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Mucopolysaccharidosis: Caregiver Quality of Life

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Abstract

The mucopolysaccharidoses (MPSs) are a group of rare genetic diseases caused by a deficiency of specific enzymes involved in catabolism of glycosaminoglycans, which causes multisystem abnormalities. Quality of life (QoL) is directly associated with physical, mental, and psychological well-being and with social relationships, including family and friends. **Aims:** To evaluate the QoL of caregivers of patients with MPS. **Methods:** Cross-sectional study using a convenience sampling strategy. The sample comprised mothers of patients with MPS seen at the Medical Genetics Service, Hospital de Clínicas de Porto Alegre, Brazil. The World Health Organization Quality of Life Assessment (WHOQOL-BREF) was used to assess QoL. **Results:** Eleven mothers of 12 patients with MPS (MPS-I = 1; MPS-II = 3; MPS-III = 3; MPS-IV = 4; and MPS-VI = 1) were included. The average WHOQOL-BREF score was 46.59, with the physical health domain scoring highest and the environmental domain scoring lowest. The lower QoL of mothers of children with MPS-II seems to be related to the worse clinical condition of these children, with more severe symptoms and greater need for help with daily activities as well as with a feeling of responsibility due to the inheritance pattern of the disease.

Keywords

mucopolysaccharidoses, quality of life, caregivers, daily activities, disabilities

Introduction

The mucopolysaccharidoses (MPSs) are a group of rare genetic diseases, with an estimated incidence of 1.3 to 4.5:100 000 live births. The MPSs are a subset of the lysosomal storage diseases (LSDs) caused by a deficiency of specific enzymes that catalyze degradation of glycosaminoglycans (GAGs), which then build up in the body and cause a variety of pathologic changes.[1-3] Seven types of MPS have hitherto been identified (Table 1).

The MPSs are inherited in an autosomal recessive pattern, with the exception of MPS-II, which is X-linked.[2] The MPSs have a chronic, progressive course and share several clinical aspects, such as multisystem involvement; hepatomegaly; heart, lung, bone, and joint problems; and visual and auditory changes.[4-6] These systemic changes can hinder performance of the activities of daily living, such as feeding, dressing, and personal hygiene, and may delay acquisition of motor skills. Respiratory and cardiac involvement affects the performance of activities such as climbing and descending stairs, walking long distances, or playing sports. Neurological regression, a characteristic of some forms of MPS, limits the independent performance of daily activities such as shopping, riding on public transportation, and managing one's own life.[7-11]

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Table 1. Clinical and Epidemiological Features of Mucopolysaccharidoses.

Disease	Eponym	Deficient Enzyme	Symptom Severity	Inheritance Pattern	Incidence[a]
MPS I	Scheie, Hurler-Scheie, Hurler	Alpha-L-iduronidase	Attenuated, intermediate, severe	AR	1:100 000
MPS II	Hunter	Iduronate-2-sulfatase	attenuated to severe	X-linked	1:162 000
MPS III-A	Sanfilippo A	Heparan-*N*-sulfatase	attenuated to severe	AR	1:128 000
MPS III-B	Sanfilippo B	α-*N*-acetylglucosaminidase	attenuated to severe	AR	1:135 000
MPS III-C	Sanfilippo C	Acetyl-CoA: α-glucosaminide *N*-acetyltransferase	attenuated to severe	AR	1:1.407 000
MPS III-D	Sanfilippo D	*N*-acetylglucosamine 6-sulfatase	attenuated to severe	AR	1:1.056 000
MPS IV-A	Morquio A	*N*-acetylgalactosamine 6-sulfatase	attenuated to severe	AR	1:201 000
MPS IV- B	Morquio B	β-galactosidase	attenuated to severe	AR	1:715 000
MPS VI	Maroteaux-Lamy	Arylsulfatase B	attenuated to severe	AR	1:248 000
MPS VII	Sly	β-glucuronidase	attenuated to severe	AR	1:2.111 000
MPS IX	Natowicz	Hyaluronidase	Mild	AR	4 cases

Abbreviations: AR, autosomal recessive; MPS, mucopolysaccharidosis.
[a]Adapted from Meikle et al.[1]

There is a wide clinical heterogeneity, being the most severe forms associated with high rates of morbidity and mortality during childhood, and neurological involvement. Patients with an attenuated phenotype may experience normal survival and absence of cognitive involvement. However, symptoms usually arise in childhood, with progressive limitations in social involvement, which mean that patients may require the support and assistance of caregivers throughout most of their lives.[12]

According to the World Health Organization (WHO), quality of life (QoL) is defined as ''individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards, and concerns.''(p. 1570)[13] The QoL is directly linked to physical, mental, psychological, and emotional well-being.[13]

A ''caregiver'' is someone, usually a relative, who takes care of or otherwise supports an ill or disabled individual. Caregivers are largely family members and predominantly women, and in fact, this role is most commonly taken on by the individual's mother.[14] Caregivers of individuals with disabilities and/or limitations are prone to reductions in QoL due to their complete dedication to the patient, which leads them to neglect their own lives.[15] Socioeconomic status, social support networks, and the characteristics of the disabled care recipient also influence QoL of caregiver. One study showed that caregivers tend to become more stressed and tired when the patient is not sleeping well or is not responding positively to treatment.[16]

Caregivers of children with chronic illness exhibit significantly lower QoL than parents of healthy children. Among the former group, parents of children with metabolic diseases reported even lower QoL than parents of children with other conditions, such as end-stage renal disease or Duchenne muscular dystrophy.[17] Within this context, the present study sought to assess QoL in mother caregivers of children with MPS.

Methods

Mothers of patients with MPS seen at the Outpatient MPS Clinic of the Medical Genetics Service at Hospital de Clínicas de Porto Alegre, state of Rio Grande do Sul, Brazil, were invited to take part in the study. A convenience sampling strategy was used whereby mothers were recruited during the MPS Symposium held in Porto Alegre in 2012. Caregiver QoL was assessed with the WHOQOL-BREF questionnaire in its version validated for the Brazilian population,[18,19] and data on demographic variables and clinical characteristics were collected by means of a questionnaire developed by the investigators. Socioeconomic stratification of the sample was performed in accordance with the 2013 Brazilian Economic Classification Criterion. For patients with MPS-I and -II, disease phenotype was classified as severe or attenuated based on the attending physician's impression as recorded in patient charts. Likewise, data on the presence or absence of cognitive impairment were collected by means of a chart review, as no IQ test results were available.

The WHOQOL-BREF instrument comprises 26 items. The closer the total score is to 100 points, the better the QoL, and lower scores denote worse QoL (Table 2). The demographics questionnaire contained items on geographic origin, age, sex, and clinical characteristics of MPS. Caregivers were asked to sign an informed consent form confirming their agreement to participate in the study and have their data made public.

The WHOQOL-BREF domain and total scores were calculated by means of the instrument's own specific scoring syntax. Results were analyzed descriptively for all caregivers and disaggregated by MPS type as were demographic and clinical data.

Results

The study sample comprised 11 mothers, including one who had 2 children with MPS. The median age was 35 years (interquartile range [IQR], 31.5-36.5 years; range, 29-43 years). Socioeconomic classification yielded the following results: A1, n = 1; B1, n = 2; B2, n = 4; and C1, n = 4. Mucopolysaccharidosis IV-A was the most common MPS type (n = 4). Most patients were male (n = 9) and had a median age of 16.5 years

Table 2. WHOQOL-BREF Domains.[a,b]

Domain	Facet
I. Physical health	1. Pain and discomfort
	2. Energy and fatigue
	3. Sleep and rest
	4. Mobility
	5. Activities of daily living
	6. Dependence on medicinal substances and medical aids
	7. Work capacity
II. Psychological	8. Positive feelings
	9. Thinking, learning, memory, and concentration
	10. Self-esteem
	11. Bodily image and appearance
	12. Negative feelings
	13. Spirituality/religion/personal beliefs
III. Social relationships	14. Personal relationships
	15. Social support
	16. Sexual activity
IV. Environment	17. Freedom, physical safety, and security
	18. Home environment
	19. Financial resources
	20. Health and social care: accessibility and quality
	21. Opportunities for acquiring new information and skills
	22. Participation in and opportunities for recreation/leisure activities
	23. Physical environment (pollution/noise/traffic/climate)
	24. Transport

[a]Adapted from The World Heath Quality of Life Assessment (WHOQOL) Group.[13]
[b]Higher scores (of 100) denote better quality of life.

(IQR, 11-20.5 years). Regarding geographic origin, 5 mothers were from the state of Rio Grande do Sul; 2 each from the states of Bahia, Minas Gerais, and São Paulo; and 1 from the state of Santa Catarina.

The most common clinical features of patients with MPS were sensory impairments (vision and hearing) and mental retardation. A need for assistive technology devices (eg, eyeglasses, hearing aids, and wheelchairs) was also reported. Patients who do not use wheelchairs have the ability to move around the place without assistance or with minimal assistance of the caregiver (Table 3).

The mean QoL score was 48.06. Regarding specific WHOQOL-BREF domains, the highest scores were found for the *physical health* domain, with a pooled mean of 56.03 points, whereas the lowest scores were found for the *social relationships* domain, with a pooled mean score of 36.11 points.

The total score of QoL revealed that caregivers of patients with MPS-I-Hurler had the lowest scores, with a pooled mean of 45.19 points. Caregivers of patients with MPS-IV-A had the highest scores, with a pooled mean of 49.30 points. Data stratified by MPS type are shown in Table 4.

Discussion

Although limited by the small sample size, the results of this study suggest that mothers of patients with MPS have low QoL. This phenomenon may be related to socioeconomic condition, clinical characteristics, and disease severity.

In this study, caregivers of patients with MPS reported lower scores than in previous studies that investigated caregiver QoL with the same instrument. One study of QoL among caregivers of patients with sickle cell anemia identified scores of 59.69 points for caregivers of patients on hydroxyurea therapy and 58.42 points for caregivers of patients who were not on said therapy.[16] Another study on the influence of social support on QoL of family caregivers of persons with disabilities identified a general QoL score of 54.06 points,[15] and a study of caregivers of physically disabled individuals found an overall QoL score of 61.02 points.[20]

The *social relationships* domain of the WHOQOL-BREF, which assesses interpersonal relations, sexual activity, and social support, exhibited the lowest scores in our sample. This suggests that the mothers interviewed may be the sole caregivers of their children and may receive little or no support from others. Previous research corroborates this hypothesis. In one study, 26.8% of caregivers stated they received no support from others in providing essential care to their children.[15] Genetic diseases are considered chronic diseases that often cause a disability. Therefore, patients and their caregivers consider the process of ''adaptation'' as part of the concept of QoL, which says ''adaptation is the process of reaching an agreement between the implications of a health disease and the observable results of this process.''(p. 1137)[21] In addition, the increased burden faced by these caregivers may reduce their involvement in social relationships and with their partners, which may have implications for reduced QoL. Factors potentially associated include degree of emotional support, disease awareness, available leisure activities, and other family members with health issues.[22]

In a study that evaluated the QOL of mothers of children with mitochondrial diseases, it was observed higher caregiver burden levels and poorer QoL, mainly related to functionality, vitality, and mental health. Caregivers also had higher levels of depression and anxiety.[23] The MPS, the pattern of inheritance of mitochondrial diseases, and the lack of information about the diseases can affect the QoL of mothers as well as can increase the anxiety and caregiver burden.

In our sample, the highest scores were found for the *physical health* domain of the WHOQOL-BREF, which consists of items that assess pain and discomfort, sleep and rest, work capacity, mobility, activities of daily living, and dependence on medicinal substances, and medical aids; nevertheless, these scores were only minimally above average. This result demonstrates that the constituent items of this domain play an essential role in caregiver QoL. As reported in the literature, enzyme replacement therapy (ERT) for MPS has beneficial effects in many clinical symptoms, reducing hepatosplenomegaly, increasing cardiopulmonary fitness, improving functional

Table 3. Profile of Patients With MPS Whose Mothers Participated in the Study.

	MPS I-Hurler (n = 1)	MPS II-severe (n = 1)	MPS II-attenuated (n = 2)	MPS III-B (n = 3)	MPS IV-A (n = 4)	MPS-VI (n = 1)
Sex (M/F)	M	M	M	F	M	M
Median age, years	2	13	13	21.5	17	18
Range			04-22	20 - 23	15 - 24	
ERT, n	1		2	–	–	1
Median duration of ERT, months	60	24	36	–	–	60
Range			18-96	–	–	
Deafness	–		–	–	2	–
Hearing aid	–		1	–	3	–
Eyeglasses	–		1	–	3	1
Cognitive disturbances	1		1	3	–	–
Wheelchair bound	–		–	3	2	–

Abbreviations: ERT, enzyme replacement therapy; F, female; MPS, mucopolysaccharidosis; M, male.

Table 4. WHOQOL-BREF Quality-of-Life Scores of Mothers Participating in This Study, Stratified by Child MPS Type.[a]

	MPS I-Hurler (n = 1)	MPS II-Severe (n = 1)	MPS II-Attenuated (n = 2)	MPS III B (n = 3)	MPS IV-A (n = 4)	MPS VI (n = 1)
Total	45.19	44.62	45.00	48.50	49.30	46.15
Physical health	50.00	51.43	54.17	57.14	61.61	46.43
Psychological	45.83	50.00	41.67	50.00	54.17	45.83
Social relationships	33.33	35.00	33.33	45.83	31.25	50.00
Environment	40.63	31.88	34.38	38.62	31.25	37.50
Self-assessed QoL	62.50	70.00	87.50	56.25	84.38	75.00

Abbreviations: MPS, mucopolysaccharidosis; MPS I-H, mucopolysaccharidosis Hurler syndrome; MPS II-A, mucopolysaccharidosis attenuated; MPS II-S, mucopolysaccharidosis severe.
[a]Higher scores (of 100) denote better quality of life.

capacity for ambulation and stair climbing, and producing subjective improvement in joint pain and stiffness. This may have been a preponderant factor in the perception of better QoL by mothers because it can make patients more autonomous in some activities of daily life and lessening the burden on caregivers.[24-32]

Analysis of caregiver QoL stratified by MPS type showed that, in the caregiver of an patient with MPS-I, only 2 domains scored higher than average; even so, both scored below 65 points. Lower scores in the *environment*, *social relationships*, and *psychological* domains may be attributable to the clinical characteristics of the child and to the physical and emotional support structure required to provide such care. The patient included in the study had the severe form of MPS-I (Hurler syndrome) and accordingly severe clinical features, including coarse facial features, progressive mental retardation, corneal clouding, airway obstruction, heart disease, hepatosplenomegaly, and skeletal deformities.[4,33] Therefore, the caregiver's lower QoL scores may be explained by the significantly greater number of responsibilities and needs related to caring for a gravely ill child.[34]

The results obtained in caregivers of children with MPS-II (Hunter syndrome) were distinct as a result of the difference in clinical manifestations between the 2 disease phenotypes. In the severe form, symptoms arise between ages 2 and 4. In the attenuated form, symptoms arise later, neurological involvement is absent or minimal, and patients survive into adulthood.[35-37,25,7] Behavioral disturbances, such as hyperactivity and aggressiveness, are common in the severe form. Only 2 studies in children with MPS-II evaluated the impact of the disease on patient QoL. The sample consisted of 96 respondents (patients and caregivers), and 14 individuals with MPS answered the questionnaire independently. The Child Health Assessment Questionnaire had low scores for activities of daily living such as hygiene and clothing. In addition, the domains of pain, stress, physical functioning, social relationships, self-esteem, and family cohesion obtained very low scores, suggesting a marked impact on QoL of them. The study results indicate that the MPS-II has a considerable impact on health-related QoL (HRQoL), with lower scores in most of the instrument's dimensions (particularly pain and self-esteem).[11]

Another study evaluated the QOL of patients with MPS also through the 2 versions of the instrument Pediatric Quality of Life Inventory (PedsQL; The PedsQL is a generic questionnaire assessment of HRQOL in children. The version of the instrument, from 8 years, consists of 23 items divided into four domains: physical, emotional, social and school function. The questionnaire is scored, total and by size, from the average of the scores of the items correspondentes. The highest score is the

best health status). The results indicate that parents and patients had lower scores in all areas of the PedsQL, and these data suggest a lower overall HRQoL.[38]

For caregivers of patients with MPS-III-b, only physical health domain scores were lower. This finding is corroborated by the literature, which states that MPS-III-B is the least severe of all MPS forms. The main complications are neurological regression and behavioral disturbances. Mucopolysaccharidosis III-B is possibly a more attenuated pheno- type than MPS III-A.[39-41]

Caregivers of patients with MPS IV-A had the highest scores in the *physical health* domain. Despite the mobility issues faced by these patients as a result of clinical features, such as dwarfism, kyphosis, scoliosis, vertebral deformities, and hyperextended joints,[5,24,42] it appears that their caregivers do not experience a need for greater physical support. Moreover, as patients with MPS-IV-A do not have mental retardation, they appear to be more independent and autonomous for activities of daily living and thus require less maternal support.

Quality-of-life assessment of caregivers of patients with MPS-VI identified low QoL scores on all domains. This finding may be associated with the clinical features of this form of MPS, which includes slow growth, skeletal deformities, joint stiffness, and upper airway obstruction as well as limited cognitive development due to sensory deficits (visual and hearing impairment) and physical limitations, which mean that mothers must provide greater care and support for activities of daily living.[43-45,20] However, we were unable to confirm this hypothesis, as the study sample included only 1 caregiver of a child with MPS-VI.

Many studies have assessed QoL in caregivers of patients with other conditions, such Down syndrome, autism spectrum disorders, and cerebral palsy.[15,22,33] However, we were unable to find any studies evaluating QoL in caregivers of patients with MPS.

According to the 2013 Brazilian Economic Classification Criterion, the average household income of families in socioeconomic classes B2 and C1 is R$2,654.00 and R$1,685.00, respectively. For families that have a disabled child with special needs, this income is often insufficient to meet even the most basic requirements. Assessment of the socioeconomic status of our sample revealed that most mothers were living in low-income or middle-income settings and that many of these mothers had to devote the majority of their time to child care, often leading them to forgo self-care and leisure activities and even to quit their jobs.[46]

In patients with MPS, disease severity and clinical characteristics such as visual and auditory changes and neurological problems that lead to mental retardation and make patients wheelchair bound may also be associated with lower maternal QoL, due to the need for increased support and dedication to help these children perform the activities of daily living.[2,3,47]

Caregivers may face strains that affect their health and well-being. Furthermore, the special needs of patients with MPS may be an additional burden and cause great concern, and this, in turn, can impact the caregiver's job performance and social life.[20]

Conclusion

The results of this study show that caregivers of patients with MPS experience low QoL, with caregivers of patients with MPS II experiencing the poorest quality. However, further studies designed to collect more data from larger samples may provide a clearer picture of the importance of assessing QoL among parents of children with MPS. Such research may enable these individuals to receive care that meets not only the needs of their children but also their own personal and emotional needs.

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