https://doi.org/10.48047/AFJBS.6.2.2024.2673-2685

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

Phenylketonuria, Mucopolysaccharidosis and Gaucher Diseases Mothers' Lived Experiences: A Phenomenon Study

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Article History

Volume 6, Issue 2, Apr-Aug 2024

Received: 10 August 2024

Accepted: 15 August 2024

Published: 15 August 2024

doi: 10.48047/AFJBS.6.2.2024.2673-2685

Abstract: Background: Inborn errors of metabolism are a heterogeneous group of disorders that have many sequels. Mothers of these children are living various experiences which need many studies and explanations.
The aim of the study: This study aimed to explore the lived experiences of mothers caring for children with some inborn errors of metabolism like phenylketonuria, gauche disease, and mucopolysaccharidoses.
Methods: Interpretive phenomenological analysis using **Braun & Clarke** approach that provides a six- phase guide and data were gathered using semi-structured interviews and the interviews were audio recorded.
Setting: The study was conducted at the Pediatric Metabolic, and Genetic Unit at Zagazig University Hospitals.
Participants:A purposive sample composed of 21 mothers whose children suffer from (10 Phenylketonuria, 5 Mucopolysaccharidoses, and 6 Gaucher Disease).
Results: The six final themes were revealed from exploring mothers' experiences including the complexity of the diagnosis process, seeking understanding, coping with the disease effects, perceived social support, concerns for the future, and access to the health care services.
Conclusion: Inborn errors of metabolism had heavy social, psychological, and financial burdens on all family members. However, this study found that mothers were most affected by psychological issues, particularly isolation. **Recommendation:** it is become essential to develop programs for helping mothers of children with inborn errors of metabolism to reduce the burden of these diseases on mothers and consequently the children and the whole family
Keywords: *Lived experiences, Mothers, Children, and Inborn errors of metabolism*

Introduction

Inborn errors of metabolism (IEMs) are a heterogeneous group of rare genetic disorders that are generally transmitted as autosomal or X-linked recessive disorders. These defects arise due to mutations associated with specific genes, especially the ones associated with key metabolic enzymes **(Bharadwaj et al., 2021)**. Environmental, epigenetic, microbiome factors and additional genes are potential modifying etiologic factors in those with inborn errors of metabolism **(Ferreira et al., 2019)**.

The estimated number of IEMs cases in a hypothetical annual Egyptian birth cohort of 2.5 million newborns is 1286. Phenylketonuria cases are expected to constitute 40%–50% of all detected cases, with a prevalence of 1: 5000 live births **(Hassan et al., 2016)**. In the inborn errors of metabolism, the clinical signs and symptoms arise from the accumulation of the toxic substrate, deficiency of the product, or both. Depending on the residual activity of the deficient enzyme, the initiation of the clinical picture may vary starting from the newborn period up until adulthood **(Mainka et al., 2021)**.

Phenylketonuria (PKU) is a rare autosomal recessive, inborn error of amino acid metabolism caused by a deficiency of the hepatic enzyme, phenylalanine hydroxylase (PAH), which catalyzes the hydroxylation of phenylalanine (Phe) to tyrosine requiring the cofactor tetrahydrobiopterin (BH4) **(Rodrigues et al., 2021)**.

Infants with PKU typically appear normal at birth. However, untreated newborns not diagnosed in the first days of life may be weak and feed poorly. Other symptoms may include vomiting, irritability and/or a red skin rash with small pimples. Developmental delay may be obvious at several months of age. Intellectual disability in PKU is a direct result of elevated levels of Phe in the brain. It can also cause depression by reducing brain levels of dopamine and serotonin. Untreated infants with PKU tend to have unusually light eye, skin, and hair color due to high Phe levels interfering with production of melanin. They may also have a musty or "mousy" body odor caused by phenyl acetic acid in the urine or sweat. Neurological symptoms are present in some untreated patients, including seizures, abnormal muscle movements, tight muscles, increased reflexes, involuntary movements, or tremors **(National Organization for Rare Disorders, 2023)**.

Gaucher disease is a rare genetic disorder characterized by the deposition of glucocerebroside in cells of the macrophage-monocyte system. The disorder results from the deficiency of the enzyme glucocerebrosidase. While Gaucher disease manifests with vast clinical heterogeneity, it traditionally has been differentiated into the following 3 clinical subtypes, delineated by the absence or presence of neurologic involvement and its progression: type 1 - nonneuronopathic Gaucher disease, type 2 - acute neuronopathic Gaucher disease, and type 3 - chronic neuronopathic Gaucher disease and two other subtypes (perinatal-lethal and cardiovascular)**(Stone et al., 2023)**.

The mucopolysaccharidoses (MPS) constitute one of the main groups of the lysosomal storage disorders and include several disorders with overlapping features and a combined incidence of 1 in 25,000 live births. The most common types are MPS I, MPS II, MPS III and MPS IV, with incidences and relative frequencies of that vary from region to region. MPS II is inherited as an X-linked recessive trait while all the others have autosomal recessive inheritance. MPS III is divided into four subtypes-A, B, C, and D; and MPD IV is of 2 subtypes IV-A and IV-B **(Swetha et al., 2021)**.

The mucopolysaccharidoses share many clinical features that may be apparent at birth but progress as the storage of glycosaminoglycans affects bone, skeletal structure, connective tissues, and organs. The age of presentation or onset varies widely. Neurological complications may include damage to neurons, pain and impaired motor function, and damage to the peripheral nervous system connects the brain and spinal cord to sensory organs. Affected children may have intellectual disabilities, developmental delays, behavioral problems, hyperactivity, depression, speech and hearing impairment, hepatosplenomegaly, hernias, short stature, coarse facial features, cloudy eyes, and thickened skin. Children with MPS also have a significantly shortened life span **(National Institute of Neurological Disorder and Stroke, 2023)**.

The management of IEMs has traditionally consisted in diet therapy and supportive therapy, but recently other treatment options have become available, including enzyme and coenzyme replacement, removal of

harmful substances, cell and organ transplantation, and gene therapy **(Fukao & Nakamura, 2021)**. Nursing care for a child with IEMs involves a multidisciplinary approach, focusing on symptom management, assessing the child's physical, psychological, and social needs, improving quality of life, providing support to the children and their family, coordinating medical appointments, and managing referrals with other healthcare team **(National Organization for Rare Disorders, 2023)**.

Aim of the study

The current study aimed to explore lived experiences of mothers caring for children with Phenylketonuria, Gaucher Disease and Mucopolysaccharidoses..

Research question:

What are the lived experiences of mothers caring for children with Phenylketonuria, Gaucher Disease, and Mucopolysaccharidoses?

Participants and methods

Research Design:A qualitative descriptive exploratory design by using interpretative phenomenological approach (IPA).

Settings: The current study was conducted at the Pediatric Metabolic, and Genetic Unit at Zagazig University Hospitals.

Participant and recruitments:

A Purposive sampling (selective sampling) was composed of **21** mothers whose children suffered from some selected diseases of Inborn Errors of metabolism; **the sample** included **10** mothers of children with Phenylketonuria, **5** mothers of children with Mucopolysaccharidoses, and **6** mothers of children with Gaucher Disease. They were represented during the study as:

(Participant 1:10):	Mothers of children with Phenylketonuria
(Participant 11:15):	Mothers of children with Mucopolysaccharidoses
(Participant 16: 21):	Mothers of children with Gaucher Disease

<u>Mothers were recruited based on the following criteria:</u>

- Mother was the primary care giver of the child.
- Age of children was up to 10 years.
- The mother's availability for the interview and willingness to share her experiences.

The sample size was determined on the basis of theoretical saturation (the point that when the new data no longer bring additional insights to the research question).

Tools of data collection:

Part I: Socio- demographic data:

It was composed of **12** open and closed ended questions about mother's age, residence, mother's education& occupation, marital status, number of children, number of affected children, child's diagnosis, age& gender, time of disease diagnosis and telephone number **(questions: 1-12)**.

Part II: Interview guide:

According to **Busetto et al., (2020)** using open-ended questions utilized in qualitative methods, the researcher can gain an in depth understanding of the study issues. The researcher is able to "understand and capture the points of view of other people without predetermining those points of view through a prior selection of questionnaire categories" so this study used semi- structured interview guide included open ended questions about **6 domains:** diagnosis process, supporting system, parenting process, challenges &problems, management of disease at home and in the community and experiences with the health care system

Data collection:

- First, the researcher reviewed the past and current available literature relevant to the current study and theoretical knowledge of various aspects of the study was done using textbooks, articles, internet periodicals and scientific journals in order to get a clear picture of all aspects related to the problem. This helped in the design of data collection tools and fieldwork.
- An official permission was obtained by submission of formal letters issued from the Dean of Faculty of Nursing, Zagazig University to the responsible authorities of the Pediatric Metabolic Genetic Unit at Zagazig University Hospitals to obtain their permission for data collection.
- **A pilot study was** conducted at the Pediatric Metabolic, Genetic Unit at Zagazig University Hospitals with the participation of two mothers of children with Inborn Errors of Metabolism. It was very useful step for the researcher to be more experienced in applying qualitative research. The two mothers involved in the pilot study were excluded from the study sample.

Procedure of conducting in- depth interview:

In qualitative research, semi-structured interviews are a hybrid of structured and unstructured interviews in that some questions are predefined while others are not. Furthermore, they allow you to focus on the topic of interest while allowing you to explore ideas that may arise throughout the interview. Semi-structured interviews are used to explore participants' thoughts and attitudes about a specific issue **(George, 2022).**

- Once a participant was deemed eligible and the aim of the study was fully explained, an interview was scheduled at a mutually-agreed upon time and location that best served the participant given the complexity and time constraints of caring for their diseased child. Participants chose to meet in the Pediatric Metabolic, Genetic Unit at Zagazig University Hospitals when they were there for healthcare-associated visits and some mothers preferred to make the interview via telephone.
- Then oral informed consent of participants was obtained. Also, they were notified that they could withdraw at any time of the interview.
- Semi-structured interviews were conducted with the use of an interview guide and were audio recorded. Participants were asked to describe their experience of having a child diagnosed with inborn errors of metabolism. Additional questions were posed based on responses to previous questions and comments. During questioning, notes were taken regarding verbal and nonverbal replies.
- To move the interview into more in-depth territory, probe questions like "I don't think I understand what you mean, can you explain more?" or "What happened after that?" were utilized. The researcher responded to the interviewee by practicing active listening, using quiet, and letting the participants feel free to express their experiences.
- Identifying information such as names& home addresses was removed. Each interview lasted approximately half to one hour depending on the degree of detailed each interviewee contributed.
- At the end of the interview, the researcher asked the participants if they had any more comments. They were also thanked for their participation.
- The researcher played the role of moderator and data collector as the researcher conducted all interviews, recorded, transcribed, and interpreted the findings.
- Also, while conducting the study the researcher was aware of personal bias and prejudgments. So, it was the researcher obligation and responsibility to follow a scientific and professional manner at all time. The researcher took every attempt to stay objective.

Coding& Analysis:

The current study used **thematic analysis approach** guided by **Braun & Clarke (2006)** who provide a six- phase guide **(Familiarization, Generating initial codes, Searching for themes, Reviewing themes, Defining and Naming themes and Write-up)**. The phases are not necessarily linear. You may move forward and back between them, perhaps many times, particularly if dealing with a lot of complex data.

Trustworthiness of data: To achieve the trustworthiness criteria; credibility, dependability, confirmability, and transferability were used in this study.

Results:

Table (1): Socio-Demographic Characteristics of Mothers Caring for Children with Inborn Error of Metabolism (n=21).

Socio-Demographic Characteristics	no.	%
Mother age (years)		
▪ ≤35	15	71.4
▪ >35	6	28.6
Mean ± SD 32.90±6.30		
Residence		
▪ Rural	15	71.4
▪ Urban	6	28.6
Employment status		
▪ Employed	2	9.5
▪ Non- employed, looking for work	1	4.8
▪ Non- employed, not looking for work	18	85.7
Educational level		
▪ Illiterate, read and write	2	9.5
▪ Lower than high school degree	0	0.0
▪ High school degree or equivalent	12	57.1
▪ Associate degree	1	4.8
▪ Bachelor's degree	5	23.8
▪ Master or PhD degree	1	4.8
Marital status		
▪ Married	19	90.5
▪ Widow	1	4.8
▪ Divorced	1	4.8
Number of children		
▪ ≤3	15	71.4
▪ >3	6	28.6
Number of affected children		
▪ 1	15	71.4
▪ 2	4	19.0
▪ 3	2	9.6
Child age (Years)		
▪ <5	11	52.4
▪ >5	10	47.6
Mean ± SD 5.23±2.83		
Time of disease diagnosis		
▪ Before one year of age	12	57.1
▪ After one year of age	9	42.9
Child gender		
▪ Male	12	57.1

▪ **Female**	**9**	**42.9**

Table (1) shows that 71.4% of mothers were 35 years or younger, with a mean age of 32.90±6.30 years and 90.5% were married. Furthermore, 71.4% of mothers were from rural areas. Regarding the employment, 85.7% of mothers were unemployed and not seeking for work. In addition, 57.1 % of them had a high school degree or equivalent. The same table reveals that 71.4% of mothers had three or less children, with only one affected child. Concerning the child age, 52.4% were 5 years or younger, with a mean age of 5.23±2.83years and 57.1% were male. Moreover, 57.1% of children were diagnosed before the age of one year.

Emergent Themes and Sub-Themes:

Theme I. The complexity of the diagnosis process:

Obtaining an accurate diagnosis can be a long journey for many patients with inborn errors of metabolism.

Subtheme 1: Delayed diagnosis:

In this study, nearly half of the mothers received at least one or more incorrect diagnosis for their children before their rare diseases were appropriately recognized. Furthermore, the majority of mothers reported consulting more than two health care professionals before receiving an appropriate diagnosis.

P (4): *" Oh …when I remember what I went through, I couldn't help but crying. I've been seeing more than four doctors in the last six years to find out about my son's illness.*

P (11, 14): *"We sought medical treatment to find the origin of my child's continuous runny nose, as well as delays in walking, talking, and teeth development. Before receiving the diagnosis, I seem to have seen more than three doctors."*

Subtheme 2: Outcomes of delayed diagnosis:

Several mothers indicated that delayed diagnosis had severe, irreversible, and sometimes life-threatening consequences such as prolonged hospitalization, incorrect therapies, learning difficulties, and speech problems. Furthermore, mothers revealed that failure of disease diagnosis was the reason for the death of other children previously.

P (10): *"I was ignorant that my son's learning difficulties, which required many speech therapy sessions until he was nine, were symptomatic of PKU. These sessions ended when we started treatment, so we didn't need them anymore."*

P (12): *"My child's condition was not diagnosed until he was five and a half years old, which led to a variety of complications. These included many surgeries on his tonsils, adenoids, and eye, as well as hydrocephaly and macular edema, which caused vision impairment."*

Theme II: Seeking understanding:

Seeking understanding refers to the mother's desire to get adequate information to understand their child's rare disease, its prognosis and the child's future needs.

Sub-theme 1: Health care professionals:

The physician was the major source of information and initial contact for all mothers in this study at the time of diagnosis. **One of the mothers literally said,** *"The presence of such doctors and nurses was a gift from God. They simplified everything for us."*

Subtheme 2: Personal research:

When their children were first diagnosed, some mothers were overwhelmed by their own lack of information, as well as their fear and confusion regarding their child's sickness and all factors associated to it, such as prognosis, drug availability, and food. All of these factors caused the mothers to be not only satisfied with the knowledge provided by health care professionals, but also to embark on a journey of discovery via YouTube and Google.

P (*2*): *"I started searching on YouTube, but owing to the intricacy of the situations I saw, this topic frustrated me."*

Subtheme 3: Other families:

All of the mothers agreed that having other families with the same disease was beneficial. We formed a Whatsapp group where we discussed the best sources to find information on the illness. **One of the mothers precisely said,** *"Several times, I would see myself hanging out with friends and having interesting conversations—as though I wasn't going to the hospital."*

Theme III: Coping with the disease effects:

Subtheme 1: Adjustment to caring for the child's special needs:

In every situation, mothers had to learn how to care for their child's special needs such as diet and medication. Each illness had a unique impact and necessitated a unique treatment strategy. For mothers, this meant altering their regular routine to include child care.

For two of the mothers, adjusting to meet the child's needs meant they would not have to work anymore. **(P: 6, 15).** Moreover, for the **participant (3)**, she had to work a part- time.

In contrast, for one mother **(P: 9)**, adjusting to meet the child needs meant she needed to work to cover the costs of the treatment, diet and multiple medical appointments.

Subtheme 2: Parental advocacy:

Because of the rarity of these genetic disorders, the participants had to look after the child's needs and also acted as advocates to make sure the child received proper care especially in the context of controlling diet.

Some mothers also talked about advocating at a wider level with the government, to obtain the necessary foods or services as one of the mothers described word- for- word in a shaky voice,

P (*6*): *"We were on constant defense with the government and the Ministry of Health to guarantee that our children had access to enough food and therapy. We also created a Facebook group to promote these rights, which were referred to as metabolic rights."*

Theme IV: Perceived social support:

Social support is so vital that it forms a distinct dimension of its own. Appreciation of the mothers' exhaustion and kind words from husbands, friends and neighbors were the basis for this support.

Subtheme 1: Adequate social support:

In this study, mothers expressed the highest mutual partner support. These mothers shared the responsibility of caring for their children with their husbands, reduced tension by talking to one other, and provided consolation when needed. Some mothers also appreciated their friends, relatives and neighbors for their financial and spiritual help.

P (1): *"I was unable to express how much my husband helped me and occasionally put in more work than I did."*

P (5, 13, 21): *"Nothing soothed me more than kind words, and I only received them from my spouse, family members, and my relatives."*

Subtheme 2: Inadequate social support:

Only two of the mothers spoke with a broken heart about their husbands' abandonment of them.

Theme V. Access to health care services:

This study's interviews showed that these children used a wide variety of medical experts (e.g., geneticists, pediatricians, ophthalmologists, dentists and surgeons) and healthcare-support services (e.g., speech therapy, neurologists, physiotherapy, psychosocial therapy).

Subtheme 1: Co- ordination of care:

IEMs are chronic, progressive illnesses that affect several body systems and require a medical care with multidisciplinary nature to handle these disorders. As a result, it is critical that these varying healthcare practitioners communicate effectively and coordinate the patient's care efficiently.

Almost all the mothers were pleased with the coordination of cares, **as one of the mothers stated,** *"Although the hospital didn't provide this kind of care [she meant multidisciplinary care], the responsible physician worked*

with nurses to provide what children needed from other medical specialties, or at the very least to guide us in the right direction."

Subtheme 2: Interaction with the medical community:

Nearly all the mothers had positive interaction with the health care staff as they said, they assisted us in getting the treatments we needed and spoke on behalf of our children if those treatments were delayed. Additionally, they consistently communicated with the Ministry of Health and Health Insurance to facilitate certain situations for us.

In terms of personal communication, their contact was excellent, and they created a Whatsapp group to assist us in every way they can.

Subtheme 3: Challenges and barriers encountered in health care services:

Participants in this study encountered a variety of barriers to accessing health care services required to manage their children's condition, including medical professionals' limited knowledge of rare disease, difficulties with medical insurance, the drug process, and the lack of health specialists in their areas of residence. Furthermore, financial difficulties related to transportation, drugs, investigations, and medical appointments.

Mothers of children with MPS& GD stated, *"The hardest thing was having to complete health insurance paperwork every two weeks so that my child could get his medication, and the worst part was having to wait more than two years for a court order to be issued so that we could start taking the medication."*

Mothers of children with PKU, *"For certain necessities, the government supplied insurance, but it wasn't enough, so we had to obtain the rest from pricy private sources."*

Theme VI. Concerns for the future:

After the initial shock of the diagnosis had worn off and the mothers demonstrated resilience and stability, they began to inquire about the child's prognosis and what to expect in general in the future. They were also anxious about having additional children in the future.

Subtheme 1: Worry about the child unpredictable future:

The need for their children to be strong and healthy was the primary issue for these mothers, who expressed severe anxiety and fear about what would happen in the future if an adequate diet (for PKU cases) and drugs were no longer available. **Almost all PKU children's mothers literally said,** *"The food that my child eats is essential to his survival; I cannot imagine what would happen to him if these products were unavailable. My heart would stop beating.* ***Moreover, some moms expressed worry about their own mortality by saying****, "I ask myself daily: who would be able to give my child the same care I provide if something happened to me?"*

Subtheme 2: Uncertainty about having more children:

With a rare genetic disorder, the key dilemma for mothers was about having more children and whether or not they would be born with the same disease. Despite the difficulties, some mothers have abandoned the concept of having children entirely, and in turn, others have taken this step; some gave birth to healthy children, while others had more sick children.

P (14), *"I never gave birth again after my daughter's disease was diagnosed, and I never will because I can hardly care for my sickly child."*

Discussion:

Theme I. The complexity of the diagnosis process

The present study revealed that obtaining an accurate diagnosis constitutes a major obstacle for children with IEMS. Nearly half of the mothers received at least one or more incorrect diagnosis for their children before their rare diseases were appropriately recognized. These hurdles often necessitated many medical consultations and extensive diagnostic testing as the majority of mothers reported consulting more than two health care professionals before receiving an appropriate diagnosis.

These finding could be explained by the fact that many genetic syndromes have overlapping features, and many syndromes are still undergoing more intensive and in-depth research to understand their causes and

symptoms better. The less we know about the rare diseases, the more likely a misdiagnosis becomes. Also, Egypt has an established newborn screening programme; but unfortunately, it is limited to discovering only some genetic diseases, not all of them.

These findings aligned with **Awada & Holcik (2022)** who conducted qualitative interviews with Canadian patients living with lysosomal storage diseases and their families to enrich and advance current understanding of their experiences with rare-disease management and health systems navigation; they reported that every participant in that study was received at least one incorrect diagnosis before their rare disease was correctly identified and most participants indicated that they had consulted more than five healthcare professionals before ultimately receiving a correct diagnosis.

Also, in the same context, 33% of children included in a study about experiences of diagnosis with rare diseases and consequences of diagnostic delays in Australia by **Zurynski et al. (2023)** received an initial incorrect diagnosis and before receiving the correct diagnosis 38% consulted ≥ 6 different doctors. Among those with a diagnosis, 37% believed the diagnosis was delayed and 27% initially received a wrong diagnosis.

The present study highlighted the fact that delay and misdiagnosis has severe, irreversible, and sometimes life-threatening consequences, such as prolonged hospitalization, incorrect therapies, learning difficulties, and speech problems. Furthermore, mothers revealed that failure of disease diagnosis was the reason for the death of other children previously.

The previous finding was matching with **Yang et al. (2020)** who performed a study about newborn screening and diagnosis of inborn errors of metabolism in china and **Abdelsattar et al. (2022)** who carried out a study about inherited metabolic disorders in a cohort of Egyptian children in Egypt.

Theme II: Seeking understanding

The present study revealed that the physician was the major and primary source of information for all mothers at the time of diagnosis and this may be due to the extreme rarity of the conditions. Also, there was a great cooperation between the genetic specialist and skilled nurses to provide mothers with more extensive information about the diet, medication, prognosis, and other health care services.

This study's finding was consistent with **Rivard& Mastel-Smith (2014)** in USA who carried out a study to describe the father's experience of having a child diagnosed with a genetic disorder and **Balakrishnan (2021)** who conducted a study about approach to diagnosis and management of inborn errors of metabolism in neonates in India.

The current study stated that when the children were first diagnosed, the mothers were overwhelmed by their own lack of information, as well as their fear and confusion regarding their child's sickness and all factors associated to it, such as prognosis, drug availability, and food. All of these factors caused the mothers to be not only satisfied with the knowledge provided by health care professionals, but also to embark on a journey of discovery via YouTube and Google and in some instances, they shared with other families who have the same diseased child the best sources of information regarding the disease, such as available services and food preparation methods.

This finding was congruent with **Rajasekar et al. (2020)** who conducted a study about parental psychosocial aspects and stressors involved in the management of inborn errors of metabolism in Canada; found that some parents educated themselves through independent research. Also, many of the parents felt confident with the healthcare team and relied heavily on their input.

Also, studies conducted by **Clifford& Minnes (2013), Shilling et al. (2013) and Gómez-Zúñiga et al. (2019)** have indicated that mutual support between families in similar situations with regard to their children's rare diseases, the encouragement they given one another, is of crucial importance. It provides parents with a kind of shared social identity, a feeling of belonging to a group, that enables them to deal with the situation better, alleviates their stress and makes them feel more empowered to manage their children's needs.

Also, **Rajasekar et al. (2020)** revealed that parents developed an increased awareness of inborn errors of metabolism in general through the meaningful connections they made with families worldwide.

Theme III: Coping with the disease effects

In the present study, mothers of PKU children used to feed them Phe-free meals that were mostly made of vegetables. Some mothers experienced stress due to the continual modifications in the preparation of this diet, which is dependent on the level of Phe in the blood. Also, it took an additional time because it was different from what the rest of the family ate.

This finding aligned with **Shaji Thomas et al. (2021)** who conducted a systematic review about health related quality of life of caregivers of children and adolescents with phenylketonuria in Oman; reported that caring for a child or adolescent with PKU is time consuming, as they must constantly plan, monitor, and measure all daily nutritional intake of their child.

Awada & Holcik (2022) and **Siddiq et al. (2016)** studies; both presented similar findings as our study regarding parental advocacy as mothers advocated to make sure that the child received proper care especially in the context of controlling diet. Also, some mothers talked about advocating at a wider level with the government, to obtain the necessary foods or services. Also, **Baumbusch et al. (2020)** who conducted a study about parents of children with rare diseases' experiences of navigating the healthcare system in Canada; revealed that parents had to advocate and fight the doctors to get services and support for their children

Theme IV: Perceived social support

In the current study, mothers expressed the highest mutual partner support. These mothers shared the responsibility of caring for their children with their husbands, reduced tension by talking to one other, and provided consolation when needed. Also, the majority of mothers appreciated their friends, relatives and neighbors for their financial and spiritual help.

In accordance, **Rajasekar et al. (2020)** reported that social and emotional support for parents came from extended family members and through Individual friendships, outside of family circles. Also, by contrast, a few parents found themselves rekindling and/or forming meaningful friendships with individuals far removed from their previous social circles as a means of getting exposure to and seeking personalized support.

The previous findings differed from **Smits et al. (2022)** who conducted a qualitative study to explore the need for care in pediatric patients with rare diseases in The Netherlands; reported that social support was expressed by several interviewees as they felt a lack of support and understanding from their family, friends or social networks.

Theme V. Access to health care services

According to the current study, after disease diagnosis and beginning treatment, almost all of the mothers were pleased with the coordination of cares provided by different health care providers and had positive interaction with them. This finding was congruent with **Witt et al. (2023)** who indicated that half of the parents reported positive contact with specialists. Also, the parents appreciated professionals showing efforts, availability, open, and honest communication.

Unlike the present study, **Awada & Holcik (2022)** reported that participants had negative impact of inadequate care coordination which caused distress and wasted both time and resources. Also, communication among healthcare professionals was often inefficient, particularly among non-specialist healthcare providers. These parents subsequently emphasized that this could result in significant safety issues and compromised patient care. Also, **Smits et al. (2022)** indicated that some parents felt that health care providers cooperated as separate islands, and miscommunication often occurred and other participants also voiced the need of good coordination of files and information between different health care professionals.

Moreover, **Somanadhan& Larkin (2016)** reported that families felt vulnerable due to the fact that collaboration and communication between healthcare providers were often fragmented and unsatisfactory. They expressed disbelief and frustration towards healthcare systems and felt that these systems had little understanding of what challenges parents of children with MPS experience in their day-to-day life. They described the current healthcare system as being like a revolving door.

Participants in this study encountered a variety of barriers to accessing health care services required to manage their children's condition, including medical professionals' limited knowledge of rare disease, difficulties with medical insurance, and the drug process. This is supported by the results of **Awada & Holcik (2022)**, and **Khangura et al. (2016)** who conducted a qualitative study about child and family experiences with inborn errors of metabolism in Canada.

Theme VI. Concerns for the future

Participants interviewed for the present study emphasized that the need for their children to be strong and healthy was the primary issue. Also, mothers expressed severe anxiety and fear about the unknown that associated with challenges surrounding the diagnosis and what would happen in the future if adequate services and drugs are no longer available. This finding aligned with **Khangura et al. (2016)** who reported that uncertainty about the child's prognosis and future was a common experience following diagnosis. For families whose children had diseases with neurocognitive manifestations, for example, challenges dealing with uncertainty regarding how the child would be affected in the long-term were described. In addition, for those whose children had diseases that were progressive and terminal, uncertainty about the child's mortality was highlighted.

With a rare genetic disorder, the key dilemma for parents especially mothers is about having more children and whether or not they would be born with the same disease. Despite the difficulties, some mothers have abandoned the concept of having children entirely, and in turn, others have taken this step; some have given birth to healthy children, while others have more sick children. This finding is supported by **Rivard& Mastel-Smith (2014).**

Also, the previous findings aligned with **Severijns et al. (2021)** who conducted a study about hereditary diseases and child wish: exploring motives, considerations, and decision-making process of genetically at-risk couples in The Netherlands; emphasized that couples were especially reluctant to opt for a natural pregnancy when the hereditary disease was fatal or if it was a disease with different clinical features among people with the same genotype as they feared for a severe expression in their child.

Also, they found that couples who experienced a neonatal death stated that they did not ever want to experience this again without genetic testing. They also mentioned the psychological strain and feelings of guilt emerging from the uncertainty whether the child is affected or not as a disadvantage of natural conception.

Conclusions:

In the light of the present study, it was concluded that obtaining an accurate diagnosis and seeking understanding of the children's rare genetic disease, its prognosis, and their future needs were life-changing. Also, mothers encountered many barriers in health care services including medical professionals' limited knowledge of rare disease, difficulties with medical insurance, the drug process, and the lack of health specialists in their areas of residence. Furthermore, financial difficulties related to transportation, drugs, investigations, and medical appointments. Another important concern was mothers' fear of having more children in the future, and this strain raised from the uncertainty about whether the child will be born affected by the disease or not.

Based upon the findings of the present study, the following recommendations are suggested:

- Improving The Health Insurance System in dealing with families to provide more transparent, timely, and patient-focused approach to accessing IEMS drugs.
- Improving access to health care and social services and encouraging more collaborative and efficient coordination of care and communication between physicians, patients, and caregivers.
- Establishing a national program which works as a roadmap to guide patients and their family through their disease journey and provide them with the information related to disease services.

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