

Review

Decoding the Orofacial Phenotype of Mucopolysaccharidosis: From Clinical Features to Dental Implications—A Narrative Review

Denis Clay Lopes dos Santos ¹, Ana Cristina Borges-Oliveira ² , Mateus Ferreira Lopes ² , Matheus Cezário ¹ , Carlos José de Paula Silva ², Sérgio Lúcio Pereira de Castro Lopes ³  and Andre Luiz Ferreira Costa ^{4,5,*} 

¹ Department of Dentistry, Cruzeiro do Sul University (UNICSUL), São Paulo 01506-000, Brazil; dclay@cruzeirosul.edu.br (D.C.L.d.S.); matheuscezario5@gmail.com (M.C.)

² Department of Social and Preventive Dentistry, School of Dentistry, Universidade Federal de Minas Gerais, Belo Horizonte 31270-901, Brazil; anacboliveira@ufmg.br (A.C.B.-O.); flwmateus@gmail.com (M.F.L.); caseodo@ufmg.br (C.J.d.P.S.)

³ Department of Diagnosis and Surgery, The Institute of Sciences and Technology, São Paulo State University (UNESP), São José dos Campos 12245-000, Brazil; sergio.lopes@unesp.br

⁴ Postgraduate Program in Dentistry, Dentomaxillofacial Radiology and Imaging Laboratory, Cruzeiro do Sul University (UNICSUL), São Paulo 01506-000, Brazil

⁵ Department of Anesthesiology, Oncology and Radiology, Faculty of Medical Sciences, University of Campinas (UNICAMP), Campinas 13083-887, Brazil

* Correspondence: alfcosta@unicamp.br

Abstract

Mucopolysaccharidoses (MPSs) are rare inherited lysosomal storage disorders in which impaired glycosaminoglycan degradation triggers a complex cascade of cellular and tissue changes with multisystemic consequences. The craniofacial complex is frequently involved, yet oral and maxillofacial abnormalities are often described as isolated findings rather than interconnected expressions of the disease. This narrative review explores the orofacial phenotype of MPSs as the result of both developmental disturbances and progressive tissue remodeling. Current evidence on craniofacial growth, temporomandibular joint involvement, dental development, eruption disturbances, follicular changes, malocclusion, and soft-tissue abnormalities is integrated with emerging concepts of MPS pathogenesis. Particular attention is given to distinguishing developmental changes, such as enamel defects and altered tooth morphology, from progressive manifestations, including condylar resorption, skeletal remodeling, and functional limitation. Imaging findings are considered not only as diagnostic features but also as potential markers of phenotypic evolution and disease burden. Orofacial involvement may have consequences extending well beyond morphology, affecting mastication, swallowing, speech, airway function, oral hygiene, and oral-health-related quality of life. Moreover, the persistence of some craniofacial abnormalities despite disease-modifying therapies highlights possible differences in tissue-specific treatment response and reinforces the importance of long-term follow-up. By connecting pathogenesis, phenotype, imaging, and function, the craniofacial complex emerges as a clinically accessible window into the broader course of MPS. Recognizing these relationships may support earlier identification of orofacial involvement, more meaningful longitudinal monitoring, individualized dental management, and closer integration of dental professionals into multidisciplinary care.



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1. Introduction

Mucopolysaccharidoses (MPSs) comprise a heterogeneous group of rare inherited lysosomal storage disorders caused by deficiencies in enzymes involved in the degradation of glycosaminoglycans (GAGs) [1–5]. Most MPS types follow an autosomal recessive inheritance pattern, with the exception of MPS II (Hunter syndrome), which is inherited as an X-linked recessive disorder [6]. The occurrence of MPS varies considerably across populations, with combined rates reported in different countries generally ranging from 1.53 to 4.8 cases per 100,000 live births. In the United States, a nationwide analysis estimated an incidence of 0.98 per 100,000 live births and a prevalence of 2.67 per million individuals [7]. In Brazil, an analysis covering births between 1994 and 2018 estimated an overall birth prevalence of 1.57 per 100,000 live births, with MPS II emerging as the most frequent subtype [6].

Consequently, partially degraded GAGs progressively accumulate within lysosomes, disrupting cellular homeostasis and ultimately affecting multiple organs and tissues. Although the underlying enzymatic defect differs among MPS subtypes, the diseases share a chronic and progressive course, with skeletal, cardiovascular, respiratory, neurological, and connective-tissue involvement of variable severity [4,5]. At the molecular level, MPSs comprise a group of monogenic disorders involving deficiencies in lysosomal enzymes that normally act sequentially during GAG degradation. Therefore, the specific enzymatic defect determines which substrates accumulate and contributes to the considerable clinical heterogeneity observed across MPS types and even among individuals with the same subtype [1,2].

More recently, the pathogenesis of MPS is now understood to extend well beyond the simple physical accumulation of undegraded material within lysosomes [3]. GAGs are biologically active molecules that are not only involved in extracellular matrix organization, but also in cell adhesion, growth, proliferation, tissue repair, and the modulation of signaling molecules [3–5,8]. Likewise, lysosomes are no longer regarded merely as cellular recycling compartments, but as dynamic regulators of metabolism, autophagy, membrane trafficking, nutrient sensing, and intracellular signaling. Consequently, disruption of GAG degradation can initiate a much broader cascade of cellular dysfunction [3].

This cascade includes secondary substrate accumulation, altered membrane composition and vesicular trafficking, impaired autophagy, mitochondrial dysfunction, oxidative stress, inflammatory activation, and dysregulation of intracellular signaling pathways [1,3]. These mechanisms help explain why a single lysosomal enzyme deficiency can ultimately produce such widespread and apparently diverse clinical manifestations. They are particularly relevant to the skeletal system, where abnormal GAG accumulation may interfere with extracellular matrix organization, collagen homeostasis, autophagy, and signaling pathways involved in chondrocyte differentiation and bone formation [3].

Within this broader biological context, the craniofacial complex represents a particularly informative site of disease expression [9,10]. Bone, cartilage, teeth, periodontal structures, dental follicles, and oral soft tissues are exposed to the same metabolic disturbance, but may respond differently according to their developmental origin, composition, and capacity for remodeling [5,10]. The resulting orofacial phenotype may therefore be viewed not simply as a collection of associated abnormalities, but as the visible expression of an underlying and evolving disturbance in tissue development, maintenance, and remodeling [10,11].

This biological diversity is reflected in the wide range of oral and maxillofacial findings described in patients with MPS. Dental development may be affected at several levels, including tooth morphology, eruption, enamel and dentin structure, and the tissues surrounding unerupted teeth. Guven et al. demonstrated that these changes may extend

beyond clinically visible abnormalities, identifying alterations in enamel organization, the enamel–dentin junction, dentinal tubules, and the protein composition of dental hard tissues in MPS I [11]. In a broader clinical cohort, James et al. also showed that oral health needs and developmental dental abnormalities vary considerably among MPS subtypes, highlighting the heterogeneous nature of dental involvement [12]. At the skeletal level, craniofacial involvement may continue to evolve over time, particularly in the jaws and temporomandibular joints. Such progression is biologically plausible, as experimental evidence has linked GAG accumulation to inflammatory signaling, cartilage degradation, and altered osteoclast activity, mechanisms capable of contributing to continuing bone and joint remodeling [13].

Although these manifestations have been recognized for decades, the evidence has developed in a fragmented manner. Much of the earlier dental and maxillofacial literature consists of case reports and studies with small patient samples, frequently centered on individual MPS subtypes or particular abnormalities [12,14]. Cavaleiro et al., for example, emphasized both the limited sample sizes of previous studies and their reliance predominantly on conventional radiographic examinations [14]. More recently, systematic synthesis has provided a broader picture of the frequency and distribution of orofacial abnormalities across MPS subtypes [5]. Nevertheless, less attention has been given to understanding how these apparently separate findings relate to one another over the course of the disease, from disturbances established during craniofacial and dental development to changes that may continue through progressive tissue remodeling.

Against this background, there is value in moving beyond a descriptive inventory of orofacial abnormalities and considering the craniofacial complex as a dynamic expression of MPS. This narrative review therefore brings together evidence on disease pathogenesis, craniofacial growth, dental development, temporomandibular joint involvement, imaging, and functional consequences to explore the orofacial phenotype from an integrated perspective. Particular attention is given to the distinction between developmental disturbances and progressive changes, and to how both may influence function and dental care. By connecting findings that have often been discussed separately, this review seeks to provide a clinically meaningful framework for interpreting orofacial involvement and its potential role in longitudinal assessment and multidisciplinary management.

Given its narrative design, the literature was selected according to its relevance to the main themes addressed, including MPS pathogenesis, craniofacial and dental manifestations, imaging findings, functional consequences, and dental implications. No formal systematic search strategy or predefined study-selection protocol was applied.

2. Clinical Spectrum and Classification of Mucopolysaccharidoses

Despite their genetic and biochemical heterogeneity, MPSs share a recognizable multi-systemic clinical spectrum. Common manifestations include coarse facial features, skeletal abnormalities, short stature, joint involvement, hepatosplenomegaly, cardiac and valvular disease, respiratory impairment, hearing loss, ocular abnormalities, and, in some forms, progressive neurological involvement. Their combination, severity, and timing vary considerably, and certain features may provide important clues to the underlying MPS type [15].

Some of these differences are particularly informative clinically. Neurological and behavioral deterioration is a prominent feature of MPS III, whereas MPS IV is distinguished by marked skeletal dysplasia and joint abnormalities with relatively preserved cognitive function. MPS VI is predominantly characterized by progressive somatic and skeletal involvement, while hydrops fetalis is a distinctive manifestation of MPS VII. The exceptionally rare MPS IX has a predominantly articular and periarticular phenotype. These patterns

should not be regarded as isolated diagnostic signs, but rather as different expressions within an overlapping and heterogeneous disease spectrum [15].

From a classification perspective, MPSs comprise seven major types (MPS I, II, III, IV, VI, VII, and IX) defined primarily by the underlying enzymatic deficiency, with further subdivisions within MPS III and IV [5]. These disorders are also represented within the International Classification of Diseases; for example, MPS I (Hurler syndrome) is designated E76.01 in the ICD-10-CM terminology [16].

3. The Craniofacial Skeleton as a Target of Progressive Disease

Craniofacial abnormalities are observed across several MPS subtypes and may involve both facial morphology and the maxillomandibular skeleton [17–19]. A tendency toward vertical facial growth, midfacial hypoplasia, high-arched palate, maxillary constriction, mandibular abnormalities, and altered condylar morphology has been repeatedly described [5,8–10,19,20]. These structural changes are not merely morphological findings; they can modify occlusion, mastication, speech, airway dimensions, and mandibular function [5].

Among these changes, involvement of the mandibular condyle deserves particular attention. Earlier reports frequently described the condyles of patients with MPS as “hypoplastic” or “flattened”. More recent evidence, however, suggests that at least part of this appearance may represent progressive condylar resorption rather than a purely developmental abnormality [8–10,18]. Schmid-Herrmann et al. [18] demonstrated marked differences in condylar involvement among MPS subtypes, with pronounced bilateral degenerative resorption particularly evident in MPS I and VI.

This distinction is important. If the abnormal condyle represented only developmental hypoplasia, its morphology would essentially reflect an alteration established during growth. Progressive resorption, in contrast, implies an evolving process that may continue to modify mandibular morphology and function over time [18]. In affected patients, loss of condylar convexity may progress to flattening, concavity, and partial or extensive destruction of the condylar head [9,10,18].

Developmental and skeletal abnormalities may also coexist with disturbances in dental maturation. As illustrated in Figure 1, panoramic radiography may reveal this broader dentomaxillofacial phenotype, with bilateral condylar underdevelopment and enlargement of the mandibular notches occurring together with a marked delay in the development and eruption of the permanent dentition relative to chronological age.



Figure 1. Panoramic radiographic features of dentomaxillofacial involvement in mucopolysaccharidosis (MPS). Representative panoramic radiograph illustrating delayed development and eruption of the permanent dentition, bilateral enlargement of the mandibular notches, and underdevelopment of the mandibular condyles.

The clinical consequences extend beyond the radiographic appearance. Progressive condylar changes can contribute to vertical facial growth, mandibular retrusion, anterior open bite, limited mouth opening, and impaired masticatory function. Moreover, the severity and expression of craniofacial involvement may vary both among MPS subtypes and among individuals with the same condition, reinforcing the heterogeneous nature of the orofacial phenotype [10]. This variability is illustrated in Figure 2, which shows representative craniofacial phenotypes in patients with MPS VI.



Figure 2. Representative craniofacial features associated with mucopolysaccharidosis type VI (MPS VI). Clinical photographs illustrating variations in facial proportions, frontal prominence, depressed nasal bridge, thickened lips, and coarse facial appearance. These features reflect the heterogeneous expression of craniofacial involvement in MPS VI.

This relationship is particularly evident in MPS VI. Kantaputra et al. [8] reported hypoplastic mandibular condyles in 93.3% of patients with MPS VI, together with anterior open bite in 86.7%, large dental follicles in 92.3%, and malposition of unerupted teeth in 92.9%. The authors proposed that abnormal accumulation of dermatan sulfate may interfere with cartilage development and with signaling pathways involved in skeletal growth, providing a biological explanation for the vulnerability of the condylar region.

Almeida-Barros et al. further demonstrated that condylar changes have measurable functional consequences. In patients with MPS IVA and VI, 88.2% showed condylar flattening and all presented condylar hypomobility. Patients with MPS VI had more pronounced limitations in mouth opening and mandibular movements, in addition to a greater frequency of condylar hypoplasia [10].

Thus, the temporomandibular joint (TMJ) may represent one of the clearest examples of how metabolic storage translates into structural damage and ultimately into functional impairment [19].

4. Dentition as a Record of Altered Development

The teeth provide another perspective on the biological effects of MPS. Unlike many soft-tissue manifestations, dental abnormalities may preserve evidence of disturbances that occurred during specific stages of odontogenesis. When viewed within the conventional classification of dental anomalies, the MPS phenotype spans multiple developmental

categories, including abnormalities of tooth number, morphology, structure, eruption, and position [5,17]. Rather than occurring independently, however, these alterations may represent interconnected expressions of the underlying metabolic disturbance. Changes in tooth number and morphology, root development, enamel formation, eruption, and dental follicle morphology have all been reported across MPS subtypes [5,10,17].

In a controlled panoramic radiographic study, Carneiro et al. [17] found significantly higher frequencies of supernumerary teeth, conoid teeth, taurodontism, impacted teeth, partially and completely bone-covered teeth, and root dilaceration in individuals with MPS than in individuals without the disease. Together with other imaging studies demonstrating concomitant dental and craniofacial abnormalities, this pattern suggests that MPS affects several stages and components of dentomaxillofacial development rather than producing a single characteristic dental anomaly [17,20].

Taurodontism is particularly recurrent. Sarmiento et al. [9] identified taurodontism in patients with MPS I, IV, and VI, together with a high frequency of tooth impaction and enlarged cyst-like dental crypts. These findings reinforce the possibility that altered GAG metabolism may interfere with odontogenesis and the surrounding tissues responsible for tooth eruption.

Enamel provides an even more specific example of this relationship. Enamel hypoplasia has been strongly associated with MPS IVA. Almeida-Barros et al. [8] observed enamel hypoplasia exclusively among patients with MPS IVA in their comparison with MPS VI. The proposed mechanism involves GALNS deficiency and pathological accumulation of keratan sulfate and chondroitin-6-sulfate within ameloblasts during the secretory stage of amelogenesis, potentially disturbing enamel formation and the enamel–dentin interface [18]. Clinically, these developmental disturbances may result in a heterogeneous dental phenotype, with variations in tooth morphology, enamel appearance, positioning, and eruption [9,10,17], as illustrated in Figure 3.



Figure 3. Clinical spectrum of dental developmental abnormalities associated with mucopolysaccharidosis (MPS). Representative intraoral photographs illustrating (A) alterations in tooth morphology and eruption, (B) variations in tooth shape and positioning, (C) dental spacing and irregular alignment, and (D,E) changes in enamel appearance and crown morphology. These findings illustrate the heterogeneous nature of dental developmental abnormalities associated with MPS.

These subtype-related differences are important because they move the interpretation of dental abnormalities beyond simple description. The dental phenotype may, at least in some circumstances, provide information about the underlying metabolic defect [6,9].

These findings show that the dental phenotype of MPS extends across several categories of developmental abnormalities rather than being defined by a single characteristic anomaly [9,10]. In clinical practice, recognizing these patterns is relevant not only for diagnosis but also because abnormalities in tooth structure, morphology, eruption, and position may influence preventive, restorative, endodontic, orthodontic, and surgical care [4,9,17,21]. The main dental and craniofacial findings reported in MPS and their potential implications for diagnosis and management are summarized in Table 1.

Table 1. Dental and orofacial manifestations of MPS: diagnostic relevance and implications for dental management.

Finding	Clinical/Radiographic Presentation	Diagnostic Relevance	Dental Implication	References
Enamel hypoplasia	Altered enamel surface/structure	Particularly associated with MPS IVA	Preventive care, caries surveillance, restorative needs	[10]
Taurodontism	Enlarged pulp chamber/apical displacement of furcation	Developmental dental marker	Endodontic complexity	[9,17]
Delayed eruption	Failure/delay of expected eruption	Common developmental disturbance	Longitudinal monitoring; orthodontic/surgical assessment	[5,17]
Impacted/malpositioned teeth	Panoramic finding	Frequent in MPS	Evaluate interference with eruption/occlusion	[8,9,17]
Enlarged pericoronal space	Enlarged follicle/cyst-like crypt	Differentiate from dentigerous cyst	Follow-up; investigate progression; surgery when indicated	[8–10]
Condylar alteration	Flattening/resorption/hypoplasia	Progressive skeletal involvement	Assess mouth opening, occlusion, and TMJ function	[8,10,18]
Macroglossia/anterior open bite	Clinical examination	Functional phenotype	Mastication, swallowing, airway, and treatment access	[5,8,10,21–23]

5. Dental Follicles and Eruption: An Overlooked Component of the Phenotype

One of the most distinctive radiographic expressions of MPS involves the developing dentition and its surrounding follicular tissues [6–9]. Enlarged pericoronal spaces, delayed eruption, altered positioning of unerupted teeth, and disturbances in root development may coexist, producing a complex radiographic phenotype [6–9]. Pericoronal alterations have been variably described as enlarged dental follicles, cyst-like dental crypts, or dentigerous cysts, which has created some inconsistency in the literature [8–10].

Sarmiento et al. [7] found enlarged cyst-like dental crypts in 75% of their series, including all patients with MPS VI, while tooth impaction occurred in approximately two-thirds of the sample. Similarly, Kantaputra et al. [8] reported large dental follicles and malposition of unerupted teeth in more than 90% of their MPS VI cohort. Beyond individual abnormalities, panoramic imaging can provide an integrated view of dental maturation and eruption, allowing comparison between the expected stage of development and the patient's chronological age. This is illustrated in Figure 1, in which a 13-year-old patient demonstrates a marked delay in the development and eruption of the permanent dentition.

When considered together with the associated mandibular and condylar abnormalities, this finding reinforces the concept that the radiographic phenotype of MPS may simultaneously reflect disturbances in dental development and craniofacial growth [7–9,12].

From a diagnostic perspective, an enlarged pericoronal space should not automatically be interpreted as a dentigerous cyst [8,9]. The literature has used different terms to describe these findings, including enlarged dental follicles, cyst-like dental crypts, and hyperplastic follicles compatible with dentigerous cysts [9,10]. This distinction is relevant because radiographic enlargement alone does not establish true cystic transformation. Nevertheless, histopathologically confirmed dentigerous cyst formation has been reported in MPS VI following surgical enucleation of an enlarged coronal follicle, suggesting that true cystic change may occur in at least some cases [8].

Taken together, these observations suggest a possible biological continuum in which altered GAG metabolism affects the follicular environment, potentially contributing to follicular enlargement, disturbances in tooth eruption and positioning, and, in selected cases, lesions with cystic features [8–10]. Although this sequence remains hypothetical, it provides a plausible framework for understanding why these radiographic findings frequently coexist in patients with MPS [8–10].

6. From Morphology to Function

Perhaps the most clinically meaningful way to interpret the orofacial phenotype is through its functional consequences. Macroglossia, maxillary constriction, altered mandibular growth, condylar degeneration, open bite, tooth impaction, and restricted mandibular movement may coexist and together contribute to functional impairment [8,10,18,19,21].

The systematic review by de Bode et al. [5] showed that condylar defects were among the most frequently reported mandibular abnormalities and that limited mouth opening occurred in approximately one-fifth of reported patients. Macroglossia, gingival enlargement, dental follicle abnormalities, enamel defects, impacted teeth, delayed eruption, and anterior open bite were also repeatedly documented across MPS subtypes.

The functional burden can be substantial [22,23]. Changed mandibular mobility and open bite may compromise mastication and swallowing [10,22], while macroglossia and reduced nasopharyngeal dimensions may contribute to respiratory impairment [21–24]. The combination of craniofacial skeletal abnormalities and soft-tissue enlargement may therefore affect airway, mastication, swallowing, speech, and oral hygiene simultaneously [21–23]. In more severely affected individuals, these limitations may also directly influence how oral examination and dental treatment can be performed, requiring adaptations in patient positioning, access to the oral cavity, and respiratory support [4,22,23] (Figure 4).

These consequences are reflected in patient-centered outcomes. Deps et al. [22] demonstrated that young individuals with MPS had a significantly greater negative impact on oral health-related quality of life than matched individuals without MPS. Particularly, malocclusion was associated with worse oral symptoms, functional limitations, wellbeing, and overall OHRQoL (Oral Health-Related Quality of Life).

This observation is important because it shifts the interpretation of malocclusion from an essentially morphological or orthodontic finding to a component of disease burden [22]. Open bite and deficient posterior occlusion can interfere with chewing and swallowing, while altered phonation and facial appearance may affect communication and social interaction [21,22].



Figure 4. Representative orofacial manifestations and challenges in dental care associated with mucopolysaccharidosis (MPS). Clinical photographs illustrating (A) anterior open bite and altered dental alignment, (B) macroglossia and restricted access to the oral cavity, (C) adapted positioning during dental examination to facilitate clinical access, and (D) the use of respiratory support during dental treatment. These illustrations highlight the functional limitations and challenges that may arise during dental care in individuals with MPS.

7. The Oral Cavity as a Window into Disease Expression

The orofacial manifestations of MPS do not follow a uniform pattern. In a recent cohort of 102 pediatric patients, Wang et al. [24] demonstrated significant differences in dental anomalies according to MPS type, with the highest prevalence observed in MPS IV and a more than sixfold greater likelihood of these abnormalities compared with MPS II after adjustment for age and sex. Developmental, morphological, positional, radicular, osseous, and follicular changes also showed distinct distributions, suggesting that the oral presentation may reflect, at least in part, the biological heterogeneity underlying these disorders [8,10,24].

An equally relevant question is whether disease-modifying therapies can influence the course of these manifestations. Available data remain limited and do not point to a uniform response. Kantaputra et al. [8] reported that two patients with MPS VI who started enzyme replacement therapy before three years of age did not develop anterior open bite. In contrast, marked condylar involvement has been documented in MPS I despite enzyme replacement therapy or hematopoietic stem-cell transplantation [18]. These observations suggest that craniofacial tissues may differ in their response to systemic therapy, with some abnormalities arising early during development while others may continue to evolve over time.

This distinction opens a relevant direction for future research. Rather than continuing to catalogue isolated oral abnormalities, longitudinal studies should clarify which manifestations emerge early, which remain stable, and which progress despite systemic treatment. A better understanding of these trajectories could help determine when dental surveillance and intervention may have the greatest impact. In this context, oral assessment

becomes more than the documentation of disease-related changes; it offers an opportunity to recognize clinically meaningful patterns, anticipate functional consequences, and integrate dental care more effectively into the long-term management of individuals with MPS [23,24].

In terms of clinical management, disease-modifying treatment and preventive oral care should be considered complementary components of MPS management [4,23]. Enzyme replacement therapy (ERT) is an important therapeutic approach for several MPS types, while hematopoietic stem-cell transplantation (HSCT) may be considered in selected patients according to MPS type and clinical presentation [4,18]. Although these therapies may improve systemic manifestations, their effects on established craniofacial and dental abnormalities appear less predictable, reinforcing the need for continued dental follow-up [8,18]. Preventive care should begin early and include regular clinical examinations, individualized oral hygiene guidance, and surveillance for caries, periodontal disease, and developmental dental abnormalities [4,23]. Particular attention should be given to eruption disturbances and other abnormalities that may require timely dental intervention [4,17,23]. Radiographic monitoring may be particularly useful when delayed eruption, impacted or malpositioned teeth, enlarged dental follicles, or skeletal changes are present [6–9]. Close coordination between dental professionals and the multidisciplinary medical team is essential, as the multisystemic nature of MPS and associated respiratory, skeletal, and functional limitations may influence both treatment planning and the safe delivery of dental care [4,5,23].

8. Limitations

Some limitations should be considered when interpreting this review. Its narrative design did not involve a systematic search or predefined criteria for study selection, which may have influenced the literature included. The evidence on orofacial involvement in MPS is also heterogeneous, reflecting the rarity of these disorders and the predominance of case reports and studies with relatively small samples. Differences in MPS subtypes, patient age, imaging approaches, and clinical outcomes further make comparisons across studies difficult. As a result, the available data do not yet allow definitive conclusions regarding the frequency, progression, or subtype-specific expression of several orofacial manifestations. At the same time, bringing these findings together helps identify consistent patterns and, importantly, areas that remain poorly understood. Future longitudinal studies involving larger cohorts and more standardized clinical and imaging assessments may provide a clearer picture of how the orofacial phenotype develops and changes over time.

9. Conclusions

The orofacial phenotype of MPS is best understood as a recognizable combination of craniofacial, dental, skeletal, and soft-tissue abnormalities rather than as a single defining feature. Coarse facial appearance altered craniofacial growth, maxillary constriction, mandibular and condylar abnormalities, macroglossia, malocclusion, delayed or disturbed tooth eruption, impacted or malpositioned teeth, enlarged dental follicles, and taurodontism, and enamel abnormalities may occur in different combinations and evolve throughout growth. No single orofacial manifestation can be considered pathognomonic for MPS, and the considerable overlap among phenotypes means that the specific MPS type cannot be reliably determined from craniofacial, dental, or imaging findings alone. Nevertheless, the coexistence of several unusual findings, particularly in young children, may provide an important clue to an underlying systemic disorder.

This places dentists in a valuable position for early recognition. During routine dental care, abnormalities in facial development, tooth morphology, eruption, occlusion, or jaw

development may become apparent before the underlying disorder has been diagnosed. In this setting, the dentist's role is not to establish the definitive diagnosis or MPS subtype, but rather to recognize an unusual pattern and recommend appropriate medical and genetic evaluation. Following diagnosis, early preventive dental care, longitudinal clinical and imaging surveillance, and close multidisciplinary collaboration are essential to preserve oral health and function as the disease evolves.

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References

1. Kobayashi, H. Recent trends in mucopolysaccharidosis research. *J. Hum. Genet.* **2019**, *64*, 127–137. [[CrossRef](#)] [[PubMed](#)]
2. Zanetti, A.; D'Avanzo, F.; Rigon, L.; Rampazzo, A.; Concolino, D.; Barone, R.; Volpi, N.; Santoro, L.; Lualdi, S.; Bertola, F.; et al. Molecular diagnosis of patients affected by mucopolysaccharidosis: A multicenter study. *Eur. J. Pediatr.* **2019**, *178*, 739–753. [[CrossRef](#)] [[PubMed](#)]
3. Fecarotta, S.; Tarallo, A.; Damiano, C.; Minopoli, N.; Parenti, G. Pathogenesis of mucopolysaccharidoses, an update. *Int. J. Mol. Sci.* **2020**, *21*, 2515. [[CrossRef](#)] [[PubMed](#)]
4. Hirst, L.; Mubeen, S.; Abou-Ameira, G.; Chakrapani, A. Mucopolysaccharidosis (MPS): Review of the literature and case series of five pediatric dental patients. *Clin. Case Rep.* **2021**, *9*, 1704–1710. [[CrossRef](#)] [[PubMed](#)]
5. de Bode, C.J.; Dogterom, E.J.; Rozeboom, A.V.J.; Langendonk, J.J.; Wolvius, E.B.; van der Ploeg, A.T.; Oussoren, E.; Wagenmakers, M.A.E.M. Orofacial abnormalities in mucopolysaccharidosis and mucopolipidosis type II and III: A systematic review. *JIMD Rep.* **2022**, *63*, 621–629. [[CrossRef](#)] [[PubMed](#)]
6. Puckett, Y.; Mallorga-Hernández, A.; Montaña, A.M. Epidemiology of mucopolysaccharidoses (MPS) in United States: Challenges and opportunities. *Orphanet J. Rare Dis.* **2021**, *16*, 241. [[CrossRef](#)] [[PubMed](#)]
7. Josahkian, J.A.; Trapp, F.B.; Burin, M.G.; Michelin-Tirelli, K.; de Magalhães, A.P.P.S.; Sebastião, F.M.; Bender, F.; De Mari, J.F.; Brusius-Facchin, A.C.; Leistner-Segal, S.; et al. Updated birth prevalence and relative frequency of mucopolysaccharidoses across Brazilian regions. *Genet. Mol. Biol.* **2021**, *44*, e20200138. [[CrossRef](#)] [[PubMed](#)]
8. Kantaputra, P.N.; Kayserili, H.; Güven, Y.; Kantaputra, W.; Balci, M.C.; Tanpaiboon, P.; Uttarilli, A.; Dalal, A. Oral manifestations of 17 patients affected with mucopolysaccharidosis type VI. *J. Inher. Metab. Dis.* **2014**, *37*, 263–268. [[CrossRef](#)] [[PubMed](#)]
9. Sarmiento, D.J.; de Carvalho, S.H.G.; Melo, S.L.S.; Fonseca, F.R.A.; Diniz, D.N.; Bento, P.M.; Mesquita, G.Q.T.B.; de Melo, D.P. Mucopolysaccharidosis: Radiographic findings in a series of 16 cases. *Oral Surg. Oral Med. Oral Pathol. Oral Radiol.* **2015**, *120*, e240–e246. [[CrossRef](#)] [[PubMed](#)]
10. Almeida-Barros, R.Q.; de Medeiros, P.F.V.; de Almeida Azevedo, M.Q.; Ortega, A.O.L.; Yamamoto, A.T.A.; Dornelas, S.K.L.; Bento, P.M. Evaluation of oral manifestations of patients with mucopolysaccharidosis IV and VI: Clinical and imaging study. *Clin. Oral Investig.* **2018**, *22*, 201–208. [[CrossRef](#)] [[PubMed](#)]
11. Guven, G.; Cehreli, Z.C.; Altun, C.; Sencimen, M.; Ide, S.; Bayari, S.H.; Karacay, S. Mucopolysaccharidosis type I (Hurler syndrome): Oral and radiographic findings and ultrastructural/chemical features of enamel and dentin. *Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endod.* **2008**, *105*, 72–78. [[CrossRef](#)] [[PubMed](#)]

12. James, A.; Hendriksz, C.J.; Addison, O. The oral health needs of children, adolescents and young adults affected by a mucopolysaccharide disorder. *JIMD Rep.* **2012**, *2*, 51–58. [[CrossRef](#)] [[PubMed](#)]
13. Simonaro, C.M.; D'Angelo, M.; He, X.; Eliyahu, E.; Shtraizent, N.; Haskins, M.E.; Schuchman, E.H. Mechanism of glycosaminoglycan-mediated bone and joint disease: Implications for the mucopolysaccharidoses and other connective tissue diseases. *Am. J. Pathol.* **2008**, *172*, 112–122. [[CrossRef](#)] [[PubMed](#)]
14. dos Santos Cavaleiro, R.M.; Pinheiro, M.D.G.R.; Pinheiro, L.R.; Tuji, F.M.; Feio, P.D.S.Q.; de Souza, I.C.N.; Feio, R.H.F.; de Almeida, S.C.; Schwartz, I.V.D.; Giugliani, R.; et al. Dentomaxillofacial manifestations of mucopolysaccharidosis VI: Clinical and imaging findings from two cases, with an emphasis on the temporomandibular joint. *Oral Surg. Oral Med. Oral Pathol. Oral Radiol.* **2013**, *116*, e141–e148. [[CrossRef](#)] [[PubMed](#)]
15. Zhou, J.; Lin, J.; Leung, W.T.; Wang, L. A basic understanding of mucopolysaccharidosis: Incidence, clinical features, diagnosis, and management. *Intractable Rare Dis. Res.* **2020**, *9*, 1–9. [[CrossRef](#)] [[PubMed](#)]
16. U.S. National Library of Medicine. Newborn Screening Coding and Terminology Guide: Mucopolysaccharidosis Type I (MPS I). Newborn Screening Coding and Terminology Guide—MPS I. Available online: <https://lhncbc.nlm.nih.gov/newbornscreeningcodes/nb/sc/condition/MPS-I.html> (accessed on 17 September 2026).
17. Carneiro, N.C.R.; Abreu, L.G.; Milagres, R.M.C.; Amaral, T.M.P.; Flores-Mir, C.; Pordeus, I.A.; Borges-Oliveira, A.C. Dental and maxillomandibular incidental findings in panoramic radiography among individuals with mucopolysaccharidosis: A cross-sectional study. *J. Appl. Oral Sci.* **2021**, *29*, e20200978. [[CrossRef](#)] [[PubMed](#)]
18. Schmid-Herrmann, C.U.; Muschol, N.M.; Fuhrmann, V.U.; Koehn, A.F.; Lezius, S.; Kahl-Nieke, B.; Koehne, T. Mandibular condyle morphology among patients with mucopolysaccharidosis: An observational study of panoramic radiographs. *Int. J. Paediatr. Dent.* **2022**, *32*, 737–744. [[CrossRef](#)] [[PubMed](#)]
19. Çoğulu, D.; Uçar, S.K.; Canda, E.; Atila, E.K.; Alpöz, A.R.; Çoker, M. Orofacial manifestations in mucopolysaccharidoses: A comprehensive clinical and radiographic evaluation of 35 pediatric cases. *Head Face Med.* **2025**, *21*, 90. [[CrossRef](#)] [[PubMed](#)]
20. Torres, R.O.; Pintor, A.V.B.; Guedes, F.R.; Cevidanes, L.H.S.; Freitas-Fernandes, L.B.; Ruellas, A.C.O.; de Souza, I.P.R. Three-dimensional dental and craniofacial manifestations in patients with late diagnosis of mucopolysaccharidosis type II: Report of 2 cases. *Oral Surg. Oral Med. Oral Pathol. Oral Radiol.* **2018**, *126*, e35–e39. [[CrossRef](#)] [[PubMed](#)]
21. Loayza, K.S.; Reis-Oliveira, J.; Carneiro, N.C.R.; Angelo-Dornas, G.L.; de Abreu, M.H.N.G.; Borges-Oliveira, A.C. Analysis of orofacial changes in children and adolescents with mucopolysaccharidosis and osteogenesis imperfecta. *Cleft Palate Craniofac. J.* **2026**, *63*, 811–817. [[CrossRef](#)] [[PubMed](#)]
22. Deps, T.D.; Carneiro, N.C.R.; Nicolau, B.; Pordeus, I.A.; Borges-Oliveira, A.C. Oral health-related quality of life of young people with mucopolysaccharidosis: A paired cross-sectional study. *Braz. Oral Res.* **2020**, *34*, e109. [[CrossRef](#)] [[PubMed](#)]
23. Deps, T.D.; França, E.C.; Valadares, E.R.; Nicolau, B.; Pordeus, I.A.; Borges-Oliveira, A.C. Oral health of Brazilian individuals with mucopolysaccharidosis. *Eur. Arch. Paediatr. Dent.* **2021**, *22*, 13–19. [[CrossRef](#)] [[PubMed](#)]
24. Wang, M.; Liu, R.; Xia, T.; Wang, Y. Dental health in pediatric patients with different types of mucopolysaccharidosis: Retrospective cross-sectional study. *JMIR Pediatr. Parent.* **2026**, *9*, e87430. [[CrossRef](#)] [[PubMed](#)]

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