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Illness, symptoms and causes of nephrotic syndrome

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Illness, symptoms and causes of nephrotic syndrome

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LICENTIAT DISSERTATION

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Professor Olof Heimbürger
Karolinska Institutet, Stockholm

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| Abstract <p>Background: Nephrotic syndrome (NS) is not a disease but a group of symptoms due to kidney damage. The condition includes heavy proteinuria, hypoalbuminemia, and oedema. NS is complex thus patients do not fully understand the condition and how it affects health. It can also be difficult for physicians and nurses to understand, because the symptoms and signs are associated with diverse diagnoses that have different prognoses.</p> <p>Aim: The overall aim of this thesis was to explore patients' experiences of illness and the clinical characteristics of persons with NS.</p> <p>Methods: In Study I, 10 participants who became diagnosed with NS were interviewed. The transcribed interviews were analysed using a phenomenological hermeneutical method. In Study II we retrieved data from the biopsy module in the Swedish Renal Registry comprising 913 patients who underwent kidney biopsy due to NS between 2014 and 2019. The patients were categorized into two groups: (a) those with biopsy indication NS (n=735) and (b) those who had laboratory parameters compatible with NS but where the main biopsy indication was not NS (n=178).</p> <p>Results: The result of Study (I) showed that patients who were newly diagnosed with NS or had a relapse with NS ended up in a state of ambiguity which is illustrated by the following themes: Feeling ill and well at the same time; Being passively adherent; Being in uncertainty and Trying to comprehend and cope. The patients were stranger in an unfamiliar world of symptoms, signs and medical treatment. Which led to profound knowledge that causes uncertainty and lack of self-management. The results from Study (II) shows that the average age of adult patients who develop NS is 56.3 years at time of biopsy and the most common causes of NS were diabetic nephropathy, membranous nephropathy and minimal change nephropathy. The most common causes of NS in "indication NS" group were membranous nephropathy, minimal change nephropathy and diabetic nephropathy. The patients in "indication NS" group had mild hematuria and moderately reduced eGFR. In general, more men developed NS except where the cause is systemic lupus erythematosus.</p> <p>Conclusions: This thesis describes two different perspectives of NS, an inside and an outside perspective. Both perspectives are of equal importance in the care of patients with NS. The most important results are that:</p> <ul style="list-style-type: none"> • Patients with NS have difficulty understanding that their symptoms are due to a kidney disease, leading to them ending up in a state of ambiguity and uncertainty. • Patients experience receiving insufficient information and a lack of professional support, which leads to difficulties achieving self-management. • The most common causes of NS in adult patients in Sweden are diabetic nephropathy, membranous nephropathy and minimal change nephropathy. • Clinical characteristics presented by patients with NS can facilitate the establishment of a diagnosis in cases where a kidney biopsy is not possible. | | |
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Illness, symptoms and causes of nephrotic syndrome

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2021



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Abstract

Background: Nephrotic syndrome (NS) is not a disease but a group of symptoms due to kidney damage. The condition includes heavy proteinuria, hypoalbuminemia, and oedema. NS is complex thus patients do not fully understand the condition and how it affects health. It can also be difficult for physicians and nurses to understand because the symptoms and signs are associated with diverse diagnoses that have different prognoses.

Aim: The overall aim of this thesis was to explore patients' experiences of illness and the clinical characteristics of persons with NS.

Method: In Study I, 10 participants who became diagnosed with NS were interviewed. The transcribed interviews were analysed using a pheno-menological hermeneutical method. In Study II we retrieved data from the biopsy module in the Swedish Renal Registry comprising 913 patients who underwent kidney biopsy due to NS between 2014 and 2019. The patients were categorized into two groups: (a) those with biopsy indication NS (n=735) and (b) those who had laboratory parameters compatible with NS but where the main biopsy indication was not NS (n=178).

Results: The result of Study (I) showed that patients who were newly diagnosed with NS or had a relapse with NS ended up in a state of ambiguity which is illustrated by the following themes: *Feeling ill and well at the same time*, *Being passively adherent*, *Being in uncertainty* and *Trying to comprehend and cope*. The patients were stranger in an unfamiliar world of symptoms, signs and medical treatment. Which led to profound knowledge that causes uncertainty and lack of self-management.

The results from Study (II) revealed that the average age of adult patients who develop NS is 56.3 years at time of biopsy and the most common causes of NS were diabetic nephropathy, membranous nephropathy, and minimal change nephropathy. The most common causes of NS in "indication NS" group were membranous nephropathy, minimal change nephropathy and diabetic nephropathy. The patients in "indication NS" group had mild haematuria and moderately reduced eGFR. In general, more men developed NS except where the cause is systemic lupus erythematosus.

Conclusions: This thesis describes two different perspectives of NS, an inside and an outside perspective. Both perspectives are of equal importance in the care of patients with NS. The most important results are that:

- Patients with NS have difficulty understanding that their symptoms are due to a kidney disease, leading to them ending up in a state of ambiguity and uncertainty.

- Patients' experience receiving insufficient information and a lack of professional support, which leads to difficulties achieving self-management.
- The most common causes of NS in adult patients in Sweden are diabetic nephropathy, membranous nephropathy, and minimal change nephropathy.
- Clinical characteristics presented by patients with NS can facilitate the establishment of a diagnosis in cases where a kidney biopsy is not possible.

Original papers

This licentiate thesis is based on the following two papers:

- I Jönsson, A., Hellmark, T., & Forsberg, A. (2020). Persons' experience of suffering from nephrotic syndrome. *Journal of Renal Care* 46(1): 45-51. Epub 2019 Nov 19.
- II Jönsson, A., Hellmark, T., Segelmark, M., Forsberg, A., & Dreja, K. Causes of the nephrotic syndrome in Sweden 2014-2019 depending on clinical presentation and demographics. *Manuscript submitted for publication.*

Paper I have been reprinted in this thesis with permission of the publishers.

Abbreviations

| | |
|----------|---|
| ACE | Angiotensin converting enzyme |
| ACR | Albumin creatinine ratio |
| ARB | Angiotensin II receptor blockers |
| CKD | Chronic kidney disease |
| DN | Diabetic nephropathy |
| eGFR | estimated glomerular filtration rate |
| ENaC | Epithelial sodium channel |
| ERA-EDTA | European Renal Association – European Dialysis and Transplant Association |
| ESKD | End-stage kidney disease |
| FSGS | Focal segmental glomerulosclerosis |
| GBM | Glomerular basement membrane |
| GFB | Glomerular filtration barrier |
| IgAN | IgA nephropathy |
| HDL | High-density lipoprotein |
| HRQoL | Health-related quality of life |
| KDOQI | Kidney Disease Outcomes Quality Initiative |
| LDL | Low-density lipoprotein |
| MCN | Minimal change nephropathy |
| MN | Membranous nephropathy |
| MPGN | Membranoproliferative glomerulonephritis |
| NS | Nephrotic syndrome |
| PCC | Person-centred care |
| PCD | Plasma cells dyscrasias |
| SLE | Systemic lupus erythematosus |
| SRR | The Swedish Renal Registry |
| VLDL | Very-low-density lipoprotein |
| WHO | World Health Organization |

Introduction

Nephrotic syndrome (NS) is not a disease but a group of symptoms due to kidney damage. The condition includes heavy proteinuria, hypoalbuminemia, and oedema (Zhou et al., 2011). The incidence of NS in adults is about three new cases per 100,000 each year (Hull & Goldsmith, 2008). NS is caused by different kidney diseases and the outcome is dependent on the disease in question, which may be a chronic kidney disease (CKD) or a disease with relapsing and remitting conditions. NS is one of the most frequent (38-40%) indication for kidney biopsy (Fiorentino et al., 2016; Jegatheesan et al., 2016). In Sweden, the rate of NS as a kidney biopsy indication is slightly lower (23%) (Swedish Renal Registry [SRR], 2020). Despite the fact that NS is a rare condition, it is serious with a high risk of life-threatening complications such as thromboembolism (Kerlin et al., 2012) infections and kidney failure (Yamamoto et al., 2020).

Patients with nephrotic-associated glomerulopathy have low health-related quality of life (HRQoL) and a high risk of depression comparable to patients treated with haemodialysis (Libório et al., 2012). Patients with CKD have reported that they need time to understand the diagnosis, manage uncertainty in illness, integrate treatment regimens into their daily routines and restore a sense of normalcy in their lives (Tong et al., 2009). However, there is limited knowledge of patients' experience of NS and how it affects their everyday life.

NS is complex; thus patients and their families do not really understand it and how it affects their health (Beanlands et al., 2017). The condition could also be complex for physicians and nurses because the clinical presentations are associated with different diagnoses and long-term outcome. Patients' experience is important in healthcare decision-making to maximize their quality of life and self-management. There is a need for both an inside and outside perspective on NS to facilitate target oriented and person-centred care, which is the rationale behind this thesis.

Background

The glomerular filtration barrier

An important part of kidney function is to eliminate waste products and maintain fluid and electrolyte balance. The first step in this process is ultrafiltration of the plasma which takes place in the glomerulus, a capillary tuft. The plasma ultrafiltrate does not contain red and white blood cells, platelets and has a very low concentration of proteins. It is the glomerular filtration barrier (GFB) that determines the composition of plasma ultrafiltration. GFB consists of three different layers. From the inside to the outside of the capillary the layers are: the fenestrated glomerular endothelium covered by glycocalyx; the glomerular basement membrane (GBM), and the podocyte foot processes with their specific junctions, slit diaphragms (Figure 1) (Garg & Rabelink, 2011; Koeppen & Stanton, 2013; Scott & Quaggin, 2015).

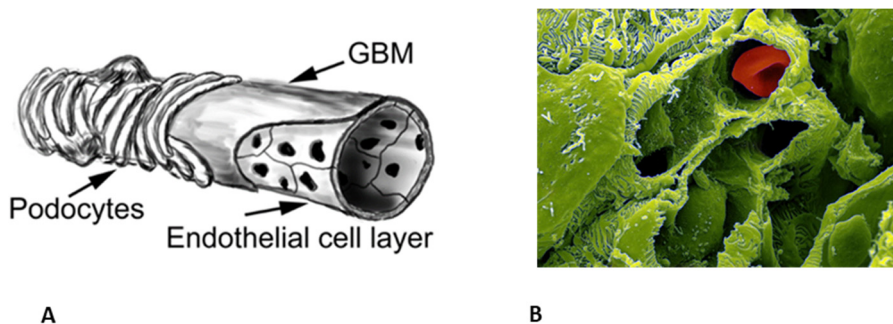


Figure 1. A. The filtration barrier of a glomerular capillary. *The endothelial cell layer* is thin and consists of small pores (60nm), known as fenestrae. The endothelial cells produce a negatively charged glycocalyx, which constitutes the first step in the filtration barrier; *The Glomerular Basement Membrane (GBM)* consists of type IV collagen, proteoglycans and laminis; *Podocytes* are large, highly specialized epithelial cells that encircle the capillaries with their foot processes and their specific junctions, termed slit diaphragms. B. Electron micrograph of the glomerular capillaries in which a red blood cell is visible.

The GFB is a complex structure that allows for high filtration rates (about 125 ml/min) of water and small molecules, including ions, urea and small proteins (Garg & Rabelink, 2011; Scott & Quaggin, 2015). The glomerular filtration occurs because there is a difference in pressure across the GFB. The hydrostatic pressure in the glomerular capillary (50 mmHg) is counteracted by the hydrostatic pressure in Bowman's space (15 mmHg) and by the oncotic pressure in the glomerular capillary (25 mmHg). The net ultrafiltration pressure is the difference between the pressures that promote filtration and those that counteract it. This result in a net ultrafiltration of 10 mmHg ($50 - 15 - 25 = 10$ mmHg) (Pollak et al., 2014).

The GFBs selective permeability of solutes depends primary on molecular size but also on molecular charge (Haraldsson et al., 2008; Scott & Quaggin, 2015). The two-pore model describes the glomerular permeability as a selective membrane consisting of a very large number of small pores with a radius between 35 and 50 Å (Öberg & Rippe, 2014) and a low number of large pores (100-120 Å) (Tencer et al., 1998; Öberg & Rippe, 2014). Molecules with a radius <20 Å are filtered freely. Molecules with a radius between 20 and 42 Å are filtered to various degree and serum albumin with a radius of 35.5 Å is filtered poorly (Koeppen & Stanton, 2013).

Proteinuria

The GFB prevents effectively but not completely proteins from being filtered to the primary urine. During normal physiological conditions, the protein content of the final urine is very low with a daily urine excretion of 40-80 mg of protein of which 10-15 mg is albumin (Garg & Rabelink, 2011; Gorriz & Martinez-Castelao, 2012). When protein levels in the urine are >300 mg/day it is defined as proteinuria. Albuminuria is defined as urine containing >30 mg albumin/day (Gorriz & Martinez-Castelao, 2012). It is defined as nephrotic-range proteinuria when the urine contains >3.5 g protein/day (Ng et al., 2018).

There are several ways of measuring protein in the urine, e.g. dipstick analysis for screening of albumin and quantitative methods to measure proteins or albumin (Gorriz & Martinez-Castelao, 2012). Previously, 24-hour urine collection was used to measure proteins in the urine, but it was time-consuming and troublesome for the patient, which could result in incorrect values. Instead of measuring the daily amount of urinary proteins, it is more reliable to measure the concentration of proteins in relation to the creatinine concentration in a urine sample. The National Kidney Foundation's Kidney

Disease Outcomes Quality Initiative (KDOQI) guidelines recommend albumin/creatinine ratio (ACR) for diagnosis in adults. Repeated measurements are necessary as there could be temporary rise of protein in the urine (Gorritz & Martinez-Castelao, 2012).

Glomerular proteinuria

Proteinuria may be due to different mechanisms in the kidney where glomerular proteinuria is the result of disturbance of the GFB (Garg & Rabelink, 2011; Glassock et al., 2015). The cause of glomerular proteinuria can be environmental, autoimmune, or genetic and may affect any layer of the GFB (Garg & Rabelink, 2011; Suh & Miner, 2013). For example, proteinuria in patients with diabetes mellitus is related to damage of the glomerular endothelial surface layer (Scott & Quaggin, 2015). Most patients (70-80%) with idiopathic membranous nephropathy (MN) have antibodies against the phospholipase A2 receptor which is expressed in podocyte in normal glomeruli (Coenen et al., 2013). Congenital nephrotic syndrome of the Finnish type is an autosomal-recessive disease where mutations have been found in the protein nephrin (NPHS1). NPHS1 is in the podocyte slit diaphragm and mutation causes an incorrect podocyte leading to NS (Kestilä et al., 1998). Alport's syndrome is due to mutations in collagen type IV causing a dysfunctional GBM (Garg & Rabelink, 2011).

Nephrotic syndrome

Causes of NS

There are a wide range of causes of glomerular damage leading to NS. It may be due to a primary kidney disease, secondary to a systemic disease, drugs, or cancer (Table 1). The cause of NS varies between children and adults. The most common cause in children is minimal change nephropathy (MCN) and in adults are MN, focal segmental glomerulosclerosis (FSGS) and diabetes nephropathy (DN) the most common causes (Jegatheesan et al., 2016; Naumovic et al., 2009). Overall, there is a predominance of men in patients with glomerulonephritis (Jegatheesan et al., 2016; Zaza et al., 2013).

Table 1. Causes of nephrotic syndrome

| Primary kidney disease | Secondary systemic disease | Other causes |
|------------------------------------|------------------------------|--|
| Focal segmental glomerulosclerosis | Amyloidosis | Cancer: Myeloma, Lymphoma |
| IgA nephropathy | Diabetes mellitus | Drugs: |
| Membranoproliferative nephropathy | Hypertension | Gold, NSAID, Penicillin, |
| Membranous nephropathy | Systemic lupus erythematosus | Captopril, Tamoxifen, |
| Minimal change disease | Systemic vasculities | Lithium |
| Proliferative glomerulonephritis | | Hereditary: Alports syndrome Congenital nephrotic syndrome |
| | | Infections: Hepatitis B and C, HIV, Mycoplasma, Syphilis, Malaria |

Signs and complications

The signs, symptoms and complications of NS are due to the high secretion of proteins (Orth & Ritz, 1998).

Oedema

Oedema is a common symptom (51%) in patients with heavy proteinuria (Gipson et al., 2016). Patients often notice that they have frothy urine, periorbital oedema in the morning and ankle oedema in the evening. The oedema can quickly develop into general oedema in the arms, legs, genitals, and ascites (McCloskey & Maxwell, 2017). The pathophysiology behind oedema in NS depends on various mechanisms. A reduction in oncotic pressure leads to fluid leaking from the intravascular space to the interstitial space (*underfilling*). The latest approach to explain oedema in NS is that renal sodium retention leads to intravascular volume expansion (*overfilling*) (Siddall & Radhakrishnan, 2012). One hypothesis is that sodium retention in NS is due to an increased activation of the epithelial sodium channel (ENaC) in the distal tubules and collecting ducts. In NS, the concentration of plasmin in the urine increases, which leads to activation of ENaC and sodium retention (Hinrichs et al., 2020).

Hyperlipidaemia

Hyperlipidaemia is common in NS and a risk factor for vascular disease such as heart disease and stroke. Total cholesterol, very-low-density lipoprotein (VLDL) and low-

density lipoprotein (LDL) are almost always increased, while high-density lipoprotein (HDL) can vary. Changes in lipoprotein metabolism in NS are due to two mechanisms: overproduction and impaired catabolism of lipoproteins. The lower level of plasma albumin the more pronounced are the changes in lipids (Orth & Ritz, 1998).

Thromboembolism

The perhaps most severe complication of NS is an increased risk of venous thromboembolism (Christiansen et al., 2014; Kayali et al., 2008). It is more common in adult patients with NS to develop thromboembolism than it is in children with NS. Pulmonary embolism and deep vein thrombosis are relatively common during the first six months after diagnosis of NS (Mahmoodi et al., 2008; Orth & Ritz, 1998). But the incidence varies depending on the causes of NS, where adult patients with MN are associated with the highest risk of developing thromboembolism (Kerlin et al., 2012; Mahmoodi et al., 2008). The risk of thromboembolism in NS is multifactorial and is associated with the level of proteinuria (Mahmoodi et al., 2008), medications and central venous catheterization (Kerlin et al., 2012). The hypercoagulable state in NS is due to increased levels of factor V, factor VIII, fibrinogen, and decreased levels of antithrombin III. Blood platelets also have an abnormally increased aggregability (Orth & Ritz, 1998).

Infections

Patients with NS have an increased tendency to develop bacterial infections, which is due to decreased levels of IgG and immunosuppressive treatment (Orth & Ritz, 1998). It is also well known that oedema of the legs increases the risk of skin infections.

Kidney function

The risk of reduced kidney function is due to the underlying disease that cause NS. The risk of end-stage kidney disease (ESKD) is strongly associated with grade of albuminuria (Carrero et al., 2017).

Diagnosis

To diagnose the cause of NS a kidney biopsy is performed if there is no contraindication. The histopathological diagnosis forms the basis for possible specific treatment and sometimes prognosis. It is also important to assess and monitor kidney function, measurement of albuminuria and plasma albumin (Carrero et al., 2017; Kidney Disease Improving Global Outcomes [KDIGO], 2012).

Treatment

The primary goal is to treat the underlying disease but also to treat symptoms and prevent complications. Symptomatic treatment includes antihypertensive and antiproteinuric therapy (Königshausen & Sellin, 2017). KDIGO's recommendation are angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARB), restriction of dietary sodium, diuretics, statins and prophylactic anticoagulation when serum albumin <25 g/L (KDIGO, 2012).

The main treatment for patients with NS is depended on the underlying disease. In primary kidney disease immunosuppressive therapy is common, e.g. corticosteroids, cyclical corticosteroid/alkylating-agent regimen (KDIGO 2012; Nishi et al., 2016).

Prognosis

The prognosis in NS depends on the underlying disease that caused NS. For example, MCN has a good prognosis where the majority receive remission during treatment. In those patients who have MN, approximately one-third receive spontaneous remission of NS. Patients who have persistent high-grade proteinuria despite treatment have a worse prognosis (Clyne & Rippe, 2015).

Illness and symptoms

A disease is often described from a biomedical or physiological model constructed as a change in biological structure or function. A 'disease state' is a scientific explanation and defined by physicians based on the patient's symptoms and signs (Toombs, 1992). Symptoms are a subjective experience of illness noticeable to the patient, comprising changes that occur because of a disease. Signs are objective indicators, radiological or laboratory examination, of a disease or pathological condition (Oxford English Dictionary, 2021).

When people are feeling unwell or have various symptoms, they often do not say that they have a specific disease. Instead, they describe how the symptoms affect their lives, which is illness. Illness is the patient's perspective and experience of symptoms and suffering (Toombs, 1992). Illness is defined by Kleinman (1988) as:

Illness refers to how the sick person and the members of the family or wider social network perceive, live with, and respond to symptoms and disability. Illness is the lived experience of monitoring bodily processes such as respiratory wheezes, abdominal cramps, stuffed sinuses, or painful joints. (Kleinman, 1988, p. 3-4).

The different perspectives on illness and disease can have an impact on the relationship between the patient and the healthcare professionals because they do not share a common view of illness. For the patient illness is a lived experience, while for the physicians it is a scientific explanation (Toombs, 1992). The physician interprets the patient's subjective description of symptoms and together with objective signs a disease is conceptualized (Cassell, 1976). In healthcare the medical perspective is dominant, but in order to understand the patient's suffering, a holistic perspective is desirable where the patient's experience is required (Kottow, 2017).

Because NS can be caused by a chronic illness or have recurring periods of relapse, the patient often has periods of close and intensive contact with healthcare professionals. Unfortunately, patients with chronic illness often experience that they are defined as separate disease units and not as a whole person (Tong et al., 2009).

What characterizes a chronic condition is (a) that there is no cure, instead management over time is essential, (b) for effective treatment, the patient must engage continuously in different health care practices, (c) the patient becomes an expert on her/his condition and must guide its management over time, and (d) patients and healthcare professionals must share complementary knowledge (Holman & Lorig, 2004).

Self-management

The term self-management is often used in the care of patients with chronic illness to create control in their lives (Kralik et al., 2004). The purpose of self-management is "helping patients to maintain a wellness in their foreground perspective" (Lorig & Holman, 2003, p. 1). There are several well-established programmes for self-management and according to Lorig & Holman (2003), the programme must be based on patients' perceived problems and encompass:

- *Medical or behavioural management*: taking medication, adhering to a special diet.
- *Role management*: maintaining, changing, and creating new behaviours or life roles.
- *Emotional management*: dealing with the emotional sequel of having a chronic condition, which alters one's view of the future.

A review of 50 articles on self-management in CKD shows that most intervention topics concern medical or behavioural management such as diet/nutrition, general CKD knowledge and medication. Few self-management interventions were involved role management and emotional management (Donald et al., 2018).

Living with a chronic illness is not linear. The patient's problems change when the disease goes into remission or relapsing. Therefore, self-management support needs to meet the patient's trajectory of problems over time (Holman & Lorig, 2004; Paterson, 2001).

In a report from 2002, the World Health Organization (WHO) drew attention to the care of patient with chronic illness. WHO stated that patients cannot be passive recipients of care but must participate in the care and the healthcare staff must support it (World Health Organization, 2002). Person-centred care (PCC) is a concept used to highlight the importance of including the patient in the care and to respect the patient as a person (Pelzang, 2010). In PCC, the perspective has changed from focusing only on diseases and their limitations to focusing on the patient's perceived health and resources (Pelzang, 2010; Wallström & Ekman, 2018)

To understand the patient's problems, physicians and nurses need to consider her/his experience and illness narrative (Tate & Pearlman, 2019). A patient's narrative provides a unique perspective, leading to an understanding that can help the patient return to self-management and a healthier life. A patient's narrative is important in meeting the patient and not just focusing on the biological marker signs (Wallström & Ekman, 2018).

Rationale

NS has traditionally been approached from a physiological or medical perspective representing an outsider perspective based on reductionism and focusing on the disease based on pathophysiology. Therefore, the patient's view of the disease and consequences for her/his daily life are missing (Thorne & Paterson, 2000). To provide person-centred care as expected in health care today both the personal and the professional understanding of the disease is equally important. The insider and outsider perspectives differ from each other in four respects; the focus on the current situation, attitude towards the disease, relevance, and perception of time. Toombs (1992) argues that both insider and outsider perspectives are valid. From a medical point of view, establishing a diagnosis and focusing on symptoms can be considered as solving a puzzle. When the diagnosis is established, the puzzle is solved. However, the patient views the disease in terms of consequences for her/his everyday life (Toombs, 1992).

The rationale behind this thesis was to explore and describe the characteristics of experienced NS. The intention was to illuminate specific areas of concern and understand the consequences of NS in everyday life in order to provide a platform for self-management support. To address the outer perspective a second rationale was to illuminate clinically useful patterns to make further sense of this complex syndrome when approaching the patients' illness experience. The main reason for this thesis is to increase our knowledge by combining the inner and outer perspective for use in care and education of patients who suffer from NS.

Aim

The overall aim of this licentiate thesis was to explore personal experiences of illness and clinical characteristics among persons with nephrotic syndrome.

The thesis is based on two studies where the specific aims were:

- To explore patients' experience of suffering from nephrotic syndrome (Study I).
- To describe the causes of nephrotic syndrome in the Swedish population and to analyse how different clinical signs are associated with different diagnoses (Study II).

Methods

Design

This licentiate thesis consists of two studies with two different designs. An inductive qualitative design was employed to explain the patients experience of living with NS (Study I) and a deductive quantitative design was used to describe and analyse causes of NS and clinical characteristics (Study II). An overview of the studies is presented in Table 2.

Table 2. Overview of the studies in the thesis

| Study | Design | Patient population | Data collection | Data analysis |
|-------|--|--------------------|------------------------|--|
| I | Inductive, Qualitative | N=10 | Open-ended interviews | Phenomenological hermeneutical |
| II | Deductive, Quantitative, cross-sectional retrospective | N=913 | Swedish Renal Registry | Descriptive statistics, Mann-Whitney test, Chi-square test, independent t-test |

Description of the study cohorts

Participants (Study I)

The participants were consecutively recruited (Polit & Beck, 2021) between February 2016 and February 2019 at Skåne University Hospital, Lund. The criteria for inclusion were patients newly diagnosed or relapse with NS, ACR >300 mg/mmol and hypoalbuminaemia <28 g/L. During the study period, there were 10 eligible patients

(6 men and 4 women) who agreed to participate in the study. The cause of NS was MN (n=7) and MCN (n=3). The mean age was 57.8 years (range 21 to 90 years).

The Swedish Renal Registry (Study II)

In Study II we retrieved data from SRR, which is a national internet-based quality register for patients with CKD in Sweden. The SRR was launched in 1991 and consists of data in seven modules: epidemiology, kidney biopsy, CKD, dialysis, dialysis access, transplantation, and quality of life. Yearly, data entry to the register is a routine procedure at outpatient clinics and dialysis units. Information that can be retrieved from the register is e.g., kidney diagnosis, clinical parameters, laboratory measures and treatment outcomes (Welander & Sigvant, 2020). The annual reports show quality data related to a very large part of care, from investigation and treatment of primary kidney disease to kidney replacement treatment, kidney transplantation, and dialysis (SRR, 2020).

The biopsy module was launched in 2015 and captured nearly 40% of all native kidney biopsies in Sweden. Older biopsies from 2013 and 2014 can also be retrospectively retrieved. Currently, almost 3,800 patients are included, and the module contains data from 20 of Sweden's 21 counties. Data in the biopsy module include age, sex, height, weight, blood pressure, kidney function, clinical chemistry, serology, biopsy indication, medications, and comorbidities (Peters et al., 2020). For biopsy indication one of the following five alternatives has to be chosen: nephrotic syndrome, acute nephritic syndrome, other acute kidney injury, CKD 1-2 and CKD 3-5.

Data collection

Open ended interviews (Study I)

For Study I data were collected through open-ended interviews and all interviews were performed by the first author. It is important to select a setting where the participants feel comfortable, undisturbed, and able to speak freely (Taylor & Bogdan, 1984). Therefore, the participants could choose time and place for the interview, which took place at the nephrology ward (n=3) and at the nephrology outpatient clinic (n=7). To ensure that the key topics were explored and covered, an interview guide was developed (Taylor & Bogdan, 1984) with the following three opening questions: "Can you please tell me what happened when you became nephrotic or ill", "Can you please tell me

how your health has changed” and “How did you discover that you were ill”. Probing questions were posed when necessary to generate narratives of the experience. The interviews lasted for a median time of 33 minutes (range 21 to 52 minutes).

The Swedish Renal Registry (Study II)

Data from kidney biopsies performed between 1st January 2014 and 31st December 2019 were included in the study.

Step 1: Three searches were performed in the biopsy module: (1) biopsy indication nephrotic syndrome, (2) ACR >300 mg/mmol and (3) urine albumin >3.5 g/24 hours. The search generated a total of 1,734 entries. Data retrieved from the module at time of biopsy included patient age, sex, weight, kidney diagnosis, blood pressure, dipstick haematuria, plasma creatinine, eGFR (CKD-EPI), plasma CRP, plasma albumin, ACR, u-albumin/24h and blood haemoglobin.

Step 2: We excluded 821 of the 1,734 entries due to duplicates (n=633), age <18 years (n=4), missing plasma or urinary albumin data (n=21), biopsy before 1st January 2014 (n=7) and biopsy indication other than NS and plasma albumin >30 g/L (n=156). After exclusions, 913 patients were included in the analyses.

Step 3: The patients (n=913) were categorized into two groups: (a) those with biopsy indication NS (n=735) and (b) those who had laboratory parameters compatible with NS but where the main biopsy indication was not NS (n=178). The most common indication for biopsy in “other indication” group was CKD 3-5 (48.3%) followed by acute nephritic syndrome (30.9%), CKD 1-2 (11.2%) and acute kidney injury (9.6%).

Data analysis

Phenomenological hermeneutical method (Study I)

To analyse the text a method for researching lived experience based on Ricoeur’s theory was chosen (Lindseth & Norberg, 2004). Ricoeur’s interpretive phenomenology is based on the view of the capable human being, i.e. “homo capax” (Ricoeur & Backelin, 2011) and the relationship to personhood and person-centeredness (Ricoeur & Blamey, 1994).

This method involves three dialectical movements between understanding and explanation. The three steps comprise naïve reading, structural analysis, and comprehensive understanding.

Naïve reading: the purpose in this step is to become familiar with the text and gain an understanding of a phenomenon. The transcribed text was read several times to grasp the meaning. We formulated our understanding in a phenomenological language and validated it with the subsequent structural analysis.

Structural analysis: this step is the methodical instance of interpretation and a way of seeking to identify and formulate themes. The text was divided into meaning units where similarities and differences were identified. The meaning units were then condensed into themes and sub-themes. During the analysis the themes and sub-themes were reflected on in relation to the naïve understanding in order to validate it.

Comprehensive understanding: in this step the text was read again as a whole bearing the naïve understanding and the validated themes in mind. The themes and sub-themes were summarized and reflected on in relation to the research question and the context of the study, i.e., patients' experience of living with NS. Our preunderstanding and experience of patients with NS were important during the interpretation. We thought of associations with relevant literature about the meaning of lived experience. Based on this literature we formulated an interpretation of the experience of living with NS.

Statistical analyses (Study II)

- All analyses were performed using IBM SPSS software (version 26.0 SPSS Inc.) for Mac.
- Categorical variables (sex and grade of haematuria) were expressed as frequencies and percentages. To compare group differences between categorical variables we used the Chi-square (grade of haematuria) and Fisher's exact test (sex).
- Normal distributed variable (age) was expressed as mean \pm standard deviation (SD) and the independent sample t-test was used to compare the groups.
- Non-parametric continuous variables (laboratory parameters, weight, and blood pressure) were expressed as medians and interquartile ranges.
- The Mann-Whitney test was used to compare the two independent groups "indication NS" and "other indication".
- P-values <0.05 were considered statistically significant

Ethical considerations

The two studies conform to the ethical principles outlined in the Declaration of Helsinki for medical research involving human being and data (World Medical Association, 2013). Most ethical guidelines for research contain three principles that have been taken into account in the two studies: (a) beneficence, (b) respect for human dignity and (c) justice (Polit & Beck, 2021).

For **Study I** ethical approval was obtained from the Regional Ethical Review Board in Lund, Sweden (Reference number: 2016/505).

Participation in the study was not considered to cause any risks to the patient. The questions during the interview were controlled by the patient, which minimized the risk of the patient to experience the issues too sensitive or threatening the integrity.

The participants received verbal and written information by the first author about the purpose of the study and data collection procedures. They were informed that participation in the study was voluntary and that they have the right to withdraw from the study and it would not affect the medical treatment or nursing. They were also informed that confidentiality would be ensured. Each participant received an identification number, and it is only the first author that has access to the identification information.

All participants gave their written informed consent.

For **Study II** ethical approval was obtained from the Regional Ethical Review Board in Stockholm, Sweden (Reference number: 2018/1591-31/2).

Permission to retrieve data was approved by SRR.

The patients have earlier given their consent that data being registered in SRR. The data we received from SRR contained only the variables that were relevant to our research. Prior to data analysis, the patients were coded, and each patient received a specific identification number.

Results

This is a summary of the results from the two studies, for more details see each papers (Paper I-II). The findings are presented from an inside perspective and from an outside perspective.

From an inside perspective (Study I)

The structural analysis revealed that patient who were newly diagnosed with NS or had a relapse with NS ended up in a state of ambiguity. Being in ambiguity were illustrated by four main themes: *Feeling ill and well at the same time*, *Being passively adherent*, *Being in uncertainty* and *Trying to comprehend and cope* (Table 4).

Table 4. Structural analysis of the meaning of being in ambiguity among 10 patients with nephrotic syndrome captured in the following main themes and sub-themes.

| Sub-themes | Main themes |
|---|---------------------------------------|
| Experiencing physical changes Not noticing or understanding symptoms Being affected by the disease but managing everyday life | Feeling ill and well at the same time |
| Avoiding asking questions Trusting healthcare professionals Feeling powerless | Being passively adherent |
| Doubting the future Wondering about causes and prognosis Questioning one's own role | Being in uncertainty |
| Seeking information Acknowledging family support Willing to make lifestyle changes | Trying to comprehend and cope |

Almost all participants stated that they were *feeling ill and well at the same time*. They had physical changes such as swollen legs, weight gain and shortness of breath but did not understand that their signs or symptoms were due to kidney disease. The participants indicated that despite physical changes, they managed their daily lives. All

participant received high doses of diuretics, which they experienced limited their social function and freedom to leave their homes.

Being passively adherent meant that the participants trusted healthcare professionals in an unreflective and obedient manner. Even when the participant did not understand the advice and prescriptions, they avoided asking questions. This approach was explained by that they were not the type of person who asked questions or that they had no interest in the disease. Despite this, some of the participants felt powerless because they were unable to influence the disease, which led to a feeling of impotence

Most of the participants stated that they had not received enough information about the disease or how they could live with it. This resulted in a state of *being in uncertainty*. They wondered what caused the disease and if they might have done something themselves that caused the condition. Some of the participants felt doubts about the future, they did not know if they would get well again or if their condition would worsen.

The participants were *trying to comprehend and cope* handle the illness in the best possible way. Some of the participants searched for information about the disease on the Internet. Those who had relatives felt that they received good support from them. Although participants were willing to make the necessary lifestyle changes, they received no guidance. They tried themselves but were left alone in a limbo that was characterized by trial and error.

The results of study I indicated that patients suffering from NS are in an unfamiliar world of symptoms, signs and medical treatment without professional guidance. The patients were not invited into a partnership and caring relationship by a nephrology nurse or physician. Therefore, they ended up at a threefold disadvantage because they (a) were at the bottom of the hierarchical structure of the healthcare institution, (b) were suffering from a severe and disabling disease affecting their existence and (c) had a complete knowledge deficit causing a cognitive disadvantage (Ekman, 2020).

The patients had a willingness to learn and understand, but the lack of guidance from healthcare professionals regarding causes, prognosis and self-management activities increased their suffering and prevented health and well-being. The participants ended up in a state of constant ambiguity and uncertainty in illness, where self-management became a mission impossible without reliable support.

From an outside perspective (Study II)

Overall the patients (n=913) with NS had a mean age of 56.3 years and there were more men than women (57.8 vs. 42.2%) at time of kidney biopsy. The patients had moderate reduced eGFR (median 48 ml/min/1.73m²) comparable to CKD stage 3. Median ACR was 486 mg/mmol and median plasma albumin was 24 g/L. Most patients (48.2%) had grade 1-2 haematuria on dipstick analysis. The diagnoses that caused severe haematuria (grade 3-4) were MPGN (14.2%), IgAN (13.4%) and MN (13.4%).

The most common causes of NS were DN (17.5%), MN (17.2%) and MCN (15.3%). There was a variation of the causes in different age groups where MCN (20.7%) and MN (13.8%) were more common in age <49 years. DN (22.8%) and MN (18.5%) were most common with age 50-70 years. The largest difference in diseases more common in men were DN (20.5 vs 13.5%) and MN (19.5 vs. 14.0%). Diagnoses more common in women compared to men included SLE (8.3 vs. 0.8%), MPGN (7.3 vs. 4.5%) and MCN (17.4 vs. 13.8%).

Patients with reduced kidney function (CKD 5) were most common in DN (23.5%), other kidney diagnosis (17.3%) and vasculitis (16.3%).

Comparing “indication NS” and “other indication”

In “indication NS” group were MN (19%), MCN (18.5%) and DN (16.5%) the most common causes of NS. In “other indication” the most common causes were DN (21.9%), IgAN (14.0%) and other kidney diagnosis (12.4%).

There were significant (p<0.001) differences between the groups regarding kidney function. The patients in “other indication” had severely reduced eGFR compared to patients in group “indication NS” who had moderately reduced eGFR (median 24 vs. 56 ml/min/1.73m²). This is comparable with CKD stage 4 vs. CKD stage 3. The group “other indication” had higher plasma creatinine than “indication NS” (median 233 vs. 106 µmol/L). The fact that the patients in “other indication” had more reduced kidney functions may be due to that most patients had diagnose DN (21.9%) followed by IgAN (14.0%). DN was also the most common diagnosis in patients with CKD 3 (21.5%), CKD 4 (29.8%) and CKD 5 (23.5%).

The “indication NS” group differed from “other indication” group when comparing blood haemoglobin (median 126 vs. 113 g/L) and grade 3-4 of dipstick haematuria (26.2 vs. 43.5%). The fact that “other indication” group had more haematuria could partly be explained by the fact that IgAN and DN were more common in this group.

Discussion

Methodological consideration

As the two studies on which this thesis is based have a different scientific design, their quality and limitations are discussed separately. In qualitative studies, the term trustworthiness is used, while the corresponding terms in quantitative studies are validity and reliability (Polit & Beck, 2021). According to (Lincoln & Guba, 1985), there are four criteria that need to be established to ensure trustworthiness: credibility, dependability, confirmability, and transferability.

Study I

A phenomenological hermeneutical method based on Ricœur's interpretation theory was chosen (Lindseth & Norberg, 2004). This method has been used previously in various qualitative studies. A phenomenological approach reveals the meaning of the lived experience of a phenomenon. Hermeneutics focuses on the interpretation of the text, in this case the transcripts of the interviews. The researcher restructures the text to find meanings that lie beneath the surface. Parts that are similar to each other are brought together into larger units (Lindseth & Norberg, 2004).

Credibility

The overriding goal in qualitative research is credibility, which refers to the truth and the interpretations of data (Lincoln & Guba, 1985). To ensure credibility two of the researchers interpreted the data together. One of the researchers has extensive experience of working with patients with NS. The other researchers did not have such experience. Consecutive sampling was used and all available participants who met the criteria were included in the study. No new perspectives emerged after eight interviews but to ensure that we achieved saturation two further interviews were conducted. The large age and gender distribution among the participants contributed to a richer variation of experience of NS.

Dependability

Dependability refers to how stable data are over time and similar conditions (Lincoln & Guba, 1985). To establish dependability, the research process is documented and can be considered replicable with similar participants and conditions.

Confirmability

Confirmability refers to objectivity and that data states the participants' answers and not the researchers' perspectives (Lincoln & Guba, 1985). Confirmability was ensured by the rich quotations from the participants that illustrated each emerging theme.

Transferability

Transferability indicates the extent to which the findings can be applied to other settings or groups (Lincoln & Guba, 1985). It is up to the reader to decide whether our findings are transferable to another context. To facilitate such a decision, we have carefully described the context of the research and that data is based on a single centre study.

Study II

A generalizable result of quantitative research is based on the study's validity and reliability (Polit & Beck, 2021).

Study II is a retrospective register study where we retrieved data from the biopsy module of the SRR. The SRR has been widely used before and found to have good validity. However, the biopsy module has not yet been validated, which can be seen as a limitation (Peters et al., 2020).

To obtain as many patients and data as possible we retrieved data over the course of six years thus the amount of data can be considered a strength for the study's validity (Polit & Beck, 2021).

Appropriate selection and variables that could respond to the purpose increases the validity of the study (Polit & Beck, 2021). Therefore, a preliminary search of variables was performed, and the final search was conducted in March 2020 after the registry has been updated.

A limitation is that one region in Sweden did not report results from native kidney biopsies in the biopsy module. There are no statistics on how many kidney biopsies are performed annually in Sweden and therefore we cannot conclude that all native kidney biopsies are registered. However, according to the annual report of the SRR it is

estimated that between 70 and 80% of native kidney biopsies are registered in the module.

Another limitation was that the clinical symptoms that patients may have due to NS are not reported to the registry. Therefore, we could not compare symptoms to clinical parameters. This would have been desirable to describe the relationship between symptoms and signs.

Discussion of the findings

The overall aim of this thesis was to explore personal experiences of illness and clinical characteristics among persons with NS. The intention was to illuminate specific areas of concern and understand the consequences of NS in the everyday life of patients. But also to provide a platform for self-management support and increase the knowledge for use in care and education of patients who suffer from NS by combining the inner and the outer perspectives.

The inner and the outer perspective of NS

Becoming a patient means entering a new context, where the environment, actions and attitudes differ from the person's everyday life. The suffering patients can experience in healthcare can be described on the basis of three different variations of suffering: 'disease suffering', 'life suffering' and 'care suffering'. 'Disease suffering' is associated with the consequences of the disease such as physical limitations, symptoms and discomfort. 'Life suffering' is related to how people in care experience their lives and the changes involved. 'Care suffering' is caused by the care situation and the presence or absence of good care (Eriksson, 2015). The result of Study I indicates that suffering from NS means being in an unfamiliar world of symptoms and signs, a 'disease suffering'. To do not understand the symptoms and signs was leading to a state of ambiguity and uncertainty for the patients, a 'life suffering'. Patients experiencing uncertainty in illness is common and are described as "the cognitive state created when the person cannot adequately structure or categorize an event because of the lack of sufficient cues" (Mishel, 1988, p. 225). The results of Study II show that different diseases cause NS, and that symptoms and signs could differ depending on the cause. Therefore, the physician may also be in a state of uncertainty before a possible kidney biopsy and the establishment of a diagnosis. In addition to the stress of suffering from an illness, there will be additional stress for the patient if the physician is unable to provide an immediate diagnosis (Beanlands et al., 2017). The physicians' 'disease state' is not the

same as the patient's experience of disease (Toombs, 1992). The patient experiences illness and is aware that something is not well in the body and feels unfamiliar. The physician on the other hand, tries to conceptualize the signs and symptoms to establish a diagnosis (Toombs, 1990).

When the location of the symptoms is inconsistent it creates uncertainty (Mishel, 1988), which is also confirmed by our results. In Study II the results show that overall patients with NS have signs of heavy albuminuria and low plasma albumin, which could indicate that the patients have symptoms of oedema. In Study I all patients experienced symptoms of oedema but did not understand why they had these symptoms. Although the participants had severe oedema, shortness of breath and difficulty breathing they stated that they had not noticed any symptoms. It can be difficult to distinguish a pattern when symptoms are characterized by contradictions regarding the intensity, frequency, and location at which they occur. When the symptoms form a pattern, there is less uncertainty and less ambiguity about the disease (Mishel, 1988).

Uncertainty in Study I may arise from the patients' experience of lack of sufficient information about the disease and condition. To provide effective information to the patient, tailored information appropriate to her/his needs, vulnerabilities and capabilities should be used (Hashim, 2017). Active listening, open-ended questions and developing functional goals together with the patient are good strategies (Constand et al., 2014; Hashim, 2017). To achieve efficient treatment and care, patients and healthcare professionals need to share knowledge with each other and become partners (Holman & Lorig, 2004).

Person-centred care (PCC)

The gap between the patient's experience of illness and the healthcare professionals' views about the current diagnosis can be reduced through the patient's participation in care (Toombs, 1992). PCC care is an approach where the patient actively participates in the planning and implementation of her/his own care in collaboration with healthcare professionals (Constand et al., 2014).

One unexpected result in Study I was that the patients were passively adherent to treatments. This can be partly explained by that it was a disease that she / he had little or no experience from. But if we assume that the patient is a capable decision-maker and active in her/his illness management, patients need to get education and social support (Thorne & Paterson, 1998) to receive empowerment. In PCC, the patient is not reduced to her/his disease (Ekman, 2020) but is regarded as a person who can tell, can act and can be responsible (Ricoeur & Backelin, 2011).

When healthcare staff deliver person-centred care, they respect and confirm the person's experience and interpretation of being unhealthy and illness. O'Hare (2018) propose five strategies for patient-centred care: (1) "listening to the patient", (2) "allowing time for the complexity of the patient's situation", (3) "being willing to go beyond the job description in order to avoid fragmented care", (4) "re-imagining what it means to provide good care" and (5) "finally being aware of the value of relationship building" (O'Hare, 2018).

Patients with chronic illness often have close contact with healthcare providers and need to have good relationships with healthcare professionals over time. In order to manage their chronic illness, patients should feel free to ask questions and receive self-management support. It is necessary to establish a partnership between patient and professional, where medication adherence, functional abilities, knowledge and self-management are discussed (WHO, 2002).

Self-management

Patients with chronic illness can change between periods of severe illness and well-being (Paterson, 2001). One of the most common causes of NS in Study I and Study II where MCN and MN. Both MCN and MN are kidney diseases that in some patients often has recurring periods of relapses and remissions (Clyne & Rippe, 2015). Self-management could help patients to maintain their well-being in periods characterised by fluctuation of illness and well-being (Lorig & Holman, 2003). Patients with chronic illness who received self-management education believed that it plays an important role in understanding the biomedical construction and consequences of the disease process (Kralik et al., 2010). The participants in Study I were willing to undertake necessary lifestyle changes, but as they received no guidance, they were in a limbo characterized by trial and error. Lack of information about NS and its treatment could hamper self-management in a profound way (Beanlands et al., 2017).

Study II shows that some of the causes (e.g. DN, vasculitis, vascular diseases) reduce the kidney function, which may lead to dialysis or transplantation in the future. In Sweden, there is a well-established organization in the care of patients with ESKD with nurse practitioner who coordinates the patients care and educates the patients. But, there is no such well-established organization for patients with NS.

A self-management programme provided by nurses in the early stages of CKD contributes to increasing the physical and mental health components of HRQoL. Self-management also strengthens the patient's knowledge and self-efficiency (Nguyen et al., 2019). It is important that self-management programmes do not focus on the

disease itself but on the patient's perceived problems (Lorig & Holman, 2003). As person-centred care focuses on the patient's narrative and partnership, it makes it possible to obtain knowledge about her/his problems.

Conclusions

Although the cause of NS is known, the condition itself is complex for patients, their relatives, physicians and nurses. The kidney disease that causes NS can be chronic or characterized by periods of remission and relapse. When caring for these patients, more focus must be placed on supporting self-management so that the patient learns to recognize and control the symptoms that may occur from time to time.

The main conclusions are that:

- Patients with NS have difficulty understanding that their symptoms are due to a kidney disease, leading to them ending up in a state of ambiguity and uncertainty.
- Patients experience receiving insufficient information and a lack of professional support, which leads to difficulties achieving self-management.
- The most common causes of NS in adult patients in Sweden are diabetic nephropathy, membranous nephropathy and minimal change nephropathy.
- Clinical characteristics presented by patients with NS can facilitate the establishment of a diagnosis in cases where a kidney biopsy is not possible.

Clinical implications and future aspects

The findings in this thesis can support new guidelines and health promotion strategies in the care of patients with NS. When caring for patients with NS the knowledge from the inside and outside perspective is essential to increase the effectiveness of the collaborative work between healthcare professionals and patients.

The main clinical implications are that:

- The care for patients with NS should be organized in a more rigorous, person-centred way. The patients' narratives and experience should form the basis for the design of a healthcare plan.
- Nurse practitioners or a nephrology nurse should ensure a continuous learning process for patients and their relatives, in addition to supporting self-management.
- When approaching the patients' illness experience clinically useful patterns should be highlighted to help patients make sense of this complex syndrome.

Future aspects

- Introduce and evaluate a self-management programme in the clinic for patients with NS.
- Study HRQoL with RAND-36 when patients are diagnosed with NS and follow-up after one year.
- Evaluate HRQoL with RAND-36 during and after treatment for NS.

Populärvetenskaplig sammanfattning

Nefrotiskt syndrom (NS) är inte en sjukdom utan ett tillstånd med en grupp symtom som orsakats av olika njursjukdomar. Symtomen vid NS är läckage av protein i urinen, lågt albumin i blodet och generella ödem. Vid NS finns det en ökad risk för komplikationer som blodpropp, infektioner och njursvikt. NS är en av de vanligaste orsakerna till njurbiopsi och patienter med NS är vanligt förekommande på njurmedicinska kliniker. Njursjukdomen som orsakar NS kan vara kronisk eller gå i skov. Tidigare forskning visar att patienter som har kronisk njursjukdom har en låg hälsorelaterad livskvalitet och hög risk för depression, jämförbart med patienter som behandlas med hemodialys.

NS är ett komplext tillstånd där patienter inte helt förstår tillståndet och hur tillståndet påverkar hälsan. Det blir därför svårt för patienterna att hantera symtomen som uppstår, vara följsamma till aktuell behandling, hantera eventuella fysiska och psykosociala problem samt göra de livsstilsförändringar som behövs. Patienterna behöver stöd vid egenvård för att kunna främja sin hälsa. Det kan också vara svårt för läkare och sjuksköterskor att förstå tillståndet eftersom symtomen och tecknen är förknippade med olika diagnoser och prognoser.

Mycket av forskning om NS har haft fokus på patofysiologi och behandling och mindre om patientens erfarenhet av att leva med NS. Ett helhetsperspektiv inom sjukvården med utgångspunkt i personcentrerad vård är önskvärt där även patientens erfarenhet synliggörs för att underlätta för stöd vid egenvård.

Det övergripande syftet med denna avhandling var att undersöka patienternas erfarenheter av NS och de kännetecknen hos personer med NS uppvisar. Avhandlingen bygger på två studier där syftet med studie 1 var att undersöka personers upplevelse av att drabbas av NS. Syftet med studie 2 var att beskriva orsakerna till NS i den svenska befolkningen och analysera hur olika kliniska tecken kan associeras med olika diagnoser.

I studie 1 intervjuades 10 patienter, sex män och fyra kvinnor, som insjuknat i NS mellan åren 2016-2019. Medelålder hos patienterna var 58 år (21-90 år). Intervjuerna analyserades med hjälp av fenomenologisk hermeneutisk metod. Resultatet visade att patienterna som insjuknade i NS:

- Kände sig sjuka och friska på samma gång. De upplevde fysiska förändringar men förstod inte att symtomen orsakades av en njursjukdom. Även om patienterna var påverkade av sjukdom klarade de av det vardagliga livet.
- Var passivt följsamma till de råd och anvisningar som läkare och sjuksköterskor gav. De undvek att ställa frågor och litade på personalen. Samtidigt kunde patienterna känna sig maktlösa.
- Kände osäkerhet och tvivel inför framtiden. De undrade över vad som orsakat tillståndet och om de själva hade orsakat det.
- Försökte förstå och hantera tillståndet genom att söka efter information. De fick stöd från närstående och var villiga till livsstilsförändringar.

Sammantaget ledde detta till att personer med NS var i ett tillstånd med tvetydighet och behövde få hjälp av vårdpersonal med information och stöd vid egenvård.

För att undersöka orsaker till NS i Sverige hämtade vi data från det nationella svenska njurregistret (Studie 2). Vi inkluderade data från patienter som blivit njurbiopsierade mellan åren 2014-2019. Vi gjorde tre sökningar i registret: (1) biopsiindikation NS, (2) albumin-kreatinin kvot >300 mg/mmol och (3) urin albumin >3.5g/dygn. Efter sökningarna hade vi 1734 träffar. Av de 1734 träffarna exkluderades: patienter <18 år, där värden på plasma albumin och urin albumin saknades, där njurbiopsi var utförd före januari 2014, där biopsiindikationen var annan än NS och plasma albumin >30g/l. Efter att ha exkluderat 821 träffar hade vi kvar 913 unika patienter som ingick i analysen där vi utförde olika statistiska analyser. Inför analysen delade vi in patienterna i två grupper: (1) biopsiindikation NS och (2) patienter där laboratorievärdena visade på NS, men biopsiindikation var inte NS, denna grupp kallade vi ”annan indikation”

Resultatet från studie 2 visade att medelåldern hos patienter som insjuknade med NS var 56 år. De vanligaste orsakerna till NS i Sverige var *diabetes nefropati*, *membranös nefropati* samt *minimal change nefropati*. Detta skiljer sig inte från många andra länder. Vid jämförelse mellan grupperna (i) och (ii) hade patienterna i gruppen ”annan indikation” mer njurpåverkan. I denna grupp var de vanligaste orsakerna till NS diabetes nefropati och IgA-nefrit, vilka ofta leder till njurpåverkan. Orsakerna till NS skiljde sig åt mellan olika åldersgrupper, där minimal change nefropati och membranös nefropati var vanligast hos personer yngre än 49 år. Diabetes nefropati och membranös nefropati var vanligare hos patienter äldre än 50 år. Generellt var det fler män med NS utom där orsaken till NS var systemisk lupus erythematosus.

Denna avhandling beskriver två olika perspektiv på NS, ett inre och ett yttre perspektiv. Båda perspektiven är viktiga i vården av patienter med NS. De viktigaste resultaten är att:

- Patienter med NS har svårt att förstå att deras symtom beror på en njursjukdom vilket leder till oklarheter och osäkerhet.
- Patienter med NS får otillräcklig information och det saknas professionellt stöd, vilket leder till svårigheter för att utföra egenvård.
- Kliniska tecken vid NS har en väsentlig inverkan på troliga diagnoser hos vuxna patienter med NS.

Även om orsakerna till NS är välkända är själva tillståndet komplicerat för patienter, närstående, läkare och sjuksköterskor. NS påverkar patienterna framgent, då eftersom orsaken till NS kan vara kronisk eller kännetecknas av perioder med remission och återfall. Vården av patienterna behöver ha mer fokus på att stödja vid egenvård så att patienten lär sig känna igen och kontrollera symtomen vid NS.

- Vården för patienter med NS bör organiseras på ett mer rigoröst och personcentrerat sätt. Patientens berättelser och erfarenheter ska ligga till grund för utformningen av en hälsoplan.
- Njursjuksköterskan bör säkerställa ett kontinuerligt lärande för patienter och deras anhöriga samt stödja vid egenvård.
- Orsakssamverkan mellan symptomen vid NS och sjukdomen (diagnosen) behöver förtydligas för att öka patienternas kunskap så de kan utöva egenvård.

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