FROM GENES TO TEETH: A SCOPING REVIEW ON DENTAL ANOMALIES AND DENTITION ALTERATIONS IN GENETIC SYNDROMES

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ABSTRACT

Introduction: Genetic disorders, resulting from specific gene mutations, often impair systemic growth and craniofacial development, with manifestations extending to the oral cavity. Many syndromes present with odontogenesis alterations, including tooth anomalies in morphology, size, number, enamel integrity, and eruption timing. These dental phenotypes may serve as an early diagnostic indicator for multidisciplinary care. Methods: A systematic search of PubMed, Scopus, and EBSCO was performed for studies published from January 2015 to June 2025. Of 184 records, 9 met the inclusion criteria. Results: Distinct syndrome-specific dental patterns were identified. Turner syndrome mainly associated with supernumerary teeth, while Otodental syndrome showed globodontia. Wolf–Hirschhorn syndrome revealed delayed eruption, microdontia, and agenesis. Down syndrome presented with agenesis and delayed eruption. Williams syndrome was characterized by microdontia and diastema, whereas Wilson's disease showed dens invaginatus. PHACE syndrome presented root anomalies, Ehlers–Danlos syndromes showed enamel hypoplasia and dentin defects, and Blepharocheilodontic syndrome demonstrated tooth agenesis and conical teeth. These patterns correlated with mutations in odontogenesis-related genes. Discussion: Dental anomalies represent consistent phenotypic manifestations in genetic syndromes. Each syndrome exhibits distinct abnormalities, as specific mutations result in variations in morphology, size, density, growth, eruption, and overall development, thereby highlighting genotype–phenotype correlations. Dentition changes may serve as non-invasive diagnostic markers, with genetic insights guiding therapy. Conclusion: Dental anomalies and dentition alterations contribute a significant phenotypic component in many genetic syndromes. Their recognition, alongside genetic testing, can improve diagnostic accuracy and promote comprehensive interdisciplinary management. Further research should refine genotype–phenotype mapping to optimize interdisciplinary care.

Key word: Dental anomalies, genetic syndromes, dentition changes

INTRODUCTION

Genetic diseases are relatively rare conditions, affecting approximately 6–8% of the global population.[1,2] It is estimated that 3.5% to 5.9% of individuals worldwide have one of approximately 7,000 rare diseases, the majority of which are of genetic origin.[1] Rare genetic diseases are usually associated with chronic conditions, are heterogeneous in nature, and are widely distributed.[2,3] These disorders typically arise from mutations in single genes or chromosomal alterations, and although the prevalence of each condition is low, their cumulative burden is substantial when considering hereditary transmission and family hist\ory.[1,3] Most genetic diseases can be observed through manifestations in body growth and dentocraniofacial development, and some of these manifestations may interfere with the patient's daily life.[2,4]

Numerous genetic syndromes exhibit identifiable phenotypic characteristics, including dental and craniofacial abnormalities. Tooth development (odontogenesis) is frequently disrupted in genetic syndromes and represents a key phenotypic manifestation.[5] The process is regulated by a complex genetic signaling system that includes epithelial–mesenchymal interactions in the embryonic development stage.[6,7] A wide range of dental abnormalities, including changes in tooth number (hypodontia, hyperdontia), morphology, size, mineralization, and eruption patterns, can be caused by mutations which regulate these pathways, including disturbances in Wnt and other important molecular cascades.[7,10] These oral and craniofacial symptoms may develop early in life, before other systemic symptoms, and are potentially relevant as clinical indicators for the underlying genetic condition.[6,7]

Odontogenesis, progresses through well-coordinated stages of initiation, morphogenesis, and mineralization, regulated by a complex interplay of genetic signals and growth factors. Fundamental regulatory mechanisms, including Wnt/β-catenin, BMP, FGF, and SHH signaling, enhance epithelial–mesenchymal interactions, while transcription factors such as MSX1, PAX9, and AXIN2 play an important role in defining tooth number, morphology, and position patterning.[6,9,10] Disruptions in these molecular pathways, whether caused by chromosomal abnormalities or single-gene mutations, might result in dental malformations such as hypodontia, supernumerary teeth, altered crown-root morphology, enamel hypomineralization, and delayed or premature eruption.[6,10,11] The phenotypic variability shown in various genetic syndromes—such as Turner, Otodental, Wolf–Hirschhorn, Down, Williams, and Ehlers–Danlos syndromes—illustrates the diverse genetic and developmental pathways involved, highlighting the significance of determining genotype–phenotype correlations for understanding along with managing these conditions.

From a clinical point of view, ,dental manifestations of genetic syndromes are of particular concern, as they may impair mastication, oral health, and aesthetics, ultimately reducing quality of life. Identifying the right multidisciplinary intervention treatments including pediatric dentists, geneticists, pediatricians, and other medical specialists can begin with early detection of dentition changes. Despite the scarcity of high-level evidence, numerous case reports, observational studies, and reviews have described the association between genetic syndromes and dental anomalies. This scoping review aims to synthesize current knowledge on dental abnormalities and dentition changes in genetic syndromes and to explore their potential as early diagnostic indicators supporting multidisciplinary care.

METHOD

1.1 Protocol

This scoping review adhered to the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews) guidelines and was structured using the PCC framework (Population, Concept, Context).

Population : Individuals diagnosed with genetic syndromes or hereditary genetic disorders

Concept : Identifying and mapping Dental anomalies and dentition alterations, including changes in tooth morphology, size, number, enamel integrity, eruption timing, and tooth density in patients with genetic syndromes

Context. : Dentition alterations are explored as potential early diagnostic indicators in any healthcare setting.

1.2 Search Strategy

A comprehensive search was conducted in PubMed, Scopus, and EBSCOhost for studies published between 2015 and 2025. Search terms included combinations of MeSH terms and free-text keywords related to: “Genetic Diseases”, “Tooth Abnormalities”, “Tooth Eruption, Ectopic”and “Anodontia”, Full search strategies are summarized in Table 1 of the original manuscript.

Tabel 1. Search Strategy

base	H/Keywords	lt
Med	'Genetic Diseases, Inborn"[Mesh])) OR "Down lrome"[Mesh]) AND "Tooth Abnormalities"[Mesh]) OR th Eruption, Ectopic"[Mesh]) OR "Anodontia"[Mesh]	
us	tic diseases OR down syndrome OR turner syndrome AND h Abnormalities OR Tooth Eruption, Ectopic OR anodontia) PUBYEAR > 2015 AND PUBYEAR < 2025 AND YEAR > 2014 AND PUBYEAR < 2025 AND (LIMIT-TO (TYPE,"j")) AND (LIMIT-TO (OA,"all")) AND (LIMIT- PUBSTAGE,"final")) AND (LIMIT-TO (DOCTYPE,"ar" ND (LIMIT-TO (LANGUAGE,"English"))	
COhost	"Genetic Diseases, Inborn+" AND MH "Tooth ormalities+" OR MH "Tooth Eruption, Ectopic" OR MH th, Unerupted" OR MH "Anodontia"	

1.3 Study Selection

Process Two reviewers (NS and IS) independently screened the titles and abstracts. Eligible studies were further reviewed in full text. Disagreements were resolved by discussion and consensus. Studies were included if they:

1.3.1 Children under the age of 16 years with a confirmed diagnosis of genetic syndromes or genetic disorders (e.g., Down syndrome, Williams syndrome, and others).

1.3.2 Studies reporting dental anomalies, including microdontia, enamel hypoplasia, not limited to hypodontia, , and delayed tooth eruption.

1.3.3 Studies addressing dentition alterations, such as variations in eruption timing, the transition from primary to permanent dentition, or irregular eruption patterns.

1.3.4 Articles published in either English or Indonesian.

1.3.5 Studies published within the last ten years (2015–2025)

Exclusion criteria included:

1.3.6 Studies addressing non-genetic dental anomalies (e.g., those caused by trauma, infection, or environmental factors).

1.3.7 Studies that do not specify the type of genetic disorder or syndrome under investigation.

1.3.8 Experimental studies conducted on animals or in vitro models (given the focus on human subjects).

1.3.9 Articles that fail to provide specific data regarding dentition anomalies (e.g., those merely referring to “dental problems” without detailed description).

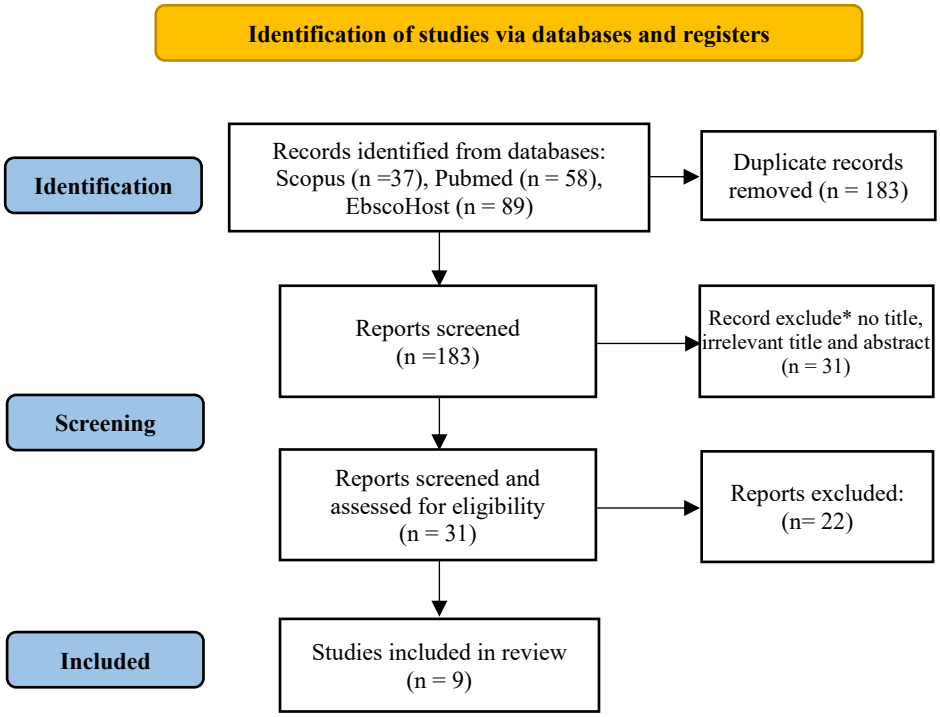

Figure 1. PRISMA flow diagram showing the election of articles included in the review.

1.4 Data Extraction and Synthesis

A standardized data extraction form was used to collect information on study design, genetic disease, mesurment tool, dental anomalies and dentition alteration and results.. A narrative synthesis was performed to map the findings and highlight methodological differences, observed manifestation, and research gaps (Table 1.)

RESULT

A total of 183 articles were screened for relevance. Only nine of them met the inclusion criteria for our research (Fig. 1). This review included wide range of study designs such as case reports, retrospective investigations, a case series, a clinical study, and one systematic review. Each study focused on specific genetic syndromes with distinct dental anomalies. The findings are categorized according to the types of dental anomalies and dentition alterations (Table 1).

In Turner syndrome, supernumerary teeth were observed in a small number of patients, while Otodental syndrome was characterized by globodontia, considered a pathognomonic finding. Microdontia, peg-shaped teeth, fused teeth, agenesis, enamel hypoplasia, and delayed

eruption were all found in Wolf-Hirschhorn syndrome strongly linked with genotype–phenotype correlations. Dental alteration such as malocclusion, agenesis and delayed eruption, were frequently observed in individual with Down Syndrome. Wilson's disease showed multiple dens invaginatus, an uncommon morphological anomaly. A small case series revealed that PHACE syndrome was also characterized by several root abnormalities. Williams syndrome was frequently characterized by microdontia and diastema. In the systematic review of Ehlers–Danlos syndromes, a significant structural anomaly included enamel hypoplasia and dentin defects. Finally, Blepharocheilodontic (BCD) syndrome was associated with conical teeth, tooth agenesis and conical teeth, representing combined numerical and morphological anomalies. Overall, the included studies demonstrate that a wide range of dental anomalies occur across different genetic syndromes (Tabel 1), with each syndrome showing a distinctive pattern of manifestations.

Among the categories of dental anomalies and dentition aleration, , the most frequently reported ones were those related to tooth size and shape tooth size and shape (Otodental, Williams, Wolf–Hirschhorn, Wilson's disease, and BCD). The presence of globodontia, microdontia, diastema, conical teeth, and dens invaginatus highlights significant morphological variation caused by genetic mutations (Tabel 2) . There were four syndromes (Turner, Wolf–Hirschhorn, Down, and BCD) showed abnormalities in tooth numbers, including supernumerary teeth, agenesis, and oligodontia These results highlight the importance of genetic dysregulation in the initiation and development of teeth. Anomalies related to tooth structure and mineralization, though less frequent, were mainly observed in Ehlers–Danlos and Wolf–Hirschhorn syndromes, particularly enamel hypoplasia and dentin defects. Down and Wolf-Hirschhorn syndromes exhibited growth and eruption disturbances, which included delayed eruption. PHACE syndrome was identified by its unique root anomalies, suggesting a rare yet clinically significant phenotype. Besides, Down and Williams syndrome frequently presented with abnormalities in the dentition pattern. Despite the fact that specific type and number of anomalies are more frequently reported, each genetic syndrome displays unique dental features.

Tabel 1. Literature Presentation data

No.	Author/year	Study Design	Genetic disease	Measurement tool	Dental Anomalies and Dentition Alteration	Category	Reported Genetic Mutation
1.	Andrade NS et al., 2019 .	Case Report	Turner Syndrome	Clinical And Radiographic Examination	Supernumerary Teeth	Tooth number anomaly	Not specified (chromosomal monosomy X)
2.	Bussaneli DG et al.,2025	Case Report	Otodental Syndrome	Clinical And Radiographic Examination	Globodontia (Enlarged, Bulbous Molars)	Tooth size/shape anomaly	Microdeletion 11q13 (FGF3 haploinsufficiency)
3.	Limeres J et al., 2020	Cross-sectional study	Wolf-Hirschhorn Syndrome	Genetic Testing, Clinical Examination	Delayed Eruption, Microdontia, Peg-Shaped Teeth, Fused Teeth, Agenesis	Tooth size/shape anomalies; tooth number anomalies; growth and eruption alteration	Deletion 4p16.3 involving MSX1
4.	Möhlhenrich et al., 2023	Retrospective study	Down Syndrome	Clinical Records	Tooth Agenesis, Delayed Eruption	Tooth number anomaly; growth and eruption alteration; dentition pattern	Trisomy 21
5.	Memis S et al., 2021	Case Report	Wilson's Disease	Clinical And Radiographic Examination	Multiple Dens Invaginatus	Tooth shape anomalies	ATP7B mutation (copper metabolism defect)

6.	Youssef MJ et al 2019.	Case Report Series	PHACE Syndrome.	Clinical And Radiographic Examination	Root Abnormalities (Multiple, Abnormal Morphology)	Dental root abnormalities	Not specified
7.	Matsuno et al., 2019	Clinical Study	Williams Syndrome.	Clinical And Cephalography Examination	Microdontia, Diastema,	Tooth size/shape anomalies; dentition pattern	7q11.23 microdeletion (ELN gene region)
8.	Kapferer-Seebacher I et al., 2020	Systematic Review	Ehlers-Danlos Syndromes	Literature Review	Enamel Hypoplasia, Dentin Anomaly	Structure/mineralization anomalies	COL1A1, COL5A1, COL5A2 mutations
9.	Kantaputra PN et al., 2018	Retrospective case-control study	Blepharocheilodontic (Bcd) Syndrome	Clinical And Radiographic Examination	Tooth Agenesis, Conical Teeth	Tooth number anomalies; tooth shape anomalies	CDH1 and CTNND1 mutations

Tabel 2. Types of Dental Anomalies Reported Across Genetic Syndromes

Category of Anomaly	Associated Syndromes	Example Manifestations	Number of Syndromes
Tooth number (supernumerary/agenesis/oligodontia)	Turner syndrome, Wolf-Hirschhorn syndrome, Down syndrome, BCD syndrome	Supernumerary teeth, agenesis, oligodontia	4
Tooth size/shape (microdontia, conical, invaginatus, globodontia)	Otodental syndrome, Wolf-Hirschhorn syndrome, Williams syndrome, Wilson's disease, BCD syndrome	Globodontia, microdontia, peg-shaped teeth, diastema, conical teeth, dens invaginatus	5
Tooth structure/mineralization	Wolf-Hirschhorn syndrome, Ehlers-Danlos syndromes	Enamel hypoplasia, dentin anomalies	2
Growth & eruption	Wolf-Hirschhorn syndrome, Down syndrome	Delayed eruption	2
Root anomalies	PHACE syndrome	Abnormal root morphology, multiple root defects	1
Dentition/occlusion pattern	Down syndrome, Williams syndrome	Malocclusion, diastema	2

DISCUSSION

Dental anomalies and dentition alterations seen in the oral cavity consistently indicate the presence of genetic disease. Although specific phenotypic manifestations differ for each genetic disease, hese features can be regarded as reliable clinical markers of underlying genetic abnormalities. Dental anomalies occur as a result of mutations in sequence of a gene or a group of genes. This condition happen because of the change to the expression or function of the encoded protein(s).[6] In general, these manifestations are related to tooth size, morphology, eruption sequence, and disruption of developmental molecular signaling pathways. More than 300 genes have been implicated in determining dentition characteristics.[6]

Dentition alterations involving changes in tooth number are commonly associated with presence of additional teeth (supernumerary) or absence of teeth (hypodontia/oligodontia), resulting from disturbances in the dental lamina or tooth germ during development.[5] This condition frequently observed in patients with genetic disorders. Across genetic syndromes, dental morphology anomalies (e.g., globodontia, conical/peg-shaped teeth, microdontia, dens invaginatus, and supernumerary teeth) cluster around disruptions of epithelial–mesenchymal signaling—especially Wnt/β-catenin, FGF, and EDA–NF-κB pathways, and key transcription factors of odontogenesis.[12,13]

In Turner syndrome, the occurrence of supernumerary teeth is not consistently present; however, this condition reflects the broad dental phenotype associated with chromosomal, particularly related to monosomy X that disrupt initiation of tooth development.[14] Supernumerary teeth are also frequently reported in Otodental Syndrome, although not as a defining feature such as globodontia, this manifestation indicates the pleiotropic nature of craniofacial involvement.[15] Such anomalies may be transmitted through autosomal dominant or autosomal recessive traits with incomplete penetrance or may be associated with an X chromosome.[6] Such anomalies cause by genetic disease have a corelation with overactivation of the Wnt/β-catenin pathway and persistence or hyperactivity of the dental lamina during odontogenesis.[16,17] Overactivation of epithelial Wnt/β-catenin signalling result to stabilisation of β-catenin or ablation of the Wnt inhibitor. β-catenin produces a large domed epithelial budding with mesenchymal condensation, thus expanding the expression regions of Wnt10b, Lef1, Bmp4, Msx1 and Msx2 and eventually leading to the formation of extra teeth.[16] Zhang et al indentified SHH signaling is essential for regulating tooth and oral development and human dentition. Moreover, enhanced expression of the BMP to the transforming growth factor (TGF)-beta in supernumerary tooth formation.[18] Ma et al

indentified heterozygous RUNX2 mutation in patient with supernumerary with genetic disease. This gene suggesting pathogenic mechanisms involving reactivation of the dental lamina and altered FGF signaling through RUNX2–TWIST1 interactions, which enable initiation of additional tooth buds. [19]

Hypodontia is one of the most common symptoms of genetic diseases involving tooth number such as Wolf-Hirschhorn syndrome, Down syndrome, Williams syndrome, and Blepharocheilodontic syndrome (BCD).[20,21,22,23] This study suggests a common pathophysiological mechanism affecting odontogenesis during the initiation stage. Distribution pattern of dental anomalies involving number differs across syndromes. In Wolf–Hirschhorn and Williams syndromes, hypodontia often involves the maxillary lateral incisors and premolars, suggesting certain tooth positions may be more vulnerable to chromosomal imbalance.[20,22] In Down syndrome, hypodontia generally presents with variable patterns, reflecting delayed development associated with trisomy 21.[21] In Blepharocheilodontic syndrome (BCD), hypodontia is usually linked with craniofacial clefts and ectodermal anomalies.[23]. Zeng et al stated that mutations in the same genes, usually EDA, EDAR, and EDARADD, which are involved in the same signal pathway essential for ectodermal structure development can cause tooth agenesi. Khan et al stated that mutations in paired-like homeodomain transcription factor 2 (PITX2) gene can involved in tooth development.[24] These inter-syndromic variations not only underscore the heterogeneity of odontogenic disturbances but also emphasize the diagnostic significance of numerical dental anomalies in differentiating syndromic entities.[25]

As anomalies of tooth number highlight disruptions during the initiation stage of odontogenesis, morphological anomalies, on the other hand, reflect defects emerging during the morpho-differentiation phase, thereby expanding the phenotypic spectrum of genetic syndromes. These anomalies typically arising during the tooth morpho-differentiation phase, which are frequently caused by genetic mutations. Globodontia, characterized by rounded, enlarged molars and unusual morphology, is one of the most common features of Otodental syndrome. The etiology of ODS is genetic, involving microdeletions in the chromosomes 11q13.3 and 20q13.1, mutations in the gene *FGF3* and alterations in the genes related to dental development, like the *BMP-4, MSX-1, DLA- 1* and *DLX-2* This supports the role of FGF signaling dysregulation in crown enlargement and altered morphology. This feature often considered as pathognomonic dental features highlighting a distinct dental phenotype in this rare genetic condition.[15] The occurrence of multiple dens invaginatus, caused by enamel and dentin infolding during odontogenesis, represent a rare but clinically relevant manifestation of Wilson's disease.[26] BCD is a manifestation of conical teeth and agenesis are

frequent, often associated with craniofacial clefts and ectodermal defects. CDH1/CTNND1 (cadherin–catenin complex) in BCD happen to cause conical teeth and agenesis, linking epithelial adhesion and neural crest dynamics to crown morphology.[23,17] In Wolf–Hirschhorn syndrome, deletions encompassing MSX1 (4p16.2) correlate with microdontia/peg-shaped teeth and agenesis, reflecting altered tooth-bud patterning by a homeobox factor.[20] The specific morphological changes observed in dental skeletal syndromes are determined by the genetic mutations and pathways they involve, which gives them distinct clinical significance.[26] Other morphology related anomalies regonized in Axenfeld–RiegerSyndrome such as taurodontism, enamel hyploplasia, microdontia, and conical teeth. Altough this additional morphology-related anomalies not part of the primary evidence base of this scoping review, illustrate the broader phenotypic heterogeneity of tooth morphology anomalies across genetic disorders and emphasize that shared disruptions in developmental signaling pathway. [26]

Tooth size anomalies further illustrate syndrome-specific developmental disturbances. These alterations typically arise during the process of odontogenesis and tightly regulated epithelial–mesenchymal signaling (Wnt/β-catenin, FGF, EDA/NF-κB) and key transcription/adhesion factors. Microdontia is another common anomaly, frequently observed in Williams syndrome, typically affecting the incisors.[22] The alteration in tooth size, consistent with craniofacial growth patterns in Williams syndrome, underscores the role of chromosomal microdeletions in tooth morphogenesis.[22] In Ehlers–Danlos syndrome (EDS), microdontia is often accompanied by enamel defects and generalized tooth fragility.[27] Microdontia (often with peg-shaped teeth) also occurs in Wolf–Hirschhorn syndrome when 4p deletions encompass MSX1, a homeobox factor for cusp patterning; haploinsufficiency shifts tooth-bud patterning toward reduced crown size.[20] The connective tissue disorders inherent in this syndrome extend its phenotypic manifestations to dental development. These data show that FGF dosage, chromatin regulation, and Wnt/EDA and MSX1-mediated patterning are the principal genetic routes to tooth size anomalies across syndromic contexts. These findings indicate that changes in tooth size are not random, but instead reflect specific developmental disturbances associated with each syndrome.

Beyond variations in tooth number, shape, and size, genetic syndromes also compromise the integrity of enamel and dentin, as anomalies of structure and mineralization arise from disruptions in matrix protein secretion, enzymatic processing, and mineral metabolism. In Wolf-Hirschhorn syndrome, enamel hypoplasia has been identified, suggesting that gene alterations influence the amelogenesis process, which occurs parallel with odontogenesis.[20] Enamel defects discovered in Ehlers-Danlos syndrome lead to heightened tooth fragility. This

condition is associated with underlying collagen defects, whereby dental anomalies may be regarded as orodental manifestations of systemic extracellular matrix disorders.[27] Similar to this, individuals with Blepharocheilodontic (BCD) syndrome commonly have abnormal tooth shape and enamel hypoplasia, which are indicators of disruptions in the mineralization stage of dental development.[23] Genes encoding enamel matrix proteins, extracellular matrix modifying enzymes, secretory pathway regulators, dentine matrix proteins, and enzymes required for tissue mineralization are commonly implicated in tooth structure and mineralization abnormalities in genetic diseases. Pathogenic variants in AMELX, ENAM, AMBN, ACP4, MMP20, KLK4, WDR72, FAM83H and related genes underlie many forms of amelogenesis imperfecta (AI), producing enamel hypoplasia or hypomineralisation through defective matrix secretion, altered proteolytic processing of enamel proteins, or disrupted ameloblast secretory function.[19] The patterns observed across these three syndromes highlight that anomalies of structure and mineralization are often interconnected within a developmental spectrum, reflecting genetic disruptions that simultaneously affect morphogenesis and amelogenesis. In addition to these syndromic findings, Angelman syndrome demonstrates hypoplastic enamel with altered protein composition in both deciduous and permanent teeth, showing that even neurodevelopmental disorders can influence enamel mineralization.[28] These additional examples, while not part of our primary evidence base, highlight that mineralization anomalies arise not only from extracellular matrix defects but also from systemic metabolic and neurogenetic disturbances, broadening the clinical framework for interpretation.

Abnormalities in tooth eruption and growth are also well established in genetic syndromes. In Down syndrome, delayed eruption of both primary and permanent dentition is common, accompanied by craniofacial growth restriction and malocclusion. As a reflection of the wider developmental problems linked to Down syndrome, delayed eruption of both primary and permanent teeth is a typical observation in the syndrome, frequently accompanied by limited craniofacial growth and malocclusion.[21] Similarly, patients with Wolf-Hirschhorn syndrome commonly have delayed tooth eruption and enamel hypoplasia, indicating that the genetic alterations producing the disorder interfere with both odontogenesis and the timing of dental development.[20] Heterozygous variants in PTH1R are a well-established cause of primary failure of eruption (PFE), producing localized failure of eruption despite an unobstructed eruption path — likely via impaired PTHrP/PTH1R signalling in dental follicle cells that disrupts osteoclast recruitment and cementum/periodontal attachment formation.[29] These results imply that eruption problems are a systemic developmental disruption associated with specific genetic illnesses rather than being sporadic.

Root anomalies, though less frequently reported than other categories, are clinically significant. In PHACE syndrome, root abnormalities such as multiple roots with irregular morphology have been described, representing a rare but characteristic phenotype.[30] A recent case series (2019) documented bilateral absence or severe malformation of the roots of the permanent first molars in children with PHACE syndrome, reinforcing the diagnostic value of radicular anomalies.[30] These anomalies may reflect disruptions in Hertwig's epithelial root sheath (HERS) signaling, involving pathways such as Wnt/β-catenin—where fine control is essential for root elongation—and SHH, both crucial for root patterning and elongation.[18] Vascular anomalies intrinsic to PHACE syndrome may further impair local odontogenic signaling, resulting in atypical root morphology. Although evidence remains limited to small case series, the presence of root anomalies underscores the diagnostic significance of radicular morphology in genetic syndromes.

CONCLUSION

Dental anomalies and dentition alterations contribute a significant phenotypic component in many genetic syndromes. Each syndrome exhibits distinct dental patterns reflecting syndrome-specific disruptions in odontogenesis. These variations correlate with alterations in key developmental pathways, including Wnt/β-catenin, SHH, FGF, and adhesion molecule signaling, thereby highlighting genotype–phenotype associations. Their recognition, alongside genetic testing, can improve diagnostic accuracy and promote comprehensive interdisciplinary management. Future research should aim to refine genotype–phenotype mapping and clarify molecular mechanisms underlying dental anomalies, with the goal of optimizing precision medicine and multidisciplinary interventions in affected individuals.

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