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Parental psychosocial aspects and stressors involved in the management of inborn errors of metabolism



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ABSTRACT

Parents of children with inborn errors of metabolism (IEM) face numerous psychosocial challenges. An increased understanding and awareness of these stressors can ensure better overall outcomes for the entire family. We conducted semi-structured, in-person interviews with ten parents to identify psychosocial stressors, strategies, and supports they utilized to overcome their challenges. Our interview guide was designed to elicit familial experiences during the pre- and post-diagnosis periods. The themes and sub-themes were identified through qualitative descriptive textual analysis of audio-recorded transcripts. Major themes identified include ambiguity of illness, changing family and spousal dynamics, and navigating the healthcare system. Sub-themes revolved around disease effects, psychological stressors, health systems, support, and facing the disease. Healthcare professionals have an opportunity to minimize the impact of negative emotional outcomes by assisting families as they navigate the experience of having a child with an IEM. Our findings can be used to develop and continue a more well-rounded, family-oriented framework for IEM management.

1. Introduction

Management of inborn errors of metabolism (IEMs) often result in psychological distress and can impact the outcomes of affected children [1]. Most IEMs are chronic conditions that require investigations and medical interventions such as repeated blood sampling, multiple hospitalizations, and gastrostomy feeding, as well as invasive procedures such as tissue biopsies, and portacaths for intravenous access, repeated imaging studies, specialized diets, and medications, respectively [1]. Parents are challenged in many ways during their child's IEM diagnosis and management, given that some conditions are diagnosed through newborn screening (NBS) programs, whereas several require extensive clinical and laboratory investigation. Despite the shorter period of uncertainty pre-diagnosis and generally positive outcomes post-diagnosis for the affected child when screened through NBS, parents reported a higher perceived familial burden compared with the perspectives of

healthcare professionals [2]. Alternatively, parents of children with a specific subset of IEMs (intoxication-type disorders) revealed that dietary requirements imposed a social and emotional burden on them, as these were initially difficult to grasp and communicate in a social environment [3]. Parents of children with mucopolysaccharidosis type III (MPS III, Sanfilippo syndrome) reported high levels of anxiety, depression, and expressed that they viewed themselves as being less goal- and future-oriented, compared with parents of children with intellectual disability [4]. Even well-adapted IEM caregivers experienced substantial stress due to the social challenges they faced while navigating systems, providers, and raising awareness of rare diseases [5]. Parents also reported feeling unsupported and devalued in their child management roles, despite gaining expertise over time [6].

Collectively, these challenges and parental stressors can potentially influence the child's overall outcomes. The following are a few examples of different factors of influence: familial cultural belief systems

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[7], employment status, access to interpreter services can impact the implementation of patient management plans [8,9] and their overall experience with clinical care. For some disorders such as phenylketonuria (PKU) [10,11] and porphyria [12] emotional dysregulations as well as psychiatric comorbidities can become challenges in providing management and care. In conditions such as Fabry disease [13] and Gaucher disease [14] clinical depression and anxiety also frequently coexist with significant pain from multisystem involvement. The situation gets more complicated as access to psychological and psychiatric services may be limited by resource constraints and competing clinical priorities amongst different service providers.

Parents or guardians are the primary caregivers and the main point of contact and collaboration for the healthcare team when managing children with IEMs. A comprehensive understanding of the difficulties, concerns, and positively implemented supports of these caregivers may enable more refined and effective care for the patients and their families. An important consideration is that the parent and child perspectives on the experience of IEM management differ across conditions [2]. To increase the specificity of parental findings, we facilitated open-ended conversations through a semi-structured design. Our project aimed to identify and better understand 1) how parents see the role of stressors at different times in their children's healthcare journey as impacting social aspects of their lives and 2) how parents recognize and handle their psychosocial difficulties.

2. Methods

2.1. Study design and participant selection

We conducted qualitative, semi-structured in-person interviews to access a broad spectrum of social, emotional, and psychological themes in parents of children diagnosed with IEMs. The inclusion criteria for selection in the study were: parents of children, under the age of 10 years, with IEMs diagnosed and managed in and around Southwestern Ontario. We employed purposive sampling to ensure representation of a range of IEMs including amino acidopathies, organic acidemias, lysosomal storage disorders, and neurodegenerative disorders. Any families with a child that passed away before or during recruitment were not contacted further. The Health Sciences Ethics Review Board at Western University (London, Ontario, Canada) approved this study and all involved parents provided informed consent before participating.

2.2. Data collection

Study investigators (AM, CP, MN, AV, BP), with expertise in IEM management and qualitative research, designed the semi-structured interview guide for this study. The interview guide focused on the process of diagnosis, the impact of diagnosis, day-to-day challenges, coping with the unknown, support systems, mental/emotional health, and gaps in support and care. Participants underwent two sets of interviews, conducted over two years (interviewed by PR). Parents were initially informed of this study either by phone or during in-person clinical consultations and then officially recruited after obtaining informed consent. Literature states that phenomenological research requires textual data from a minimum of six individuals to ensure rich and robust descriptions [15,16]. To accommodate the accepted sample size requirement, our study included ten parents from different families. All interviews were audio-recorded, following consent from parents, and transcribed by an experienced medical transcriptionist. Transcripts were then verified independently against audio recordings and hand-written notes by a member of the research team (PR, SG). Discrepancies were not noted.

2.3. Data analysis

Transcripts from the first set of interviews were subjected to qualitative descriptive analyses [15,16]. The first five interview transcripts were independently analyzed by three members of the research team (PR, MN, AM) to identify emerging themes. Following the corroboration of findings, a revised interview framework was collaboratively developed to delve deeper into these emerging themes, allowing them to be featured prominently in the remaining interviews. Triangulation of findings between the three members was used to avoid potential bias in identifying emerging themes. All textual analyses were performed in NVivo (OSR International Pty Ltd., Version 10) and Atlas.ti (Scientific Software Developments, Version 8). Study investigators (MN, AM) verified codes and theme and sub-theme classifications, through regular discussions and meetings to ensure that the saturation and theme identification was consistent. We used the revised semi-structured interview framework in the second round of interviews, conducted two years later to enable investigators to member-check their findings. In brief, member checking is a qualitative research technique, commonly used to ensure the credibility and trustworthiness of thematic findings [16]. Parents participated in another round of interviews based on the themes identified, with their responses analyzed and compared to previous textual findings for consistency.

3. Results

3.1. Participants

Ten parents (nine women, one male) participated in our study, representing seven different IEMs. The IEMs covered in this study include mucopolysaccharidosis Type VI [MPS Type 6], methylmalonic and propionic acidemia [MMA], primary carnitine deficiency [CUD], Menkes, Mitochondrial Encephalopathy, Lactic acidosis, and Stroke-like episodes [MELAS] and PKU. All IEMs listed follow an autosomal recessive inheritance pattern, except for Menkes (X-linked) and MELAS (maternally inherited). Some parents ($n = 3$) managed more than one child with an IEM diagnosis. Both rounds of interview times ranged from 30 to 90 min. All parents were fluent in English, educated higher than high school and most lived in London, Ontario, Canada or surrounding regions (Table 1). Parents reported many common experiences in their interviews, despite being exposed to different caregiving challenges and diagnostic journeys. We identified three key overarching themes: ambiguity of a child's illness and family life; changes in their social and spousal dynamics; and maneuvering the healthcare system and social services. The subsequent text discusses prominent subthemes that emerged.

3.2. Effects of ambiguity surrounding illness on parents

Parents experienced uncertainty as they faced their child and/or children's illness (Table 2). The distinct aspects of the parents' lives that were impacted during periods of uncertainty were as follows: coping with the uncertain diagnostic odyssey, understanding the childcare needs, recognizing changing family dynamics, and navigating challenges in professional development. Lengthy diagnostic processes and often unclear clinical pictures challenged parents to cope under uncertain circumstances, leading to many instances of self-blame (Table 2, [1a-b]). Mothers with children affected by either mitochondrial or X-linked diseases expressed more self-directed guilt over their role as carriers (Table 2, [1c]).

Post-diagnoses, a few parents continued to report experiencing elevated levels of anxiety. Some reported a lack of comprehension (Table 2, [2a]), due to an inability to cope with the emerging quality of life expectations and management needs of their children (Table 2, [2b]). However, some noted that the provision of a diagnosis allowed them to focus on understanding and improving the quality of life for

Table 1
Parent demographics.

Characteristics	No. of Parents (n = 10)
Gender	
Male	1
Female	9
Age	
25–34	1
35–44	4
45–54	3
55–60	2
Education	
Community College or Technical College	6
University Degree – Undergraduate Studies	2
University Degree – Graduate Studies	1
Trade	1
Region/ Location	
Kitchener/Waterloo [city]	1
Mooretown [township]	1
London [city]	4
Windsor [city]	2
Hamilton [city]	1
Kincardine [municipality]	1
Marital Status (present)	
Married	6
Separated	2
Divorced	2
Number of Biological Children*	
1	3
2	4
3	3
Annual Household Income	
< \$50,000 CAD/year	2
\$50,000–100,000 CAD/year	5
> \$100,000 CAD/year	3
Number of Children Diagnosed with IEM	
1	8
2	2

* number of biological children reported is inclusive of child with IEM.

their child, which detracted from feelings of anxiety (Table 2, [2c]).

Family dynamics were noticeably affected post-diagnoses, as ambiguity caused by new lifestyle changes contributed to uneasiness in certain aspects of parenting, particularly for parents (n = 7, Table 1) with unaffected children. Several parents independently brought up the role of food in parenting, with special dietary requirements impacting all family members (Table 2, [3a]). Older children in most participating families were typically healthy and active in extracurricular activities. Management of the IEM affected sibling imposed on the other unaffected children (Table 2, [3b]), consequently demanding more from the parents/ primary caregivers to meet the needs of all their children. Many mothers in our study mentioned that their unaffected children were more likely to opt against having children of their own later in life (Table 2, [3c]), due to their exposure to extensive lifestyle and emotional challenges.

Financial stability and development are the other important aspects of the parents' lives that were impacted post-diagnosis. Parents reported decreases in professional progression, satisfaction, and opportunities (Table 2, [4a–c]). Parents also reported that the costs associated with IEM management imposed a disproportionate financial burden on working parents (Table 2, [4a–c]).

3.3. Parents identify changes in their social and spousal relationships

As the IEM management transferred primarily to parents, they actively developed support systems for themselves and their families (Table 3). These took the form of online (international) disease-support groups, family and friend networks, and consultations with mental health professionals and mentors. Online connections enabled parents to feel supported outside of the healthcare teams (Table 3, [1a–c]).

Table 2
Ambiguity regarding child's illness and family life – example quotes*

Sub-theme 1: Coping with the diagnostic processes of a rare disease

[1a] Participant (001): “I just wanted somebody to tell me what was wrong and, you know, so we could get on with whatever we needed to do”

[1b] Participant (006): “know that my husband at the time was very upset and you know perhaps even took some of the blame on himself, thought that maybe it was because genetically it's got to come from both parents, you know there is a level of responsibility in that. I know that he had a hard time coping with it.”

[1c] Participant (007): “Mothers that are carriers for diseases ... the guilt you feel of being a carrier ... you feel like a failure because women in society are supposed to have babies [very emotional] ... it's one failure after another”

Sub-theme 2: Difficulty comprehending child's prognosis and quality of life

[2a] Participant (006): “I certainly think that when she was younger there was more concern and being uncertain as to what it would like in six months, what it would look like in a year, you know now there's hardly any anxiety at all when it comes to looking at further down the road”

[2b] Participant (002): “There are some things out there that are very scary to the family because we don't know what the future holds, you know, what's the life expectancy? Is there a life expectancy? Umm, you know, will he have to have a port-a-cath forever? Will he develop at a normal rate with his friends? Will he make friends?”

[2c] Participant (009): “It is tough to tell the future for sure because ahh, for instance, last year we never knew that umm kidney transplant and liver transplant were something that were even in the future”

Sub-theme 3: Managing affected and unaffected children

[3a] Participant (008): “We got the call; and to me that was just like ‘oh my god’ the most devastating thing in the world. My son wouldn't be able to eat meat umm, it sounds crazy but...you want to share all the pleasures in life that you find the most pleasurable”

[3b] Participant (001): “We have had to rearrange different; everything gets rearranged when you are coming here once a week, all of a sudden their activities are affected too, right. So, if we are coming on a Wednesday, we try not to schedule gymnastics on a Wednesday or you know, whatever it is. I think we've done a pretty good job of managing that. Our kids are getting older now too so it's getting easier,

[3c] Participant (003): “I can tell you, my oldest daughter says she is never going to have children because of that, because she has seen what can happen”

Sub-theme 4: Impact on parent/caregiver employment and career aspirations

[4a] Participant (002): “I had to take an extended maternity leave because we were in the hospital for so long, there was so many needs, and then not being able to put him into daycare, I wasn't able to go to work... not knowing if he's going to get sick, what if he has to go for a transplant, what company would want to keep me since I have all of this that I have to attend to, my job doesn't seem like a priority.”

[4b] Participant (005): “...even when you're planning your career and planning for advancement in the workplace it's like okay well if I apply for that job am I going to be overlooked because I have this flexible work schedule or could I not apply for that job because I know I'm going to need a day off every week or whatever, so I think it does affect it pretty hugely, like your day to day life.”

[4c] Participant (001): “think the practical part is always rolling around in the back of our head. I think it is always well maybe I will have to quit work in 5 years from now, maybe [name omitted] will progress to the point where he needs more care, or more attention or more of my care”

* text provided has been truncated at appropriate points for brevity.

Parents noted they developed an increased awareness of inborn errors of metabolism in general through the meaningful connections they made with families worldwide (Table 3, [1a]). Parents of children affected by more clinically severe conditions (e.g. MELAS) expressed concerns about the disparity in healthcare support across different countries, due to their increased awareness from making meaningful connections with other parents (Table 3, [1c]).

Increased childcare responsibilities, dysfunctional communication, and emotional distress contributed to changes in spousal relationships and dynamics during and post-diagnosis (Table 3, [2a–c]). Divorced parents discussed the dissolution of their marriages and noted prolonged stress associated with the lengthy diagnostic processes, demanding lifestyle changes, and fractured communication as contributing factors (Table 3, [2a–b]). Alternatively, six parents in our study remained married and relayed their increased feelings of connectedness with their spouses (Table 3, [2c]).

Social support for parents came from extended family members and through forging new friendships. Participating parents accepted that

Table 3
Active building of support systems for themselves – example quotes.

Sub-theme 1: IEM disease communities

[1a] Participant (002): “But also, other families, if you could be set up with another family that has already been there, same diagnosis presented the same... I found an online support group that's worldwide and it's a closed group, it's only for families affected by methylmalonic acidemia, any subtype ... it's families around the world, I have met people in New Zealand, I've met people in New Jersey, they have a child who have the same disorder, some have had transplants, some have not had transplants... I found that a very big support for us.”

[1b] Participant (004): “Every time I went to a PKU conference at the beginning I learned so much from different people. People would bring in stuff. I brought in all my recipes that [name omitted] loved. That was huge, that was so big.”

[1c] Participant (010): “I did come across United Mitochondrial Foundation which is based out of the states, which again is hard because their medical system is completely different from our medical system and a group of Canadians that met, I can't remember what year it was, they all sat at the same table and they started Mito-Canada”

Sub-theme 2: Experiencing marital vulnerability

[2a] Participant (008): “I think that for the most part, I know that I for the most part have been able to cope with it, my husband and I have separated and I think a lot of the reasoning can be that our coping skills are not the same...[text omitted for brevity]...it's hard to always be on different levels on dealing with and coping with things...[text omitted]...there have been a lot of things that have gone on in our lives that have been very eventful I guess you could say, which kind of changes how you cope and deal with everything.”

[2b] Participant (006): “I went in rock bottom. Like I went in hearing the worst-of-the-worst and he went in hearing the best-of-the- best...in the end that wasn't bad I think because it kind of balanced each other off kind of thing, and we met in the middle”

[2c]: Participant (009): “My husband and I had to really work on our communicating to want to have advocate for her and be there to support each other because it was a very trying time.”

Sub-theme 3: Bolstering familial relationships and accepting limitations of familial support

[3a] Participant (002): “They still try to feed him meat. My family doesn't understand that he's PKU and he doesn't eat meat. ‘What do you guys have? [name omitted] you want some steak or some chicken?’ And [name omitted] just looks up at them ‘Are you kidding me?’ (laughing) They don't even hear it. They don't understand it. They don't...”

[3b] Participant (006): “You know, my parents, which was my family support, they certainly were very concerned, and you know there's still not a really firm understanding I think of the disorder, even amongst close family members.”

[3d] Participant (010): “I don't know, I feel guilty for my husband knowing that he married me that I didn't know I had this...even my parents, they can't grandparents like they want...”

Sub-theme 4: Re-evaluating social circles

[4a] Participant (005): “The friends don't want to bother you. You don't open the door for them, not literally, but you don't let them in and eventually they feel like and we've noticed that friend feel bad because their kids are fine and they feel like you might resent them and so that's something that, and we don't, and I think people don't understand that, and they probably feel bad and think ‘you don't want to see me, my kids are healthy’ and it's easy if she said if you don't open that door and say ‘yeah sure we could use dinner for tomorrow night or if you could come over and have tea with me once a week’, if you don't let them, I think you could easily isolate yourself”

[4b] Participant (001): “I had a friend, not even a close friend actually, a friend that I hadn't connected to for a little while, so she was kind of removed from our whole family situation, and I actually found her a huge support because she was removed from it all, I guess, like I hadn't talked to her for a couple of years and she was a big, I don't know, a big outlet for me...she had a big role in getting me through it.”

* text provided has been truncated at appropriate points for brevity.

though extended family provided management support, their overall disease awareness was limited and communication with them was challenging at times (Table 3, [3a–b]). An interesting recurrence was that mothers of children with mitochondrial diseases expressed extensive guilt towards their spouses, children, and extended family (Table 3, [3c]) for necessitating childcare support. This was not a commonality across all parents interviewed.

Individual friendships, outside of family circles provided parents with social and emotional support. Parents described two opposing friendship trajectories that occurred in their lives, post-diagnosis. Previously established friendships and workplace camaraderie slowly

Table 4
Maneuvering healthcare system and social services – example quotes.

Sub-theme 1: Educating and updating themselves with disease information

[1a] Participant (008): “I took charge of it and I researched everything and you know, I looked for the best care that she could get, as far as the vitamins go and the management, and all the things that are best for her, and even though we were doing the vitamins and that, she was adjusting to the ketogenic diet, she was having GI issues and all the other things so I put my focus on providing her the best care and giving her the best quality of life.”

[1b] Participant (003): “I think a lot of people the first thing they do is go to the internet, which isn't always a good thing to do. I did do some research online. I find the team here incredibly knowledgeable so asking questions from the team, if I think of something I can ask [physician-name omitted] or [dietician name omitted] and then research from NIH they do all kinds of papers with actual studies done, so actually reading some stuff that has happened.”

Sub-theme 2: Learning to actively communicate with physicians

[2a] Participant (009): “The whole system can be a little scary because it's all these experts, so I feel that you're almost left to just believe whatever the doctor says and so that was my experience, that we had to believe that my daughter was okay, and yet I felt that she wasn't and then we kept getting told no it isn't. So, knowing who to call or what to do was difficult right.”

[2b] Participant (002): “But, I can imagine coming from someone like my husband who had no medical background, he still in terms of if we go to London and they talk about [name omitted] he doesn't know, sometimes they throw in medical terminology and he has to stop them and say I don't understand what that means, or he doesn't understand why this doctor has to see [name omitted] if he has a metabolic disorder, but then you have to link the kidneys in the methylmalonic acidemia and such.”

[2c] Participant (001): “I think the biggest challenge was just understanding, one of the biggest challenges was understanding who do I talk to find out what I need to know today. Who is going to give me that answer? How do I get in touch with them right now so they will talk to me? That part was somewhat challenging some days.”

Sub-theme 3: Utilizing and staying connected with healthcare team

[3a] Participant (008): “Our situation here is very unique, we do almost all of the care here. [name omitted] has a Port-A-Cath, I access it myself, I run my own antibiotics, IV antibiotics, I can mix my own, I rerun fluids a couple of nights a week and I have a really good relationship with our doctors, that took years to come though, where we have to trust that I can run things here at home to the best of my ability”

[3b] Participant (002): “Absolutely, there's the metabolic conference that's held here every year that the medical genetics team puts on that puts you in contact with people locally who have all different types of disorders, and then there's also vendors there where you can, in your community, you can try new, what help is out there, anything from extra money for diapers through Easter Seals, which I had no idea you could even do that, or some respite through different country clubs or CCAC, the metabolic conference is a great idea. The fact that they actually hold it, not only do they have support like that but they go into having some motivational speakers or talks about the specific disorders, like discussion groups, and actually learning more about the disorders by having a scientist or a doctor come in and explain it to people.

[3c] Participant (005): “There really is a lot of support because if we need something, if we need a letter written, if we need something to follow [name omitted] along with, it's just a phone call away and basically within one or two days it's usually taken care of, even if there's a doctor that's away, there's always another doctor that can come in and replace or take care of that issue that we have.”

Sub-theme 4: Seeking personal development individually and for immediate family

[4a] Participant (010): “I'm a caregiver, I'm a nurse in the home, I'm still the mom and now I'm working outside the home because [name omitted] been stable but it's tough and I'm finding that I'm needing to take time for me and that's hard too, I feel guilty, yet I need it because if I'm not taking care of myself I'm not good to anybody else, so that's very important.”

[4b] Participant (006): “I certainly sought out counselling for myself, I sought out some family counselling that included my older daughter at the time ... these are all things that I think have helped to create a better perspective for myself ... feel like I'm in a much better position to make choices.”

[4c] Participant (008): “I am pretty much a person who doesn't really go to other people for support, I am not very good at asking for help, I do have a social worker, I have had her since my other daughter was, well, probably under one when we got her. She is about the only person I go to. I have seen a psychologist, but I did go to her after my daughter died, just coping with that.”

* text provided has been truncated at appropriate points for brevity.

eroded due to low disease awareness in colleagues and their ensuing discomfort with dissimilar childcare compared to their respective children (Table 3, [4a]). 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 (Table 3, [4b]).

3.4. Parents evolve into assertive navigators of the healthcare system

Parents' roles evolved as child management progressed and influenced their overall approach to the healthcare team and system at large (Table 4). As increased management needs emerged, parents participating in our study actively educated themselves about the disease. They focused on minutiae pertaining to child care (inclusive of dietary restrictions, physical activity, emotional and intellectual stimulation) through regular communication with genetic counselors and/or healthcare professionals, reading extensively about disease progression, and maintenance of a thorough log of their child and their research (Table 4, [1a]). Although some educated themselves through independent research, many of the parents felt confident with the healthcare team and relied heavily on their input (Table 4, [1b]).

Despite expressed confidence in their healthcare team post-diagnosis, parents categorized their initial interactions as being difficult, passive, and reactive (Table 4, [2a]). The magnitude of novel information relayed in a short period contributed to them feeling overwhelmed during the pre-diagnostic uncertainty (Table 4, [2b]). Most parents expressed recognizing and determining the appropriate utilization of available resources as the main challenges navigating the healthcare system (Table 4, [2c]).

These communication gaps acted as barriers, exacerbating anxiety, and confusion experienced by the family. To overcome this, some parents took specific, active steps to increase communication with the healthcare teams – including involving themselves in the healthcare and maintaining regular contact with at least one of the healthcare professionals (Table 4, [3a]), attending the metabolic family workshops held by the team to better acquaint themselves, connecting with families in the clinic or the same region (Table 4, [3b]) and engaging and updating their family physicians to better accommodate their child's needs (Table 4, [3c]).

The continued assertive role parents played in their own self-care was another notable and distinct development. Many parents actively sought professional help and guidance for their mental health (Table 4, [4a]) and subsequently encouraged their unaffected children to follow similar practices (Table 4, [4b]). Resources availed included psychiatrists, community religious leaders, and psychologists.

4. Discussion

IEMs are rare and medically complex conditions to manage. Finding extensive disease awareness and supports can be challenging for families [9]. Our findings support existing literature, specifically in relation to psychosocial stressors experienced by primary caregivers in the early diagnostic period that identified increased depression, anxiety, and compassion fatigue in primary caregivers as a result of psychosocial stressors associated with managing children with either terminal or progressive inborn errors of metabolism [4,17,18]. We captured a more in-depth trajectory of psychosocial stressors and relevant supports in these parents as their child's disease progressed and associated child management increased. Parents projected self-awareness in terms of their emotional and mental health deterioration and demonstrated a strong will to incorporate positive outlets. One aspect of these outlets included friendships. A study [8] in the Netherlands identified emotional support as being protective for parental health-related quality of life and the loss of friendship as a risk factor for health-related quality of life impairment in parents of children with IEMs. Our findings support the loss of established friendships but also

elucidate an interesting concept of developing new relationships instead of continuing the societal isolation previously described. This, along with the increased personal health and self-care amongst parents, acceptance of limitations of support systems [19], and assumption of an active role [6] in navigating the healthcare system all bolster the idea of a “new normal” [5] and “self-organization” [20].

A review of the literature indicates that chronic and/or terminal illnesses in their children can impact their parents' spousal relationships in a mixture of negative [21,22] and overall positive [23] manner. Our findings were consistent with this, as some parents expressed increased strength in their marital relationships due to shared experiences of uncertainty and emotional isolation. Whereas, others reported dissolution of their marriage, and increased feelings of loneliness, assumed responsibility and burden, that typify something described previously as a “lone parent” [24,25]. Financial struggles were consistent with findings of other studies [4,6,8,26], with parents undergoing a significant adjustment period of fluctuating incomes. Many of these financial and employment changes persisted after the diagnosis. However, employment impact and changes to career aspirations is a complex and layered issue and might be difficult to address from a healthcare team perspective.

4.1. Increased maternal guilt in mitochondrial/X-linked disorders

Each IEM presents a unique clinical and management challenge and imparts a different effect on parents and families [5,7,8,17,18,26]. Diagnoses of mitochondrial (MELAS) and X-linked (Menkes) disorders may be perceived as stressors for mothers as they are the primary genetic contributors [27]. As reported earlier, three mothers in our study expressed increased self-blame and guilt about their genetic role in contributing to their child's mitochondrial or X-linked IEM. We believe that these preliminary findings are noteworthy and suggestive of a developing theme. Further research assessing differences in maternal psychosocial experiences across IEMs [27,28] is warranted.

4.2. Study scope, limitations, and strengths

Our study highlighted the overarching concerns, stressors, and coping activities in a specific population of caregivers who were consistently responsible for the care of IEM-affected children. The qualitative information attained elucidates personal experiences beyond the scope of validated questionnaires. The unique and common experiences shared by participating parents contribute to the evolving knowledge about the challenges and supports in place in our current healthcare system. We present in-depth parental experiences across six different IEMs. It is important to consider the variance of presentation, inheritance patterns, diagnoses and other aspects of disorders categorized as IEMs. These differences manifest as unique psychosocial challenges specific to the illness, that cannot be fully appreciated when considering IEM disorders in general. Although we acknowledged some emerging themes that were unique to certain disorders, to identify more established themes, further investigation into the unique family experiences is warranted. Furthermore, of the 10 parents interviewed, two had a second child with IEM. The experience of having this second child may have resulted in unique family dynamics and responses to the diagnostic process, which were not investigated further in our study.

A potential limitation of our study (inclusive of two in-person interviews) is that our recruitment process may have selected for parents who may have been more likely to cope well with their child's illness. Though this study primarily discussed maternal experiences, due to participant availability, future research focused on gaining a better perspective of the paternal role in managing children with IEMs would be beneficial. It was noteworthy that many mothers were forced to give up a career or make more pronounced lifestyle changes to accommodate the care of their child(ren). This resulted in most fathers, including the one interviewed, to be the sole earners in their families and

more removed from direct care of the child(ren). These changes in lifestyles and gender roles may play a role in the parent's perspective about IEM management and more study of these differences is warranted.

A noted observation during our study was the evident improvement in parental well-being using clinic-associated support programs, such as workshops on self-compassion, mindfulness, resiliency training and emphasis on addressing mental and emotional healthcare needs. The implementation of positive self-care strategies expressed by parents showcase the benefits of a supportive healthcare team. Our findings continue to highlight the need for healthcare professionals to incorporate more comprehensive education paradigms and psychosocial supports for parents throughout the affected child's management.

5. Conclusion

Continuous improvement and implementation of tertiary support systems within the healthcare system for the primary caregivers of children with IEMs contributes to better overall long-term outcomes for both the affected child and family. We discuss the various stages of disease management through the parental perspective. Our findings describe a multitude of stressors like prolonged uncertainty, decreased social contact, demanding childcare, and identify how each parent handled the challenges at various stages of their child's diagnosis and treatment. Many reported the benefits of self-care while discussing how they navigated challenges in maintaining their spousal relationships and the associated self-blame. Continuing to build a network of support with patient groups and facilitating connections from the onset might assuage some uncertainty and anxiety expressed during the diagnostic periods and subsequent management.

Authors and contributors

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Appendix A

A.1. Participant demographic questionnaire

Parent Questionnaire

1. What gender do you identify with?

? Female

? Male

? Other: _____

2. What is your age? _____

? What is your present marital status?

? Married

? Separated

? Divorced

? Never married

? Other: _____

4. What was your marital status at the time of your child's diagnosis?

? Married

? Separated

? Divorced

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Animal rights

This study does not involve any experimentation on animal subjects.

Declaration of Competing Interest

All authors agree with the following responses:

1. All financial support for this work has been provided through the Department of Pediatrics, London Health Sciences Center.
2. There are no financial relationships with any entities to disclose.
3. Please see response 1.
4. No non-financial interests to disclose.
5. No relevant patents or copyrights are pending.
6. No authors hold any relationships and/or affiliations with any of the participants in this study.

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- ? Never married
 ? Other: _____
5. How many children do you have?
 ? 1
 ? 2
 ? 3 or more
 ? Other: _____
6. What primary ethnic identity do you identify by?
 ? African American/Canadian
 ? Asian American/Canadian
 ? Caucasian
 ? Hispanic
 ? Middle Eastern
 ? East Indian
 ? Aboriginal
 ? Other (please specify): _____
7. Which city do you live in or live closest to?
 London
 Other: _____
8. What is the highest level of education that you have completed?
 ? None
 ? Elementary school
 ? High school diploma
 ? Community college or technical college
 ? University degree – undergraduate
 ? University degree – graduate (Master’s or PhD)
 ? Professional degree
 ? Other (please specify): _____
9. What is your total household income from all resources?
 ? < \$50,000/year
 ? \$50-100,000/year
 ? \$100,000/year
 ? > \$100,000/year
10. Are you a health care professional?
 ? Yes
 ? No
 ? Other: _____
11. What is the language spoken most often in your home?
 ? English
 ? French
 ? Other (please specify): _____
-

A.2. First interview question guide

Question Guide (For parents of child/children with an IEM)

The following questions will be asked by the interviewer (student) once ethics approval is obtained and informed consent is obtained. The interviewer will use probes to understand the participant’s perspective more fully and will allow some flexibility to pursue areas of concern with respect to psychosocial health identified by participants. This interview guide will be modified on an on-going basis, as data from the study emerge. It will also be adapted to suit the particular characteristics of the participant (e.g., whether the participant is a mother, father, teenage child; the presence of other family members in the household, etc.).

1. Please describe the process of diagnosis of IEM for your child. **[probing questions]**
 - a. What experiences would you categorize as challenges during this time?
 - b. What resources (at that time) did you feel were useful?
 - c. What resources (looking back) do you think would have been useful?
2. Post diagnosis, how was your family impacted? **[probing questions]**
 - a. How was your social life impacted?
 - b. If your child (affected) was attending pre-school or school, how did the diagnoses impact those experiences?
 - c. How were your family dynamics and the unaffected siblings’ lives impacted?
3. What are (currently, post-diagnosis) some challenges in your day-to-day life as you manage your child’s IEM? **[probing questions]**
 - a. What would you identify as challenges/ difficulties as they pertain to dietary restrictions and/or dietary management of your child?
 - b. What would you identify as challenges/ difficulties as they pertain to traveling and/or being mobile with your child?
 - c. What would you identify as challenges/ difficulties as they pertain to monitoring your child’s condition?
 - d. What would you identify as challenges/ difficulties as they pertain to administering treatment and/or trying new treatments for your child?
 - e. How would you describe your daily interactions and experiences as it relates to your immediate family?
4. How do you assess and handle the unknown nature and/or course of the metabolic disease in your child? **[probing questions]**
 - a. If your child had previously been admitted to the hospital on short notice, how would you describe your thoughts and/or experiences during those times?
 - b. If your child has presented with new issues/health concerns, how would you describe your thoughts and/or experiences during those times?
 - c. How would you describe your reactionary actions and/or behaviors in your management of the IEM?
5. Please describe what supports/ support systems you relied on to cope with the management of your child’s IEM? **[probing questions]**
 - a. What role did your friends play in this regard?
 - b. What role did your extended family and/or relatives play in this regard?
 - c. What role did your immediate family play in this regard?
 - d. If you consulted a social worker and/or psychologist, what role did they play in this regard?

- e. If you consulted a spiritual mentor and/or leader, what role did they play in this regard?
- f. If you consulted the internet, what specific online resources were utilized, and how?
- g. If you consulted support groups, what role did they play and what specific resources did they provide?
6. Please describe how the diagnosis and subsequent management of your child's IEM impact your mental and emotional health? [*probing questions*]
 - a. From your perspective, how was your child's (affected) mental and emotional health impacted over the course of the IEM diagnosis and management?
 - b. From your perspective, how were your other children's (unaffected) mental and emotional health impacted?
 - c. From your perspective, how was your significant other's mental and emotional health impacted?
7. Please describe specific supports and/or resources currently in place for you and your family in our metabolic/neurometabolic clinics?
8. If you have sought professional consultation for yourself at any time (pre- and post-diagnosis), please describe your overall experiences as they pertain to access to psychological/psychiatric services?
9. Please describe any gaps you identify currently in support services/ resources in the clinical and/or community setting?
10. Please describe your suggestions for the development and/or improvement of these services going forward?

A.3. Member checking interview question guide

Challenges of Parents of Children with Inborn Errors of Metabolism (IEM)

Themes:

- 1) Uncertainty of illness
- 2) Support systems
- 3) Navigating the health care system

Interview guide: (Questions for the parents in the second interview)

Note: Prior to beginning the interview explain to participants that re-interviewing them is part of the data collection process to ensure researchers are accurately capturing the information provided by the participants the first time around. Explain it is their opportunity to agree with what has been offered or to refute it (part of the process and it is okay if researchers are interpreting what they are saying incorrectly – with no fear of repercussions if they do not agree).

The questions this time are centered on three themes that were repeated within the multiple interviews that were done the first time around.

1) Uncertainty of illness:

(Main questions) *Please describe the impact of the uncertainty that often surrounds a diagnosis of IEM?*

- a. Emotionally?
- b. Practically? (for parent and the family)
- c. Were there any strategies or things you did to manage the uncertainty?

2) Support Systems:

(Main question) *Please describe what/who your most valuable supports were during the times you found most difficult i.e. time of diagnosis, when you went home?*

- a. What kind of support would have been helpful?

3) Navigating the health care system:

(Main question) *Participants interviewed earlier for this study talked about their experiences of now having to be involved with the health care system which for some was a new experience. Please describe what this was like for you?*

- a. Challenges?
- b. Positive experiences?
- c. What/who did you find helpful in navigating this big system?

4) Concluding remarks/ questions:

Please let me know if there is anything else you feel like sharing and/or we should know. Do you have any questions for me?

Thank you for your time.

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