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Patient experience and healthcare priorities in childhood steroid sensitive nephrotic syndrome

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Patient experience and healthcare priorities in childhood steroid sensitive nephrotic syndrome

by

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Abstract

Childhood idiopathic steroid sensitive nephrotic syndrome (SSNS) is characterized by sudden and unexpected onset of body swelling, massive proteinuria and hypoalbuminemia. The chronic recurrent relapses and side effects of its treatment can impact patients' and caregivers' experiences of the disease. The aims of this qualitative study were to explore the experiences and healthcare priorities of children with SSNS and their caregivers. We interviewed 28 participants that comprised 10 children aged 9 to18 years (6 boys and 4 girls) and 18 caregivers over the internet on Microsoft Teams between January and April 2021. Using qualitative description and thematic analysis, we identified three themes related to the diagnostic journey of childhood nephrotic syndrome (unexpected distressing symptoms, elusiveness of diagnosis and confronting the diagnosis) and three themes related to the experiences of children living with SSNS and their caregivers (disruption of normalcy, regaining control and dependable social support system). Four actionable needs and care priorities of participants were identified: desire to be heard, understanding the cause of nephrotic syndrome, alleviating the burden of steroid regimen and enhanced social support availability. Our study provides insights into several strategies that healthcare professional could adopt to improve the diagnostic experience of children and their caregivers in search of a diagnosis of nephrotic syndrome and care of patients and their families. Also, our findings have the potential to inform the design and conduct of future research in priority setting and treatment of childhood SSNS.

Keywords: nephrotic syndrome, steroid sensitive nephrotic syndrome, experiences, priorities, children, caregivers, qualitative research

Preface

This manuscript-based dissertation consists of two manuscripts that are linked through their focus on experiences and care needs of children with childhood nephrotic syndrome and their caregivers. Dr Augustina Okpere led the conceptualization, protocol design and implementation, data analysis and initial draft of the manuscripts. Dr. Okpere received substantial guidance from her research committee (Drs. Susan Samuel, Meghan Elliott, Kathryn King-Shier and Lorraine Hamiwka) throughout the phases of the thesis development. All authors contributed important intellectual content and provided critical reviews of the manuscripts.

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Dedication

This work is dedicated to my family, Sebastian, Oseremen, Onosetale and Ebosetale Okpere. It would not have been possible without your love and perseverance.

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List of Abbreviations

SSNS	Steroid sensitive nephrotic syndrome
CKD	Chronic kidney disease

Chapter 1 Introduction

Childhood idiopathic nephrotic syndrome is a chronic kidney disorder characterised by generalised body swelling, massive proteinuria and hypoalbuminemia (Noone, Iijima, & Parekh, 2018). Globally, the estimated incidence of nephrotic syndrome is between 2 - 7 per 100,000 children (Chanchlani & Parekh, 2016). Geographical and ethnic differences have been documented with higher rates reported among children of South Asian and African descent (Banh et al.; 2016; McKinney et al., 2001; Srivastava, Simon & Alon, 1999). The incidence of idiopathic nephrotic syndrome in children in the United States of America is 2 per 100,000 children less than 16 years of age (Schlesinger et al., 1968). In Canada, the incidence is 4.7 per 100,000 children aged 1 to 18 years (Banh et al; 2016). The peak age at diagnosis is 1 to 4 years with male preponderance (McKinney et al., 2001; Schlesinger et al., 1968). The exact cause is unknown. Genetic mutations in the structure and function of the kidney's filtration barrier, disorders in the immune system and environmental factors have been postulated (Noone et al., 2018; Niaudet & Boyer, 2016, p. 841).

Steroid sensitive nephrotic syndrome (SSNS) runs a remitting and relapsing course. Approximately 80 – 90% of patients with nephrotic syndrome will achieve remission with corticosteroid therapy. These patients are referred to as having SSNS. About 10 – 20% of cases will not respond to corticosteroid therapy; this is known as steroid resistant nephrotic syndrome (Koskimies et al.,1982; Mckinney et al., 2001). The disease often spans throughout childhood, during the period of physical growth as well as social, emotional and intellectual development and frequently extends into adulthood (Fakhouri et al., 2003; Ruth et al., 2005). The clinical course of SSNS is that of either prolonged remission [24%], infrequent relapses with recurrence of body swelling and massive urinary protein loss [22%] or frequent relapses/steroid dependence [53%] (Koskimies et al.,1982)

Corticosteroids are the first-line agents for inducing remission in patients with SSNS. (Niaudet & Boyer, 2016; Wanner, 2012). Remission is defined as trace or negative protein in urine and resolution of body swelling (Niaudet & Boyer, 2016; Gibson et al, 2009). The aim of treatment is to reduce or stop protein loss from the kidneys. The relapsing and remitting nature of the disease predisposes affected children to higher cumulative doses of steroids over a prolonged period. Prolonged use of steroids in children can lead to complications such as growth retardation (Donatti et al., 2003), poor bone health (Leonard et al., 2004), obesity (Foster et al., 2006), hypertension (Klepikov, Kutyrina & Tareyeva, 1988), cataract (Brocklebank, Harcourt & Meadow, 1982) and behavioral disturbances (Mishra et al., 2010).

Corticosteroid sparing agents are commonly used to minimize the side effects of corticosteroids. Patients with steroid dependence (defined as 2 consecutive relapses during corticosteroid therapy or within 14 days after cessation of therapy) or frequent relapses (defined as 2 or more relapses within 6 months of initial response or 4 or more relapses within a period of one year) have complicated medical courses and high cumulative steroid dosing (Gibson et al, 2009; Wanner, 2012). As a result, corticosteroid-sparing agents such as cyclophosphamide, cyclosporine, tacrolimus and rituximab are often used as alternatives for managing disease burden and minimizing steroid side effects. However, these second line agents also have associated risks such as damage to the gonads (Rivkees et al., 1988), kidney damage, hypertrichosis and gingival hyperplasia (Ishikura et al., 2008, Iijima et al., 2002) and lung fibrosis (Sellier-Leclerc et al., 2013) and behavioral abnormalities (Mishra, 2010). From the care provider's perspective, it is challenging to manage patients with SSNS, keep them free of side effects, and help them achieve high quality of life.

Childhood SSNS impacts the quality of life of affected children. Quality of life is a multidimensional construct with no universal definition (WHOQOL, 1998; Wallander, & Schmitt & Hoot, 2001). The World Health Organization defined quality of life as "an individual's perception of their position in life in the context of the culture and value system in which they live and in relation to their goals, expectations, standards and concerns" (WHOQOL, 1997). Wallander et al., 2001, pp. 574) defined it as "the combination of objectively and subjectively indicated well-being in multiple domains of life considered salient in one's culture and time, while adhering to universal standards of human rights". Quality of life is commonly assessed within the dimensional framework of physical, social and psychological domains (Wallander et al., 2001). In children with SSNS, the remitting and relapsing course, and chronicity of the disease impose psychological, social and emotional burden on affected patients and their caregivers which impacts their quality of life (Ruth et al., 2004; Mishra et al., 2015). Ruth et al (2004) in a single centre cross-sectional study conducted in Germany to examine the quality of life in 45 patients aged 3 to 19 years with SSNS from 45 families revealed that affected children have impairment in social functioning as well as psychosocial adjustment both at home and in school compared to healthy controls. In another study from the United States, Selewski et al. (2015) found that the duration of childhood nephrotic syndrome significantly impacts health related quality of life. In this study, children aged 8 to 17 years with longer disease duration had poor social and school functioning on validated measures. Mishra and colleagues (2015) showed that parents of children with nephrotic syndrome have lower health-related quality of life compared to controls.

Patients' experiences of a disease give insight into their needs and disease burden. Patients' experiences of a disease is different from their quality of life. While patients' personal view of their health status, symptom burden and satisfaction with health services can be captured by certain

instruments such as patient-reported outcome measures (PROMs) or patient-reported experience measures (PREMs) (Welding & Smith, 2013), some authors have argued that patient experience spans beyond experience with healthcare services to include the experience of coping with and dealing with the illness (Needham, 2012; Shale, 2013). A narrative review by Wolf et al. (2014) identified several concepts to consider with regards to the definition of patient experience. Firstly, patients' experiences reflect occurrences and events that happen independently and collectively across the continuum of care. Secondly, patient experience is more than satisfaction with healthcare services. Thirdly, patient experience is strongly tied to their expectations beyond clinical outcomes or health status. Finally, patient experience is tied to the principles and practices of patient-and family-centered care. Overall, patients' experience of a disease includes their lived experiences, clinical interactions with healthcare providers, and care. In chronic diseases such as SSNS, patients' experiences therefore encompass experiences of getting a diagnosis, chronic treatments, health practices and life-changing experience which may impact all aspects of life.

There is paucity of data about children and their caregivers' experience with nephrotic syndrome. The few reported studies on experience with nephrotic syndrome were conducted in adults with nephrotic syndrome and parents of children with the disease. A previous study conducted in Canada and United States of America employed focus groups and individual interviews to explore perspectives about the learning needs of adult patients and parents of children with nephrotic syndrome (Beanlands et al., 2017). The participants reported that the complexity of the disease, its treatment and delays in diagnosis impacted the way they coped with the disease. However, the authors did not explore the participants' experiences of getting a diagnosis of nephrotic syndrome. Delayed diagnosis and misdiagnosis of a chronic disease in a child may led to feelings of anxiety, guilt, anger, and mistrust of the healthcare providers among caregivers

(Kharrazi & Kharrazi, 2005). In Sweden, Jonsson et al. (2020) conducted telephone interviews with 10 adults living with nephrotic syndrome; the participants described their experience as feeling ill and well at the same time, being passively adherent to treatment, being in uncertainty due to lack of information and understanding of the disease and trying to comprehend and cope with the disease. There are no data about the experiences of pediatric patients in search of a diagnosis of childhood nephrotic syndrome nor the perspectives of children living with SSNS and their caregivers.

The pediatric patient's experience has been examined for chronic kidney disease (CKD) but not SSNS. Patients with SSNS rarely develop CKD, a more severe complication of nephrotic syndrome. CKD is defined as abnormalities of kidney structure or function for greater than 3 months, with implications for health (KDIGO, 2013). Nicholas and colleagues (2011) explored the lived experiences and perceptions of 25 Canadian children and adolescents aged 7 to 18 years with kidney failure undergoing dialysis treatment. The children described multifaceted experiences and perspectives ranging from not feeling normal, frequent absences from school to relying on family, friends, and health care providers. Tong et al. (2013) explored the experiences and perspectives of 27 Australian individuals aged 12 to 24 years with CKD. The participants who were awaiting kidney transplant described feelings of inferiority and insecurity about their future, which were countered by a sense of resilience and adjustment mentality. SSNS, unlike CKD, is characterized by unpredictable relapses with recurrence of edema and massive proteinuria. The experiences of children living with SSNS have not been described.

A child's experience of a chronic disease could be impacted by the child's relationship and interactions with individuals in the surrounding environments or ecological systems. The ecology of childhood describes the relationship between a developing child and the environment

(Bronfenbrenner, 1979). Bronfenbrenner (1979) described the nested arrangement of these ecological environments that are centered around the child and the influence of the environment on child development. These different environments are referred to as the micro-, meso-, exo-, and macrosystems (Bronfenbrenner, 1979). The developing individual is considered a dynamic entity that moves progressively from one ecosystem to another. The relationship between individuals and their environments is viewed as transactional and reciprocal and exchanges among the different systems bring changes to one another over time (Bronfenbrenner, 1979). The innermost level of environment is known as the *microsystem*. It is the smallest and immediate environment of the child and comprises the caregivers, siblings, peers, friends, school, health services, church and community environment (Bronfenbrenner, 1979). The experiences of a growing child with SSNS could be intertwined with child's relationship and interactions with the different elements of this ecosystem (Figure 1).

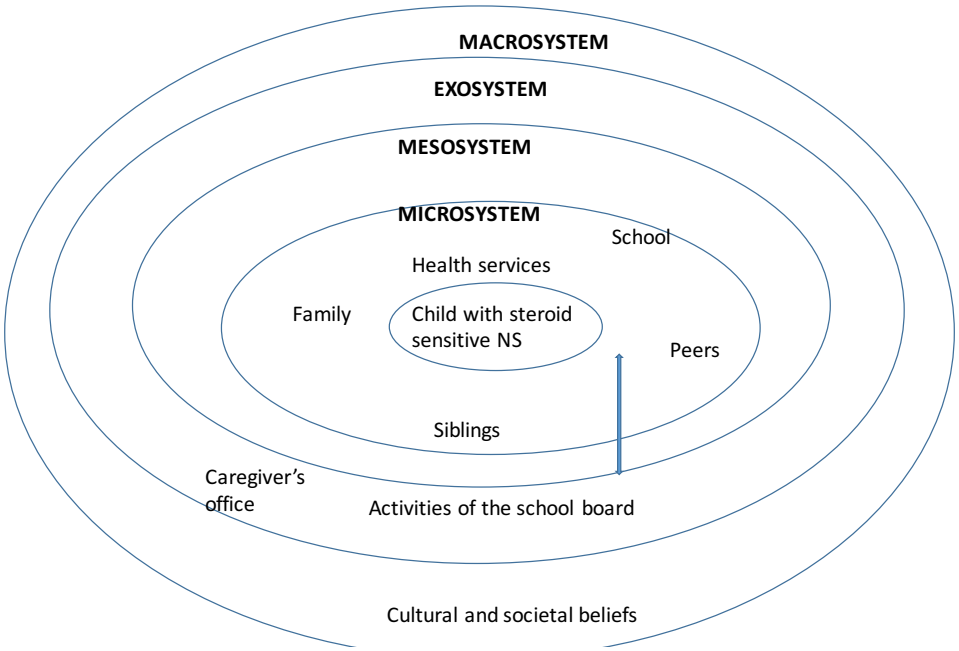

Figure 1: The ecosystem of a child with chronic illness. Adapted from the Ecology of Human Development (Bronfenbrenner, 1979).

The *mesosystem* comprises the interrelations among two or more settings within the microsystem in which the child participates (blue arrow). For example, the interactions between caregivers and healthcare providers and between the child and his/her siblings or peers could impact on the child and family's experience of living with the disease. The *exosystem* refers to one or more settings that do not involve the developing person as an active participant, but in which events occur that affect what happens in the setting containing the developing person (Bronfenbrenner, 1979). A child's exosystem may include the caregiver's place of work, the caregiver's network of friends and the activities of the local school board. For instance, loss of job by a caregiver of a child with SSNS would indirectly impact on the child's experience of living with the disease as the experiences of caregivers are intertwined with that of the child. The *macrosystem* is the largest and most distant ecosystem and is comprised of societal elements such as cultural beliefs, societal polices, political and economic systems that could influence the child's growth, development and experiences. The implication of this is that a chronic disease in a growing child occurs in a hierarchy of these nested ecosystems that are interrelated (Patterson & Garwick, 1994) and that the experiences in search of a diagnosis of a chronic illness and living with the illness could be impacted by the child's relationship and interactions with the surrounding environments.

Chronic diseases create strain within the family structure by their interaction with the individual, family or other ecological system. The family system constitutes a vital part of the child's immediate environment. A problem in any member of the family affects all members of the family (Kazak, 1989). Parents and caregivers play a central role in the care of children with chronic diseases. The meaning and demands of a child with a chronic illness change with the child's development and the developmental changes occurring in the family such as caregiver's

employment status or the arrival of a new child (Kazak, 1989). A family's understanding of the meaning of a chronic illness and its ability to cope with the demands of the disease are critical in maintaining stable family structure and function (Patterson & Garwick, 1994; Rolland, 1988). The outcome of the family's response is conceptualized in terms of family adjustment and family adaptation and is reflected on the physical and mental health of members of the family especially the caregivers (Patterson & Garwick, 1994; Rolland, 1988). The family's response to the child's illness also has profound impact on the development and well-being of the child (Kazak, 1989). This could impact on the child's experience of living with the disease. This implies that "chronic illness happens to a family, not just an individual" (Patterson & Garwick, 1994, p. 131). SSNS like other childhood chronic diseases, causes strain within the family structure. A previous study by Mitra & Bannerjee, (2011) showed that nephrotic syndrome causes significant mental and economic stress on families and higher rate of depression among caregivers of children with nephrotic syndrome compared to a control group of primary caregivers of children with minor illnesses.

Patient experience of chronic illness could also be impacted by factors inherent in the individual and nature of the disease. Based on the author's (AO) clinical experience, and informed by Bronfenbrenner's framework described above, potential factors that could impact a child's experience with SSNS beyond the ecological environment include the child's characteristics and the complexities surrounding the nature and management of SSNS (Table 1). These potential factors guided this research about the experiences of children with SSNS and their caregivers.

Table 1: Potential factors that could impact patient's and caregiver's experience in SSNS

Potential Factor	
a)Individual factors	• Age • gender • Presence of co-morbidities
b)Environmental factors	• Family structure • Socioeconomic status • Peer relationship • School and hospital policies • Access to health and social services • Social support
c)Disease-related factors	• Uncertainties about the cause of nephrotic syndrome • Lack of biomarkers to guide therapy or predict prognosis* • Duration of disease • Frequency of relapse • Dependence on steroids to induce remission • Side effects of prolonged steroids • Choice of second line agents • Regular monitoring and urine test at home

* (Stone, Magella & Bennett, M.R. 2019)

The potential disease-specific factors that could impact children's and caregivers' experiences with SSNS are multifactorial and includes the relapsing and remitting nature of the disease, side effects of the medications as well as absence of a biomarker to monitor response to the treatment and predict prognosis. Given these complexities, it is therefore important for healthcare providers to understand patients' and caregivers' views and priorities in the management of the disease. Patients' priorities are the personal health needs and preferences that patients hope to achieve through their health care (Tinetti et al., 2016). In clinical practice, physicians focus on clinical, physical, biochemical and endpoint outcomes of disease such that the priorities that are important to the patient such as the burden of the disease, shared decision making, and social function are often overlooked (Lee, et al., 2010). Aligning healthcare priorities and perspectives of patients and their families with that of the healthcare professionals in decision making is the cornerstone of patient-centered care, which is providing care that is respectful of,

and responsive to, patients and their families' preferences, needs and priorities in a way that ensures that patient values guide all clinical decisions (IOM, 2001). It encompasses a shared-decision approach between the patient and their families and the healthcare professionals to provide quality healthcare to patients as well as including patients and families in healthcare research. While outcome priorities including kidney function, survival, physical activity, lifestyle restrictions and growth, have been ascertained in the research context in children with CKD by Hansson et al. (2019), to our knowledge, there have been no published reports on the care priorities of children with SSNS.

Rationale

Despite the knowledge and understanding of the complexities of the nature and treatment of SSNS, and the potential impact on the affected children and their caregivers, there have been no reports on the experiences and healthcare priorities of children living with SSNS and their caregivers. Knowledge of the experiences of children and their caregivers in search of a diagnosis of this rare disease and their experiences with the disease in their everyday lives provides healthcare professionals and decision-makers valuable information about patients' needs, care priorities and burden of illness (Rand, Dunn & Slade, 2019). Therefore, there is need for an in-depth exploration of the experiences, perspectives, and priorities of children living with SSNS and their caregivers in order to improve care of this population of patients and their families.

The overall aim of this study was to explore the experiences and healthcare priorities of children with SSNS and their caregivers.

The research questions are:

1. How do 8 to 18-year-old children with SSNS and their caregivers describe their experiences living with the disease?

2. What are the perspectives of 8 to 18-year-old children with SSNS and their caregivers about the treatment strategies that they received for SSNS?
3. What do 8 to 18-year-old children with SSNS and their caregivers view as care priorities?

Overview of Thesis

In this manuscript-based thesis, we employed qualitative description methodology and semi-structured interviews to explore the experiences and healthcare priorities of children with SSNS and their caregivers.

In chapter one, we present an overview of childhood SSNS, the challenges of its treatment and the rationale for our study. In chapter 2, we discuss research methods including the nuances of conducting child and family interviews. In chapter 3, we report the findings of the diagnostic journey of children and their caregivers in search of a diagnosis of nephrotic syndrome. We use the broad term nephrotic syndrome in this section because the child's response to steroid therapy is unknown at the time of diagnosis. In chapter 4, we present our finding related to the experiences of children living with SSNS and their caregivers. Finally, we present the implications of the findings of our study and recommendations for medical practice by integrating the findings from the two manuscripts in chapter 5.

Chapter 2 Methods

Study Design

We applied qualitative description as described by Sandolewski (2000 & 2010) to explore participants' experiences with SSNS. Qualitative description is particularly useful in health science research to explore research questions that are relevant in clinical practice. It entails a kind of interpretation of lower inference and presentation of rich descriptions of individuals' experiences in everyday language while remaining close to the data (Sandelowski, 2000 & 2010).

Theoretical Framework

Bronfenbrenner's Ecology of Human Development (Bronfenbrenner, 1979) provided a guiding framework for understanding the social and environmental factors that might influence the experiences of a child with a chronic illness. The Ecology of Human Development describes how interactions between a child and the environment influence growth and development. In using this theoretical framework, we situated our study across the development of a child, and we presumed that interactions between a child with SSNS and their family members, healthcare providers, peers, and school community could impact on their experiences with the disease. Thus, the Bronfenbrenner's Ecology of Human Development informed our research objectives and the interview questions around contextualization of the interactions and relationships between participants and individuals in their environments. In addition, the framework also contributed to an overall discussion of our study findings. However, our study was primarily inductive and exploratory.

Population and Setting

We studied children with SSNS and their caregivers enrolled in the Canadian Childhood Nephrotic Syndrome (CHILDNEPH) project at the Alberta Children's Hospital who had consented

to be contacted for future studies. The CHILDNEPH project was established in 2011 and was designed to develop a transformative model of care by building a longitudinal cohort of children with SSNS to study the variations in care and an understanding of the pathogenesis of nephrotic syndrome and patient-oriented outcomes (Samuel, 2017). The cohort consists of 328 children aged 1 to 18 years recruited from 2013 to 2019 in 11 participatory sites across Canada (Dart et al., 2021), 48 of which are enrolled at the Alberta Children's Hospital in Calgary.

Sampling and Recruitment

We employed purposive sampling (Patton, 2002) to identify eligible children with SSNS and their caregivers in the CHILDNEPH cohort at the Alberta Children's Hospital. The eligibility criteria were children and adolescents aged 8 to 18 years with idiopathic SSNS; primary caregivers who reside with the child with SSNS and ability to communicate comfortably in English language. Patients with co-existing medical conditions that would impact on the ability to participate in the study such as global developmental delay or cerebral palsy and patients with chronic kidney disease with an estimated glomerular filtration rate of less than 60/min/1.73m^2, were excluded from the study. Specifically, a maximum sampling strategy (Patton, 2002; Suri, 2011) was used to explore experiences across a range of participants characteristics including age and gender categories, and disease duration. Eligible caregivers of affected children less than 8 years were also identified to capture the experiences of individuals who have younger children living with SSNS. We chose to exclude children aged 7 years and below because the reliability and validity of self-reports in these age categories have not been demonstrated (Matza et al., 2013). We tried to recruit other patients and their families outside the CHILDNEPH cohort through their care providers, but our efforts were unsuccessful.

The CHILDNEPH team provided information about eligible patients and their families

enrolled in the CHILDNEPH project to one investigator (A.O.) who contacted the caregivers through electronic mail that included information about the study and an invitation to participate. A follow-up invitation was sent after one week to those that did not respond. Interviews were scheduled for the participants who responded affirmatively through email correspondences, telephone calls and text messages. A $20 electronic gift card was offered to each child and caregiver participant as reimbursement for their time and contributions. All electronic gifts cards were sent to the caregivers through electronic mail.

Ethical Considerations

These manuscripts are part of a Master's degree Thesis. Ethical approval for this study was obtained from the Conjoint Health Research Ethics Board at the University of Calgary (REB20-0860) and the Head of the Nephrology clinics at the Alberta Children's Hospital. Researchers often encounter many gatekeepers such as caregivers to gain access to children to participate in research (Hill, 2005). In this study, we respected the child's autonomy to make personal decisions to participate in this study. The purpose of the study, risks and benefits of the study were explained to the children in an age and developmentally appropriate language. All minor participants aged 8 to 10 years and 11 to 13 years provided assent for the study. Caregivers of the minors provided parental consent and adults and mature minor participants aged 14 to 18 years provided informed consent. All consent forms are presented in the supplemental materials. To ensure confidentiality, a unique identifier was assigned to each participant and only de-identified interview excerpts were presented in the final report. We reported this study in accordance with the guidelines of the Consolidated Criteria for Reporting Qualitative research (COREQ)(Tong, 2007).

Data collection

Semi-structured interviews were used to explore the experiences of participants. 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.

The primary interview guide was used for participants aged 10 - 18 years and was adapted for use in children aged 8 - 9 years and caregivers (Supplementary material). The interviews explored the experiences of the participants in getting a diagnosis of childhood nephrotic syndrome and their experiences with SSNS through open-ended questions and prompts to elicit information. The interview guides were designed based on the clinical experience of the researcher, the thesis committee input, literature review and the theoretical framework of the Bronfenbrenner's Ecology of Human Development (Bronfenbrenner, 1979). The interview guides were pilot tested with an adolescent patient and a caregiver of a child with SSNS and revisions were made to one question and interview technique based on feedback. The interview guide offered a focused structure for discussion to ensure that the same basic lines of inquiry were pursued in each interview (Patton, 2002, p. 345). As qualitative research is a reflexive and iterative process (Mauthner & Doucet, 2003), minor revisions (ordering of some questions but not the content) were made to the interview guides following each of the first 3 interviews.

For a long time, researchers have relied on caregivers as primary informants for data on children's feelings and perspectives. This is due to the misconception that children lacked the cognitive capacity to recall events related to their feelings and emotions (Faux, Walsh & Deatrick, 1988; Lamb et al., 1994). However, evidence has shown that children as young as 3 to 6 years can provide reports about themselves and their own health (Dayan & Ziv, 2012; Ponizovsky-Bergelson et al., 2019). These findings position children as 'competent and social actors who are experts in their own lives" (Clark & Statham, 2005) However, interviewing children could be a complex and challenging task and there are additional methodological and ethical considerations to improve the

rigor and success of the interview process. An understanding of the child's language, cognitive and social skills is essential to ensure successful interviews with children (Hughes & Baker, 1990, p. 29). Children's acquisition of language, cognitive and social skills increase with increasing age. Therefore, we designed the interview guides using languages that are appropriate to the children's developmental stages. Hence, we used two different interview guides for the children.

Children's ability to recall past events pertaining to self depends on their level of cognitive development. Research has shown that children from the age of 2 years possess autobiographic memory, defined as memory of information and specific events with respect to time and place pertaining to self. (Flvush et al., 1991, Howe & Courage, 1997). Children from this early age have the cognitive ability to store information in their memory and recall past experiences. Recall of events is influenced using cues such as 'tell me more about that'; the number of details elicited using cued invitations increases with increasing age (Hershkowitz, 2001). Therefore, we used prompts to aid the recall of events by the participants. Lamb et al. (2003) in a study to determine the influence of age on the amount and quantity of information provided by children aged 4 to 8 years to different types of free-recall prompts demonstrated that action cues elicited information from the children irrespective of age while only the 8-year-old children provided more detailed information in response to time-segmenting cues. Time- segmenting cues, unlike action-based cues which seek more information about a pre-disclosed event, explore information about what happened before or after the event, during the time between two such events, or at the same time as the event. Thus, responses to time-segmental cues require more cognitive demand than action-based cues (Lamb et al., 2003). In this study, we employed time-segmenting cues to explore events including events surrounding symptoms of nephrotic syndrome and relapses of SSNS.

Choosing an appropriate research setting is another important factor to consider before the

interview (Valentine, 1999). Interviewing children in familiar environments such as the home or school may enable the child to communicate freely without embarrassment (Morison, Moir & Kwansa, 2000). On the other hand, some children may consider questions about their personal lives to be intrusive in the home environment (Hill, 2006). Nonetheless, interviews in home settings allow the researcher to observe the child's environment and play area as well as the interaction between the child and other members of the family (Bushin, 1996). In this study, the interviews were conducted virtually using Microsoft Teams™ while the participants were at their homes and all children were offered the opportunity to have their caregivers present during the interviews.

Establishing and maintaining rapport with the child before the interview fosters trust and allays discomfort. In this study, the interviewer established rapport with the participants by asking them questions about their friends, school and family. Early interactions with the child also offer opportunity to perform a rough assessment of the child's linguistic and social developmental stage (Morison et al., 2000). The child's attention span should be considered in determining the duration of the interview. Faux et al., (1988) recommended a duration of 30 to 45 minutes depending on the child's age. However, a report by Shapka et al. (2016) revealed that virtual interviews may take longer time to complete compared to in-person interviews. Therefore, in this study, we estimated the duration of the interview to be 45 to 60 minutes.

The child's emotions during the interview may influence his or her continued participation in the study. Hence, we structured the interview guides to begin with the least distressing questions, progressing to more sensitive topics as the child felt comfortable with the interviewer (Morison et al., 2000). The interviewer's response to the child's answers may also impact on the child's emotions and could be vital in maintaining rapport and sustaining the child's cooperation. The

response could be non-verbal and verbal acknowledgements, rephrasing or summarizing the child's answers and probing for clarifications (Morison et al., 2000). Hence, we used words such as 'You did so well in explaining that' as well as repeating or rephrasing their answers to portray an understanding and acceptance of their feelings (Hughes & Baker, 1990, p. 60). However, children and their caregivers may experience emotional distress during interviews. Therefore, we provided children and their families with the telephone number of the Alberta Health Mental Health Services that they could call for psychological support.

The caregivers were also interviewed separately to explore their own experiences. We anticipated that two caregivers may consent to participate together in a dyadic interview. Dyadic interviewing is an interview technique that allows interaction between two individuals in response to open-ended questions. The term dyadic interview has been described in different ways across the literature. Morgan (2013) referred to dyadic interview as a broad method of qualitative data collection from joint interview of two individuals who may not necessarily have a prior relationship. Eiskovits & Koren (2010) classified separate interviews of two individuals by the same interviewee in the same interview space and separate interviews of two individuals performed simultaneously by different interviewees in their dyadic model. Caldwell (2014, p. 488) defines dyadic interview as "a qualitative approach that recognizes the existence of an interdependent relationship between two individuals, embracing this phenomenon as a source of information rather than attempting to control for it". In this discussion, we refer to dyadic interview to mean joint interview of two individuals who have a prior relationship. Dyadic interviews allow participant to jointly explore the research topic by sharing and comparing information to co-construct knowledge (Morgan, 2013). There are different modalities of conducting dyadic interviews. Firstly, a joint interview is conducted with the two participants at

the same time by one interviewer. Secondly, the interviewer may conduct separate interviews followed by joint interviews with the same participants. In the third model, the interviewee conducts a joint interview which is followed by individual interviews with the same participants (Caldwell, 2014). Joint interaction offers an opportunity to observe two individuals share their stories and study the interactions between them. The separate interviews provide complementary information and increases trustworthiness through data triangulation (Lincoln & Guba, 1985). In analyzing data from dyadic interviews, researchers may choose to analyze the narrative of each participant separately or the dyad combined depending on the study's research questions and the dyadic interview structure (Caldwell, 2014). In dyadic analysis, the procedure for analyzing individual narratives is similar to that performed in qualitative studies on individual level. In addition, the researcher, examines the themes emerging from each participant's narrative by assessing contrasts and overlaps between the individual narratives (Eiskovits & Koren 2010). When the dyad is the unit of analysis, attention must be paid to the relationship between the participants (Morris, 2001; Morgan, 2013), and whether the participants speak of individual or joint experiences (Seale, Charteris-Black, Dumelow, et al., 2008). Furthermore, one must avoid attributing one participant's persistent comment as shared versions of events (Morgan, 2013).

Field notes were taken during and immediately after the interviews to record observations and initial thoughts. Socio-demographic data including participants' age, gender, ethnicity, educational level, date of diagnosis of nephrotic syndrome, relapses and caregiver's occupation were collected from participants electronically prior to the interview.

All interviews were conducted by one investigator (A.O.) on Microsoft Teams, a secure, web-based video platform. All interviews were audiotaped on Microsoft Teams and transcribed verbatim by one investigator (A.O.). The transcripts were uploaded into NVivo (QSR International

Pty Ltd., Version 12, 2018), a qualitative data organization, coding, and retrieval system.

Data Analysis

We used thematic analysis at the semantic level as described by Braun and Clarke (2006) as the method through which patterns within the data were identified, analyzed, interpreted, and reported. Thematic analysis is a theoretically flexible analytical method that is useful in examining individuals' perspectives, highlighting similarities and differences, and generating insights into their participants experiences (Braun & Clarke, 2006).

Codes and themes were derived directly from the data rather than fitting the data into a pre-existing coding frame or analytic preconceptions (Braun & Clarke, 2006). In this study, data collection and analysis took place concurrently. One investigator (A.O.) engaged in thorough and repeated reading of transcripts, generated initial codes to organize the data into meaningful groups. A second investigator (M.J.E.) independently coded the first two transcripts to contribute to coding scheme development. Investigators met regularly throughout this stage to refine and finalize the coding scheme, which occurred after the first 12 transcripts and was applied to subsequent transcripts.

Codes were sorted into potential themes by identifying repeated, similar, and differing patterns across the data set while ensuring that all relevant data were captured in the identified themes. The themes were reviewed to check for coherent patterns in relation to the coded data extract and the entire data set (Braun & Clarke, 2006). Themes were further refined, and clear theme definitions were generated. In the final phase, the meanings of our findings were interpreted in relation to the research questions. Findings were discussed regularly among the research team to ensure that the final themes addressed the research questions. In this study, data saturation,

defined as the point at which additional relevant data is no longer attainable (Fusch & Ness, 2015), was achieved after 25 interviews.

Due to the iterative nature of the interviews and data analysis, two distinct areas of the participants experiences emerged: the experiences of getting a diagnosis of nephrotic syndrome and experiences of living with the SSNS. These two areas focus on the experiences of the participants at distinct chronological periods of having the disease. These areas therefore merited their own separate assessment. We therefore present our findings in two separate manuscripts: the diagnostic journey of childhood nephrotic syndrome and experiences and healthcare priorities of living with SSNS.

Methodological Rigor and Reflexivity

To ensure methodological rigor in this study, we employed Lincoln and Guba's four criteria of trustworthiness: credibility, confirmability, transferability and dependability (Lincoln & Guba, 1985). Maximum variation purposive sampling identified children of different ages groups with varied duration of living with nephrotic syndrome and experiences (Patton, 2012). The research team comprised of nephrology and qualitative research experts who were involved in the development of the study protocol, interview guides and data analysis. Careful probing using time-segmenting cues and free recall prompts were employed to elicit rich and comprehensive data. Credibility was ensured by prolonged engagement with the data, investigator triangulation and writing of memoirs. An audit trail of the analytical procedure describing how the findings were derived from the data were kept to strengthen the confirmability of our results. Participants demographic characteristics and directs quotes were provided to enhance transferability of our findings to other settings (Sandelowski, 1986; Lincoln & Guba, 1985). Furthermore, a detailed description of the study procedure was provided to ensure the replicability of our findings.

In conducting this research, I reflected constantly on my disciplinary position as a Pediatric Nephrology Fellow. My interest in the topic was inspired by one of my patients and her caregiver who shared their experiences with SSNS with me in a street market. Their story provided insight into the difficulties and challenges patients with SSNS and their families encounter which may not be discussed in the clinical setting and enabled sensitivity in the way I approached the topic with the participants of the present study. In addition, I was reflexive on how my knowledge of the disease, beliefs and personal experiences as a mother could influence the process of data collection and interpretation.

Chapter 3: Diagnostic journey of childhood nephrotic syndrome

Abstract

Background: Childhood nephrotic syndrome is a rare disease that is characterized by sudden onset of body swelling, massive proteinuria and hypoalbuminemia. Lack of recognition of the symptoms may lead to unnecessary delays in diagnosis and treatment.

Aim: To explore the experiences of children with nephrotic syndrome and their caregivers in their search of a nephrotic syndrome diagnosis.

Study design: Qualitative description

Methods: Semi-structured interviews of children (aged 9 to 18 years) and their caregivers were conducted virtually using Microsoft Teams between January and April 2021. Thematic analysis as described by Braun and Clarke was used to analyze the data.

Results: The participants comprised of 10 children aged 9 to18 years (6 boys and 4 girls) and 18 caregivers. Three themes that describe participants' experiences in search of a diagnosis of nephrotic syndrome were identified: unexpected distressing symptoms, elusiveness of diagnosis and confronting the diagnosis. Children with nephrotic syndrome and caregivers experience anxiety and fear due to the unexpected symptoms of nephrotic syndrome and lack of knowledge about the disease. Perceived diagnostic delays and misdiagnosis at primary care facilities contributed to multiple consultations with different care providers.

Conclusion: The experiences of children with nephrotic syndrome and their caregivers in search of a diagnosis may be impacted by their beliefs and perceptions of the symptoms, lack of knowledge about the disease and perceived diagnostic delays and misdiagnosis by their healthcare providers. Strategies to promote awareness and understanding of this rare disease are needed to improve the diagnostic experiences of patients and their caregivers.

Keywords: nephrotic syndrome, diagnosis, experiences, children, caregivers, qualitative research

Background

Childhood idiopathic nephrotic syndrome is a rare disease of the kidney characterized by abrupt and progressive body swelling, massive proteinuria and hypoalbuminemia (Noone, Iijima & Parekh, 2018). Some patients may present with complications such as acute kidney injury (Rheault et al., 2015), infections (Hingorani et al., 2002), growth retardation (Garin et al., 1989) and abnormal clotting (Kerlin et al., 2009). The diagnosis of nephrotic syndrome is confirmed by identification of massive proteinuria (protein: creatinine ratio of >200mg/mmol in spot urine) and low serum albumin levels of < 25g/dl in the setting of generalized body swelling (Niaudet & Boyer, 2016; Gibson et al., 2009). Most cases of childhood nephrotic syndrome are steroid responsive (Koskimies et al., 2001; Mckinney et al., 2001), therefore, prompt diagnosis and initiation of steroid treatment can lead to rapid resolution of symptoms in most patients.

The diagnosis of any childhood disease begins with consultations between physicians and patients and their families about their experiences with the symptoms of illness. The physician then uses clinical experience and laboratory investigations to delineate the disease at the heart of the illness experience. This is referred to as the 'diagnostic moment' (Jutel, 2011, p 62). For patients with rare diseases, the lack of recognition of disease-specific symptoms may lead to multiple consultations with different health care providers, misdiagnosis, unnecessary delays in investigations and treatment before a definitive diagnosis is made (Zurynski et al., 2017). For these patients and their families, this is not a moment, but a journey often characterized by uncertainties and profound distress (Price &Walker, 2014). A previous survey of caregivers of children with nephrotic syndrome by Hollis et al., (2018) showed that the delays in diagnosis of nephrotic syndrome in children occurred mainly in primary care settings, with most cases being diagnosed as allergies. To our knowledge, there has been no published report about the in-depth experiences

of children with nephrotic syndrome and their caregivers in their search for a diagnosis of childhood nephrotic syndrome

An appreciation of the diagnostic experiences of children and their caregivers could inform how healthcare providers approach the diagnostic process and how patients and their families can be supported along this journey. In this present study, we aim to explore the experiences of children with SSNS and their caregivers in their search of a nephrotic syndrome diagnosis.

Methods

Qualitative description methodology was used to explore participants' experiences in their search for a diagnosis of nephrotic syndrome. Qualitative description is used in health science research to explore research questions that are relevant in clinical practice. It entails low inference interpretation and data presentation in everyday language while remaining close to data (Sandelowski, 2000 & 2010). We employed the Bronfenbrenner's Ecology of Human Development (Bronfenbrenner, 1979) as a guiding framework for understanding how interactions between the child with nephrotic syndrome and their caregivers with individuals in their environment could impact their diagnostic experiences. This framework guided the development of our study objectives, framing of interview questions and contributed to the discussion of our results.

We recruited children aged 9 to 18 years from the Canadian Childhood Nephrotic Syndrome (CHILDNEPH) cohort (Samuel, 2017) at the Alberta's Children's Hospital using maximum variation purposive sampling (Patton, 2002). All participants provided informed consent for the study.

We explored the participants perceptions and reactions to the symptoms of nephrotic syndrome, experiences in search of a diagnosis and their reactions to the diagnosis using semi-

structured interviews which were conducted virtually using Microsoft Teams™. The interviews were conducted from January to April 2021 by one investigator (A.O), who also recorded observations and initial analytical thoughts in field notes. The interviews were audio-taped and transcribed verbatim, and the transcripts were analyzed thematically as described by Braun and Clarke (2006).

Results

Sample Characteristics

Of the 38 eligible families of children with SSNS approached, 28 individuals from 15 families consented to an in-depth semi-structured interview. Of those who did not participate, 1 family declined, 4 families initially agreed to participate but did not consent to the study and 18 families did not respond to our invitation. In one family, both parents participated in the study but their child did not agree to join the study. All but two children were symptom free and were not taking any nephrotic syndrome medication at the time of the interview. Of the 28 participants, 10 were children with nephrotic syndrome (6 boys and 4 girls; age range 9 to 18 years) (Table 1) and 18 were caregivers (8 males and 10 females) (Table 2). Twenty-five interviews (18 individual, 4 children's interview with a parent present and 3 father-mother dyads) were conducted between January and April 2021. The average duration of interviews was 49 minutes.

Table 1: Characteristics of Children with steroid sensitive nephrotic syndrome (N = 10)

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	11
Asian	3
Other	4
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(s) present	4
No Caregiver present	6

Table 2: Characteristics of Caregivers of children with steroid sensitive nephrotic Syndrome (N = 18)

Characteristics	Number of participants
Gender	
Male	5
Female	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
Ethnicity	
White Caucasian	11
Asian	3
Other	4

The diagnostic journey of childhood nephrotic syndrome

In discussing their experiences in search of a diagnosis for sudden and unexpected symptoms, participants described their reactions to the symptoms, perceived delays in diagnosis or misdiagnosis. They also described how they were prepared to contribute to the treatment plans despite their lack of understanding of the nephrotic syndrome. Overall, participants expressed motivation to move past the diagnosis and learn about NS and its treatment. Three themes that describe participants experiences leading from onset of symptoms to meeting with nephrology team were identified: 1) unexpected distressing symptoms; 2) elusiveness of diagnosis; and 3) confronting the diagnosis.

Unexpected distressing symptoms

Participants' reaction to the abrupt and unexpected onset of symptom of body swelling, their perceptions and beliefs about the symptoms and the emotional reactions to the persistence of the symptoms are described in this theme.

Participants described the sudden, unprovoked onset of swelling of the body that caused alteration in physical appearance. While children emphasized gross physical changes, caregiver participants noted more subtle and progressive changes and a departure from previous state of health. One child participant who developed the symptoms at the age of 7 described his scrotal swelling as following:

> My pee grew big… (boy, 9 years old)

Many caregiver participants used words like 'puffiness', 'looking like a balloon' 'getting fatter' 'unrecognizable' and 'distorted face' to describe their children's appearances. One caregiver participant whose child's symptom progressed gradually said:

> ...we kind of 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. (female, caregiver)

Participants described a range of perceived beliefs and perceptions about the cause of their symptoms. One child participant who noticed her leg swelling in a gymnastics class at school said:

> And we [herself and her friends] thought that my feet were broken… (girl, 16 years old)

At the beginning, some caregiver participants described the progressive weight gain resulting from the body swelling as normal growth. A few caregiver participants ascribed the symptom to familiar and relatable medical conditions such as allergies or injuries on the feet.

Both adolescent and caregiver participants described being concerned, afraid, anxious and worried as the body swelling persisted and making a decision to search for the diagnosis of the unusual symptoms. One adolescent participant who developed the symptoms at the age of 11 years said:

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

Elusiveness of diagnosis

This theme reflects on participants' emotional reactions to a perceived mischaracterization of symptoms by healthcare providers.

Some participants particularly caregivers, described a perceived minimization of symptoms by healthcare providers to whom they reached out about their concerns. Some caregivers who visited primary care centers with their children in search of a diagnosis expressed feelings of being dismissed by physicians who may not have appreciated the significance of the presenting symptoms and thus did not carry out the appropriate investigations to identify their cause. For some caregiver participants, this prompted the feelings of disappointment and mistrust in the primary healthcare team. One participant who described her child as gaining weight rapidly 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...We were disappointed with the family doctor…I didn't believe them because I was sure something was going on. (female, caregiver)

Some participants described feelings of disappointment and helplessness as their children were subjected to unnecessary investigations and treatment for other conditions such as allergies or constipation in primary healthcare facilities. This frequently led to delays in diagnosis, which, in turn, delayed initiation of appropriate therapies. One participant whose child was treated with

cortisone nasal spray for allergies after repeated primary care visits because of the body swelling said:

> It was super frustrating. I was not happy clearly because I mean, when we finally figured her out, she was pretty bad. So, it took a very long time for a 3-year-old to go through that. (female, caregiver)

One caregiver participant whose child was admitted for peritonitis, a complication of ascites resulting from nephrotic syndrome shortly after diagnosis described the following:

> So, over the couple of months, I went to at least 6 different doctors…but he had all these strange symptoms and nobody took blood, nobody took stool or urine samples…I guess that my main regret is that I didn't fight harder maybe, and my main complaint is that nobody fought for me... (female, caregiver)

Confronting the diagnosis

Participants' emotional reactions upon arriving at a diagnosis of nephrotic syndrome and motivation to overcome their fears and learn about the disease and its management are described in this theme.

All but 2 children received the diagnosis of childhood nephrotic syndrome at tertiary hospitals shortly after presentation.

Caregiver participants described a wide range of emotions following receipt of the diagnosis. Many participants expressed initial feelings of relief upon finally receiving a diagnosis after a prolonged period of uncertainty and frustration and later, feelings of sadness and uncertainties as they learned more about nephrotic syndrome and the implications of living with the condition. In contrast, some participants described being heartbroken at the news and used terms like 'shocked', 'worried', 'scared', 'devasted', 'lost' and 'overwhelmed' to describe their

reactions. One participant whose affected child was her only child at the time of diagnosis described the following:

> Oh like, your world was crushing down when you get told that your son has a rare kidney disease and that they don't know much about it…it was definitely much overwhelming and scary and very hard at first when we were told about it. (female, caregiver)

Some caregivers described feelings of guilt and the perception that their actions while pregnant or caring for the child may have contributed to their nephrotic syndrome. Accordingly, one participant who had two other 'healthy' children before the child with nephrotic syndrome stated the following:

> Devasted. 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, there is no known cause, apparently, I still felt like I did something wrong. (female, caregiver)

A majority of the participants described having no knowledge of nephrotic syndrome prior to the diagnosis. However, they expressed motivation to move past the diagnosis and learn to adapt and manage the disease. They most often learned about it from their friends, specialist care team and nephrotic syndrome pamphlets while some sought information from the internet to help them comprehend and understand nephrotic syndrome. One adolescent who developed nephrotic syndrome at 9 years of age described her learning experience as follows:

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

One caregiver participant spoke about learning about nephrotic syndrome from a parent who is a friend of hers at the parking lot of her child's school. She spoke about how this friend looked at her child and said:

> She looked nephrotic! (female, caregiver)

Many participants described cordial interactions with members of the care team and appreciated the professional support they received from the care team in preparation for managing and living 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. So, we left there pretty comfortable that we as a family would be able to manage going forward with him. (female, caregiver)

Discussion

Our study highlights the challenges that patients and their caregivers encounter in their journey in search of a diagnosis of childhood nephrotic syndrome. In characterizing participants experiences, we identified three themes related to patients' and providers' appreciation of symptoms, perceptions of delayed diagnosis or misdiagnosis, and children's and caregivers' 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 to for support mischaracterized these manifestations as common and relatable conditions, such as allergies, particularly during the early stages of the disease. The increasing severity and persistence of symptoms evoked feelings of apprehension that prompted their continued search for a diagnosis.

To our knowledge, this is the first study in which the experiences of children with nephrotic syndrome and their caregivers in search of a diagnosis for childhood nephrotic syndrome were explored. The findings from this study are consistent with a previous report by Beanlands et al. (2017) which revealed that adult patients with nephrotic syndrome also lacked an understanding of the cause of their symptoms and only sought medical help when their symptoms worsened. This lack of awareness of the symptoms of childhood nephrotic syndrome among children and their caregiver in our study could be attributed to the rarity of the disease which occurs in 2 to 7 per 100,000 children (Chanchlani & Parekh, 2016). It is therefore not surprising that all but one adult participant who has nephrotic syndrome in our study had no prior knowledge of this condition.

This study showed that some physicians in some primary care settings lacked knowledge of childhood nephrotic syndrome. Consequently, its symptoms were either minimized, dismissed, or misdiagnosed, which contributed to delays in getting the right diagnosis at the community health facilities. A previous report by Hollis et al. (2018) revealed that childhood nephrotic syndrome was incorrectly diagnosed as allergies in some family and walk-in clinics in Canada contributing to diagnostic delays. Similarly, previous studies in which participants' experiences of other rare disease were explored showed that primary care physicians' lack of knowledge of the disease potentially led to delayed diagnosis and mistreatment (Kharrazi & Kharrazi, 2005; Zurynski et al., 2017). On the other hand, our study showed that participants received accurate and prompt diagnosis at tertiary hospitals. This disparity could be explained by the fact that nephrologists at the tertiary care hospitals have extensive training in nephrotic syndrome and other rare diseases. In contrast, primary care physicians in the community, who receive general training to recognize common diseases and acute, severe illnesses, may not be skilled in recognizing uncommom, more chronically evolving illnesses (Phillips & Haynes, 2001). Nonetheless, a preliminary diagnosis of

childhood nephrotic syndrome in the presence of generalized body swelling is achievable by a simple dipstick urinalysis which demonstrates massive proteinuria in a spot urine sample. This contrasts with most rare diseases that require sophisticated, invasive, expensive, time-consuming, and sometimes genetic procedures for diagnosis. The dipstick urinalysis is a simple, non-invasive, cost-effective test that can be performed in many clinic settings to alert the care team to a potentially serious underlying condition and prompt additional testing or specialist referral. As our study demonstrated, an expedited diagnosis might assuage the fear and uncertainty that accompanying the initial manifestations of childhood nephrotic syndrome. The findings of our study provide insight into the development of targeted strategies that could help address a potential knowledge gap in this area to improve the diagnostic experience of patients and their families.

The burden of misdiagnosis and diagnostic delays are unfortunate realities for patients and their caregivers. In the United States, about 5% of all medical conditions are misdiagnosed in outpatient settings each year (Singh et al., 2014) and approximately 30% of the annual healthcare budget is spent on unnecessary services (IOM, 2013). Delays in diagnosis or misdiagnosis could cause devastating physical and psychological consequences to the patients and their caregivers. Physical harm to the patient could result from inappropriate treatment, delayed treatment, and disease deterioration (Schiff et al., 2009). In our study, one of the children who was misdiagnosed by 6 different physicians over a period of months was admitted for peritonitis shortly after confirmation of his diagnosis. Although early diagnosis of nephrotic syndrome may not have necessarily prevented this complication, a delayed diagnosis could have potentially increased his risk of complications of peritonitis such as sepsis, septic shock, organ failure or death (Karvellas et al., 2015). A previous qualitative study showed that incorrect diagnosis and diagnostic delays of cystic fibrosis, another rare disease, in children led to frustrations, uncertainties, anxieties and

worries among their caregivers (Kharrazi & Kharrazi, 2005). Our study further emphasizes the doubt, worries, frustrations and guilt experienced by caregivers, many of whom described feeling responsible for their children's diagnoses and diagnostic delays, and the potential for mistrust of the primary care system.

Our study also showed that despite the deep emotional distress associated with a diagnosis of nephrotic syndrome, caregivers were resolute in their pursuit of the truth about their children's unusual and disconcerting symptoms. The caregivers in our study expressed initial relief upon arriving at a diagnosis, but this was followed by deep frustration, fear and worries as they began to grasp the implications of this condition. This pattern of behaviour is not uncommon among families dealing with rare diseases (Esquivel-Sada & Nguyen, 2018; Granero-Molina et al., 2020). These findings suggest a potential role for psychological support of these patients and their families beginning from the time of diagnosis.

Lack of knowledge about the trajectory and prognostic uncertainties of chronic diseases can further contribute to worries and psychological distress to patients and their families (Cohen, 1993). Provision of information to patients and their families is a key component of patient centered care (IOM, 2001). Educating children and their caregivers who had just received a diagnosis of childhood nephrotic syndrome is an important support structure in the management of the disease. Information and education empower patients to develop confidence, motivation and self-determination to deal with disease and improve treatment adherence. (Ludman et al., 2013)

The Bronfenbrenner's ecology of human development (Bronfenbrenner, 1979) informed our understanding of how interactions between children with SSNS and their caregivers and their ecological environments could impact their experience and perception of the symptoms of the disease as well as their diagnostic journey. Findings from our study revealed that the children's

perceptions of the symptoms of nephrotic syndrome and their learning experiences may be impacted by their interactions with their friends and healthcare providers in the tertiary hospital. On the other hand, our findings suggest caregivers' experiences in getting a diagnosis of nephrotic syndrome for their children and their learning experiences are impacted additionally by their interactions with healthcare providers in the community and tertiary hospitals in their ecological environment.

Strengths and Limitations

A major strength of our study is that we employed qualitative study design to explore the experiences of children with nephrotic syndrome and their caregivers in obtaining a diagnosis of childhood nephrotic syndrome. Our findings offer a valuable contribution to the scant knowledge base in this area. Additionally, the findings of our study could inform the establishment of strategies and programs that could improve awareness of nephrotic syndrome in the general population and the diagnostic experiences of children and their caregivers.

One of the limitations of our study is that our sample was limited to children and their caregivers who were enrolled in the CHILDNEPH project at the Alberta Children's Hospital in Calgary, Alberta. The views of the participants in our study may not reflect those of patients/caregivers who were not enrolled in the CHILDNEPH project, some of whom may have had lived with the disease for a longer duration than those in the CHILDNEPH cohort. Also, the perceptions of the children and their caregivers in our study may not be reflective of those that declined to participate in the study nor those of children with nephrotic syndrome and their caregivers in other settings. However, our maximum variation sampling across age, gender and disease duration categories captured a wide range of experiences that could be transferrable to other populations and settings. A further limitation is that we employed dyadic interviews of two

caregivers with the risk of one participant dominating the discourse (Seale et al, 2008). This may limit the amount of data collected from the other participant. Also, the presence of both participants in the interview space may influence the disclosure of sensitive topics by the participants (Morris, 2001).

Conclusion

The experiences of children with SSNS and their caregivers in search of a diagnosis may be impacted by their beliefs and perceptions of the symptoms, lack of knowledge about the disease and perceived diagnostic delays and misdiagnosis by their healthcare providers. Strategies to promote awareness and understanding of this rare disease are needed to improve the diagnostic experiences of patients and their caregivers. Our study also provide insight to the need for psychological and emotional support for children and their caregivers beginning from the time of diagnosis.

Chapter 4: Patients' and caregivers' experiences with childhood steroid sensitive nephrotic syndrome

Abstract

Background: Childhood steroid sensitive nephrotic syndrome (SSNS) runs a relapsing and remitting course. Children with nephrotic syndrome and their caregivers have poor quality of life. The experiences of children with SSNS and their caregivers have not been reported.

Aim: To explore the experiences and healthcare priorities of children with SSNS and their caregivers.

Study design: Qualitative description

Methods: Semi-structured interviews were conducted with children living with SSNS and their caregivers over a period of 3 months from January to April 2021. The data were analyzed thematically.

Results: There were 28 participants that comprised of 10 children aged 9 to18 years (6 boys and 4 girls) and 18 caregivers. Over 70% of the caregiver participants were employed. Three themes that describe participants' experiences were identified: disruption of normalcy, regaining control and dependable social support system.

Conclusion: Children with SSNS and their caregivers experience disruptions in their lives as a result of recurrent relapses, side effects of steroid medication and disease uncertainties. Despite these challenges, children and their caregivers demonstrated resilience and strength to regain control while retaining hope for a cure. Strategies to provide psychological support for children with SSNS and their families should be developed and implemented.

Keywords: steroid sensitive nephrotic syndrome, experiences, children, caregivers, qualitative study

Background

Steroid sensitive nephrotic syndrome (SSNS) is the most common form of idiopathic nephrotic syndrome in children. Despite a high rate of response to steroid therapy, over 75% of the patients will experience a relapse (Koskimies et al.,2001; Mckinney et al., 2001). A previous study by Ruth et al. (2004) showed that steroid dependence and treatment with immunosuppressive medications had significant negative impact on the quality of life of children with SSNS. As a result of these complexities, patients and their caregivers must make important and challenging decisions in choosing therapies based their values and priorities in addition to treatment effectiveness (Montori et al., 2008).

The family system constitutes a vital part of the child's immediate environment. A chronic illness in a child may impact other members of the child's family (Kazak, 1989). Caregivers of children with chronic illnesses bear responsibilities of taking care of the needs of the children in addition to their usual parenting roles because of demands on disease-specific treatment and care (Raina et al., 2005). Caregivers of children with SSNS monitor relapses and remissions, ensure adherence to steroid medication schedules and dietary restrictions and watch for signs of steroid toxicity and complications of nephrotic syndrome that might warrant intervention. Furthermore, caregivers may cease employment to devote full attention in caring for the child with chronic illness (Kazak, 1989). This implies that the experiences of a child with SSNS may be closely interwoven with those of their caregivers. Caring for children with chronic illness may be detrimental to the health and wellbeing of the caregivers (Raina et al., 2005). A previous quantitative study showed that caregivers of children with nephrotic syndrome have poor quality of life compared to caregivers of healthy children in the control group (Mishra et al, 2015). However, to our knowledge, there has been no reports about the perceptions, values, and priorities

of children with SSNS and their caregivers.

Having a greater understanding of the experiences of children and their caregivers living with SSNS could provide healthcare professionals and decision-makers valuable information about patient's needs, care priorities and burden of illness. This could help inform supportive interventions for patients and their families (Luxford & Sutton, 2014). Thus, the purpose of this study was to explore the experiences and healthcare priorities of children living with SSNS and their caregivers.

Methods

We employed qualitative description to explore the experiences of children living with SSNS and their caregivers. Qualitative description involves interpretation of low inference and staying close to the data. The Bronfenbrenner's Ecology of Human Development (Bronfenbrenner, 1979) guided our understanding of social factors in the participants' environment that could impact their experiences of SSNS. This framework informed our study objectives, interview questions around interactions and relationships between participants and individuals in their environments and contributed to an integrated discussion of our study findings.

Maximum variation purposive sampling (Patton, 2002) was used to recruit children aged 9 to 18 years from the CHILDNEPH cohort at the Alberta Children's Hospital. All participants provided informed consent for the study. Semi-structured interviews were conducted from January to April 2021 to explore participants' experiences with the aid of interview guides with open-ended questions. The interview guides were structured to elicit information across the following topic areas: (i) treatment of SSNS; (ii) relapses; (iii) impact on daily life: family life, learning, work, extracurricular activities, vacations; (iv) relationships with peers, friends, school community, care providers and work colleagues; (vi) healthcare priorities and unanswered questions; (vii) outlook,

(viii) coping with the disease and (ix) communicating with other children and families dealing with SSNS. The interviews were conducted by one investigator (A.O) over the internet using Microsoft Teams™ from January to April 2021. Observations during the interview and initial analytical thoughts were recorded in field notes. We audio-taped the interviews and transcribed them verbatim. We used thematic analysis as described by Braun and Clarke (2006) to analyze the data.

Results

Sample Characteristics

We conducted a total of 25 interviews with 28 participants. A total of 23 families contacted did not participate in the study. There were 10 children aged 9 to 18 years with SSNS, including 6 boys and 4 girls (Table 1). Many of the children had lived with SSNS for more than 6 years. There were 18 primary caregivers, 13 females and 5 males. The majority (22) of the participants were Caucasians (Table 2).

Table 1: Characteristics of Children with steroid sensitive nephrotic syndrome (N = 10)

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	11
Asian	3
Other	4
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(s) present	4
No Caregiver present	6

Table 2: Characteristics of Caregivers of children with steroid sensitive nephrotic Syndrome (N = 18)

Characteristics	Number of participants
Gender	
Male	5
Female	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
Ethnicity	
White Caucasian	11
Asian	3
Other	4

In the following sections, participants' experiences with childhood SSNS and healthcare priorities are described.

1. Experiences with childhood SSNS

In discussing their experiences living with SSNS, participants described their fears and worries related to the initial symptoms of body swelling, losing control of their daily lives, relapses and their treatment as well as the uncertainties surrounding the disease etiology and prognosis. Overall, participants described being resilient and adapting their life goals to accommodate SSNS into their lives. Three themes associated with living with SSNS were identified: (i) disruption of normalcy; (ii) regaining control and (iii) dependable social support.

Disruption of normalcy

This theme reflects participants' expressed disruption of normal life related to the initial

symptoms of body swelling, repeated, uncontrollable relapses, side effects of steroids and uncertainties surrounding the disease etiology and trajectory.

Children with SSNS described a feeling of low self-esteem due to excessive weight gain from steroid treatment or disease-related edema. They discussed feeling unhappy about other children shaming them because of their weight and not being able to fit into their clothes. One child who developed the disease at the age of 4 years and had a total of 33 relapses which were treated with steroids over a period of 5 years said the following:

> …I couldn't fit in my clothes and my jacket didn't fit anymore...It makes me feel like there is an empty space. I cannot fit in like the others. (boy, 10 years old)

Children also discussed feeling of frustration and helplessness with the unpredictability and repeated relapses of SSNS. They perceived the relapses as continuous and constant events that were beyond their control. One adolescent participant who had frequent relapses said:

> Well, it was just kind of a constant thing. It was like I would relapse, then I would take the medicine, then I would get better for a month or two then I would relapse again. And so, it was just continuous cycle… definitely, it was an annoyance. (boy, 18 years old)

Caregiver participants conveyed feelings of disappointment, frustration and helplessness when they perceived that neither the steroid regimen nor second line agents could adequately prevent relapses in their children. Some talked about feeling overwhelmed when ensuring that their child adhered to the medication schedule during treatment of relapses.

Both children and caregiver participants also described frustration and helplessness related to behavioral changes and mood swings associated with steroid medications. Some children discussed feelings of sadness about being different from their peers and being unable to participate

in physical activities because of their inability to control their abnormal behaviors associated with steroid medication. One child participant who was diagnosed with nephrotic syndrome at the age of 7 years and whose mum described him as being very hyperactive while taking steroids said:

> I will run around, I wasn't really myself. I didn't like it…Because I can't be myself around my friends. (boy, 9 year old)

Children also spoke about being unhappy with the restrictions in their social life because of repeated relapses. They talked about being angry with the frequent school absenteeism and isolation from friends. Some described having difficulty with learning and completing homework during such times. Many described feeling disappointed about limited participation in physical activities because of weight gain, low energy and tiredness related to taking steroids. Some of them who were athletes spoke about disappointment in having to quit competitive sports in the school. One adolescent participant who is a professional gymnast said:

> Well, when it is season [competition period] and I am puffy, I usually just like take a day or two off. But when it is worse, I might just like quitting the season and yeah. It just makes me feel a little bit upset. (girl, 10 years old)

Many caregivers also described disruption in their social lives because of the overwhelming responsibility of managing their child's disease. Some spoke about frustration with the disruptions to their work schedules to keep up with doctors' appointments and frequent laboratory investigations.

> …it is very hard because, sometimes, I always want to change my schedule especially that time when he is very very sick because I have always to take him to the hospital. And also, that time we are living in [City D] and every time we need to travel from [City D] to the tertiary hospital in [City A]. So, I am always trying to

> find the solution to get a day off or at least working in the evening. (female, caregiver)

Both children and caregiver participants described being in a state of constant apprehension because of the uncertainties surrounding their SSNS etiology, prognosis and long-term medication side effects. Adolescent participants and their caregivers described how worries about SSNS could extend into adult life. One caregiver of an adolescent who developed nephrotic syndrome at the age of 3 years said:

> But she's 16 now, and she has it. Does it mean that she has it for life or she just has to live with it? And because she's 16, when she reaches 18, will she get referred to another specialist because then she is out of pediatric care?... I guess what I worry about is how it will be in her adult life. (female, caregiver)

Both children and caregiver participants described feeling unhappy about a salt restricted diet. Children used words like 'horrible' and 'disgusting' to describe the taste of low sodium meals while caregiver participants discussed having difficulties preparing low salt meals separate from the meals of other members of the family each time the child relapsed. One caregiver whose child had had 33 relapses said:

> At that time, I was struggling to do separate meals, like I have to cook his different and mine, trying to handle everything. It was really hard… I don't have the time to make him a separate pot and the rest of the family separate pot. (female, caregiver)

Regaining control

The theme of regaining control describes participants attempts at striving for normalcy, coping skills and cautious expressions of optimism about the future.

Many children described how they adjusted their interests to fit SSNS in their lives. Some

who were unable to perform competitive sports due to weight gain and low energy discussed switching to other extracurricular activities that require less physical exertion. One adolescent participant who enjoyed playing soccer, volleyball and basketball before he was diagnosed with nephrotic syndrome said:

> I think if I hadn't gotten nephrotic syndrome, I would have been doing sport my whole life, so far. Yeah, it definitely kind of stopped that for me. And I got involved with other things instead that won't require as physical [activity]... Eventually, I got involved in theatre, live theatre... (boy, 18 years old)

Furthermore, some children described a proactive involvement in monitoring themselves for symptoms of relapses. While younger children discussed checking their body for signs of edema, older children spoke about performing dipstick urinalyses whenever they noticed edema. Many children spoke about taking oral steroid medication despite its bitter taste and large pill burden.

Some caregiver participants whose children tended to relapse during steroid tapering described making their own adjustments to the tapering schedule to achieve what they perceived as a better response for their child or by using alternative treatments (e.g. garlic and Zoya) to induce remission.

In discussing how they coped with the SSNS, some children described controlled disclosure of their illness and isolation from friends as a way of sheltering themselves from being ridiculed by their peers. Adolescent participants spoke about being very conscious of their appearance and wearing very loose clothes to disguise their weight gain.

Despite the setbacks in some aspects of life goals, some children maintained a positive outlook about their future and spoke about how SSNS has influenced their choice of career and the motivation to help other people. One high school participant who is aspiring to study medicine

in the University said:

> …I want to take...all three sciences so that I can be a doctor. I have already started going for that because I think that I wouldn't have really known what I wanted to do so badly without having that [SSNS]...That has definitely pushed me to what I want to do. (girl, 16 years old)

On the other hand, many caregiver participants conveyed difficulty in coming to terms with their children's disease. Nevertheless, many spoke about being resilient for their children, never giving up and trying to live as normal a life as possible. A few participants reflected on how their experiences might compare with others they perceived as worse off. Others described techniques to distract themselves from their child's illness such as immersing themselves in their work, or how an altruistic mindset led them to sacrifice their life goals to focus on their children. One caregiver who has been unemployed since his child's nephrotic syndrome diagnosis said:

> So, basically, I have not applied for a single job since June 2020… (male, caregiver)

Despite the relative calm experienced during remission induced by steroids and some second line medications, most participants viewed the future with cautious optimism. They expressed a desire to return to normal life without relapses or need for steroids. While some participants spoke about hope for a spontaneous cure of the SSNS, a few expressed doubts about outgrowing the disease.

Dependable social support network

Participants' support networks included external support structures that they perceived as helpful in alleviating the challenges of living with SSNS such as families, friends, healthcare providers, colleagues, school communities and support groups.

Both younger children and adolescents described receiving support from close and understanding friends from school. They talked about their friends comforting them whenever they could not participate in physical activities during relapse. A few adolescents described receiving support from their schoolteachers who gave them extended time to submit their homework whenever they had a relapse. Children did not discuss their caregivers as part of their support network. Many children perceived the nephrology care team as caring and dependable. Whereas younger children described satisfaction with their encounters with the care team such as having toys available during hospital visits, older children described being grateful for the holistic care and sincere interest of the care team in their wellbeing and other aspects of their lives. One child participant said:

> Well, it's usually, like they pay a close attention to how I am acting and what I am feeling… Yeah, and they also like try and help the best they can with the medicine and take care of the side effects. (girl, 10 years old)

Many caregiver participants described their families as invaluable for helping alleviate the burden of living with SSNS. They viewed their families as key sources of assistance with care for other children in the family as well as providing emotional support. Caregiver participants viewed the school community, especially the teachers, as instrumental in providing learning support for their children whenever they missed school because of a relapse of SSNS. Some caregiver participants described understanding and supportive friends, some of whom took it upon themselves to assist them during relapse such as preparing homemade low salt meals. One participant said:

> Close friends that have asked, like my close friend who baby sat him…She even baked bread and said 'I took the salt off' and she baked him special bread. When

> he had relapses, she would show up at my door with like 5 loaves of baked bread that had no salt in it. (female, caregiver)

Some spoke about colleagues at work who adjusted participants' schedules to enable them to accommodate doctors' appointments.

Many participants perceived the professional care team as a strong and dedicated support system within and outside the hospital. Many caregiver participants expressed trust and confidence in the expertise of the professional care team. They appreciated the care team's accessibility and availability to answer their questions without judgment. One caregiver participant spoke about receiving emotional support from other caregivers in a nephrotic syndrome support group on social media. Many participants expressed disappointment in not knowing any other families affected by SSNS and the absence of a nephrotic syndrome support group in their communities to whom they could turn for support.

2. Participants' needs and care priorities

Participants perceived important needs and care priorities in childhood nephrotic syndrome were embedded throughout the 3 reported themes on experiences with SSNS. Four actionable needs and priorities were identified: (a) desire to be heard; (b) understanding the etiology of nephrotic syndrome; (c) alleviating the burden of steroid regimen and (d) enhanced social support availability

Desire to be heard

Many caregiver participants spoke about the desire to be listened to by their healthcare providers. Some described perceived dismissal of their worries and concerns about their children's sudden onset of body swelling by their healthcare providers. One caregiver said the following:

> And they [healthcare providers] just missed it as an allergic reaction or something. But I wasn't convinced of it, I was actually upset that there wasn't any further testing done… I just felt dismissed. (female, caregiver)

A few caregivers whose children were steroid dependent discussed disappointment in having only one standardized, 'fast' steroid tapering schedule and the desire for individualized steroid tapering regimen. One caregiver whose child relapses during steroid tapering said:

> So, he kept relapsing and kept relapsing because we realized that he was not responding to the regular schedule of tapering prednisone. It was even scarier for us. So, we asked the doctors, and we asked the nurses, but we were told no, keep the schedule the way it is. But we knew it's not working for him. So, in this, we had no support from the [Hospital A] on finding a better tapering schedule for him. They just use a very rigid tapering schedule that didn't work for him. (female, caregiver)

An understanding of the cause of nephrotic syndrome

A majority of caregiver participants conveyed the desire to have better understanding of the underlying nephrotic syndrome etiology or trigger. One caregiver participant whose child is 4 years old said the following:

> My priority number one is obviously to know the source. (male, caregiver)

Alleviating the burden of steroid regimen

Some children viewed provision of a more palatable form of steroid therapy or an alternative medication as a first line agent as a way of encouraging them to adhere to treatment as an important priority in the treatment of SSNS. One child participant who does not want to take oral steroid again said:

> Well, I feel like it needs to taste better, and I think they should make it so one does not need to take as much. If they get a hold on that, it will do a lot. (girl, 10 years old)

Enhanced social support availability

Many children spoke about the need to connect and share experiences with other children living with SSNS. When asked about a nephrotic syndrome support group, one adolescent participant said:

> I feel it would be good for people especially with younger children that it is hard to understand. And asking people their experience would be good. (girl, 16 years old)

Many caregiver participants spoke about the need to connect and share experiences with other caregivers of children with SSNS beginning from the time of diagnosis. One caregiver whose child was diagnosed at 17 months said:

> It would be interesting and obviously, you will have you put your name on a list but even saying hey, here is some names in your local region to get together with… But yeah, those kind of this might be of interest and I feel like we are also a fairly good example for the others, the new ones that would be like it is okay, it does get better and having that connection maybe earlier on might have been beneficial… (female, caregiver)

Discussion

In characterizing participants' experiences, we identified themes: disruption of normalcy, regaining control and dependable social support. Despite experiencing disruptions and restrictions in their normal lives due to repeated relapses of SSNS and its treatment, participants demonstrated

resilience and strength in striving for stability by adjusting their life goals, being proactively involved in surveillance and treatment of relapses and developing internal coping strategies to overcome the challenges. The participants' expressed top care priorities evoked by feelings of dismissal by their healthcare providers, knowledge gaps about the etiology of the disease and needs for individualized steroid regimen and nephrotic syndrome support networks. Overall, the experiences of children living with SSNS and their caregivers may be impacted by the interactions between them and their families, friends, healthcare providers and school communities.

To the best of our knowledge, this is the first study that explored the experiences and healthcare priorities of children and their caregivers living with SSNS. We identified similar themes reported in previous studies of experiences of adults and caregivers of children living with nephrotic syndrome, including contending with uncertainties, lack of knowledge and learning to manage nephrotic syndrome (Jonsson, Hellmark & Forsberg, 2020; Beanlands et al., 2017). Similar teams were also reported among children and young adults living with chronic kidney disease (Tong et al., 2012; Nicolas et al., 2011). Our study provides additional insights into the experiences of young children with a chronic remitting and relapsing illness.

Our study showed that children with SSNS may have low self-esteem and experience a loss of control of their lives because of their unpredictable relapses, the side effects of steroid medications, limitations in their social lives and dietary constraints. Physical limitations and other constraints imposed by rare diseases can impact patients' emotional, psychological and social adjustments as well as general wellbeing (Barlow et al., 2007). Therefore, multidisciplinary strategies including psychosocial, nutrition rehabilitation and occupational therapy aimed at improving patient's self-worth, confidence and coping with disruptions in life goals should be incorporated early in the management of childhood SSNS.

Caregivers of children with chronic illnesses assume the responsibility of maintaining the child's complex treatment needs and care schedules in addition to their usual parenting responsibilities (Raina et al., 2005). Our study showed that caregivers experience disappointments, frustrations, worry and grief due to repeated relapses, failure of steroid therapy to induce prolonged remission and uncertainties surrounding the disease trajectory. A recent systematic review revealed that parents of children with chronic disease have increased incidence of depression and anxiety compared to parents of healthy children (Cohn et al., 2020). A previous quantitative study by Esezobor et al. (2020) showed that caregivers of children with nephrotic syndrome experience psychological distress. Therefore, the findings of our study further highlight the need for psychological and emotional support for caregivers of children with SSNS.

Our study illuminated that the uncertainties surrounding the etiology and prognosis of SSNS may influence the way participants coped with the disease. Mishel (1988) defined illness uncertainty as "the inability to determine the meaning of illness-related events". It is a cognitive state that is created when a person cannot adequately structure or categorize an event because of the lack of sufficient cues. McCormick (2002) described illness uncertainty as encompassing 6 attributes: ambiguity, inconsistency, vagueness, unpredictability, unfamiliarity, and lack of information. Our study identified lack of knowledge about SSNS and long-term complications of medications; unpredictability of relapses and complexity of the treatment as important factors contributing to illness uncertainty in SSNS. Therefore, exploring and addressing sources of uncertainty and developing ways to address the concerns of children and their families should be incorporated as key components of patient-centered care in SSNS.

A cornerstone of patient-centered care is aligning the healthcare priorities and perspectives of patients and their families with that of the healthcare professionals in decision making (IOM,

2001). The findings of our study provide insight into the emotional and psychological distress experienced by patients and their caregivers living with SSNS as a result of repeated uncontrollable relapses and uncertainties about the disease etiology and prognosis. Our findings emphasize a need for provision of psychological and emotional support for patients and their families beginning from the time of diagnosis of childhood nephrotic syndrome. Furthermore, healthcare teams should strive to continuously assess, understand, and address the concerns of children with SSNS and their caregivers over the course of the illness. The identified care needs and priorities of participants in our study provide insight into other opportunities for healthcare providers to enhance patient-centered care.

The framework of the Bronfenbrenner's Ecology of Human development (Bronfenbrenner, 1979) informed our understanding of how interactions between children with SSNS and their caregivers and their ecological environments could impact their experiences of living with the disease. Findings from our study revealed that participants' perceptions about the disease may be impacted by their interactions with their families, friends, healthcare providers, and schoolteachers in their immediate ecological environment. Additionally, the experiences of children with SSNS and their caregivers may be impacted by the activities in the exosystem, the environment where the child is not present.

Strengths and Limitations

A major strength of our study is the rigorous application of qualitative methodology to provide insight into the experiences of children with SSNS and their caregivers. Another strength of our study was our inclusion of both children living with nephrotic syndrome as well as their caregivers, which allowed us to comprehensively examine the issue under study. We integrated the different perspectives of children and their caregivers to provide an overall thematic

representation of their experiences. Furthermore, the findings of our study are strengthened by the inclusion of the perspectives of the children rather relying on their caregivers as primary informants. In addition, the findings of our study could inform the implementation of strategies such as provision of psychological support and creation of a childhood nephrotic syndrome group support group to improve the care of children and their families living with the disease. Finally, the findings of our study could inform the design and conduct of future research in enhancing the taste of oral steroids and individualizing steroid tapering regimen in childhood SSNS.

A limitation of our study is recall of events and experiences by participants depending on the time elapsed since the children's diagnosis. This bias was mitigated by carefully defining the research questions and refining the language of questions in the interview guides to prompt recall of events. A further limitation in interviewing children is that the presence of a caregiver during the interview may have influenced the child's responses. Children may limit their responses or withhold sensitive information when their caregivers are present (Mauthner, 1997; Gardner & Randall, 2012). To mitigate this limitation, the interviewer established rapport, strived to build trust with the children, asked questions in non-threatening ways and offered to interview older children without their caregivers present.

Conclusion

Children and their caregivers living with SSNS experience disruption in their life related to recurrent relapses, side effects of steroid medication and uncertainties and lack of knowledge of nephrotic syndrome. Despite these challenges, children and their caregivers demonstrated resilience and strength to regain control while retaining hope for a cure. Strategies to provide psychological and social support for children with SSNS and their families should be developed and implemented.

Chapter 5 Implications and recommendations for medical practice

Childhood nephrotic syndrome is a rare disease characterized by sudden and unexpected onset of body swelling. The chronic recurrent relapses and side effects associated with treatment impacts on patients' and caregivers' experience of the disease. Using a descriptive qualitative approach, we explored the experiences of children with SSNS and their caregivers in their search for a diagnosis as well as their experiences and healthcare priorities living with the disease. Our findings were presented in two manuscripts. Manuscript One detailed the diagnostic journey of children with nephrotic syndrome and their caregivers in search of a diagnosis. Data from this manuscript revealed the challenges and frustrations that children with nephrotic syndrome and their caregivers encounter in their search for a diagnosis from the onset of symptoms to meeting with the nephrology care team. We identified themes related to symptoms and diagnosis of nephrotic syndrome: unexpected distressing symptoms, elusiveness of diagnosis and confronting the diagnosis. In Manuscript Two, we presented the experiences of children and their caregivers living with SSNS. Three themes related to losing control and striving for stability were identified: disruption of normalcy, regaining control and dependable social support. Overall, data from both manuscripts revealed that SSNS symptoms, relapses, treatment and uncertainties impacts on the experiences of children and their caregivers living with the disease.

Findings from Manuscript One showed that symptoms of nephrotic syndrome were mischaracterized by participants as a relatable condition such as allergy in its initial stages. The increasing severity and persistence of symptoms evoked feelings of anxiety and worry that prompted their continued search for a diagnosis. Data from Manuscript Two revealed that the chronic recurrence of symptoms (relapses) and disease treatment evoked the feelings of frustrations, loss of control, low-self-esteem, and helplessness. These findings suggest a potential

role for psychological support for all patients and their families living with SSNS beginning from the time of diagnosis.

Knowledge gaps and uncertainties about childhood nephrotic syndrome were consistent finding across both manuscripts. Prior to their diagnosis, participants lacked knowledge of nephrotic syndrome. After many years of living with the disease, participants still had unanswered questions regarding the disease etiology and prognosis. Findings from our study suggest opportunities to enhance awareness and understanding of this rare disease to improve the experiences of young children living with the disease and that of their families. In addition, there is need for the care team to continuously assess, understand and address the concerns of children with nephrotic syndrome and their families.

Although participants did not fully understand the implications of the diagnosis of nephrotic syndrome, they expressed a motivation to move past the diagnosis and learn to adapt and manage the disease. Participants developed trust in the specialist care team and appreciated the professional support they received from the members of the team in preparing to manage and live well with the disease. Data from Manuscript Two revealed that participants remained resilient over time despite the disappointments and frustrations with uncontrollable relapses and behavioral changes and mood swings associated with steroids. They developed strategies to regain control while hoping for a cure.

To our knowledge, this is the first study to explore the diagnostic journey of children and their caregivers in getting a diagnosis of childhood nephrotic syndrome and their experiences living with SSNS. Our study provided insights into several strategies that healthcare professional could adopt to improve the diagnostic experience and care of children and their families living with the disease. The findings from our study revealed that there is lack of awareness of symptoms

of childhood nephrotic syndrome among children and their caregivers. To improve awareness and recognition of symptoms of childhood nephrotic syndrome, healthcare professionals and policy makers should develop strategies to educate the general public about the symptoms of this rare disease. This would go a long way to mitigate symptom mischaracterization by children and their caregivers.

Furthermore, the findings of our study highlight the knowledge gap among community healthcare providers about childhood nephrotic syndrome which often led to delays in diagnosis and misdiagnosis. These findings could provide insights for developing and implementing targeted strategies to address a potential knowledge gap among community healthcare providers about childhood nephrotic syndrome with the aim of improving the diagnostic experience of children and their caregivers. Additionally, findings of our study could inform policy makers and stakeholders to enact policy on basic investigations such as dipstick urinalysis that should be performed for children with edema presenting at any health facility for early detection of massive proteinuria and other urinary abnormalities.

The findings of our study provide insight into the negative emotional and psychological distress experienced by children and their caregivers living with childhood idiopathic SSNS as a result of the recurrent symptoms and uncertainties about the disease etiology and prognosis. These findings provide insights into the need for psychological support for children and their families beginning from the time of diagnosis.

Also, the findings of our study highlight the need for a childhood nephrotic syndrome support group. Such a group would foster interactions and sharing of experiences between children and families dealing with childhood nephrotic syndrome This finding could provide insight into development of a nephrotic syndrome support group beginning from the time of diagnosis.

Finally, participants care priorities and needs were compactible across both manuscripts. These findings provide insights into opportunities to enhance patient-centered care in the management of childhood nephrotic syndrome.

Directions for future research

Our study provides an understanding of the challenges and needs of children with SSNS and their families that could inform future research to address patients and caregivers' healthcare priorities. Furthermore, the findings of our study reinforced the need for continued research for alternative medications to steroid as first line medication for treatment of childhood. Also, the findings of our study could inform the design and conduct of future randomized controlled trials on different steroid tapering regimens for children with SSNS. Additionally, the findings of this study could inform studies to reduce steroid pill burden and improve the taste oral steroid medication used in the treatment of SSNS.

Finally, further work using established, systematic processes for priority setting is needed to build on our qualitative findings and establish healthcare priorities of children with SSNS and their caregivers. In this way, actionable priorities can contribute to a research and evidence-informed care agenda that uphold principles of patient- and family-centered care and strive to meet patients' needs.

Knowledge Translation Plans

An end-of-grant knowledge translation will be used to disseminate our research findings to patients with SSNS, their caregivers, healthcare providers and policymakers. Our goals are to increase knowledge and awareness about the experiences of children and their families in searching for a diagnosis of nephrotic syndrome and living with SSNS and to inform future research on SSNS. We will disseminate our findings to primary care providers' by submitting an abstract of our

findings to primary care physicians' and strategic patient-oriented research (SPOR) conferences. We will submit the manuscript on diagnostic journey of childhood nephrotic syndrome to the Canadian Family Physician journal. A summary of our findings will be submitted to medical educational reviews to be used in medical undergraduate and residency training. Children and their families will be briefed in face-to-face meetings or virtual workshops using slide presentations prepared in plain language. We will communicate our findings to pediatric nephrologists through virtual meetings and publication of the experiences of children with SSNS and caregivers in a peer-reviewed journal. The results of our study will be communicated to the Alberta Health Services Policy makers through briefs and infographics. Finally, future direction will consist of knowledge synthesis in the form of a qualitative meta-synthesis of the experiences and perspectives of adults with nephrotic syndrome.

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SUPPLEMENTARY MATERIAL I: ASSENT FORM FOR 8 TO 10 YEARS TO PARTICIPATE IN A STUDY

TITLE: Patient experience and healthcare priorities with steroid sensitive nephrotic syndrome

WHO IS PAYING FOR THE STUDY: [redacted]

PEOPLE DOING THE STUDY: [redacted]

[redacted]

We want to tell you about a research study we are doing. A research study is a way to learn more about something. We are asking you to be in the study because we want to learn more about how children with nephrotic syndrome feel. About 30 people will be in this study.

We want to tell you about some things that will happen to you if you join this study.

If you join this study, we will ask you questions for about 1 hour using the internet. Your parents can be present if you want.

You will not be hurt if you join the study. You will not miss school too.

If you are in the study, it may not help you to get better. It may help us to know how children with this condition feel.

When we have finished, we will write a report. We will not write your name in the report. We may use the answers from everybody to do another study in nephrotic syndrome.

You do not have to join this study. It is up to you. You can say yes, or you can say no. It's OK if you say yes and then you change your mind later. If you want to stop, tell us or your parents that you want to stop. No one will be mad at you if you do not want to be in the study or if you say yes now then want to stop later.

Before you say yes or no, you can ask us any question. If you join, you can ask questions at any time. Just tell us or your parents that you have a question.

If you join the study, we will give your family a $20 gift card.
We will talk to your parents about this study. You can also talk to them before you decide.

If you want to ask a question later, you can call or
tell your parents to call [redacted]

DO YOU WANT TO JOIN THIS STUDY?

□ Yes □ No

_____ _____

Name of Child Date

_____

Name of Person who received assent

_____ _____

Signature of Person who received assent Date

We will give you a copy of this paper to keep.

SUPPLEMENTARY MATERIAL II: ASSENT FORM FOR CHILDREN AGED 11 – 13 YEARS TO PARTICIPATE IN A STUDY

TITLE: Patient experience and healthcare priorities with steroid sensitive nephrotic syndrome

SPONSOR: [redacted]

INVESTIGATORS: [redacted]

[redacted]

[redacted]

INTRODUCTION

A research study is a way to find out new information about something. People don't need to participate in a research study if they don't want to participate.

You can talk this over with your parents/guardians before you decide whether or not to participate. We will also ask your parents/guardians to give their permission for you to take part in this study. But even if they say "yes", you can still decide not to do this. Your parents or guardians can be present during the interview if you want.

WHY ARE WE DOING THIS STUDY?

You are being asked to take part in this research study because we are trying to learn more about the experiences of children with steroid sensitive nephrotic syndrome.

WHY AM I BEING ASKED TO BE IN THE STUDY?

We are inviting you to be in the study because we want you to share your experiences living with steroid sensitive nephrotic syndrome. About 30 people will be in this study.

WHAT WILL HAPPEN IF I TAKE PART IN THIS STUDY?

If you decide that you want to be part of this study, we will ask you some questions about your experience with nephrotic syndrome that would last for approximately 45 to 60 minutes. The interview will take place over the internet. We will record the interview. It's OK if you say yes and then you change your mind later. If you want to stop, then all you have to do is tell us or your parents/guardian you want to stop. No one will be mad at you if you don't want to be in the study or if you say yes now then want to stop later. If you decide to stop, we will not use your answers to write the report.

ARE THERE ANY POTENTIAL RISKS OR DISCOMFORTS THAT I CAN EXPECT FROM THIS STUDY?

You will not be hurt if you decide to participate in the study. You will not miss school if you take part in the study. If you experience discomfort or distress during the interview, we will offer to take a short break, change the topic, or stop the interview. We will also advise you to call the Alberta Health Services' Mental Health Help Line at 877 303 2642.

WILL THE STUDY HELP ME?
If you are in the study, it may not help you to get better or benefit you. The study may help us to understand how patients with steroid sensitive nephrotic syndrome feel and want they want from their doctors and nurses caring for them.

WILL THE STUDY HELP OTHERS?
This study might find out things that doctors and nurses could use to make the care for patients with steroid sensitive nephrotic syndrome better. We may use the answers from everybody to do another study in nephrotic syndrome in future.

WHO WILL SEE THE INFORMATION COLLECTED ABOUT ME?
The information collected about you during this study will be safely kept in the University of Calgary server. Nobody will read it except the people doing the research. The study information about you will not be given to your parents/guardians. The researchers won't tell your friends or anyone else that you are in this study or share any information about you. We will not put your name in the final report.

DO I HAVE TO BE IN THE STUDY?
You don't have to be in the study. It is up to you. No one will be upset if you don't want to do this study. You can say yes, or you can say no. You can also take more time to think about being in the study. No one will be mad at you if you don't want to be in the study, or if you say yes now then want to stop later. After the interview, you have 1 week to change your mind.

WHAT DO I GET FOR BEING IN THE STUDY?
Your family will receive a $20 electronic gift card at the beginning of the interview.

WHO CAN I CONTACT IF I HAVE QUESTIONS ABOUT THIS STUDY?
If you have any questions, contact [redacted] you can ask any questions that you may have about the study. If you have a question later that you didn't think of now, either you can call or have your parents call [redacted] You can also take more time to think about being in the study and also talk some more with your parents about being in the study.

WOULD YOU LIKE TO BE IN THIS RESEARCH STUDY?
If you decide to be in the study, then please write your name below. You can change your mind and stop being part of the study at any time. All you have to do is tell us. It's okay. The researchers and your parents won't be upset with you

☐ Yes, I want to be in this study. ☐ No, I don't want to do this.

_____

Name of Participant

_____ _____

Signature of Participant Date

SIGNATURE OF PERSON OBTAINING ASSENT

_____
Name of Person who received assent

_____ _____
Signature of Person who received assent Date

You will be given a copy of this paper to keep.

SUPPLEMENTARY MATERIAL III: PARENT/GAURDIAN CONSENT FOR A CHILD AGED 8 TO 13 YEARS TO PARTICIPATE IN RESEARCH

TITLE: Patient experience and healthcare priorities with steroid sensitive nephrotic syndrome

SPONSOR: [redacted]

INVESTIGATORS: [redacted]

INTRODUCTION

A research study is a way to find out new information about something. People don't need to participate in a research study if they don't want to participate.

This consent form will give you information about the research study, and what your child's participation will involve. If you would like to ask questions, please ask.

We are inviting your child to join this study because your child visited the Alberta Children's Hospital for treatment of a kidney disease called nephrotic syndrome. Your child's participation in this research study is voluntary.

WHY ARE WE DOING THIS STUDY?

Your child is being asked to take part in this research study because we are trying to learn more about the experiences of children with steroid sensitive nephrotic syndrome.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

About 25 to 30 people will take part in this study in Calgary.

WHAT WILL HAPPEN IF MY CHILD TAKES PART IN THIS RESEARCH STUDY?

If you decide that your child should join the study, we will ask them some questions about their experiences with nephrotic syndrome that would last for approximately 45 to 60 minutes. The interview will take place over the internet. We will record the interview.

HOW LONG WILL MY CHILD BE IN THIS STUDY?

Your child's participation in this study will last approximately 45 to 60 minutes.

ARE THERE ANY POTENTIAL RISKS OR DISCOMFORTS THAT I CAN EXPECT FROM THIS STUDY?

Your child will not be hurt if they participate in the study. Your child will not miss school. If your child experiences any discomfort or distress during the interview, we will offer to take a short break, change the topic, or stop the interview. We will also advise you to call the Alberta Health Services' Mental Health Help Line at 877 303 2642.

WILL THE STUDY HELP MY CHILD?

If your child is in the study, it may not help them to get better. The study may help us to understand how patients with steroid sensitive nephrotic syndrome feel and want they want from their doctors and nurses caring for them.

WILL THE STUDY HELP OTHERS?

This study might find out things that doctors and nurses could use to make the care for patients with steroid sensitive nephrotic syndrome better. We may use the answers from everybody to do another study in nephrotic syndrome in future.

WHO WILL SEE THE INFORMATION COLLECTED ABOUT MY CHILD?

The information collected about your child during this study will be kept safely locked up in a computer. Nobody will read it except the people doing the research.

DO MY CHILD HAVE TO BE IN THE STUDY?

Your child does not have to be in the study. It is up to you. It's OK if you say yes and then you change your mind later.

WHAT OTHER CHOICES DOES MY CHILD HAVE IF THEY CHOOSE NOT TO PARTICIPATE?

You are free to say no to your child participating in the study. Your decision will not affect the medical care your child receives.

CAN MY CHILD STOP BEING IN THE STUDY?

Yes. You can decide to stop your child's participation at any time without penalty. Tell the researchers if you are thinking about stopping or decide to stop. If you decide to withdraw your child from the study, then all you have to do is tell us. If you decide that your child should stop, the information collected will be used in the study unless you tell us not to use your child's information.

WITHDRAWAL OF STUDY DATA

You may request that your child's data be withdrawn from the study for up to 1 week after the interview.

WILL MY CHILD BE PAID FOR PARTICIPATING, OR DO I HAVE TO PAY FOR ANYTHING?

Your family will receive a $20 gift card at the beginning of the interview. You will not pay for participating in this project.

WILL INFORMATION ABOUT MY CHILD'S PARTICIPATION BE KEPT CONFIDENTIAL?

Any information your child provides is confidential. Any information mentioned in the interview that may identify your child will not be transcribed. Information that will identify your child will not be kept with the research data. Your child's personal information will be removed from the data and will be kept separate from the research data in the University of Calgary server and will only be accessible to the research team. Any personal information your child provides will not be included in the final report. No information identifying your child will be transferred to any agency.

HOW LONG WILL INFORMATION FROM THE STUDY BE KEPT?

Information collected during this study will be kept for 5 years in conformity with the University of Calgary Data Retention Policy after which the data will be destroyed in accordance with University of Calgary Policy.

WHOM MAY I CONTACT IF I HAVE QUESTIONS ABOUT THIS STUDY?

You may contact [redacted] with any questions or concerns about the research or your participation in this study.

If you have any questions concerning your rights as a possible participant in this research, please contact the Chair, Conjoint Health Research Ethics Board, University of Calgary at 403-220-7990.

HOW CAN I FIND OUT ABOUT THE STUDY RESULTS?

Participants and their families will be informed about the result of the study in face-to-face meetings or virtual workshop.

WHAT RIGHTS DOES MY CHILD HAVE IF THEY TAKE PART IN THIS STUDY?

- You have a right to have all of your questions answered before deciding whether to allow your child take part in the study
- Your decision will not affect the care your child receives at the Alberta Children's Hospital
- If you decide that your child should take part, your child may leave the study at any time

WOULD YOU LIKE YOUR CHILD TO BE IN THIS RESEARCH STUDY?

By signing this form, you are agreeing for your child to participate in an interview to learn about experiences in steroid sensitive nephrotic syndrome. This does not mean that you are waiving

your legal rights nor does it release the investigators or involved institutions from their legal and professional responsibilities.

Name of Child

SIGNATURE OF PARENT OR LEGAL GUARDIAN

Name of Parent or Legal Guardian

Signature of Parent or Legal Guardian | Date

SIGNATURE OF PERSON OBTAINING CONSENT

Name of Person Obtaining Consent | Contact Number

Signature of Person Obtaining Consent | Date

SIGNATURE OF THE WITNESS

Name of Witness

Signature of Witness | Date

A signed copy of this consent form will be given to you to keep for your records and reference.

SUPPLEMENTARY MATERIAL IV: CONSENT FORM FOR ADULTS AND MATURE MINORS AGED 14 -18 YEARS TO PARTICIPATE IN A STUDY

TITLE: Patient experience and healthcare priorities in children with steroid sensitive nephrotic syndrome.

SPONSOR

INVESTIGATORS:

INTRODUCTION

Dr. and associates from department of Community Health Sciences at the University of Calgary are conducting a research study.

This consent form is only part of the process of informed consent. It should give you the basic idea of what the research is about and what your participation will involve. If you would like more detail about something mentioned here, or information not included here, please ask. Take the time to read this carefully and to understand any accompanying information. You will receive a copy of this form for your records.

You were identified as a possible participant in this study because your child visited the Alberta Children's Hospital for treatment a kidney disease called nephrotic syndrome. Your participation in this research study is voluntary.

WHY IS THIS STUDY BEING DONE?

The purpose of the study is to explore the experience, perspectives and care priorities of children living with steroid sensitive nephrotic syndrome.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

About 25 to 30 people will take part in this study in Calgary.

WHAT WILL HAPPEN IF I TAKE PART IN THIS STUDY?

We are inviting you to take part in a face-to-face interview that will take approximately 45 to 60 minutes. The interview will take place over the internet using University of Calgary Microsoft Teams at a scheduled time. If you prefer another location, that could be arranged. All interviews

will be audio-recorded and transcribed.

HOW LONG WILL I BE IN THIS STUDY?

Your participation in this study will last approximately 45 to 60 minutes.

ARE THERE ANY POTENTIAL RISKS OR DISCOMFORTS THAT I CAN EXPECT FROM THIS STUDY?

There are no known harms associated with this project. If, during the interview, a question is not applicable to you or you feel uncomfortable answering, just let me know. You can refuse to answer any specific questions during the interview or stop the interview at any time.

ARE THERE ANY POTENTIAL BENEFITS IF I PARTICIPATE?

If you agree to participate, there may or may not be of direct benefit to you. However, based on the results of this study, the information will contribute towards the improvement of care and future research in childhood steroid sensitive nephrotic syndrome.

WHAT OTHER CHOICES DO I HAVE IF I CHOOSE NOT TO PARTICIPATE?

You are free to choose not to participate in the study. If you decide not to take part in this study, there will be no penalty to you.

CAN I STOP BEING IN THE STUDY?

Yes. You can decide to stop at any time without penalty. Tell the researchers if you are thinking about stopping or decide to stop. If you decide to withdraw from the study, information collected up to the time of withdrawal will be retained and used in the study unless you specifically request otherwise.

WITHDRAWAL OF STUDY DATA

You may request that your data be withdrawn from the study for up to 3 months after the interview.

WILL I BE PAID FOR PARTICIPATING, OR DO I HAVE TO PAY FOR ANYTHING?

Upon completion of the interview, your family will receive a $20 gift card. This will be sent to you through electronic mail. You will not incur any costs by participating in this project.

WILL INFORMATION ABOUT MY PARTICIPATION BE KEPT CONFIDENTIAL?

Any information you provide is confidential. Any information mentioned in the interview that may identify you will not be transcribed. No identifiable information about you will be kept with the research data. All identifiable information about you will be replaced with a code. A master

list linking the code and your identifiable information will be kept separate from the research data. The data and personal identifiers will be encrypted and password-protected and will be stored in a computer in the University Calgary servers and will only be accessible to the research team. Any personal identifiers provided will not be included in the final report. No information identifying you will be transferred to any agency.

HOW LONG WILL INFORMATION FROM THE STUDY BE KEPT?

Information collected during this study will be kept for 5 years in conformity with the University of Calgary Data Retention Policy after which the data will be destroyed in accordance with University of Calgary Policy.

CONTACT FOR FUTURE RESEARCH

University of Calgary researchers may contact me in the future to ask me to take part in other nephrotic syndrome research studies

- ❑ YES
- ❑ NO

IF I SUFFER RESEARCH RELATED INJURY, WILL I BE COMPENSATED?

In the event that you suffer injury because of participating in the research, no compensation will be provided to you by Roy and Vi Baay Chair in Kidney Research, the University of Calgary, Alberta Health Services or the Researchers. You still have your legal rights to seek damages.

WHOM MAY I CONTACT IF I HAVE QUESTIONS ABOUT THIS STUDY?

You may contact [redacted] with any questions or concerns about the research or your participation in this study.

If you have any questions concerning your rights as a possible participant in this research, please contact the Chair, Conjoint Health Research Ethics Board, University of Calgary at 403-220-7990.

HOW CAN I FIND OUT ABOUT THE STUDY RESULTS?

Participants and their families will be informed about the result of the study in face-to-face meetings or virtual workshops.

WHAT RIGHTS DO I HAVE IF I TAKE PART IN THIS STUDY?

Taking part in this study is your choice. You can choose whether or not you want to participate. Whatever decision you make, there will be no penalty to you.

- You have a right to have all of your questions answered before deciding whether to take part.
- Your decision will not affect the standard medical care your child receives at the Alberta Children's Hospital
- If you decide to take part, you may leave the study at any time

HOW DO I INDICATE MY AGREEMENT TO PARTICIPATE?

By signing this form, you are indicating your agreement that you will participate in an interview to explore patient experiences and healthcare priorities. Your signature indicates that you have understood to your satisfaction the information regarding your participation in the research project. In no way does this waive your legal rights nor release the investigators or involved institutions from their legal and professional responsibilities. You are free to withdraw from the study at any time without jeopardizing your child's healthcare.

_____
Name of Participant

_____ _____
Signature of Participant Date

_____ _____
Name of Person Obtaining Consent Contact Number

_____ _____
Signature of Person Obtaining Consent Date

A signed copy of this consent form will be given to you to keep for your records and reference.

SUPPLEMENTARY MATERIAL V: PRIMARY INTERVIEW GUIDE FOR ADOLESCENTS AGED 10 TO 18 YEARS

Preamble

My name is Augustina Okpere. Thank you for agreeing to speak with me today. I am interviewing children with steroid sensitive nephrotic syndrome (SSNS) and their caregivers. I am interested in learning about your experience living with SSNS. Your experiences are very important to us to better understand SSNS. Don't worry if you do not understand some questions. I am here to help. Feel free to ask me questions. You may not have thought about some questions, and it is okay to say you don't know.

Are you in a place where you have some privacy and feel comfortable to talk? If so, we can begin the discussion ……

1.Tell me about the time you had the body swelling.
- Probe how they felt, what they did, how the news of the diagnosis was received
- Probe experience with diagnosis and treatment; coping/feeling

2. What it is like having to take steroids (prednisolone)?
- Probe relapse, compliance, side effects

3. Tell me about any other medicines you have had to take for your kidney problems
- Probe decision making process, experience with the drug, alternative medications

4. Tell me about how your kidney problem (nephrotic syndrome) has affected the way you live your life?
- Probe school, friends, extracurricular activities, vacations
- Probe what they think the future will look like, hopes and goals for the future.

5. What things are important to you concerning your health (priorities)
- Probe challenges in care, unanswered concerns/questions, priorities
- Probe how concerns are addressed by health teams

6. If you met another kid who was just starting to go through the same kidney problem that you went through, what would you tell him/her?
- Probe gaps in care/knowledge
- Probe what they wish they had known at the start, what things could help/hinder as they go forward.
-

7. Is there anything else you want to say?

SUPPLEMENTARY MATERIAL VI: INTERVIEW GUIDE FOR CHILDREN AGED 8 – 9 YEARS

Preamble

My name is Augustina Okpere. Thank you for agreeing to speak with me today. I am interviewing children with steroid sensitive nephrotic syndrome (SSNS) and their parents. I am interested in learning about how you feel. Your experiences are very important to us to better understand SSNS. Don't worry if you do not understand some questions. I am here to help. Feel free to ask me questions. You may not have thought about some questions, and it is okay to say you don't know.

Do you feel comfortable to talk? If so, we can begin the discussion ……

1.Have you been to the Children's Hospital?

Tell me about the time you went to the Children's Hospital.

- Probe why they went to the hospital
- Probe what happened in the hospital, how they felt

2.Tell me about the time you had the body swelling.

- Probe how they felt, what they did, how the news of the diagnosis was received
- Probe experience with diagnosis and treatment; coping/feeling

2. Let's talk about your medicine.

- Name of the medicine
- Probe relapse, compliance, side effects

3. Tell me about any other medicine you have had to take for your swelling/kidney problem

- Probe decision making process, experience with the drug

4. What is it like to have this problem with your kidneys?

- Probe school, friends, extracurricular activities, vacations

5. What things do you worry about when you visit the doctor?

- Probe challenges in care, unanswered concerns/questions, priorities

6. If you met another kid who was just starting to go through the same things as you, what would you tell him/her?

7. Is there anything else you want to say?

SUPPLEMENTARY MATERIAL VII: INTERVIEW GUIDE FOR CAREGIVERS

Preamble:

My name is Augustina Okpere. Thank you for agreeing to speak with me today. I am interviewing children with SSNS and their caregivers. I am interested in learning about your child's experience living with SSNS and your own experience. Your experiences are very important to us to better understand how to care for children with SSNS. Don't worry if you do not understand some questions. I am here to help. Feel free to ask me questions. You may not have thought about some questions, and it is okay to say you don't know.

Are you in a place where you have some privacy and feel comfortable to talk? If so, we can begin the discussion ……

1.Tell me about the time your child was first diagnosed with nephrotic syndrome/kidney problem
   - Probe how they felt, how the news of the diagnosis was received

2. What it is like for your child to take steroids
   - Probe relapse, compliance, side effects

3. Tell me about any other medicine your child has taken for nephrotic syndrome?
   - Probe decision making process, experience with the drug

4. Tell me about how nephrotic syndrome has affected your child's life
   - Probe school, friends, extracurricular activities, vacations

5. Tell me about what is important to you about your child's health and health care
   - Probe challenges in care, unanswered concerns/questions, priorities

Let's turn to how you are coping with your child's diagnosis

6. Tell me about how your child's nephrotic syndrome has affected your life
   - Probe work, social life, family

6. If you met another parent whose child has just been diagnosed with nephrotic syndrome, what would you tell him/her?

7. Is there anything else you want to say?