Living with Glutaric Aciduria Type 1: Experiences of Adolescents and Their Families Living in Germany

Glutarik Asidüri Tip 1 ile Yaşamak: Almanya'da Yaşayan Adölesanların ve Ailelerinin Deneyimleri

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ABSTRACT

Objective: This study was conducted to investigate the effects of treatment of a child with glutaric aciduria type-1 diagnosis on the health-related quality of life of a child and his family via in-depth interviews.
Methods: The study was conducted in qualitative research design in the pediatric metabolism department of a university hospital in Germany. The inclusion criteria of the study were as follows: a family 1) with a child followed up with glutaric aciduria type-1 and who was exposed to a (tryptophan and) lysine restricted-diet, 2) with other healthy siblings aged between 10 and 25 years, and 3) who agree to participate in the study. The study was carried out in the framework of a biopsychosocial-spiritual model with a child (n=4) who was followed up with glutaric aciduria type-1 and his family. A total of 10 interviews were conducted. The interview records were transcribed and analyzed.
Results: In the study, 4 main domain and 11 themes were determined according to the biopsychosocial-spiritual model. The physical effects of the disease, the positive effects of treatment, and limitations were the themes in the biological domain. The psychological domain included themes named as psychological reactions to the disease, adaptation to the treatment process, coping strategies, and future concerns. The domain of social effects explained themes such as family and environment communication-interaction. In the spiritual domain included the meaning and objective of life and belief-values.
Conclusion: Living with glutaric aciduria type-1 disease and treatment received was found to have multiple effects on the quality of life of children and their families.

Key Words: Adolescent, family, metabolism, quality of life.

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ÖZET

Amaç: Bu çalışma glutarik asidüri tip 1 tanısıyla izlenen bir çocuğun tedavi almasının çocuk ve ailenin sağlıkla ilişkili yaşam kalitesine olan etkilerini derinlemesine görüşmelerle incelemek amacıyla yapılmıştır.
Yöntem: Çalışma Almanya'da bir üniversite hastanesinin pediatrik metabolizma bölümünde temel nitel araştırma deseninde yapılmıştır. Çalışmanın dahil edilme kriterleri 1) glutarik asidüri tip 1 tanısıyla izlenen ve lizinden kısıtlı (ve triptofan) diyet alan 2) ve 10-25 yaş arasında başka sağlıklı kardeşleri olan çocuk 3) çalışmaya katılmayı kabul eden ailedir. Araştırma, çalışmanın kriterlerine uyan Glutarik asidüri tip-1 tanısıyla izlenen bir çocuk ve ailesiyle (n=4) biyopsikososyal-spiritüel model çerçevesinde gerçekleştirilmiştir. Toplamda 10 görüşme yapılmıştır. Görüşme kayıtları metin haline getirilmiştir ve analiz edilmiştir.
Bulgular: Çalışmada modele göre 4 temel alan ve 11 tema belirlenmiştir. Hastalığın fiziksel etkileri, tedavinin pozitif etkileri ve sınırlılıkları biyolojik alanda yer alan temalardır. Psikolojik alanda hastalığa yönelik psikolojik tepkiler, başetme stratejileri, gelecek kaygıları ve tedavi sürecine uyum temaları yer almıştır. Sosyal etkiler alanı aile içi iletişim-etkileşim ve çevre ile iletişim-etkileşim temalarını açıklamaktadır. Spiritüel alanda ise yaşamın anlamı ve amacı ve inanç-değerler olmak üzere iki alt tema yer almıştır.
Sonuç: Glutarik asidüri tip 1 hastalığıyla yaşamanın ve alınan tedavinin çocuk ve ailenin yaşam kalitesi üzerine çok yönlü etkileri olduğu belirlenmiştir.

Anahtar Sözcükler: Adölesan, aile, metabolizma, yaşam kalitesi

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INTRODUCTION

Glutaric aciduria type-1 (GA1) is a rare autosomal-recessive hereditary neurometabolic disease that is due to deficiency of glutaryl-coenzyme A dehydrogenase (1). The prevalence of the disease is 1 in 100,000. The estimated incidence in Germany is 1 in 112,700 newborns (2).

GA1 requires lifelong treatment and monitoring. It is often accompanied by macrocephaly, encephalopathic crises during catabolism is a typical feature, symptoms such as delayed speech and motor development, permanent dystonia, and irreversible brain injury are often observed (3,4). Patients with GA1 suffer from mental retardation as well as emotional and behavioral problems. These symptoms affect all family members in addition to the child (5).

Hereditary metabolic diseases can affect intrafamilial interactions, social lives of parents, the interactions between spouses and other siblings, and may have a financial impact (6,7). Gramer and coworkers (8) stated that in metabolic diseases, especially in situations where the diet is important, the burden of care is high and burnout is frequent in affected families. The international guideline on GA-1 recommends that the psychosocial effects of diagnosis and treatment should be evaluated as part of routine follow-up in both affected individuals and their families (9).

The physical, social and psychological effects of chronic diseases on the life of the affected individual and his family, often has an impact on health-related quality of life (10). The perspective of affected families is very important in determining the experiences, needs, and expectations of families, especially in rare metabolic diseases. It is necessary to listen to all family members, especially young people in the family, to understand the effect of living with metabolic disease and receiving dietary treatment on health-related quality of life (11).

Only few studies on GA1 exist (12). There are no studies on the experiences and quality of life of families regarding the disease and treatment process. The present study is thought to address this gap in the field by focusing on the effects of the disease and treatment process and the opinions and experiences of young individuals. For this reason, this study was carried out to determine the impact of living with the diagnosis of GA1, which is a rare condition and a target disease of newborn mass screening in Germany using the tandem-MS technique. Diet and other treatments have an impact on the health-related quality of life of the patient and his/her family.

Theoretical Framework

Since chronic disease affects the individual in many aspects including biological, social, and psychological terms and also has an effect on the quality of life concept, our study employed the biopsychosocial-spiritual model. The theoretical framework and interview questions of the study were designed based on the biopsychosocial-spiritual model developed by Sulmasy (13). Figure 1 shows the form of the model as adapted to the current study. The questions prepared according to the model can be found in Appendix 1.

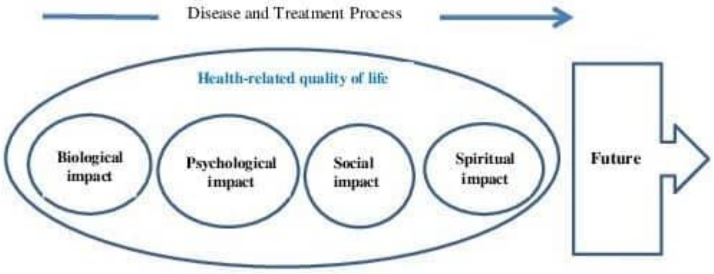

Figure 1: Adaptation of the biopsychosocial-spiritual model to the current study

MATERIALS and METHODS

The study was carried out in the basic qualitative research design. The basic qualitative research design was thought to be appropriate for this study. The study used the purposive sampling method. The inclusion criteria of this study were as follows: a family 1) with a child who was diagnosed with GA1 and who was exposed to a (tryptophan and) lysine restricted-diet, 2) with other healthy siblings aged between 10 and 25 years, and 3) who agreed to participate in the study. Diagnosis of GA1 was based on clinical and neuroimaging findings and confirmed by blood tandem mass spectrometry (TMS) and/or urine gas chromatography and mass spectrometry (GC/MS) and/or genetic analysis. After all, there were 5 children with GA1 cared for in the paediatric outpatient clinic for inborn errors of metabolism at Hannover Medical School. The family included in the study met the inclusion criteria and were easy open to communicate about their situation. In the study, patient, mother, father, and sibling titles were used to keep the anonymity of individuals. The family was invited to read and sign a consent form permitting the interviews. No vote by the ethical review commission was required as the interviews were essential in the clinical context to define the outcome of disease.

Instrumentation and Procedures

In-depth, semi-structured interviews were held with the families who agreed to participate in the study (Appendix-1). The interviews were conducted by the first author. The family was informed about the study, and a consent form was obtained for their participation in the study. The first interview was held with the patient, who was followed-up in the outpatient clinic, and subsequently the mother, and the father as well as siblings (when applicable) were interviewed. The first meeting was performed in a quiet treatment room of the policlinic. During the interview, the speech, gestures, and mimics of the participants were observed by the researcher. Other interviews were conducted in a quiet room in the family's home. A total of 10 interviews including 3 interviews with the mother and father separately with one-week interval, and two interviews with each of the two children of the family. The interviews lasted approximately 30 minutes to an hour. The median interview time was 45 minutes in parents and 30 minutes in children. During the interviews, a voice recorder was used after the permission of the participants was obtained.

The framework of the biopsychosocial-spiritual model leading the interviews was as follows:

- Physical effects of the disease, positive effects of the treatment, and limitations of the treatment were analyzed in the biological area.
- The first psychological responses to the disease, compliance with the treatment and nutrition program, coping strategies, and future concerns were analyzed in the psychological field.
- Intrafamily communication and interaction, and communication and interaction with the environment were analyzed in the field of social effects.
- Understanding the purpose of life and the effect of belief/values were analyzed in the spiritual field.

Data Analysis

The content was evaluated by considering the thematic analysis steps developed by Braun and Clarke (14). Before starting the content analysis, the interviews in the audio recordings were first listened to and transcribed. The transcription of the audio records of the interviews was made by the researchers themselves to prevent data loss. Ten interview texts were reviewed several times by two researchers, and the researchers noted their impressions. The interviews, which were transcribed during the analysis, were coded sentence by sentence to have more comprehensible outcomes. A "code list" was created using the coded-sentences data. Later, themes that could explain these codes under certain categories were identified. Similar codes were classified into clusters and then a table containing these themes was created to see these individual concepts, which were later organized in groups, and to observe the connections between each of them. For the validity of the data, the coded themes and statements were submitted to the opinion of an expert in the field. Figure 2 provides a summary of the main categories and emerging themes.

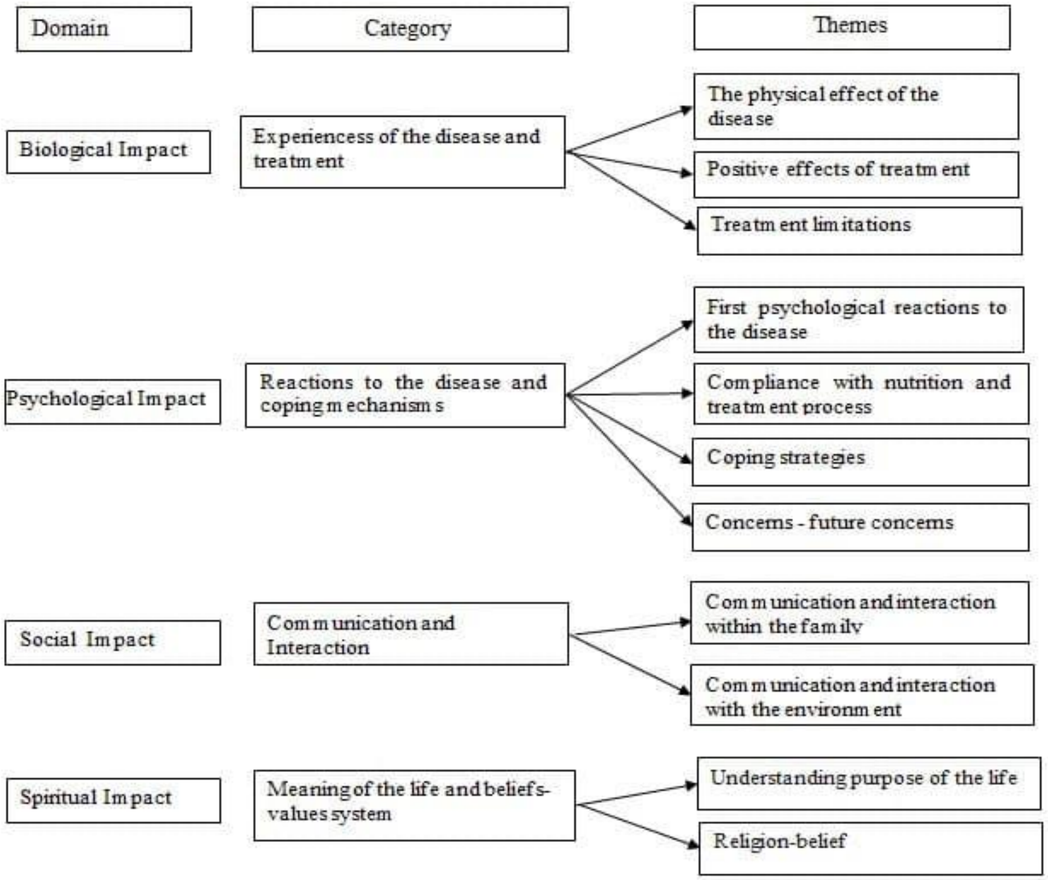

Figure 2: Main categories and emerging themes

Participants

The child, who was followed up with the diagnosis of GA1, was 15 years old and attending a school for the physically disabled. He stated that he loved nature and animals very much. He said moving, running, and dancing were highly important for him. His elder brother, who was 17 years old, was a high school student and he was very interested in cars. The father was 41 years old, and the mother was 40 years old. The father worked in a cleaning company and the mother worked as an elderly care technician in a nursing home.

RESULTS

Effects of living with glutaric aciduria type 1 and the treatment program

The themes determined as a result of the interviews were illustrated in the field of the biopsychosocial-spiritual model. Since the parameters of the model have a dynamic structure in interaction with each other, some overlaps may have occurred in the sub-items of the themes (Figure 3).

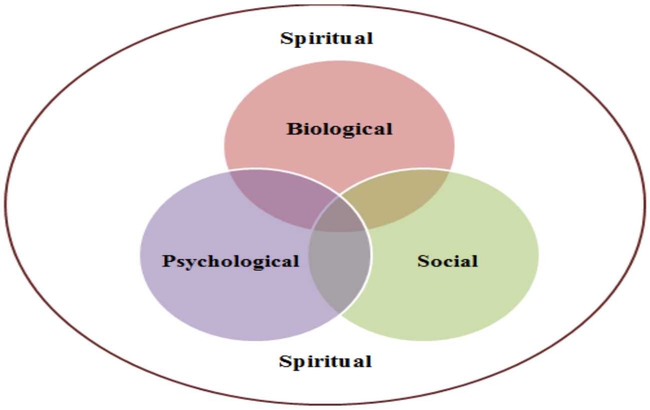

Figure 3: Biopsychosocial-spiritual model for living with glutaric aciduria type I

Biological effects

"I noticed that my child was different" Physical effects of the disease

> "On the day I gave birth, I said there was something wrong and weird with my child. My baby's head was very big and long. He did not cry. I had noticed something was wrong with my baby" (The Mother).
>
> "My child started walking and talking at the age of four. When he started walking, he constantly fell to the ground. His knees and head were always in sores. The wounds on his knees never disappeared" (The Father).

"*Nutrition plan and medical treatment was our hope*" *Changes and benefits coming with nutrition and medical treatment*:

> "Nutrition was important for my child. What foods contained lysine and tryptophan and what did I need to give him? The nutritionist taught them to me. My child recovered when he paid attention to his diet (The Mother).
>
> "Child development teachers suggested animal therapy to better use the energy of our child and to speed up his speech. We went horse-riding for two days a week. My child's speech improved. It healed my child. We still continue horse-riding" (The Father).

"*Diet compliance alone may sometimes be inadequate*". *Limitations of the Treatment Program:*

> "We paid attention to my child's diet, but he seemed as if he did not have much strength. I searched for the issue a lot, and I found articles claiming that vitamin support would be good. Then, multivitamin support was added to his treatment. After the vitamin supplement he received with his special formula, my child revived, recovered" (Mother).
>
> "It was forbidden to give fish and meat derivatives for the first 6 years. It was our chance to apply not only the nutrition program, but also the combination of occupational therapy, speech therapy, work-activity, and animal therapy" (Father).

Psychological Effects

"When I first heard it, I was totally wrecked; I was shocked." The first reaction of the family to the disease:

> "I felt all my world got wrecked when the chief physician of the district hospital where I gave birth said my child had a problem… We learned that our child had a rare disease ... When I first heard it, I was shocked" (The Mother).
>
> "I was preparing to take my wife and baby to our house. My wife told me that our child was sick ... I couldn't accept it, I was in shock ... I accused my wife of what has happened to us, telling her that it was because of her concerns" (Father).

"*Our first six years were like a horror movie.*" *Compliance with nutrition and medical treatment*:

> "We are a family that loves eating meat. My child is unable to eat meat because of his diet. The dietitian said that we should not eat meat near the child … and that the child should get used to this situation. She told us to eat the meat and give the bone to the child. I resented it so much; I was so sorry" (The Mother).
>
> "People around us often accused us by asking how we ate in front of our child and how we tolerated this situation. It was a very difficult situation for us. It was difficult, but we got used to it" (The Father).

"*Running away this process or keep going*". *Coping strategies:*

> "My child was sick ... I was thinking if there was a need to go to ergo therapy, speech disorder unit. I thought those in Europe and my wife were exaggerating it. I walked away from my family for a while; I ran away ... I could not cope" (The Father).
>
> "I was ready to welcome all kinds of difficulties. I accepted it. The doctor said we were lucky to diagnose it early, and I even evaluated it as good news… Because I was a mother; I had to continue for my child" (The Mother).
>
> "When I noticed my brother's illness, I was not aware of the situation much. He was different, but everyone loved him. For a while, I pretended as if there was no such disease. I used to join my friends when they made fun of my brother. But now I think much differently (The Brother).

"*I have concerns*" *Future concerns:*

> "I do not think that he will be able to protect his property and money in the future. If somebody asks for the 100 Euros he has, he gives it" (The Mother).
>
> He is a child who can be fooled easily. He doesn't want to break anyone's heart.... I have concerns ... After five years of working, Germany gives my son a chance to retire. I know that my child will not depend on anyone, even without us. However, there must be someone who will support him, who will love him like his mother, father, or wife (The Father).
>
> "My brother is a pure and friendly person. Therefore, he can be fooled. I can predict what may happen in the future. As his elder brother, I will protect him from now on; I will guide him" (The Brother).

Social Effects

In-Family Communication and Interaction

"*Changes when we were separated and when we were together with my husband*". *Communication between spouses*:

> "I neglected myself and my husband so much. I gained 60 kilos at once. I was badly-groomed. My husband and I were separated for a while because he did not understand me at the beginning. When we came over our problems with my husband, we had considerable progress in our child's illness" (The Mother).
>
> My wife and I have collaborated against challenges later, though we could not do it at first. I have tried to alleviate her burden because she worked. As partners, we have succeeded it together, and we continue our struggle (The Father).

"*I could not accept for a long time*". *Communication between siblings:*

> "My brother is trying to show his love by smelling my T-shirt. I get very angry when he approaches me like this. I couldn't accept it at first. But now I see him more fortunate. I will support him throughout my life" (The Elder Brother).

"My two children are different from each other, but he is my child". Parent-child relationship:

> My child is different from children of his age; he has different characteristics. I spent a lot of time with him. I was interested in my little boy so much because of his illness. During this time, I bought whatever my older son asked for so that he would not be affected (The Mother).
>
> My eldest son is introverted, and my little son can establish communication so quickly. We had to deal more with one of our children during the illness process. Sometimes I am thinking if my other child was quiet and introverted because of this (The Father).

Communication and Interaction with the Environment

"Nature and animals are very important to us". Communication and interaction with nature and animals:

> "We sent him to a gardening course because we know his interest in it. His teachers said that he was very successful and very happy while doing" (The Mother).
>
> "For him, life seems to exist in nature and the love of animals. Nature and animals have made a great contribution to my child's recovery. Horse riding training has speeded up his speech and rehabilitated my child" (The Father).

"Continuity of communication with the health professionals is very important" Communication with the health professionals:

> The doctor and dietitian were vitally important to us… I investigated a lot of things. I shared what I found with the doctors; they supported me (The Mother).
>
> Continuity of communication with the healthcare professionals was very important. We got support. If there had been someone available at the beginning for managing and directing everything, things would have been easier for families (The Father).

Spiritual Impact

"*My child is my miracle*". *Understanding the purpose of life*:

> My child is my miracle. We would not be happier if we had a child with no health problems at all instead of him. The meaning of my life and my perspective has changed… (The Mother).
>
> I have realized how important it is to be healthy in life. The meaning and purpose of life at the moment is that my family and children are healthy and together (The Father).

"*My belief in myself has made this process easier*". *My beliefs and values:*

> That I have been able to successfully overcome this process is the result of my belief that I can do it. I have focused on the facts that I can do for my child, not on superstitions (The Mother).
>
> I have talked to religious people to ask for prayers… I was more focused on faith and beliefs, especially at the time of the first diagnosis. My child's illness had a major impact then. Turning to religion and faith relieved me especially in the early days of the process (My Father).

DISCUSSION

Biological Effects

The family mentioned the importance of diet in the treatment of the child, and they said they observed developments in the child when the diet was applied. In GA1, a lysine-restricted diet and amino acid- formula (with lysine-free, low tryptophan content) are important to support adequate growth and development as well as preventing metabolic crises and encephalopathy (15). In our study, the family mentioned that they attached great importance to carnitine supplementation and diet to support the child's growth and especially brain development. However, the carnitine and micronutrient approach in the treatment of GA1 is based on a few cross-sectional studies and reports of some case studies in the literature. Evidence-based studies for medical treatment of patients followed-up with the diagnosis of GA1 are needed (15).

The family in our study reported that the diet regimen supported their quality of life to some extent, and that treatment was more effective with multiple treatment approaches such as speech and language therapy, and animal therapy. Liégeois and Morgan reported that it was important to start speech therapy in children with metabolic disease, which is responsible for 76% of speech disorders (16). The treatment approach found in the literature was observed to coincide with the treatment approach that the child and the family were directed in our study. However, after evaluating the child in GA1, we noticed that evidence-based studies were needed regarding the treatment and therapy approaches that families could be directed to.

Psychological Effects

In our study, the parents stated that they were shocked when they first heard the diagnosis after birth. In the literature, the moment when families first learn the diagnosis is depicted as the most difficult time to bear (17). The mother had a rapid transition to the acceptance stage with her maternal instinct and taking on the care responsibility. The father, on the other hand, showed reactions in the form of accusing the mother and moving away for a while. In the literature, the perceptions of society regarding the roles of the mothers and fathers are also effective. When the differences between fathers and mothers in terms of reactions to chronic diseases are examined, studies can be seen to generally focus on mothers as the mother is the main caregiver and the father is mostly engaged in financial affairs (18,19). The existence of evidence-level studies that will determine the differences between the mother and father is important in terms of eliminating the gap in the field (18,20).

Family members may have difficulty coping with the time-consuming care and different medical and dietary treatments of the patient (17). In our study, the father reported that several treatment methods were administered and he tried to get away from the disease process for a while as he could not cope with it.

Also, the mother mentioned that she spent efforts for her child with her maternal instinct, she suppressed some emotions to cope and tried to be strong. Similar to our study, Golfenshtein et al. (21) stated in their study that mothers tried to be strong by suppressing their emotions for their children in cardiology intensive care and that they coped with it in this way.

In genetically hereditary metabolic diseases, the mental state of the individual is affected (22). Individuals with mental retardation can make up a group that believes others readily and is open to neglect and abuse. For this reason, parents' concerns for the future increase in these situations (23). In our study, the family thought their child believes everyone and can be easily fooled because he could not do calculations for simple monetary matters. In the literature, it is seen that families with children who are followed up with the diagnosis of metabolism have concerns about how their children live in adulthood, the conditions that may be experienced in transition to independence and their safety (12,24). In chronic diseases, parents' concerns about their children's future affect their quality of life.

Social Effects

Taking/giving care to a child with hereditary metabolism disease affects the marriage relationships, the development of other siblings, and the relationship with other people around them (10,25). In our study, the mother stated that she focused her attention on her sick child more and that this affected the relationship between the spouses. In the study of Pelentsov et al. (19) most of the parents whose children were followed up with a rare disease mentioned that the disease process brought the spouses closer to each other, while some parents stated that the mother was often busy with caring the child and that the father worked for earning money, which prevented parents from spending time together (19).

In social communication and interaction, communication with nature and animals has positive effects on the development of children. In our study, the family stated that being in touch with nature and doing gardening made the child realize what he could do and that therapy with animals such as horse riding speeded up the child's speech. Studies have reported that these therapies support the development of the child and increase psychological well-being in children with speech delay (26), children with mental disabilities (27), and children with cerebral palsy (28). The combination of approaches such as animal therapies and medical therapy in neurometabolic diseases are thought to provide progress in the treatment and growth of the child.

Spiritual effects

In life-threatening situations, the patient and the family increasingly need spiritual resources such as hope, inner confidence, empowerment, loving and being loved, harmonious relationships, religious practices, relationships, and seeking meaning (29,30). The mother in our study reported that she made sense of her child diagnosed with glutaric aciduria as her miracle and that she found happiness in life with this perspective. The mother stated that the process shaped the meaning and purpose of life. The father added that the meaning and purpose of life came from being healthy, and so he understood it better. In our study, the other sub-themes discussed in the spiritual dimension of the disease were "my beliefs and values". The mother mentioned that her belief in what she could do as a caregiver facilitated the process rather than religious belief. The father, on the other hand, mentioned that embracing his religious belief gave hin relief in the early stages of the diagnosis. In the study of Büssing et al. (31) the effects of the disease process on spiritual needs in individuals with disease-causing cancer and chronic pain was studied in Germany in four areas. These included religious needs (praying, attending a religious ceremony, reciting religious/spiritual books, etc.), need for inner peace/tranquility (desire to be in a place where you will find silence and peace, experiencing the beauty of nature, talking to someone about fear and anxieties), and existential needs (31).

CONCLUSION

GA1 affects the quality of life of the patient and the family in many ways. According to the results of the study, it is important to know the factors affecting health-related quality of life to be able to plan and implement an appropriate approach to the family and child followed-up with this diagnosis. One of the limitations of the study was that it was conducted with a small sample size. On the other hand, holding an in-depth qualitative interview with the family constituted the strength of the study.

Conflict of interest
No conflict of interest was declared by the authors.

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REFERENCES

1. Heringer J, Boy N, Burgard P, Okun JG, Kölker S. Newborn screening for glutaric aciduria type i: benefits and limitations. International Journal of Neonatal Screening 2015; 1(2): 57-68.
2. Heringer J, Boy SN, Ensenauer R, Assmann B, Zschocke J, Harting I, et al. Use of guidelines improves the neurological outcome in glutaric aciduria type I. Ann Neurol 2010; 68(5):743-752.
3. Couce ML, López-Suárez O, Bóveda MD, Castiñeiras DE, Cocho JA, García-Villoria J, et al. Glutaric aciduria type I: outcome of patients with early-versus late-diagnosis. Eur J Paediatr Neurol 2013;17(4):383-389.
4. Viau K, Ernst SL, Vanzo RJ, Botto LD, Pasquali M, Longo N. Glutaric acidemia type 1: outcomes before and after expanded newborn screening. Mol. Genet. Metab. 2012;106(4):430-438.
5. Zeltner NA., Landolt MA, Baumgartner MR, Lageder S, Quitmann J, Sommer R, et al. Living with intoxication-type inborn errors of metabolism: a qualitative analysis of interviews with paediatric patients and their parents. In JIMD Reports 2016; 31: 1-9.
6. Mlčoch T, Puda R, Ješina P, Lhotáková M, Štěrbová Š, Doležal T. Dietary patterns, cost and compliance with low-protein diet of phenylketonuria and other inherited metabolic diseases. Eur J Clin Nutr 2017; 72(1):87–92. doi:10.1038/ ejcn.2017.102.
7. Siddiq S, Wilson BJ, Graham ID, Lamoureux M, Khangura SD, Tingley K et al. Experiences of caregivers of children with inherited metabolic diseases: A qualitative study. Orphanet J. Rare Dis. 2016; 11(168): 1–10. doi:10.1186/s13023-016-0548-2.
8. Gramer G, Haege G, Glahn EM, Hoffmann GF, Lindner M. Burgard P. Living with an inborn error of metabolism detected by newborn screening—parents' perspectives on child development and impact on family life. J Inherit Metab Dis 2014;37(2):189-195.
9. Boy N, Mühlhausen C, Maier EM, Heringer J, Assmann B, Burgard P et al. Proposed recommendations for diagnosing and managing individuals with glutaric aciduria type I: second revision. J Inherit Metab Dis 2017;40(1):75-101.
10. Fidika A, Salewski C, Goldbeck L. Quality of life among parents of children with phenylketonuria (PKU). Health Qual Life Outcomes 2013;11(1):54.
11. Drew SE, Duncan RE, Sawyer SM. Visual storytelling: a beneficial but challenging method for health research with young people. Qual. Health Res 2010;20(12):1677–1688.
12. Piercy H, Machaczek K, Ali P, Yap S. Parental experiences of raising a child with medium chain acyl-CoA dehydrogenase deficiency. Glob Qual Nurs Res 2017;4:1-8.
13. Sulmasy DP. A biopsychosocial-spiritual model for the care of patients at the end of life. Gerontologist 2002;42:24–33.
14. Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol 2006;3(2): 77–101.
15. Gallant NM, Leydiker K, Wilnai Y, Lee C, Lorey F, Feuchtbaum L et al. Biochemical characteristics of newborns with carnitine transporter defect identified by newborn screening in California. Mol Genet Metab 2017;122(3):76-84.
16. Liégeois FJ, Morgan AT. Neural bases of childhood speech disorders: lateralization and plasticity for speech functions during development. Neurosci Biobehav Rev 2012;36(1):439-458.
17. Hockenberry M. Wilson D, Rodgers C. Wong's Essentials of Pediatric Nursing. 10th ed Missouri: Elsevier-Mosby*;* 2016.
18. Foody C, James JE, Leader G. Parenting stress, salivary biomarkers, and ambulatory blood pressure: a comparison between mothers and fathers of children with autism spectrum disorders. J Autism Dev Disord 2015; 45(4):1084-1095.
19. Pelentsov LJ, Fielder AL, Laws TA, Esterman AJ. The supportive care needs of parents with a child with a rare disease: results of an online survey. BMC family practice, 2016;17(1):88.
20. Yogman M, Garfield CF, Committee on Psychosocial Aspects of Child and Family Health. Fathers' roles in the care and development of their children: the role of pediatricians. Pediatrics, 2016;138(1). doi: 10.1542/peds.2016-1128.
21. Golfenshtein N, Deatrick JA, Lisanti AJ, Medoff-Cooper B. Coping with the stress in the cardiac intensive care unit: can mindfulness be the answer? J Pediatr Nurs;37:117–126.
22. Yilmaz, G. Mothers with disabled children: needs, stress levels and family functionality in rehabilitation. Scand J Caring Sci. 2020;34(2):524-532
23. Quiroz HJ, Parreco J, Easwaran L, Willobee B, Ferrantella A, Rattan R, et al. Identifying populations at risk for child abuse: a nationwide analysis. J Pediatr Surg 2020;55(1):135-139.
24. Freedman R, Sahhar M, Curnow L, Lee J, Peters H. Receiving enzyme replacement therapy for a lysosomal storage disorder: a preliminary exploration of the experiences of young patients and their families. J Genet Couns 2013;22(4):517-532.
25. Grant S, Cross E, Wraith JE, Jones S, Mahon L, Lomax M et al. Parental social support, coping strategies, resilience factors, stress, anxiety and depression levels in parents of children with MPS III (Sanfilippo syndrome) or children with intellectual disabilities (ID). J Inherit Metab Dis 2013;36(2):281-291.
26. Anderson HK, Hayes SL, Smith JP. Animal Assisted Therapy in Pediatric Speech-Language Therapy with a Preschool Child with Severe Language Delay: A Single-Subject Design. IJAHSP 2019;17(3):1.
27. Nedzinskaitė U, Mažeikaitė J, Paleckaitis M, Stankevičius R. Canine-assisted therapy and the improvement of physical characteristics in disabled children: a pilot study. Sveik. Moksl**.** 2019;29: 6.
28. Elmacı DT, Cevizci S. Dog-assisted therapies and activities in rehabilitation of children with cerebral palsy and physical and mental disabilities. INT J ENV RES PUB HE 2015;12(5):5046-5060.
29. Ramezani M, Ahmadi F, Mohammadi E. Spirituality in contemporary paradigms: An integrative review. Evidence Based Care 2016;6(2):7-18.
30. Saad M, De Medeiros R, Mosini AC. Are we ready for a true biopsychosocial–spiritual model? The many meanings of "spiritual". Medicines 2017;4(4):79.
31. Büssing A, Föller-Mancini A, Gidley J, Heusser P. Aspects of spirituality in adolescents. International Journal of Children's Spirituality, 2010;15(1):25-44.

Appendix I. Interview guides for semi-structured interviews

Parents Experiences

- Tell me about a typical week with your family
- Tell me about your experiences about the diagnosis of glutaric aciduria type I
- What do you tell when you are told that “living with a child who is being followed up with glutaric aciduria”?
- What are your experiences with the treatment process?
- What would you like to say when you think about your children's future?
- What are your coping strategies?
- What are your supports?
- How did this affect your plans? (family life, choices, lifestyles, decision-making processes ...)

Prompts relating to child/children

Medical treatment

- How does your child describe the disease condition?
- What are your child's thoughts on the glutaric aciduria process according to you?
- Diet plan;
  - a) How did it affect your child?
  - b) How did it affect family members?

Psychosocial

- What are your child's likes to do?
- How is your child's communication with the environment?
  - a) Friends
  - b) Teachers
  - c) Family
- What is the approach of the people around you to your child?
- What can you say when you consider the psychosocial effects of treatment on your child?
- What are the stressful situations your child experiences in this process?
- What would you say about how your child coped in stressful situations?
- What are your other child's thoughts/reactions about his/her sibling's disease?

Spiritual

- What would you like to say about the meaning / purpose / well-being of life?
- Your well-being;
  - a) Disease
  - b) How did treatment (diet therapy and others) affect?

Interview guide for semi-structured interviews with siblings

- What do you like to do in daily life? (school, friends, etc.)
- What are your experiences of having a sibling who is being followed up with the diagnosis of glutaric acid type 1?
  - a) What does it mean for your family?
  - b) What does it mean to you? How did it affect your life? How do you feel?
  - c) How can you explain this situation to someone who wants to learn something about glutaric aciduria?
  - d) What is the reaction of friends and the environment to the disease?
  - e) What kind of explanation was given to you about this situation of your brother?
  - f) Some children have to be treated. They meet many doctors and nurses. What do you think about this? What are the things you say “it would be better for my sibling if it were done”?
  - g) How did the diet (tryptophan and lysine restricted diet) affect your sibling?
- What would you say about coping in stressful situations?
- What do you want to say when you say the meaning / purpose of life / spirituality / well-being?