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ORIGINAL RESEARCH

Audiological and Ophthalmological Manifestations in Patients with Mucopolysaccharidosis: A Retrospective Single-Center Study

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ABSTRACT

Mucopolysaccharidoses (MPS) are rare inherited lysosomal storage disorders caused by deficiencies of enzymes responsible for the degradation of glycosaminoglycans. Progressive accumulation of glycosaminoglycans affects multiple organ systems, including the auditory and visual systems, and may significantly impair quality of life. This study aimed to retrospectively evaluate the auditory and ophthalmologic findings of patients diagnosed with MPS and to emphasize the importance of multidisciplinary follow-up. Medical records of 45 patients diagnosed with MPS and followed at the Division of Pediatric Metabolism, Uludağ University Faculty of Medicine, between January 2010 and December 2024, were retrospectively reviewed. Demographic characteristics, MPS subtypes, and audiological and ophthalmological findings were recorded. The mean age of the patients was 13.3±5.7 years, and the mean age at diagnosis was 4.39±3.5 years. Of the patients, 55.5% were male. The most common MPS subtypes were type IVa (28.8%) and type III (24.5%). Corneal opacity was detected in 46.6% of the patients, whereas hearing impairment was present in 15.9%. These findings demonstrate that auditory and visual systems are frequently affected in patients with MPS. Early diagnosis, regular sensory system screening, and multidisciplinary management are essential to improve clinical outcomes and quality of life in these patients.

Keywords: Mucopolysaccharidosis. Hearing loss. Corneal opacity. Multidisciplinary approach.

Mukopolisakkaridoz Olgularında İşitme ve Görme Bulguları: Tek Merkez Tecrübesi

ÖZET

Mukopolisakkaridozlar (MPS), glikozaminoglikanların lizozomal yıkımından sorumlu enzimlerin eksikliği sonucu ortaya çıkan nadir kalıtsal lizozomal depo hastalıklarıdır. Glikozaminoglikanların ilerleyici birikimi birçok organ sistemini etkileyebilir ve özellikle işitme ve görme sistemlerinin tutulumu hastaların yaşam kalitesini önemli ölçüde azaltabilir. Bu çalışmada, mukopolisakkaridoz tanısı ile izlenen hastaların işitsel ve oftalmolojik bulgularının retrospektif olarak değerlendirilmesi ve multidisipliner izlemin öneminin ortaya konması amaçlanmıştır. Uludağ Üniversitesi Tıp Fakültesi Çocuk Metabolizma Bilim Dalı'nda Ocak 2010–Aralık 2024 tarihleri arasında izlenen 45 MPS hastasının tıbbi kayıtları geriye dönük olarak incelenmiştir. Hastaların demografik özellikleri, MPS alt tipleri ile işitme ve göz muayene bulguları değerlendirilmiştir. Hastaların ortalama yaşı 13,3±5,7 yıl, ortalama tanı yaşı 4,39±3,5 yıl olup olguların %55,5'i erkekti. En sık görülen MPS alt tipleri Tip IVa (%28,8) ve Tip III (%24,5) idi. Hastaların %46,6'sında kornea opasitesi, %15,9'unda ise işitme kaybı saptandı. Bulgularımız MPS hastalarında işitme ve görme sisteminin sıklıkla etkilendiğini göstermektedir. Bu nedenle erken tanı, düzenli duyusal sistem taramaları ve multidisipliner izlem hastaların klinik sonuçlarını ve yaşam kalitesini iyileştirmek açısından önemlidir.

Anahtar Kelimeler: Mukopolisakkaridoz. İşitme kaybı. Kornea opasitesi. Multidisipliner yaklaşım.

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Mucopolysaccharidoses (MPS) are lysosomal storage disorders resulting from impaired glycosaminoglycan (GAG) degradation. Although most MPS subtypes are inherited in an autosomal recessive manner, MPS type II (Hunter syndrome) follows an X-linked recessive inheritance pattern[1,2]. Deficiency of these enzymes leads to progressive accumulation of GAGs in cells and tissues. Over time, this accumulation affects various systems, including the skeletal, cardiovascular, respiratory, hepatobiliary, central nervous, and sensory systems[3–5]. Involvement of sensory systems, particularly hearing and vision, represents an important complication that negatively

affects the quality of life and educational performance of patients with MPS. These manifestations predominantly emerge during childhood. Although conductive hearing loss is most commonly observed, sensorineural and mixed types may also occur. Eustachian tube dysfunction, serous middle ear effusion, tympanosclerotic changes, and abnormalities of the temporal bone are among the most frequently reported pathophysiological mechanisms[6–8]. Visual impairment in MPS patients may result from corneal opacity, retinal degeneration, optic atrophy, and glaucoma. In particular, corneal accumulation of GAGs reduces corneal transparency and may lead to progressive visual loss[9–11]. Previous studies have reported that the prevalence of hearing loss in patients with MPS ranges between 20% and 80%. Visual impairment tends to occur earlier and more severely in MPS types I, IV, and VI[8,12,13]. These findings highlight the importance of early diagnosis, multidisciplinary follow-up, and timely initiation of appropriate therapies in influencing disease progression[14–16].

In this study, auditory and visual findings in patients diagnosed with MPS were retrospectively evaluated. The frequency of sensory system involvement, distribution according to MPS subtypes, and related clinical outcomes were examined. The findings are presented to emphasize the importance of multidisciplinary follow-up and routine sensory system screening in patients with MPS.

Materials and Methods

In this retrospective study, medical records of 45 patients diagnosed with MPS and followed at the Division of Pediatric Metabolism, Uludağ University Faculty of Medicine, between January 2010 and December 2024, were retrospectively reviewed. Demographic characteristics, sex, age, MPS subtype, presence of parental consanguinity, and audiological and ophthalmological findings were evaluated. Audiological assessments were performed using standard audiological tests, and ophthalmologic examinations were conducted by pediatric ophthalmologists.

Results

The mean age of the 45 patients with mucopolysaccharidosis included in the study was 13.3±5.7 years, while the mean age at diagnosis was 4.39±3.5 years. Of the patients, 55.5% were male and 44.5% were female. The rate of parental consanguinity was 53.3%. Regarding the distribution of MPS subtypes, **MPS type IVa was the most common subtype (28.8%), followed by type III (24.5%), type VI (17.7%), type I (13.3%), type II (11.3%), and type VII (4.4**%). The demographic and clinical characteristics of the study population are summarized in Table I. No statistically significant difference was observed between sex distribution and impairment in hearing or visual functions **(p > 0.05).**

When the auditory and visual findings of the 45 MPS patients were examined in detail, sensory system involvement appeared to be a common component of the clinical course. These complications may directly affect the cognitive, social, and educational development of affected individuals. Hearing evaluation revealed decreased hearing function in 7 patients (15.9%). Among these cases, 57% had conductive hearing loss, 28% had mixed hearing loss, and 14% had sensorineural hearing loss.

Table I. Demographic Characteristics and Audiological/Ophthalmological Findings of Patients with Mucopolysaccharidosis (n = 45)

Variable	Value
Age, years (mean ± SD)	13.3 ± 5.7
Age at diagnosis, years (mean ± SD)	4.39 ± 3.5
Male sex, n (%)	25 (55.5)
Female sex, n (%)	20 (44.5)
Parental consanguinity, n (%)	24 (53.3)
Hearing impairment, n (%)	7 (15.9)
Corneal opacity, n (%)	21 (46.6)
Association between sex and hearing/visual impairment	Not significant (p > 0.05)

Ophthalmologic evaluation revealed corneal opacity in 21 patients (46.6%). This finding was most frequently observed in MPS types I, IVa, and VI. The distribution of MPS subtypes, hearing loss patterns, and ophthalmological findings are presented in Table II.

Table II. Distribution of MPS Subtypes, Types of Hearing Loss, and Ophthalmological Findings Among Patients with Mucopolysaccharidosis

MPS subtype	n (%)
MPS Type IVa	13 (28.8)
MPS Type III	11 (24.5)
MPS Type VI	8 (17.7)
MPS Type I	6 (13.3)
MPS Type II	5 (11.3)
MPS Type VII	2 (4.4)
Type of hearing loss (n = 7)	
Conductive hearing loss	4 (57.1)
Mixed hearing loss	2 (28.6)
Sensorineural hearing loss	1 (14.3)
Ophthalmologic findings	
Corneal opacity	21 (46.6)
Most affected MPS subtypes	Types I, IVa, and VI

Discussion and Conclusion

Mucopolysaccharidoses (MPS) are lysosomal storage disorders characterized by a broad clinical spectrum and multisystem involvement. Sensory system involvement is particularly important both during the diagnostic process and throughout long-term follow-up In this study, auditory and visual findings in patients with MPS were retrospectively evaluated, and the importance of a multidisciplinary approach was emphasized. Hearing loss is a common and often progressive complication in patients with MPS. In the study conducted by Hauer et al., the prevalence of hearing loss reached up to 80%, whereas our study detected hearing impairment in 15.9% of patients[5]. Differences in diagnostic age, duration of follow-up, audiological screening techniques, and sample size may explain this discrepancy. Conductive hearing loss is commonly associated with middle ear effusion, Eustachian tube dysfunction, and temporal bone abnormalities. Lampe et al. reported that mixed and sensorineural hearing losses become more frequent in advanced stages of the disease[8].

Regarding visual impairment, Clarke reported that patients with MPS type I frequently exhibit corneal opacity accompanied by optic nerve involvement and retinal degeneration[2]. Corneal opacity has been reported to show a progressive course in patients with MPS type IVa, significantly affecting quality of life. These findings are supported by 15-year follow-up data reported by Lampe et al. Sawamoto et al. emphasized that early diagnosis and regular monitoring may help control visual complications[8,16].

In our study, corneal opacity was detected in 46.6% of patients with MPS types I, IVa, and VI. These findings are consistent with the literature and support the progressive nature of corneal involvement, particularly in patients with MPS type IVa. Although no statistically significant association was observed between MPS subtypes and auditory or visual system involvement ($p>0.05$), our results clinically suggest that MPS types III, IVa, and VI may be more frequently associated with sensory system impairment. These findings highlight the importance of individualized multidisciplinary follow-up. Sawamoto al. reported that the intensity of GAG accumulation increases in parallel with systemic involvement and may influence the severity of sensory system damage[16]. Although enzyme replacement therapy (ERT) improves visceral manifestations and motor function, its impact on sensory system involvement appears limited. Studies conducted by Harmatz et al. in MPS VI and Muenzer et al. in MPS II have demonstrated that ERT does not lead to significant improvement in hearing or visual functions [12,13]. Sawamoto et al. suggested that emerging therapeutic approaches such as gene therapy and intrathecal administration strategies may offer more effective treatment options for sensory system involvement in the future[16].

Corneal GAG accumulation reduces transparency and may lead to severe visual impairment by affecting visual acuity. Simultaneous impairment of hearing and vision in patients with MPS may lead to substantial limitations in language acquisition, cognitive development, academic performance, and social integration, particularly in children during developmental periods. These neurosensory impairments often emerge early in the course of the disease and tend to progress over time.

Consequently, this condition not only decreases quality of life at the individual level but also increases the need for special education and rehabilitation services, thereby contributing to the burden on healthcare systems. For this reason, systematic multidisciplinary evaluation protocols initiated at the time of diagnosis, along with regular audiological and ophthalmological monitoring, are of critical importance for preventing secondary morbidity and preserving functional capacity in patients with MPS.

In conclusion, our study demonstrates that hearing and visual impairments are common in patients with MPS and significantly contribute to disease burden. Early diagnosis, multidisciplinary monitoring, and timely supportive interventions are essential for optimal management. Regular audiological and ophthalmological screening performed by multidisciplinary teams is crucial to improve the quality of life of patients diagnosed with MPS.

Researcher Contribution Statement
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