Disease Burden: Lived Experience of Mothers Caring For Children With Inborn Errors of Metabolism

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Abstract

Background: **Background:** Inborn errors of metabolism are chronic conditions that have many consequences. Mothers of these children are facing different challenges which are underdetermined.

The aim of the study: This study was aimed to analysis the disease burdens of mothers caring for children with some inborn errors of metabolism.

Methods: Interpretive phenomenological analysis using **Braun & Clarke** approach that provides a six- phase guide and it was conducted on 21 motherss whose children suffer from (10 Phenylketonuria, 5 Mucopolysaccharidoses, and 6 Gaucher Disease) and data were gathered using semi-structured interviews and the interviews were audio recorded.

Results: The five final themes were revealed from disease burdens of mothers caring for children with inborn errors of metabolism including Emotional/ Psychological impacts, familial impacts, social impacts, physical impacts, and financial impacts.

Conclusion: Inborn errors of metabolism had a heavy social, psychological, and financial burdens on all family members. However, this study found that mothers were the most affected by psychological issues, particularly isolation.

Recommendations: 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 on the children and the whole family.

Keywords: Disease Burden, Mothers, Children, and Inborn errors of metabolism.

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Introduction

Inborn errors of metabolism (IEMs) are a diverse group of more than 1000 genetic disorders resulting in reduced activity of an enzyme, structural protein, or transporter molecule in a metabolic pathway **(Chimney, 2022).** Although the incidence of each specific disease is rare, collectively IEMs are common and affect 1 in 800 live births **(Ismail et al., 2019).**

The signs and symptoms of these disorders are due to the defect in a metabolic pathway and the aggregation of the defective pathway's metabolites, which are poisonous can cause cell destruction. Additionally, the lower-path metabolite deficiency is effective in disease pathogenesis. This pathogenesis can affect one or more systems **(Sulaiman &Al-Owain, 2019).** Inborn errors of metabolism have a substantial contribution to intellectual disability, seizure, metabolic acidosis, hyperammonemia, ataxia, coma, liver damage, cataract, kidney failure, kidney cyst, cardiomyopathy, pericarditis, sudden infant death syndrome (SIDS), neurological disorders in children **(David , 2018).**

Children with chronic diseases have complex care needs. Inborn errors of metabolism are categorized as rare and chronic conditions that need lifelong support, protection, care, and treatment **(Pilevar et al., 2019).** Caring for a child with IEMs requires specific and lifelong dietary management, which requires constant planning, monitoring, and measurement of the child's daily nutritional intake. Moreover, there might be additional management requirements, such as medical appointments, frequent blood tests, occupational therapy, and speech therapy**(Chimney, 2022).**

Additionally, these children have psychological problems, such as anxiety, depression, social isolation, and low self-confidence and their quality of life is lower than that of their peers **(Adib-Hajbaghery et al., 2019),** and they frequently experience a sense of loss that results in chronic sorrow **(Mitchell et al., 2020).** Their parents and caregivers' physical, psychological, and social health is also affected. These diseases increase parenteral and familial stress, and the more parenteral stress, the less psychological parent-child psychological adjustment. Parents experience depression, sleep disorders, and low quality of life and have more struggles than other families **(Batchelor & Duke, 2019).**

Aim of the study

The current study aimed to identify and analysis the disease burdens of mothers caring for children with some inborn errors of metabolism.

Participants and methods:

Research Design

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.

Settings: 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) and **fulfilled the following criteria:**

- Mother is the primary care giver of the child.
- Children aged up to 10 years.
- Mother available for interview and willing to share experiences.

(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

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.

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 disease burdens.

Procedure of conducting in- depth interview:

- 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. Participants chose to meet in the Pediatric Metabolic, Genetic Unit at Zagazig University Hospitals 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?" were utilized.

- 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)**.

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

Results:

Part I:Characteristics of the Studied Participants

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.

Part II: Thematic Analysis:

Five themes were emerged from the interview discussion about disease burdens of mothers caring for children with inborn errors of metabolism including Emotional/ Psychological impacts, Familial impacts, Social impacts, physical impacts, and Financial impacts.

Theme 1: Emotional/ Psychological impacts:

Subtheme 1: Initial response:

Among the participants in this study, grief, anxiety, stress, emotional exhaustion, shock, denial, acceptance and depression were all noted. Some mothers outlined myriad factors that

contributed to greater stress, but delayed diagnosis was frequently cited as one of the most crucial. While seeking a diagnosis, mothers frequently engaged in anxiety-inducing efforts to explain symptoms that doctors assigned to other health conditions.

P (4, 13, 18, and 20): *"After years of worrying about the symptoms for which I could find no explanation, I was glad to find out that I could treat him and he would not die like his former brothers."*

P (3): *"I was devastated to hear the terrible news, and I sobbed continuously until I developed postpartum depression and had extreme hallucinations about killing my daughter, which necessitating care from a psychiatrist."*

P (14): *"Since I found out about my daughter's illness, I've been living in denial about it and have told everyone she is fine, even though I visit the hospital on a weekly basis for treatment."*

P (15): *"I felt guilty since my husband and I were to blame for our child's illness.....What would have happened if we hadn't married?"*

Subtheme 2: Current response (The effect of time):

When mothers were asked how they felt about their child's disease now, after time allowed them to assimilate the information and understand the nature of the disease, its prognosis, and treatment, **18 mothers** showed acceptance of their children's condition.

Even at the time of the interview, one mother **P (14)** expressed her denial, saying, "I do not accept from anyone, not even myself, the idea that my daughter is sick with a rare disease."

Another mother **P (15)** expressed feelings of guilt after knowing that the disease was caused by a genetic problem, saying, *"It was helpful to know what caused it but, at the same time, it mainly told me that it was my fault."*

Also, mother **P (9)** expressed her concern about the everyday challenges of managing their child's needs, saying, *"I felt very anxious due to the requirements of daily life including special diet, treatment, and continuous follow up of the disease."*

Theme 2: Familial impacts:

As a result of the new challenges that have entered the family, such as day-to-day management of the disease, meeting the child's needs, multiple visits to health care centers to receive treatment in the presence of the other children, and a husband who had needs that must be met, all of these factors led to some family problems that may sometimes end in divorce.

Subtheme 1: Maintaining the marital relationship:

All of the mothers were married to the affected child's fathers at the time of diagnosis and continued to be so, with the exception of two mothers, one of whom had already divorced and the other was facing divorce.

Moreover, in response to questions regarding how the child's genetic disease had affected their relationships with their spouses, they either remembered getting closer or experienced no change.

All participants expect P 14, 17: *"My husband was the one who helped me the most and was usually there with our other children when I went to the hospital with my sick child; on occasion, he even went instead of me. Despite this, my marriage remained strong."*

P (14): *"My ex-husband and I actually got divorced because he didn't want to have ill children anymore and because he constantly viewed me as guilty."*

P (17): *"I had to endure a lot in order to become pregnant, and I was only able to conceive my daughter using Intracytoplasmic Sperm Injection (ICSI). After knowing about my daughter's illness, my husband started looking for a new wife because he wanted more healthy children, and I was threatened with divorce."*

Subtheme 2: Maintaining the relationship with the child's siblings:

When one or more children demand more time, attention, and adaptations than others, family dynamics might be disrupted. Siblings of children with genetic disorder experienced a wide range of emotions in this study, including anxiety, anger, jealousy, and worry about their future and their sibling death.

P (2, 4, 6, 7, 9): *"The fact that I had to devote a lot of time and energy to take care of his sibling bothered me the most since it made him feel jealous and that I didn't love him as much as him or her."*

P (15, 20): *"The stresses of my child's illness put a strain on me, causing me to become overly anxious, which impacted my relationship with my kids and made them anxious as well."*

P (10): *"Due to the age gap between him and his brothers and the death of his father, his brothers frequently worry about him, which causes numerous conflicts and family issues."*

Theme 3: Social impacts:

During their journeys with the child genetic condition, mothers in this study faced a number of social problems. Social isolation was highlighted as a major challenge for both mothers and their children as a result of various factors, including the disease's psychological and physical implications. Furthermore, the managing process, which frequently included a lifetime of day-to-day care, frequent medical appointments, providing care at home and communicating with health care team to ensure their children's needs; all of these factors hindered mother's social inclusion and interaction with others , as well as their autonomy and freedom.

P (1, 4, 5, 6): *"Due to everyday challenges like food preparation, doctor visits, and frequent hospitalization, I even became isolated from my family and neighbors, and I stopped taking part in almost all of their activities."*

P (11, 12, 14, 15): *"The numerous questions regarding my child's sickness, as if I were being investigated for a crime, made me feel unhappy, embarrassed, and separated from all of my family."*

The social lives of their children were a significant source of stress for mothers in this study, particularly when their children were unable to attend activities such as parties or holidays due to

food limitations. Some mothers were anxious about their children being excluded and bulled, particularly at school.

P (3, 5, 6): *"It was difficult for me to attend my relatives' birthday parties, and when we did, I brought my child's own food so he didn't feel different from the others."*

P (19, 21): *"My son's vision was not good. Other pupils at school showed disregard for his medical condition. I became tense and nervous about this."*

P (12, 13, 14): *"I was so terrified that I never sent my child to school, and if it hadn't been for the requirement for Health Insurance, I would not have enrolled him."*

Theme 4: Physical impacts:

Different physical symptoms were experienced by some of the mothers in this study. These symptoms included headaches brought on by overthinking about the prognosis of the illness and the child's future, as well as back pain and hypertension. On the other hand, other mothers had no changes in their physical condition and instead considered their child's disease a challenging journey.

P (4, 6, 7, 19, 21): *"I frequently had headache due to overthinking about everything regarding my child, particularly the disease's treatment and prognosis."*

P (10): *"In the early months of my son's sickness, I experienced hypertension."*

P (11, 14, 15): *"Because this condition impacted my child's bones, I had to carry him/her all the time, which affected my lower back."*

P (1, 5, 20): *"I never felt physically affected by my child's condition since I always considered it a gift from God."*

Theme 5: Financial impacts:

Two mothers' ability to keep a paid job had been damaged by dealing with rare genetic illnesses **(p: 6, 15)**. This difficulty was further compounded by the multiple medical appointments and daily home care needed to manage the disease and income was then impacted by this. Furthermore, one mother **(p: 3)** switched from a full-time to a part-time job.

Expenses associated with attending numerous medical appointments and significant travel expenditures were mentioned as another cost for families. Moreover, many mothers required additional costs for special diet, essential health care and social services related to the disease symptoms and complications. These expenses and services placed additional financial strain on families.

P (17): *"Every time, I had to take my child in a private car, which was incredibly expensive."*

P (20): *"Every week, I had to spend a lot of time, effort, and money traveling from my home city to the hospital, which is located in another city."*

P (1, 4, 19): *"My child required speech therapy and learning difficulties sessions in addition to the medical care for the illness, which I was unable to pay for."*

P (11, 12, 13. 14, 15, 21): *"Almost every week, we had to visit a different physician, such as an ophthalmologist, cardiothoracic surgeon, or orthopedist. We also needed to undergo through a lot of pricey investigations, examinations, and testing."*

Discussion:

Among the participants in this study, grief, anxiety, stress, emotional exhaustion, shock, denial, acceptance and depression were all noted at the first time of disease diagnosis. Also, some mothers outlined myriad factors that contributed to greater stress, but delayed diagnosis was frequently cited as one of the most crucial.

These findings were in harmony with the results of the study by **Shirdelzade et al. (2023)** in Iran; who aimed to explore mothers' lived experience who caring for children with inborn errors of amino acid metabolism; revealed that mothers experienced grief, sorrow as soon as they found out their children's diagnosis, and some denied the disease and tried to provide some hope for themselves to bear the difficulties. Also, **Ismail et al. (2019)** who conducted a study about inborn errors of metabolism in the era of untargeted metabolomics and lipidomics; stated that these problems are common among mothers caring for children with IEMS including negative feelings, anger, denial, and depression.

On contrary, **Kolemen et al. (2021)** who made a study to evaluate the parents' anxiety levels before and after the diagnosis of their child with a rare genetic disease in Turkey; declared that there was a significant decrease in the anxiety levels of the families after diagnosis especially mothers.

In the current study 18 mothers **(86% of participants)** shown acceptance of their children's condition when they were asked how they felt about their child's disease during the interview and this could related to the time allowed them to assimilate the information, understand the nature of the disease, its prognosis and treatment.

In the same line **Haw& Henriques (2021)** who conducted a study about exploring how mothers of a child with a genetic disorder experience in UK, reported that the participants used many different coping strategies to deal with the distress of having a child with a genetic disorder but most frequently they described using 'acceptance'.

Conversely, **Shirdelzade et al. (2023)** in Iran; reported that the more time that passed after disease diagnosis and the more signs and symptoms appeared, the more psychological problems mothers experienced, such as depression, emotional exhaustion, anxiety, and in some cases, they even needed to go to a psychiatrist and start treatment.

The results of our study showed that all of the mothers were still married to the affected child's fathers at the time of diagnosis, with the exception of two, one of whom had already divorced and the other was facing divorce. Moreover, in response to questions regarding how the child's genetic disease had affected their relationships with their spouses, they either remembered getting closer or experiencing no change.

These results agreed in some parts with **Somanadhan& Larkin (2016)** as they reported that parents' marital relationships had become markedly strained as one of the families separated

following their child's diagnosis. Also, **Rajasekar et al. (2020)** revealed that out of 10 parents, (6 parents) remained married and relayed their increased feelings of connectedness with their spouses.

Family dynamics can be disrupted when one or more children require more time, care, and adjustments than the others. For this reason, some participants in the current study highlighted that their healthy children have gone through a wide range of emotions, including anxiety, anger, jealousy, and worry about their future and their sibling death.

In the same line with the results of the current study, **Witt et al. (2023)** who made a study about living with a rare disease-experiences and needs in pediatric patients and their parents in Germany; revealed that the interviewed parents mentioned ignoring and suppressing their needs and desires, harming family life and exceptionally healthy siblings. Also, **Somanadhan& Larkin (2016);** reported that parents attention predominantly focused on their sick child resulting in their healthy child often being left out and emotionally disrupted.

Haukeland et al. (2019) who conducted a study about emotional experiences among siblings of children with rare disorders in Norway; found that the disease prognosis lead to worry and a variety of negative emotions, such as fear, nervousness, sadness, grief, and feelings of jealousy .Also, Participants described emotional distress in relation to the possible or probable early death of their sibling.

Social isolation was highlighted as a major challenge for both mothers and their children in the present study as a result of various factors, including the disease's psychological and physical implications. Furthermore, the managing process, which frequently includes a lifetime of day-to-day care, frequent medical appointments, providing care at home and communicating with the health care team to ensure their children's needs; all of these factors hindered mother's social inclusion and interaction with others , as well as their autonomy and freedom.

In accordance, **Shirdelzade et al. (2023)** in Iran stated that most mothers with a child with IEMS preferred not to communicate with others and chose isolation for multiple reasons, including the amount of time caring for their children, wanting to avoid others' judgmental looks, and also to avoid answering others' numerous questions about the child's condition. Therefore, they selected self-imposed isolation instead of socialization. Also, these findings supported by **Boettcher et al. (2021)** systematic review to investigate the quality of life in parents of children with different rare diseases as they affirmed that parents of children with rare diseases reported loneliness, and more stress than parents of children without a disease.

The results of the current study showed that most study participants had a significant source of stress regarding their children social lives particularly when their children were unable to attend activities such as parties or holidays due to food limitations. Also, some mothers were anxious about their children being excluded and bulled particularly at school.

The previous results were supported by **Witt et al. (2023)** who found that some of the children reported experiences of mobbing and social exclusion, especially in school.

Also, **Siddiq et al. (2016)** who conducted a qualitative study about experiences of caregivers of children with inherited metabolic diseases in Canada; reported that many families' vacations

were described as requiring a lot of planning and preorganization as they had to pack all of their necessary food and bread in addition to their clothes.

In the current study two mothers' ability to keep a paid job had been damaged by dealing with rare genetic illnesses. This difficulty was further compounded by the multiple medical appointments and daily home care needed to manage the disease and income was then impacted by this. Also, one mother switched from full-time to part-time job. This finding was congruent with **Rajasekar et al. (2020)** who reported that the costs associated with IEM management imposed a disproportionate financial burden on working parents.

These results were in harmony with **Hassanin et al. (2022)** who conducted a systematic review about the psychosocial impact of parenting a child with a lysosomal storage disorder in The United Kingdom and **Siddiq et al. (2016)**; found that some family caregivers took a leave of absence from their occupation and sacrificed career opportunities in order to accommodate this immense level of care.

The present study showed that the expenses associated with attending numerous medical appointments and significant travel expenditures were mentioned as another cost for families with children suffering from a rare disease. Also, many mothers require additional costs for special diet, essential health care and social services related to the disease symptoms and complications. These expenses and services place additional financial strain on families.

These study findings agreed with **Hatirnaz et al. (2023)** who reported that the number of rare disease centers in Turkey is still not at the required level, and the experienced physicians reside in more central cities like Istanbul, Ankara, and Izmir. This issue forces patients to travel to these cities for proper treatment and healthcare. Also, the results of our study aligned with the results of **Gündüz et al. (2023)** who applied a study to determine out-of-pocket health expenditures of patients with inborn errors of metabolism during follow-up and treatment processes and to determine the economic burden on the families in turkey as they found that 69% of participants had difficulty finding accommodations and reported travel expenses.

Conclusions:

Based upon the findings of the present study, it can be concluded that 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:

1. Improving access to health care and social services and encouraging more collaborative and efficient coordination of care and communication between physicians, patients, and caregivers.

2. 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.

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

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