

Oral health status in patients with mucopolysaccharidoses

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The aim of this study is to assess oral clinical and radiological findings of patients with mucopolysaccharidoses (MPS) which are a group of rare inherited disorders of glycosaminoglycan catabolism. In this retrospective and descriptive study, records of all patients with MPS over 3 years of age managed at Division of Pediatric Metabolism, who were all referred to Department of Pediatric Dentistry for evaluation of their oral health status were assessed. Oral examinations were performed in 30 patients with determination of DMFT/S, dmft/s, dental plaque and gingival indices and panoramic radiological assessment was performed in 12 patients. Twenty-seven (90.0%) patients had dental caries and 19/21 (90.5%) had gingival inflammation. Radiological examination in 12 patients with panoramic image showed short mandibular ramus (100.0%), enlarged dental follicles (83.3%), taurodontism (75.0%), flat mandibular notch (66.7%). In association with the bone structure and morphology of the jaws, 11 patients (91.7%) had trabecular variation similar to osteoporotic disease. Condylar defect was observed in all patients, which might lead to temporomandibular joint disorders. Pulp chamber with three horns, which had never been reported in MPS before, was observed in panoramic images of 2 of 7 patients with MPS-VI. Oral clinical and radiological changes are very common in this population of MPS patients. These changes may impair opening of the mouth, eating and chewing and thus affect their quality of life. Regular dental counseling, preventive applications and dental treatments must be included in multidisciplinary team approach of MPS patients to provide better oral health.

Key words: mucopolysaccharidosis, dentistry, oral health, panoramic oral radiology.

Mucopolysaccharidoses (MPSs) are a group of heterogeneous, progressive, multisystemic lysosomal storage disorders caused by deficiencies of several lysosomal enzymes required for glycosaminoglycan (GAG) breakdown. The overall prevalence of the 7 distinct types of MPS (I, II, III, IV, VI, VII, and IX) may range from 1.9 to 4.5 per 100,000 live births, with regional variations.¹⁻⁵ It is expected to be higher in Turkey than that of the developed world due to the high rate of consanguineous marriages (25%).⁶

Although clinical findings vary with the type of MPS, main clinical features include

short stature, macrocephaly, characteristic coarse facies, umbilical and inguinal hernias, developmental delay, skeletal dysplasia with dysostosis multiplex, limited joint mobility or joint laxity, hearing loss, ocular involvement, neurodegeneration with dementia, heart disease, respiratory distress and hepatosplenomegaly.⁷⁻⁹ Therefore, a multidisciplinary treatment approach is essential for the diagnosis, treatment, and follow-up of patients with MPS.¹⁰ MPS patients also present with oral findings that can be observed clinically or radiologically. Oral features commonly reported in MPS include thick lips, anterior open bite,

gingival hyperplasia, diastemas, macroglossia, high palate and condylar defects.¹¹⁻¹⁵ A higher prevalence of dental caries, malocclusion, poor periodontal health, and delayed eruption of teeth, cystic lesions or enlargement of the dental follicle may also be present.^{12,13,16}

Patients with MPS are a challenge for dentists due to complicated mental and physical disabilities. If treatment under general anesthesia becomes necessary, oral health providers need to be aware of associated risks of anesthesia due to difficulties with airway management and comorbid multisystemic involvement, especially cardiorespiratory problems.¹⁷

Dentists may encounter patients with MPS because of orofacial findings. Greater awareness of MPS will enable early referral, diagnosis and treatment, which may improve patients' quality of life and illness outcomes, since specific treatment modalities including enzyme replacement therapy and hematopoietic stem cell transplantation are available for some types of MPS. The present study aimed to investigate the oral health status of 30 MPS patients followed in a single center.

Material and Methods

This retrospective and descriptive study was performed by the approval of the Local Ethical Committee of Non-Interventional Clinical Studies in compliance with the Helsinki Declaration (Project No: GO 17/774). We assessed the records of all patients with MPS managed at a University Hospital, Faculty of Medicine, Division of Pediatric Metabolism between January 2013 and December 2015, who were all referred to Department of Pediatric Dentistry for evaluation of their oral health status. The sample consisted of all the patients whose parents allowed them to participate in the study by signing an informed consent. MPS patients over 3 years of age with complete primary dentition were evaluated; whereas those with uncooperative behavior were excluded.

Data were obtained from interview, clinical and radiological evaluations. The parents completed an oral health questionnaire performed by two investigators for each patient at the time of the dental examinations. Questions in relation to the type of MPS, age, gender and presence of other comorbid illnesses, complaints about oral

health, tooth-brushing frequency were included in the questionnaire. Clinical evaluations were performed by one of two experienced pediatric dentists. Anterior open bite, dental caries, plaque index and gingival inflammation were noted by clinical examination. The total number

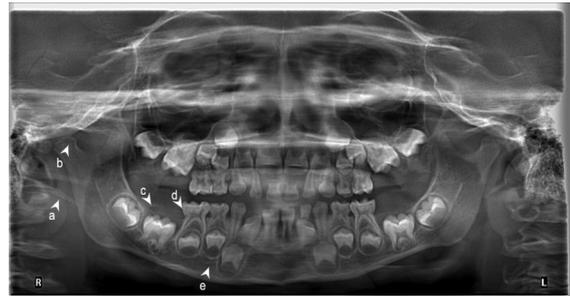


Fig. 1. Radiological findings in a patient with MPS-VI (patient no.1): malformed styloid ligament (a), (Eagle's syndrome), condylar defect (b), enlarged dental follicle (c: 46, 36, 26), pulp chamber with three horns (d: 75, 85), trabecular variation like osteoporotic bone (e).



Fig. 2. Radiological findings in a patient with MPS-VI (patient no. 7): condylar defect (a), prominent mandibular angulus (b), impacted teeth (c: 47, 48, 28, 18), root dilacerations (d: 15, 36, 46), trabecular variation like osteoporotic bone (e), ectopic teeth (f: 18, 28), taurodontism (g: 16, 26, 36, 46, 17, 27), flat mandibular notch (h).

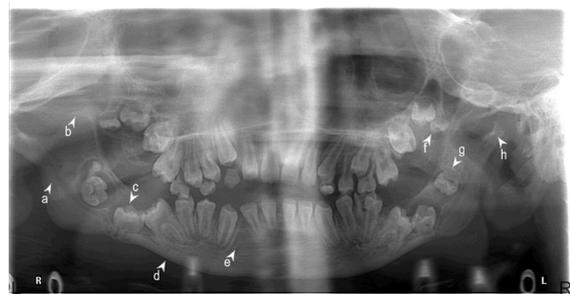


Fig. 3. Radiological findings in a patient with MPS-II (patient no.12): short mandibular ramus (a), malformed coronoid process (b), impacted teeth (c: 36, 46, 47, 37), enlarged dental follicle (c: 37, 38, 47, 48), thin mandibular inferior cortex (d), trabecular variation like osteoporotic bone (e), supernumerary and ectopic teeth (f, g), condylar defect (h).

Table I. General Characteristics of Patients with Mucopolysaccharidoses (MPS).

Characteristics (n=30)	n	%
Age, years		
4-6	11	36.7
7-11	15	50.0
14-27	4	13.3
Gender		
Female	13	43.3
Male	17	56.7
MPS type		
MPS-I	2	6.7
MPS-II	3	10.0
MPS-IIIA	4	13.3
MPS-IIIB	2	6.7
MPS-IVA	6	20.0
MPS-VI	12	40.0
MPS-VII	1	3.3
Co-morbid illnesses	23	76.7
Intellectual disability	15	50.0
Parental consanguinity	27	90.0
Sibling with MPS	13	43.3

of decayed, missing and filled teeth (DMFT/dmft) and surfaces (DMFS/dmfs) were recorded for each patient using a mirror and explorer in accordance with World Health Organization criteria and methods. Dmft/s for primary teeth, DMFT/S codes for permanent teeth are involved in. Gingival index of Silness-Löe for gingival inflammation were used.^{18,19}

Digital panoramic images were obtained by Veraview IC5 device (Morita Corporation, Japan) to help in the diagnosis and dental treatment planning. Eighteen patients could not cooperate for obtaining a panoramic image, therefore a total of 12 patients could be evaluated with panoramic images by a single experienced radiologist for the presence of root dilacerations, taurodontism, impacted teeth, enlarged dental follicle, delayed tooth eruption, diastema, pulpal obliteration, short mandibular ramus, irregular mandibular cortex, malformed coronoid process, malformed styloid ligament, condylar defect, a flat mandibular notch and trabecular variation. Delayed tooth eruption and diastema were also supported clinically. Statistical analysis was performed by using SPSS

for Windows 21.0 (IBM Corp. Released 2012. Armonk, NY: IBM Corp.). Number, percentage, mean, standard deviation, median, 1st and 3rd quartiles, minimum and maximum values were estimated for descriptive statistics. The normality of the distributions was analyzed by Shapiro-Wilk test.

Results

Table I shows the general characteristics of the patients. We evaluated 30 patients (17 males and 13 females) with the median age was 8 years (minimum-maximum: 4-27; 1st quartile 6.0 years, 3rd quartile 10 years). All patients were evaluated clinically but only 12 patients could be evaluated radiologically. It was observed that a greater number of patients had MPS-VI 40% (n=12) and parental consanguinity was present in 90% (n=27) of the patients and 43.3% had a sibling with MPS. A higher number of males (56.7%) were observed especially for MPS-II (100%) and MPS-VI (66.7%). Intellectual disability and other comorbid illnesses were recorded in 50% and 76.7% of patients, respectively. 43%

Table II. Oral Health Indices of Patients with Mucopolysaccharidoses.

Dental health indices		Gingival health indices	
dmft (n=26*)	5.50 (0.0-14.00)	Plaque index (n=21***)	1.09 (0.63-2.24)
dmfs (n=26*)	8.00 (0.0-57.00)		
DMFT (n=17**)	0.0 (0.0-4.00)	Gingival index (n=21***)	1.38 (0.03-2.43)
DMFS (n=17**)	0.0 (0.0-16.00)		

The total number of decayed, missing and filled teeth (DMFT/ dmft) and surfaces (DMFS/dmfs) were recorded. Dmft/s for primary teeth, DMFT/S codes for permanent teeth are involved in.

Data is presented as median (minimum-maximum)

*dmft/dmfs values could not be evaluated in 4 patients due to permanent dentition.

**DMFT/DMFS values could not be evaluated in 9 patients due to primary dentition.

***9 patients could not be evaluated due to uncooperative behavior. PI and GI values were evaluated only in 21 cooperative patients.

(13/30) of patients did not have a toothbrush and they stated having never brushed their teeth. Most commonly reported oral health complaints were mouth breathing (16/30) followed by tooth decay (14/30).

Clinically, 27/30 (90.0%) patients had dental caries and 19/21 (90.5%) had gingival inflammation. The quantity of plaque and gingival bleeding of 21 patients were checked clinically and were recorded using Silness and Løe plaque index (PI) and gingival index (GI). The median, minimum and maximum values of DMFT, DMFS, dmft, dmfs, PI, GI indices are presented in Table II.

Radiological examination in 12 patients with panoramic image showed short mandibular ramus (100%), condylar defect (100%), enlarged dental follicles (83.3%), taurodontism (75%), a flat mandibular notch (66.7%) (Fig.1; Fig.2). Pulp chamber with three horns were observed in primary teeth of two patients. Anterior open bite (46.7 %) was present in about half of all patients. In association with the bone structure and morphology of the jaws, 11 patients (91.7%) were observed to have trabecular variation similar to osteoporotic disease. The inferior cortex of the mandible was thinner in one patient with MPS-I, one with MPS-II and five with MPS-VI (Fig.3). Condylar defect such as abnormal morphology of condyles was observed in all patients and malformed coronoid process in 7 patients, which might lead to temporomandibular joint abnormalities.

A summary of findings from the panoramic images is presented in Table III.

Discussion

Epidemiological surveys concerning all types of MPS are still very scarce because of the low prevalence of these diseases.⁸ Data on MPS prevalence in Turkey is not available, but it is expected to be higher than that of the developed world, due to the high rate of consanguineous marriages (25%).⁶ Parental consanguinity was present in 90% (n=27) of our patients.

The more common types of MPS in different populations have shown considerable variation.³ MPS-VI was the most common type in this study, similar to the Turkish patient population living in Germany.³ Many of our patients (76.7%) had comorbid conditions such as cardiorespiratory, visual or hearing problems secondary to underlying MPS. Early diagnosis and multidisciplinary treatment approach are essential because many patients with MPS are at risk of multisystem impairment and significant morbidity, including dental problems.²⁰

In the present study, majority of the patients with MPS had serious dental caries and gingival inflammation. The literature contains mainly case reports regarding oral manifestations in patients with MPS. However, there are a few studies evaluating oral health status with plaque index, gingival index, DMFT/DMFS and radiologically.^{8,15} Ninety percent of MPS patients in this study had dental caries, which was higher than the study by James et al.¹², who reported dental caries in 50% of their MPS patients. In the present study, the average of dmft was 5.27 and the average of DMFT was 2.12, whereas James et al.¹² reported the

Table III. Radiological Findings of Patients with Mucopolysaccharidoses (MPS).

Patient*	Type of MPS	Root dilaceration	Taurodontism	Impacted teeth	Enlarged dental follicle	Delayed tooth eruption	Diastema	Short mandibular ramus	Thin mandibular inferior cortex	Malformed coronoid process	Malformed styloid ligament	Condylar defect	Flat mandibular notch	Trabecular variation
1	VI	-	-	-	+	-	+	+	+	-	+	+	-	+
2	VI	+	+	+	+	-	+	+	+	+	-	+	+	+
3	VI	+	-	+	+	+	+	+	+	+	-	+	+	+
4	VI	+	+	+	+	+	+	+	-	-	+	+	+	+
5	IVA	-	+	-	-	-	+	+	-	+	+	+	+	+
6	VII	+	+	+	+	-	+	+	-	+	-	+	+	+
7	VI	+	+	+	+	+	+	+	-	-	+	+	+	+
8	VI	-	+	-	+	-	+	+	+	+	-	+	+	+
9	IVA	-	+	-	-	-	+	+	-	-	-	+	-	-
10	VI	-	-	-	+	+	+	+	+	+	-	+	+	+
11	I	+	+	-	+	+	-	+	+	-	-	+	-	+
12	II	+	+	+	+	+	+	+	+	+	-	+	-	+

*18 patients could not cooperate for obtaining a panoramic image, therefore 12 patients could be evaluated

mean dmft as 3.21 and the mean DMFT as 1.67 in the MPS population. The family income and level of parental education, which was not assessed in our study as well discrepancy of oral health practices of patients, comorbid diseases, could be the reasons of the higher dental caries indices compared to the study by James et al.¹²

It was reported that the increase in caries in MPS patients may be associated with a decrease in salivary flow rate and more acidic pH than in controls. Salivary flow rate and salivary pH were not evaluated in our study. However, 50% of our patients have intellectual disability as well as a problem of manual dexterity and nearly half of the patients do not brush their teeth. 53.3% of the patients also complained about mouth breathing, which may have contributed to poor hygiene of the mouth and consequently, tooth decay. All these factors may explain the high prevalence of caries in our MPS patients.

The mean plaque index and gingival index (1.30±0.48, 1.22±0.65) showed moderate plaque accumulation and moderate gingival inflammation requiring regular oral hygiene and plaque removal. While 90.5% of 21 MPS patients showed gingivitis in the present study, James et al.¹² reported 43% of MPS patients exhibited gingivitis. Elanor et al.²¹ reported 17 of 25 MPS patients needed periodontal treatment requiring oral hygiene, plaque or calculus removal.

Clinically, some findings such as microdontia^{15,21,22} and presence of tooth abrasion (occlusal wear)²³, flat and wide palate²¹, high-arched palate^{13,22} enlargement of alveolar process^{13,21,22}, macroglossia^{13,21} tongue protrusion²⁴ thick lips²¹ enamel hypoplasia^{14,21,25} and gingival hyperplasia^{13,15,22-24} abnormal frenulum¹⁵ were not evaluated in the present study. However, other clinical manifestations such as anterior open-bite^{15,23}, diastemas^{15,21,22}, and delayed eruption^{13,15,24}, were observed in both present study and other studies.

All MPS patients with radiological evaluation in our study (12/12) had short mandibular ramus and condylar defect. Nakamura et al.²⁶ reported that 71% (29/41) of patients with MPS were observed with a condylar defect. With regard to radiological findings of other studies; impacted teeth^{8,27}, taurodontism^{14,15,27}, changes in coronoid process⁸, delayed dental

eruption^{8,27} and enlarged dental follicle^{8,24,27} were observed as reported in the literature. Other radiological manifestations described in the literature such as pulp obliteration^{8,14,28}, cervical constriction²¹, root shortening^{17,21}, delay in germ formation⁸, were not detected in the present study. However, trabecular variations like osteoporotic bone^{24,27}, malformed styloid ligament²¹ and mesioangular tipping of impacted teeth and root dilacerations⁸, and thin mandibular inferior cortex,^{24,27} which were observed in our study have rarely been reported in the literature.

We realized pulp chamber with three horns in primary teeth of two patients, which had not been reported previously in MPS. We observed trabecular variation (such as enlargement of bone marrow) in 91.6% of the MPS patients and thin mandibular inferior cortex in 58.3% of the patients, which was slightly more common than that observed by Sarmiento et al.²⁷ (50%). The accumulation of glycosaminoglycans in the bone tissues of the jaws leads to these features, which were previously reported in a case study.²⁴ A flat mandibular notch was present in 66.6% of our patients, in line with a report by Antunes et al.⁸

The results of this study should be interpreted with awareness of its limitations. As this was a non-representative descriptive study that enrolled the patients who visited the metabolic clinic during a certain time period, the patients may not represent the whole MPS population. Factors such as the level of parental education and family income, which can influence the child's oral health status were not evaluated in this study. Prospective cohort studies with control groups may be required to elucidate whether mucopolysaccharidoses have a causal relationship with gingival inflammation or dental caries.

Since these patients do require special care, it is essential to educate and motivate the parents as well as the patients to provide a good oral hygiene. Complex procedures requiring sedation or general anesthesia may be high-risk in MPS patients due to various anatomic and cardiorespiratory problems which makes it even more crucial to promote regular visits to the dentist. Regular dental counseling, preventive applications and dental treatment must be included in the multidisciplinary team approach of MPS patients.

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