orthodontic treatment outcomes. Increased IL-6 levels are associated with acute inflammation and greater root resorption, while P2RX7 variations and prolonged orthodontic treatment may further increase EARR risk[56].

The **Vitamin D Receptor** influences bone growth, immune response, and osteoclast formation through the RANKL/OPG pathway. Polymorphisms in the Vitamin D receptor gene have been associated with bone density changes and External Apical Root Resorption during orthodontic treatment.

Osteopontin plays a key role in odontoclast activation and root resorption, with certain OPN gene variants linked to increased susceptibility to EARR.

The **RANK/RANKL/OPG** Pathway regulates osteoclast activity and bone resorption. OPG protects against excessive resorption by blocking RANKL, while gene polymorphisms in OPG are associated with EARR variation.

Wnt Signaling Pathway influences bone formation by regulating the OPG/RANKL pathway. Reduced Wnt signaling may lead to spontaneous root resorption and decreased bone mass.[57]

Syndromes And Malocclusion

Severe skeletal malocclusions may be associated with genetic syndromes affecting craniofacial development. Chromosomal abnormalities such as deletions, transpositions, or enlargements can cause micrognathia, facial asymmetry, and other dentofacial deformities. Imbalances between genetic and environmental factors increase the severity of these malformations. Syndromes may alter the growth of one or both jaws, leading to abnormal arch relationships. Early diagnosis is important and is often

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based on oral abnormalities and radiographic findings, with orthodontists frequently being the first to identify these conditions. The paper highlights management strategies and summarizes the key features and inheritance patterns of related syndromes[58-60].

Various syndromes according to maxillary and mandibular features, maxillary deficiency, mandibular deficiency, mandibular prognathism ,maxillary and mandibular deficiency, maxillary deficiency and mandibular prognathism are explained in tables 1-6.

Current Knowledge On Genetic Of Malocclusion

Genetic factors significantly influence susceptibility to malocclusion, with many dental and facial traits showing high heritability. Features such as facial dimensions, dental spacing, arch dimensions, and tooth size discrepancies are strongly inherited, while overbite and overjet are more affected by environmental factors[61-63]. Familial studies suggest autosomal dominant inheritance with incomplete penetrance in Class III malocclusion, whereas Class II malocclusions may involve polygenic inheritance and variable expressivity. The high prevalence of malocclusion in craniofacial birth defects further supports a genetic basis, with around 150 genes/loci linked to craniofacial conditions associated with malocclusion[64,65].

Human genetic mapping methods used to identify malocclusion risk loci include linkage and association analyses. Linkage studies detect rare variants with major effects in families, while association studies identify common variants with smaller effects in larger populations. Advances such as genome-wide association studies (GWAS), next-generation sequencing, and meta-analysis have improved complex trait mapping, though research on malocclusion genes is still developing. Most studies focus on Class III malocclusion, with associations reported on chromosomes 1 and 12. However, inconsistent findings across populations suggest significant genetic heterogeneity among different ethnic groups.[66-70]

Conclusion

The integration of genetics into orthodontics is transforming diagnosis and treatment by enabling more personalized and predictive care. Genetic factors influence malocclusions, jaw structure, and susceptibility to orthodontic problems. Genetic testing can help identify individuals at risk for complex conditions, allowing early intervention and customized treatment plans. This approach encourages collaboration between orthodontists, genetic counselors, and other healthcare professionals to ensure accurate interpretation and effective management. However, ethical concerns such as patient privacy, informed consent, and genetic discrimination must be carefully addressed. Advances in genetic research and genomic technology are expected to further improve precision in orthodontic treatment, leading to more individualized and effective patient care.

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Table.1 Classification of various syndromes according to maxillary and mandibular features

S. No.	Condition	Etiology	Striking Features
1.	*Van der Woude syndrome (VWS).*	Autosomal dominant/recessive and environmental (IRF6)	Cleft lip and palate or palate only- Lower lip pits,-Partial syndactly of fingers and toe,- Dental anomalies including underdeveloped maxilla, collapsed maxillary dental arch and- Sparse hair
2.	Cleidocranial dysplasia	Autosomal dominant (RUNX2)	- Underdeveloped or absent clavicle,- Prominent face head,- Hyper telorism,- Brachycephaly,- Over retained deciduous teeth,- Supernumerary teeth,- Reduced height of lower third of face,- Underdeveloped maxilla (skeletal class3tendency)
3.	Papillon-lefevre syndrome	Genetic (CTSC-CATHEPSIN C GENE)	- Palmer planter keratosis, - Early onset form of aggressive periodontitis- Gingival enlargement- Ulceration and pocket (vertical) formation,- Retrognathic maxilla,- Retroclination of mandibular incisors and- Upper lip retrusion,- Decreased lower facial height
4.	Stickler syndrome	Autosomal dominant/autosomal recessive (COL2A1, COL11A1, COLL1A2)	-Midface hypoplasia,- myopia,- anteverted nares,- hearing loss,- cleft of soft palate,- fairly small SNA and SNB angles,- steep mandibular plane- incisors of both arches retroclined,-large overjet and overbite
5.	Down syndrome	Trisomy of 21st chromosome	- Mental retardation,- epicanthal folds, and- flat facial profile,- abundant neck skin,- simian crease,- congenital heart disease,- gap between first and second toe,- brachycephaly,- folded or dysplastic ears,- open mouth.

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Table 2: Syndrome having maxillary deficiency

S. No.	Condition	Etiology	Striking Features
1.	Occlusofaciocardiodental syndrome	x-lined dominant (BCOR gene)	- Congenital cataract,- hypertelorism,glaucoma,nasolacrimal duct obstruction.-long narrow face high nasal bridge,- broad or pointed nose,- bifid nose,- ear deformity,- cleft palate.- atrial septal defect,- ventricular septal defect- mitral valve defect.- Radiculomegaly (canine or multiple),- open apexs of maxilla and mandibularpremolars,- dilacerations of roots,- oligodontia,- constricted maxilla,- maxillary and mandibular dentoalveolar heights are greater than normal
2.	Kabuki syndrome	Multifactorial (KMT2D ,MLL2,KDM6A)	- Flatness of cheeks below the eyes,- lower face is disproportionately long,- may class 1, 2, 3 malocclusion,- high arch palate,- cleft palate,- lexity of TMJ,- central incisor – shovel shaped
3.	Freeman Sheldon syndrome	Multifactorial (MYH3)	- Stiff immobile flat midface and elongated philtrum,- rounded cheeks and small nose- dimpling of chin,- microstomia
4.	Crouzon's syndrome	Mutation of gene (FGFR2)	-Exorbetism,-retromaxillism- paradox retrognathia,- class3 malocclusion,- high arch palate,- hearing loss

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Table 3: Syndrome having mandibular deficiency

S. No.	Condition	Etiology	Striking Features
1.	Pierre- robin syndrome	Matter of debate but some support compression mechanicalor positional theory (SOX9)	Mandibular retrognathia in ramal height (bird faces)- cleft palate, -severe upper airway obstruction at birth.
2.	Treacher-Collins syndrome	Autosomal dominant (TCOF1, POLR1C, POLRID)	Symmetrically hypoplastic- lowest call, docon slanting palpebral fissures
3.	Silver Russell syndrome	Most cases sporadic/ autosomal dominant (H19 AND IGF2)	-Pseudo hydrocephaly,- frontal bossing,- triangular facies,- small and pointed chin with hypoplastic mandible,- high arch palate,- congenital absence of lateral incisors andpremolars,- upper lip vermillion is thin, corners of mouthcone turned down.

Table 4: Syndrome having mandibular prognathism

S. No.	Condition	Etiology	Striking Features
1.	Gorlin syndrome	Autosomal dominant (PTCH1)	- Basal cell carcinoma,- widened, fused or rudimentary ribs,- fronto parital bossing,- hypertelorism,- mandibular prognathism,- crynecomastic, mandibular and maxillary- odontogenic keratocyst (twice as frequent in mandible in 8th molar and canine area)- carnivorous teeth with shovel canine and premolar,- cleft lip and palate.
2.	Marfan syndrome	Autosomal dominant (FBN1 GENE)	Marfanoid habitus,- dolichostenomelia, arachnodactyly,- ectopia lentis,- fusiform and dissecting aneurysm ofaorta,- mandibular prognathism.
3.	Hemifacial microstomia	Autosomal dominant/recessive	- Unilateral or bilateral asymmetricallyhypoplastic ears and mandibular ramus,- ear tags/ or pits,- micrognathia,- variable cleft lip and palate,- epibulbar dermoid- vertebral anomalies,- cardiac defects,- renal anomalies and other abnormalities.

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Table 5: Syndromes having both maxillary and mandibular deficiency

S. No.	Condition	Etiology	Striking Features
1.	Turner syndrome	Numerical / structural aberration of x chromosome (MONOSOMY X)	- Low posterior hair line,- webbing of neck,- broad chest and widely spaced nipples,- coarctation of aorta,- short stature,- facies showing premature aging- Strabismus,- blue sclera,- color blindness,- total length of cranial base is reduced,- retrognathic maxilla and mandible toanterior and posterior lower facialheights,- upper posterior facial heights,- protruded maxillary central incisors.
2.	OMENS plus syndrome	Vascular insult leads to hematoma formation Disruption of mesodermal cell migration (RAG1 AND RAG2 GENES)	- Hypoplastic orbit,- zygomatic region,- maxilla and mandible, noseasymmetry,- philtrum oblique,- mouth had a cleft like extension of leftangle,- microdontia- partial anodontia,- non pnuematization of Sinus

Table 6: Syndrome having maxillary deficiency and mandibular prognathism

S. No.	Condition	Etiology	Striking Features
1.	Saethrechotzen syndrome	-Autosomal dominant (TWIST1GENE)	- Palpabral ptosis,- myopia,- eagle nose with deviated system,- malformed ear with low insertion- cardiac and renal anomalies,- cryptorchidism,- deafness,- maxillary retrusion withmandibular prognathism,- upper lateral incisors sharp ormissing,- TMJ ankylosis

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