The Diagnostic Journey of Childhood Idiopathic Nephrotic Syndrome: Perspectives of Children and Their Caregivers

Augustina Okpere, MBBS, MSc\textsuperscript{1}, Susan Samuel, MD, MSc\textsuperscript{1,2}, Kathryn King-Shier, RN, PhD\textsuperscript{3}, Lorraine Hamiwka, MD\textsuperscript{1}, and Meghan J. Elliott, MD, MSc\textsuperscript{2,4}

Abstract

Background: Childhood nephrotic syndrome is a rare kidney disease characterized by sudden onset of edema, massive proteinuria, and hypoalbuminemia. Rare diseases can have a long and difficult trajectory to diagnosis.

Objective: We aimed to explore the experiences of children with nephrotic syndrome and their caregivers in their search of a nephrotic syndrome diagnosis.

Design: An exploratory, qualitative descriptive study design.

Setting: The Alberta Children's Hospital outpatient nephrology program in Calgary, Alberta, Canada.

Sample: Children aged 9 to 18 years with steroid-sensitive nephrotic syndrome and their caregivers.

Methods: We undertook semi-structured interviews with children (alone or with a caregiver present) and their caregivers using a question guide suitable to their age and role. We used a thematic analysis approach to inductively code the data and characterize themes related to our research question.

Results: Participants included 10 children aged 9 to 18 years (6 boys and 4 girls) and 18 caregivers (8 men and 10 women). We characterized 3 themes related to participants' experiences in search of a diagnosis of nephrotic syndrome: (1) unexpected and distressing symptom onset, (2) elusiveness of a diagnosis, and (3) encountering a diagnosis. Children with nephrotic syndrome and their caregivers described experiencing initial anxiety due to their unusual and unexpected symptom onset and lack of awareness about the disease. Perceived diagnostic delays and incorrect diagnosis early in the course of the disease contributed to multiple consultations with a variety of care providers. Overall, participants expressed a desire to move past their diagnosis, learn about nephrotic syndrome, and engage in their treatment plans.

Limitations: The views expressed by participants may not reflect those of individuals from other settings. The time elapsed since participants' nephrotic syndrome diagnosis may have influenced their recall of events and reactions to this diagnosis.

Conclusions: In characterizing the diagnostic experiences of children and their caregivers, our study provides insight into how patients with nephrotic syndrome and their caregivers can be supported by the healthcare team along this journey. Focused strategies to increase awareness and understanding of nephrotic syndrome among healthcare providers are needed to improve patients' and families' diagnostic experiences.

Abrégé

Contexte: Le syndrome néphrotique infantile est une néphropathie rare caractérisée par l’apparition soudaine d’un œdème, d’une importante protéinurie et d’une hypoalbuminémie. La trajectoire jusqu’au diagnostic d’une maladie rare peut être longue et difficile.

Objectif: Nous voulions sonder l’expérience des enfants atteints du syndrome néphrotique et celles de leurs soignants pendant le processus d’un diagnostic de syndrome néphrotique.

Conception: Étude descriptive exploratoire et qualitative.

Cadre: Le programme de néphrologie ambulatoire de l’Alberta Children’s Hospital de Calgary (Alberta) au Canada.

Participants: Des enfants (9 à 18 ans) atteints du syndrome néphrotique sensible aux stéroïdes, et leurs soignants.

Méthodologie: Un questionnaire adapté selon l’âge et le rôle a servi de guide pour les entrevues semi-structurées menées avec les enfants (seuls ou en présence d’un soignant) et leurs soignants. Nous avons utilisé une approche d’analyse thématique pour coder les données de façon inductive et caractériser les thèmes liés à notre question de recherche.
The diagnosis of childhood disease can be difficult, and often begins when patients and their families consult with their physicians to understand the cause of their symptoms and how they may be helped. These encounters often take place in the primary care setting, where physicians elicit information about symptoms, identify physical findings, and try to understand the impact of the illness on the patient’s and family’s physical and emotional wellbeing. Physicians then apply their knowledge and clinical experience to choose focused, and appropriate, investigations to arrive at a diagnosis. The communication of a diagnosis and the patient’s response to this information together have been termed the “diagnostic moment,” which can impact patients’ subsequent experiences of health and illness. For children with rare diseases, such as nephrotic syndrome, this moment often represents more of a journey characterized by uncertainty and distress as they navigate new symptoms and seek to establish their underlying cause.

Rare diseases are conditions that affect fewer than 1 in 2000 people, which collectively encompass a spectrum of approximately 7000 disorders affecting over 300 million people worldwide. As most rare diseases have a genetic basis, they often rely on sophisticated genome testing and correct identification of characteristic phenotypic features to arrive at a diagnosis. The limited experience of many clinicians with recognizing or managing most rare diseases, including nephrotic syndrome, means that affected children often experience multiple consultations with different clinicians, errors in diagnosis, and unnecessary delays in arriving at a diagnosis and therapeutic plan. A previous survey of caregivers of children with nephrotic syndrome suggested lower diagnostic success in primary care settings than in emergency or pediatric care settings. Half of affected families reported being incorrectly diagnosed with allergies, which in many cases contributed to perceived diagnostic delays ranging from days to months.
The burden of diagnostic delays and misdiagnosis are unfortunate realities for patients and their families living with rare diseases, such as nephrotic syndrome. In addition to the uncertainty and concern surrounding the future of affected individuals, delays in establishing a correct diagnosis can lead to interval disease deterioration and adversely influence patients’ trust in the healthcare system and how they seek care for subsequent health concerns. To our knowledge, no published reports have explored the in-depth experiences of children with nephrotic syndrome and their caregivers in their search for a diagnosis. An appreciation of these individuals’ diagnostic experiences would help justify targeted strategies to enhance disease recognition, improve diagnostic processes, and support patients and their families along their journey. In this qualitative study, we explored the experiences of children with nephrotic syndrome and their caregivers as they sought a diagnosis, including how their symptoms were recognized and their reactions to the diagnosis.

Methods

Study Design and Setting

We used a qualitative descriptive approach to explore participants’ experiences in their search for a diagnosis of nephrotic syndrome. Qualitative description is particularly useful in health services research to explore research questions that are relevant to clinical practice. This approach was well suited to our study objectives, as it enabled us to examine a complex issue among both children and adult caregivers and provide rich descriptions of participants’ experiences using accessible language and remaining close to their own accounts. We studied children with steroid-sensitive nephrotic syndrome and their caregivers receiving care at the Alberta Children’s Hospital in Calgary, Alberta, Canada. We reported this study in accordance with the Consolidated Criteria for Reporting Qualitative research (COREQ; Supplemental Table S1).

Participant Selection

We used purposive sampling to identify eligible children and their caregivers from the approximately 50 participants registered in the Canadian Childhood Nephrotic Syndrome (CHILDNEPH) database in Southern Alberta. We employed maximum variation sampling purposively across a range of participant characteristics, including age, gender, and disease duration, to identify heterogenous patterns that cut across different cases. We included patients with varying disease duration to explore their recollections and the perceived significance of their diagnosis over time. Eligible participants included English-speaking children and adolescents aged 8 to 18 years with idiopathic steroid-sensitive nephrotic syndrome and primary caregivers who reside with the child. Children younger than 8 years were excluded, as younger children are not consistently able to provide comprehensive accounts of their illness experience. However, caregivers of children less than 8 years of age were eligible to capture the experiences of caring for younger children living with nephrotic syndrome. Children with co-existing medical conditions, such as global developmental delay or cerebral palsy, and those with chronic kidney disease (estimated glomerular filtration rate ≤ 60 ml/min/1.73 m2) were excluded because of the potential impact of these conditions on nephrotic syndrome presentation, complexity, and diagnosis.

A clinical member of the team approached eligible children and their caregivers to introduce the study and provide study-related information. An investigator (A.O.) corresponded by email with interested individuals who confirmed consent to contact, inviting them and their children to participate in this study. All minor participants aged 8 to 13 years provided assent for the study. Caregivers of minors provided parental consent and adults and mature minors aged 14 to 18 years provided informed consent. All participants were given a CAD$20 gift card as reimbursement for their participation. The study was approved by the Conjoint Health Research Ethics Board at the University of Calgary (REB20-0860).

Data Collection

Semi-structured interviews were used to explore participants’ perceptions of symptom onset, experiences in search of a diagnosis, and reactions to this diagnosis. This approach enabled participants to discuss their experiences in response to open-ended questions and the opportunity for the interviewer to ask follow-up questions based on participants’ responses. Interview guides were designed based on the clinical experience of the research team and literature review and used language appropriate to the children’s developmental stages. The primary interview guide was developed for participants aged 10 to 18 years and adapted for use with children aged 8 to 9 years and caregivers (Supplemental Table S2).

All interviews were conducted virtually by 1 investigator (A.O.), a graduate student and pediatric nephrology trainee, using the Microsoft Teams web-based platform (Microsoft Corporation) while participants were at their homes. Children were offered the option of interviewing separately or with their caregivers present. Caregivers were also interviewed separately or jointly as a parent–parent dyad. Dyadic interviews allowed interactions between participants with prior relationships to produce rich data arising from both perspectives. The interviewer summarized participants’ responses to them regularly during the interviews and asked for feedback, clarification, or elaboration as necessary to ensure accurate capture of their experiences and perspectives. Field notes were taken during and immediately after the interviews to supplement transcripts and document reflexive insights that arose during interviews. Participants’ socio-demographic data were collected electronically on the University of
Calgary’s REDCap server prior to the interviews to summarize the sample and inform purposive sampling. All interviews were audio recorded and transcribed verbatim by 1 investigator (A.O.). Transcripts were uploaded into NVivo (QSR International Pty Ltd., Version 12, 2018) to enable data organization.

Data Analysis

Data collection and analysis took place iteratively, whereby emerging concepts from interviews were explored in subsequent interviews and analysis. We undertook thematic analysis at the semantic level, whereby patterns within the data were identified, analyzed, interpreted, and reported. For dyadic interviews where both individuals contributed their own distinct perspectives, the interview was treated as a single unit of analysis. This meant that these interviews were coded, analyzed, and interpreted in such a way that we identified key messages and patterns from the transcript as a whole and integrated findings across transcripts. As both parents’ experiences were anchored to the same patient (the child with nephrotic syndrome), analysis of dyadic transcripts as a single unit is appropriate. For children’s interviews where a parent was present, only the responses of the child were analyzed.

One investigator (A.O.) engaged in thorough and repeated reading of transcripts and generated initial codes directly from the data. A second investigator (M.J.E.) independently coded the first 2 transcripts to contribute to coding scheme development. The coding scheme was finalized after the first 12 transcripts and applied systematically to subsequent transcripts with only minor adjustments made to code definitions. Codes were sorted into potential themes which were refined to ensure connections among themes and with the coded dataset. Data saturation, the point at which additional relevant data is no longer attainable, was achieved after 25 interviews. We ensured methodological rigor through attention to criteria for trustworthiness in qualitative research and reflexivity throughout data collection, analysis, and interpretation. We maintained an audit trail for all analytical procedures.

Results

Sample Characteristics

Of 38 eligible families of children with nephrotic syndrome approached, 28 individuals from 15 families consented to an interview. Of those who did not participate, 1 family declined, 4 families initially agreed to participate but did not provide consent, and 18 families did not respond to our invitation. In 1 family, both parents participated in a dyadic parent–parent interview, but their child did not participate. In total, we conducted 25 interviews involving 28 participants (18 individual interviews, 4 child interviews with a parent present, and 3 father–mother dyadic interviews) that lasted an average of 49 minutes. Ten participants were children with nephrotic syndrome (6 boys and 4 girls; age range 9 to 18 years) and 18 were caregivers (8 men and 10 women) (Tables 1 and 2). All children were diagnosed with nephrotic syndrome in the outpatient setting, 7 of whom had received their diagnosis more than 6 years previously. All but 2 children were in remission (i.e., symptom free and not taking any nephrotic syndrome medications) at the time of the interview.

The Diagnostic Journey of Childhood Nephrotic Syndrome

In discussing their experiences in search of a diagnosis, participants described their symptom onset and trajectory, their reactions to the symptoms, and perceived delays and errors in diagnosis. Overall, participants expressed a desire to move past their diagnosis, learn about the condition, and address its implications. In the following sections, we elaborate on 3 themes characterizing participants’ diagnostic journey: (1) unexpected and distressing symptom onset, (2) elusiveness of a diagnosis, and (3) confronting the diagnosis.

Unexpected and distressing symptom onset. Participants’ experiences of abrupt and unexpected onset of body swelling, their perceptions and beliefs about symptom causes, and their emotional responses to symptom persistence are described in this theme. Participants reported a sudden, unprovoked onset of diffuse body swelling that altered the children’s physical appearance. While children emphasized gross physical changes, caregiver participants noted more subtle and progressive changes that reflected a departure from their child’s previous state of health. One child participant who developed symptoms at age 7 years described his scrotal swelling as follows:

My pee pee grew big . . . . (Boy, 9 years old)

Caregiver participants used words like “puffiness,” “looking like a balloon,” “getting fatter,” “unrecognizable,” and “distorted face” to describe their children’s appearances. One caregiver whose child’s symptom progressed gradually said,

We noticed that she was puffy in the morning on the face, eyes, especially cheeks. And then, after a few days, we noticed that there was a lot of puffiness around her ankles. (Woman, caregiver)

Initially, some caregiver participants attributed the progressive weight gain resulting from diffuse body swelling to physiological growth. Others ascribed symptoms to familiar and relatable medical conditions, such as allergies or musculoskeletal injury of the feet. One child participant who noticed her leg swelling during a gymnastics class said,
We [herself and her friends] thought that my feet were broken. (Girl, 16 years old)

Although some younger children and caregiver participants expressed a lack of concern at symptom onset, their apprehension grew when symptoms persisted or progressed beyond what they considered a “normal” response to the suspected cause. Some adolescent and caregiver participants described how being increasingly “concerned,” “afraid,” “anxious,” and “worried” prompted a search for a diagnosis. One adolescent participant who developed symptoms at the age of 11 years said,

The swelling was a little strange to me. For the first time, I had fear. (Boy, 18 years old)

**Elusiveness of a diagnosis.** This theme encompasses participants’ reactions to perceived mischaracterization of symptoms by healthcare providers upon presentation. Several participants, particularly caregivers, explained how they felt that healthcare providers from whom they sought initial assessment about their concerns tended to minimize their children’s symptoms. Some caregivers described feeling dismissed by physicians who may not have initially appreciated the significance of their children’s symptoms and thus would not have carried out the appropriate investigations to identify nephrotic syndrome as their cause. Several caregivers described how this prompted feelings of disappointment and mistrust in the healthcare system. One participant who recalled her child’s rapid weight gain said,

She [physician] said that my toddler looked fine and he’s perfectly healthy. She couldn’t find any issues with him. I remember, she was asking me, “Look at him. does he look like a sick child?” Then she said, “Go home, he is a perfectly healthy child.” So, she sent us home with no diagnosis or no future investigations or plan. I didn’t believe them because I was sure something was going on. (Woman, caregiver)

Several caregivers described feeling helpless as their children were subjected to investigations and treatments for other conditions, such as allergies or constipation. They wondered if by advocating more for their child, they would have arrived at a corrected diagnosis sooner than by waiting for symptom progression or lack of effect of treatment for these more common conditions. They suggested that delays in diagnosis resulted in delayed initiation of appropriate, directed therapies for nephrotic syndrome. One participant whose child was treated with nasal sprays for suspected allergies during primary care encounters for body swelling said,

| Characteristics                  | Number of participants |
|----------------------------------|------------------------|
| Gender                           |                        |
| Boy                              | 6                      |
| Girl                             | 4                      |
| Child’s age group                |                        |
| 8-9 years                        | 5                      |
| 10-13 years                      | 2                      |
| 14-18 years                      | 3                      |
| Ethnicity                        |                        |
| White Caucasian                  | 6                      |
| Asian                            | 2                      |
| Other                            | 2                      |
| Location of residence            |                        |
| Rural or small population center (<1000) | 2                |
| Medium population center (1000-29,999) | 2            |
| Large urban population center (≥100,000) | 6            |
| Time since diagnosis of Nephrotic Syndrome |            |
| ≤6 years                         | 3                      |
| >6 years                         | 7                      |
| Relapses in the last 6 months    |                        |
| ≤2 relapses                      | 10                     |
| >2 relapses                      | 0                      |
| Other children in the family     |                        |
| Yes                              | 10                     |
| No                               | 0                      |
| Interview of participants <13 years |                |
| Caregiver present                | 4                      |
| No caregiver present             | 6                      |

| Characteristics                  | Number of participants |
|----------------------------------|------------------------|
| Gender                           |                        |
| Men                              | 5                      |
| Women                            | 13                     |
| Educational level                |                        |
| High school graduate             | 3                      |
| Some technical school/diploma    | 3                      |
| University degree                | 9                      |
| Graduate school (MSc/PhD)        | 3                      |
| Employment status                |                        |
| Full-time                        | 10                     |
| Part-time/self-employed          | 3                      |
| None                             | 5                      |
| Location of residence            |                        |
| Rural or small population center (<1000) | 4                |
| Medium population center (1000-29,999) | 3            |
| Large urban population center (≥100,000) | 11            |
| Ethnicity                        |                        |
| White Caucasian                  | 11                     |
| Asian                            | 3                      |
| Other                            | 4                      |
It was super frustrating. I was not happy, clearly, because when we finally figured her out, she was pretty bad. It took a very long time for a 3-year-old to go through that. (Woman, caregiver)

Another caregiver participant whose child was admitted shortly after diagnosis for peritonitis, a complication of nephrotic syndrome, described:

Over a couple of months, I went to at least 6 different doctors, but he [child] had all these strange symptoms, and nobody took blood, nobody took stool or urine sample. My main regret is that I didn’t fight harder, and my main complaint is that nobody fought for me. (Woman, caregiver)

Encountering a diagnosis. This theme encompasses participants’ responses to arriving at a diagnosis of nephrotic syndrome and their motivations to learn about the disease and confront its management. Some caregiver participants described traveling long distances to a tertiary care hospital to obtain or confirm a diagnosis. Caregivers and adolescent participants indicated that once their symptom constellation was recognized as characteristic of nephrotic syndrome, they underwent the necessary testing to confirm the diagnosis.

Caregiver participants described a wide range of emotions following receipt of their children’s diagnosis. Many expressed initial relief after a prolonged period of uncertainty and frustration, and later, sadness and uncertainty as they learned more about nephrotic syndrome and its implications for day-to-day living. Others described dismay at their diagnosis and used terms like “shocked,” “worried,” “devastated,” “lost,” and “overwhelmed” related to their initial reactions. One participant, whose only child was affected, said,

“Your world [comes] crushing down when you get told that your son has a rare kidney disease and that they don’t know very much about it. It was definitely very much overwhelming and scary and very hard at first when we were told about it. (Woman, caregiver)

Some caregivers described feelings of guilt and the perception that their actions while pregnant or caring for the child may have contributed to the onset of nephrotic syndrome. Accordingly, 1 participant who described having 2 other “healthy” children before the child with nephrotic syndrome stated,

“Devastated. I felt really bad. I felt it was somehow my fault. I felt very broken. Even though all the doctors will say it’s not your fault [and] there is no known cause, I still felt like I did something wrong. (Woman, caregiver)

Most caregiver and adolescent participants described having no knowledge of nephrotic syndrome prior to their diagnosis. They expressed a desire to move past their “label” and learn to adapt and manage the disease. Some described turning to trusted resources such as care teams experienced in nephrotic syndrome and informational pamphlets offered by kidney organizations, while others sought advice from internet resources to help them navigate their newly diagnosed condition. One adolescent who developed nephrotic syndrome at 9 years of age described her understanding of nephrotic syndrome as follows:

I didn’t really know what it was. They [nephrology care team] kind of talked to us because that would be like the first time that you are on steroids, so they had to explain everything to us. (Girl, 16 years old)

Many participants described empathetic interactions with members of the care team and appreciated the coordinated support services available from their care providers and in the community to help them prepare and live well with the disease. One caregiver said,

“The staff at the hospital was fantastic with explaining what it was, how it’s managed and what the potential long-term effects could be. We left there comfortable that we as a family would be able to manage going forward. (Woman, caregiver)

Discussion

Our study highlights the challenges that patients and their caregivers encounter during their search for a diagnosis of childhood nephrotic syndrome. We characterized 3 themes related to children’s and caregivers’ recognition of symptoms, perceptions of delayed diagnosis or misdiagnosis, and emotional and actionable responses to diagnostic confirmation. While symptoms of diffuse body swelling were difficult to ignore, participants described how they and their providers to whom they turned initially for assistance mischaracterized these manifestations as common and relatable conditions, such as allergies, particularly during early disease stages. The increasing severity and persistence of symptoms evoked feelings of apprehension that prompted participants’ continued search for and confirmation of a diagnosis.

To our knowledge, this is the first study to explore the experiences of both children and their caregivers related to the diagnosis of childhood nephrotic syndrome. Findings from our study are consistent with a previous report by Beanlands et al,37 which suggested that adult patients with nephrotic syndrome also misunderstood and misattributed the cause of their symptoms and only sought medical help when their symptoms worsened. A lack of awareness of the symptoms of nephrotic syndrome among children and their caregivers in our study could relate to the rarity of the disease. The uncertainty surrounding symptom onset and desire for diagnostic confirmation prompted caregivers to advocate for their children in their search for a diagnosis so they could move forward confidently with a care plan.

Some participants described empathetic interactions with members of the care team and appreciated the coordinated support services available from their care providers and in the community to help them prepare and live well with the disease. One caregiver said,

“The staff at the hospital was fantastic with explaining what it was, how it’s managed and what the potential long-term effects could be. We left there comfortable that we as a family would be able to manage going forward. (Woman, caregiver)

Discussion

Our study highlights the challenges that patients and their caregivers encounter during their search for a diagnosis of childhood nephrotic syndrome. We characterized 3 themes related to children’s and caregivers’ recognition of symptoms, perceptions of delayed diagnosis or misdiagnosis, and emotional and actionable responses to diagnostic confirmation. While symptoms of diffuse body swelling were difficult to ignore, participants described how they and their providers to whom they turned initially for assistance mischaracterized these manifestations as common and relatable conditions, such as allergies, particularly during early disease stages. The increasing severity and persistence of symptoms evoked feelings of apprehension that prompted participants’ continued search for and confirmation of a diagnosis.

To our knowledge, this is the first study to explore the experiences of both children and their caregivers related to the diagnosis of childhood nephrotic syndrome. Findings from our study are consistent with a previous report by Beanlands et al,37 which suggested that adult patients with nephrotic syndrome also misunderstood and misattributed the cause of their symptoms and only sought medical help when their symptoms worsened. A lack of awareness of the symptoms of nephrotic syndrome among children and their caregivers in our study could relate to the rarity of the disease. The uncertainty surrounding symptom onset and desire for diagnostic confirmation prompted caregivers to advocate for their children in their search for a diagnosis so they could move forward confidently with a care plan.
The presenting symptoms of nephrotic syndrome often mimic common, relatable childhood illnesses such as allergies. As with other rare diseases, the misattribution of early nephrotic syndrome manifestations to more common conditions can delay appropriate investigations. In our study, many participants perceived that initial mischaracterization of their symptoms contributed to diagnostic, and thus therapeutic, delays, which is similar to other studies exploring patients’ diagnostic experiences with rare conditions, including hemophilia and cystic fibrosis. Participants also experienced heightened concern upon confirmation of a nephrotic syndrome diagnosis after being reassured in early encounters. Our study’s findings align with results from the previously described survey suggesting children presenting with diffuse body swelling are often first thought to have allergies when presenting to their primary care team, which is not surprising given the similar manifestations and the fact that allergies are much more common and amenable to prompt treatment.

Taken together, this suggests that although most physicians are aware of rare diseases, such as nephrotic syndrome, they may not encounter them frequently enough in practice to immediately recognize their significance. A preliminary diagnosis of childhood nephrotic syndrome can be made by assessing for dependent edema, which is the most common and observable presenting symptom of this condition, and performing a simple dipstick urinalysis to demonstrate significant proteinuria and confirm the diagnosis. This contrasts with other rare diseases that often require sophisticated, expensive, and sometimes invasive procedures to establish a diagnosis. Dipstick urinalysis is a simple and cost-effective test that can be performed in many clinic settings to alert the care team to a potentially serious underlying condition necessitating additional testing or specialist assessment. As participants in our study suggested, an expedited diagnostic process could assuage the worry and uncertainty that accompany initial nephrotic syndrome manifestations.

Reports suggest that approximately 5% of all medical conditions are misdiagnosed in outpatient settings each year, and up to one-third of annual healthcare budgets are spent on unnecessary services. As supported by our study’s findings, delays or errors in diagnosis can lead to adverse physical and psychological health outcomes resulting from inappropriate treatment, delayed treatment, and disease deterioration. For example, many caregivers in our study described feeling responsible for their children’s condition and for delays in obtaining a diagnosis, which contributed to guilt and regret. Participants also questioned the extent to which their delay in diagnosis and initiation of treatment might impact the child’s disease course, response to therapy, and future physical and social development. In addition to the similar frustrations, uncertainty, and worry identified among children and caregivers living with other rare diseases, such as cystic fibrosis, these experiences can contribute to mistrust of primary care providers, to whom patients often first turn with health concerns, and of the healthcare system more broadly. This mistrust may adversely influence how and where people seek medical attention for future health concerns, which can further perpetuate challenges to diagnosing rare diseases in an overburdened healthcare system.

Patients with rare diseases often lack knowledge about their illness trajectory and prognostic implications of their condition. Provision of relevant and timely information to patients and their families is a key component of patient-centered care and ensures that patients’ and caregivers’ needs and preferences are integrated into clinical decisions. For children with nephrotic syndrome and their families, our findings suggest that disease education and support should begin at the time of diagnosis and come from multiple sources in a concerted team-based approach. Whereas nephrology care teams are often best positioned to share information about patients’ expected disease course and treatment options, primary care teams would have a critical role in supporting children’s wellbeing and ongoing routine health maintenance. Our findings also suggest that strategies to promote symptom recognition and expedited diagnosis of this condition in primary care settings are needed, as this is where affected patients often first present. Such strategies could include continuing medical education initiatives to reinforce health practitioners’ awareness of nephrotic syndrome, widespread access to dipstick urinalysis at the point of care, and enhanced communication mechanisms between primary and nephrology care teams to enable prompt consultation and advice when nephrotic syndrome is suspected.

Our findings offer valuable insight into the diagnostic hurdles children and their families face related to childhood nephrotic syndrome. However, we acknowledge some study limitations. As our sample was limited to participants in a single nephrology center, included views may not reflect those of individuals who reside in other settings. However, our maximum variation sampling across age, gender, and disease duration categories captured a wide range of experiences that we anticipate are transferrable to similar contexts. We also did not explicitly examine socio-cultural influences on the diagnostic experiences of children and their families and suggest this as an area for future dedicated study. Another limitation of our study is that recall of events and experiences by some participants may be limited depending on the time elapsed since the children’s diagnosis. This was mitigated by carefully defining the research questions and refining the language used in the interview guides to prompt recall of events. For most participants, the nephrotic syndrome diagnosis represented a significant event in their lives and one about which recollection of important details was maintained. A further limitation posed by our use of dyadic interviews is the potential for 1 participant to dominate the discourse. This was mitigated by directing questions to both participants and analyzing their responses to the same questions individually. Finally, a limitation of interviewing children is that the presence of a caregiver during the interview may influence the child’s responses. The interviewer used verbal and non-verbal techniques to establish trust and
rappor with the children and offered to interview older children without their caregivers present.

Conclusion

Children with nephrotic syndrome and their caregivers related their diagnostic experiences to beliefs about the nature of symptoms, lack of disease-related knowledge, and perceived diagnostic delays and misdiagnosis by healthcare providers. Initial feelings of apprehension were largely alleviated upon confirming a diagnosis, which enabled participants to engage in discussions about disease implications with their care team. Strategies to promote recognition of this rare disease in primary care settings, where affected patients often first present, are needed to improve patients’ diagnostic experiences. Our findings also provide insight into the importance of supporting the informational and emotional needs of affected children and families throughout their diagnostic journey.

Acknowledgments

This work would not have been possible without our amazing patient partners, participants, and staff of the Canadian Childhood Nephrotic Syndrome (CHILDNEPH) project. We are grateful to the Roy and Vi Baay Chair in Kidney Research in Canada for providing funding support for this project.

Ethics Approval and Consent to Participate

This study was approved by the University of Calgary’s Conjoint Health Research Ethics Board (REB20-0860). Caregivers of minors provided parental consent, and adults and mature minors aged 14 to 18 years provided informed consent.

Consent for Publication

Not applicable.

Availability of Data and Materials

This study used individual, participant-level data collected during interviews. We are unable to make our dataset available due to restrictions on sharing potentially identifiable data as outlined in our Research Ethics Board certification. Inquiries related to this study’s dataset can be directed to the corresponding author.

Author’s Note

Not applicable.

Author Contributions

Research idea and study design: AO, SS, MJE, KKS; data collection: AO; data analysis/interpretation: AO, MJE; supervision and mentorship: MJE, SS. Each author contributed important intellectual content during manuscript drafting or revision and agrees to be personally accountable for the individual’s own contributions and to ensure that questions pertaining to the accuracy or integrity of any portion of the work, even one in which the author was not directly involved, are appropriately investigated, and resolved, including with documentation in the literature if appropriate.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iD

Meghan J. Elliott https://orcid.org/0000-0002-5434-2917

Supplemental Material

Supplemental material for this article is available online.

Data Sharing Statement

This study used individual, participant-level data collected during interviews. We are unable to make our dataset available due to restrictions on sharing potentially identifiable data as outlined in our Research Ethics Board certification. Inquiries related to this study’s dataset can be directed to the corresponding author.

References

1. Noone DG, Iijima K, Parekh R. Idiopathic nephrotic syndrome in children. Lancet. 2018;392(10141):61-74.
2. Chanchlani R, Parekh RS. Ethnic differences in childhood nephrotic syndrome. Front Pediatr. 2016;4:39.
3. Banh TH, Hussain-Shamsy N, Patel V, et al. Ethnic differences in incidence and outcomes of childhood nephrotic syndrome. Clin J Am Soc Nephrol. 2016;11(10):1760-1768.
4. McKinney PA, Feltbower RG, Brocklebank JT, Fitzpatrick MM. Time trends and ethnic patterns of childhood nephrotic syndrome in Yorkshire, UK. Pediatr Nephrol. 2001;16(12):1040-1044.
5. Fakhouri F, Bocquet N, Taupin P, et al. Steroid-sensitive nephrotic syndrome: from childhood to adulthood. Am J Kidney Dis. 2003;41(3):550-557.
6. Rheault MN, Zhang L, Slewski DT, et al. AKI in children hospitalized with nephrotic syndrome. Clin J Am Soc Nephrol. 2015;10(12):2110-2118.
7. Hingorani SR, Weiss NS, Watkins SL. Predictors of peritonitis in children with nephrotic syndrome. Pediatr Nephrol. 2002;17(8):678-682.
8. Kerlin BA, Blatt NB, Fuh B, et al. Epidemiology and risk factors for thromboembolic complications of childhood nephrotic syndrome: a Midwest Pediatric Nephrology Consortium (MWPNC) study. J Pediatr. 2009;155(1):105-110, 110.e1.
9. Sarkar U, Bonacum D, Strull W, et al. Challenges of making a diagnosis in the outpatient setting: a multi-site survey of primary care physicians. BMJ Qual Saf. 2012;21(8):641-648.
10. Heritage J, McArthur A. The diagnostic moment: a study in US primary care. Soc Sci Med. 2019;228:262-271.
11. Jutel AG. Putting a Name to It: Diagnosis in Contemporary Society. Baltimore, MD: The Johns Hopkins University Press; 2011.
12. Price E, Walker E. Diagnostic vertigo: the journey to diagnosis in systemic lupus erythematosus. Health (London). 2014;18(3):223-239.
13. Black N, Martineau F, Manacorda T. Diagnostic odyssey for rare diseases: exploration of potential indicators. Policy Innovation Research Unit. https://piru.ac.ae/assets/files/Rare%20diseases%20Final%20report.pdf. Published 2015. Accessed September 17, 2022.

14. Richter T, Nestler-Parr S, Babela R, et al. Rare disease terminology and definitions—a systematic global review: report of the ISPOR rare disease special interest group. Value Health. 2015;18(6):906-914.

15. Haendel M, Vasilievsky N, Unni D, et al. How many rare diseases are there? Nat Rev Drug Discov. 2020;19(2):77-78.

16. Global Genes. RARE disease facts. https://globalgenes.org/rare-disease-facts. Published 2021. Accessed September 5, 2022.

17. Zurynski M, Kharrazi LD. Delayed diagnosis of cystic fibrosis and the family perspective. J Pediatr. 2005;147(suppl 3):S21-S25.

18. Carmichael N, Tsipis J, Windmueller G, Mandel L, Estrella E. “Is it going to hurt?”: the impact of the diagnostic odyssey on children and their families. J Genet Couns. 2015;24(2):325-335.

19. Merelle ME, Huisman J, Alderden-van der Vecht A, et al. Early versus late diagnosis: psychological impact on parents of children with cystic fibrosis. Pediatrics. 2003;111(2):346-350.

20. Sandelowski M. Whatever happened to qualitative description? Res Nurs Health. 2000;23(4):334-340.

21. Sandelowski M. What’s in a name? qualitative description revisited. Res Nurs Health. 2010;33(1):77-84.

22. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. Int J Qual Health Care. 2007;19(6):349-357.

23. Samuel S, Scott S, Morgan C, et al. The Canadian Childhood Nephrotic Syndrome (CHILDNeph) project: overview of design and methods. Can J Kidney Health Dis. 2014;1:17.

24. Rodriguez-Lopez S, Chanchlani R, Dart AB, et al. Characteristics associated with variation in corticosteroid exposure in children with steroid-sensitive nephrotic syndrome: results from a Canadian Longitudinal Study. Kidney360. 2021;2(12):1960-1967.

25. Patton MQ. Qualitative Research & Evaluation Methods. Thousand Oaks, CA: Sage Publications; 2002.

26. Suri H. Purposeful sampling in qualitative research synthesis. Qual Res J. 2011;11:63-75.

27. Matza LS, Patrick DL, Riley AW, et al. Pediatric patient-reported outcome instruments for research to support medical product labeling: report of the ISPOR PRO good research practices for the assessment of children and adolescents task force. Value Health. 2013;16(4):461-479.