

CLINICAL FEATURES IN NEPHROTIC SYNDROME PATIENTS: A CASE REPORTMade Maylisca Theresia Mulya Diprasta¹, Lavenda Diarnasa Zihara Safira², LevinaLarassanti³, M. Shadiqul Amin⁴, Ronald Pratama Adiwinoto⁵

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Edema, Proteinuria,
Hypercholesterolemia**Abstract**

Nephrotic Syndrome is a glomerular disease characterized by edema, massive proteinuria >3.5 grams/day, hypoalbuminemia <3.5 grams/day, hypercholesterolemia, and lipiduria. Nephrotic syndrome has a variety of metabolic effects that impact the individual. Some episodes of nephrotic syndrome are self-limited, and some respond to specific therapy, while others are chronic. A 49 year old female patient complained of frequent sweats at night and chills in the morning. Then, the patient complained that his legs had been swollen since he left the hospital until now. Apart from that, edema also occurs in the lower extremities. The management given is general management such as rest, low cholesterol, low salt, fluid restriction <1500ml, and a protein diet. Treatment of edema with diuretics, treatment of proteinuria, treatment of hypertension and history of stroke, as well as causal treatment according to the etiology of nephrotic syndrome. The patient has undergone management planning and treatment therapy for nephrotic syndrome.

Corresponding Author: Ronald Pratama AdiwinotoEmail: adiwinoto.ronald@hangtuah.ac.id**INTRODUCTION**

Nephrotic syndrome is a glomerular disease characterized by edema, massive proteinuria >3.5 grams/day, hypoalbuminemia <3.5 grams/day, hypercholesterolemia, and lipiduria (Kaluku, 2023). Nephrotic syndrome has various metabolic effects that impact individuals. Some episodes of nephrotic syndrome are self-limited, and some respond to specific therapy, while others are chronic conditions (Kharisma, 2017). Nephrotic syndrome can be caused by primary and secondary glomerulonephritis due to infection, malignancy, connective tissue disease, drugs or toxins, and due to systemic disease. The cause of nephritic syndrome in adults is associated with systemic diseases such as diabetes mellitus, amyloidosis, or systemic lupus erythematosus. The following is the classification and causes of nephrotic syndrome (Parmadi & Pratama, 2020).

The mechanism of edema in nephrosis syndrome is due to changes in cells in the glomerular basement membrane. This causes the membrane to become hyperpermeable (because it is porous), so a lot of protein is lost in the urine (proteinuria). The large amount of protein lost in the urine causes serum albumin to decrease (hypoalbuminemia) (Eriguchi et al., 2017). A lack of serum albumin results in a lack of serum osmotic pressure. Capillary hydrostatic pressure in tissues throughout the body becomes higher than capillary osmotic pressure (Darwish & Lui, 2019). Therefore, edema occurs throughout the body. The more fluid that collects in the tissue (edema), the less the plasma volume stimulates the aldosterone secretion to retain sodium and water. This retained water will also come from the capillaries and worsen the edema (Putra, 2020). The existence of other factors that also play a role in the formation of edema can be demonstrated by the observation that some

patients with nephrotic syndrome have normal or increased intravascular volume and normal or decreased plasma renin and aldosterone levels. Hypothetical explanations include intrarenal defects in sodium and water excretion or the presence of circulation agents that increase capillary walls' permeability throughout the body and the kidneys.

Globally, the incidence of nephrotic syndrome in children aged less than 18 years is 2 to 7 cases per 100,000 per year. Nephrotic syndrome occurs more often in boys, but in adulthood, there is no difference in incidence between men and women. In the pediatric population, nephrotic syndrome is most often caused by minimal change disease. In contrast, in the adult population, diabetic nephropathy is the most common cause of nephrotic syndrome (Piccini et al., 2023). In the United States, diabetic nephropathy-associated nephrotic syndrome occurs with an incidence of 50 cases per 1 million adult population. In South Asia, including India and Pakistan, kidney biopsy findings of nephrotic syndrome patients show the same pattern as in Western countries. However, in Middle Eastern and African countries, nephrotic syndrome is associated with urogenital schistosomiasis infection (Sinnakirouchenan, 2021).

Meanwhile, the national incidence rate of nephrotic syndrome in Indonesia is not yet known. Several observational studies in local referral hospitals indicate that nephrotic syndrome in Indonesia is more common in boys, the same as global data (Suwantopo et al., 2020). In Indonesia, there have been reported incidents of 6/100,000/year in boys and girls with a ratio of 2:1 (Albar & Bilondatu, 2019). Meanwhile, the incidence that occurs in adults is 3/100,000 people. Around 80% to 90% of NS cases in adults are idiopathic, which means the leading cause is unclear. Meanwhile, for kidney disease in general, the prevalence in men (0.3 %) is higher than in women (0.2%). Based on age characteristics, the highest prevalence is in the age category over 75 years (0.6 %), where an increase begins at 35 years and over.

The diagnosis of nephrotic syndrome (SN) in adults can be made if there is massive proteinuria (= 3.5 g per 24 hours) or equivalent to = 3.5 g/gCr at spot urine, hypoalbuminemia (= 3.0 g/dL), edema, as well as dyslipidemia (Piccini et al., 2023). Meanwhile, according to the Indonesian Pediatric Association (IDAI), the diagnostic criteria for nephrotic syndrome (SN) is massive proteinuria (> 40 mg/m² body surface area/hour, or 50 mg/kg/day, or urine protein/creatinine ratio at > 2, or dipstick = 2+), hypoalbuminemia (< 2.5 g/dL), edema, and can be accompanied by hypercholesterolemia (> 200 mg/dL) (IDAI, 2012).

RESEARCH METHODS

A 49 year old female patient complained of frequent sweats at night and chills in the morning. In October 2022, the patient admitted to suffering from MRS for three days because his blood sugar was 300 mg/dl, blood pressure 190/150, and left side weakness. later, he was diagnosed with a stroke. January 2023, MRS patient returned for three days because blood sugar was 46 mg/dl, dizziness, weakness, shaking; and since then, the patient no longer takes diabetes medication. Then, the patient complained that his legs were swollen since he was last discharged from the hospital in January 2023. The swelling was initially in the left leg, then swelling in the right leg. His legs were said to be difficult to walk on, and the patient was assisted with a cane every day. The patient's bladder and bowel movements are regular. Classic clinical manifestations of NS include edema on the face, especially in the morning when waking up, which is characterized by swelling of the eyelids. Other symptoms that patients may complain of are foamy urine, fatigue, shortness of breath, decreased appetite, weight gain due to edema, red rash, photosensitivity, arthralgia and neuropathic pain. On physical examination, nephrotic syndrome (SN) can show protein malnutrition which causes loss of body mass accompanied by massive proteinuria. However, these signs may be masked by weight gain due to concomitant edema. Increased blood pressure can be detected by checking vital signs. On chest examination, a trachea may be pushed, decreased vocal fremitus on palpation, abnormal deafness of the hemithorax on percussion, and decreased or absent breath sounds on auscultation. This indicates the presence of pleural effusion. If ascites is present, a dull, shifting feeling may be found on abdominal

examination. Other physical findings include xanthelasma due to severe hypercholesterolemia, SLE rash, Muehrcke's lines on nails due to hypoalbuminemia, easy bruising and neuropathy in amyloidosis, positive occult blood examination in the SN due to gastrointestinal malignancy, and on fundoscopic examination diabetic retinopathy can be found.

RESULTS AND DISCUSSION

Nephrotic syndrome (SN) is a clinical condition with symptoms of proteinuria, hypoalbuminemia, edema, and hypercholesterolemia. If undiagnosed or not treated immediately, interstitial edema will increase proximal tubular pressure, which causes a decrease in glomerular filtration rate (GFR) and kidney failure (Amalia, 2018). The kidney glomeruli of Nephrotic Syndrome patients are damaged so that protein can pass through the glomerular membrane and come out in the urine. This condition is called proteinuria. Damage to the glomerular membrane in Nephrotic Syndrome sufferers is usually so severe that much protein is excreted in the urine. This condition is known as massive proteinuria.

Based on the etiology, NS is divided into three: congenital, idiopathic/primary, and secondary. Nearly 90% of NS cases in children are idiopathic. Based on the histopathological picture, there are several forms of Nephrotic Syndrome. The most common forms are minimal lesions (85%), focal segmental glomerulosclerosis (10%), diffuse proliferative mesangial (3%), and membranoproliferative glomerulonephritis (2%). These four forms are part of idiopathic NS. Based on the response to corticosteroid therapy, it is divided into Steroid Sensitive Nephrotic Syndrome (SNS) and Steroid Resistant Nephrotic Syndrome (SNRS). NS classification based on response to corticosteroid therapy is often found in clinics today. Nephrotic syndrome with minimal histopathological lesions generally (80%) responds well to steroid administration. At the same time, the features of focal segmental glomerulosclerosis, diffuse proliferative mesangial, and membranoproliferative glomerulonephritis are generally resistant to steroid administration (Manalu, 2019).

The SN diagnosis is based on clinical symptoms, which are often characterized by edema that first appears in the area around the eyes and lower extremities. Blood pressure increases in 25% of children, and diarrhea from intestinal edema and respiratory distress from pulmonary edema or pleural effusion can be found. In some instances, it can be accompanied by hypertension and hematuria (Ramatillah et al., 2019). The patient is said to have relapsed nephrotic syndrome if proteinuria ≥ 3.5 g /day occurs after complete remission has been achieved for > 1 month. Based on the results of previous medical records, this patient was said to be suffering from nephrotic syndrome and had undergone complete treatment in 2015, but currently (in 2017), the patient was again diagnosed with nephrotic syndrome because the patient was found to have urine protein (+3), albumin 2.4 g / dl and total cholesterol 396 g/dl. So, it is said that the patient has relapsed nephrotic syndrome (Wiguna & Sudhana, 2019).

The pathophysiology of nephrotic syndrome includes edema, hyperlipidemia, thromboembolism, infection, anemia, and bone disorders. Theories regarding the occurrence of edema in nephrotic syndrome are the theory of underfilling and primary sodium retention. Based on the underfilling theory, edema is caused by a decrease in intravascular fluid volume (hypovolemia) due to a decrease in plasma oncotic pressure caused by hypoalbuminemia. A decrease in plasma oncotic pressure causes intravascular fluid to escape into the interstitial space, resulting in hypovolemia. Hypovolemia causes blood flow to the kidneys to decrease and triggers the release of aldosterone. This hormone will cause sodium and fluid retention, resulting in edema (Tjiptaningrum & Aulia, 2019). Pathogenic mechanisms that are thought to occur in NS can be divided into three large groups: (1) due to immunological processes with environmental and endogenous factors that act as triggering and risk factors that aggravate glomerular abnormalities, (2) due to biochemical abnormalities, usually in congenital abnormalities such as genetically inherited metabolism of proteins, lipids and carbohydrates, (3) due to hemodynamic abnormalities that disrupt the integrity of the glomerular capillary circulation (Raharja, 2014).

The typical leading causes of nephrotic syndrome are intrinsic kidney diseases, such as membranous nephropathy, minimal change nephropathy, and focal glomerulosclerosis. Secondary causes may include systemic diseases like lupus erythematosus, diabetes mellitus, and amyloidosis. Congenital/hereditary focal glomerulosclerosis can occur due to genetic mutations in podocyte proteins, such as podocin, nephrin, or cation channel protein 6. Nephrotic syndrome can also be caused by drug abuse (Piccini et al., 2023), including heroin. Secondary causes of nephrotic syndrome are as follows:

- a. Diabetes mellitus
- b. Immune: lupus erythematosus, antibody vasculitis, Berger's disease, acute post-infectious nephritis of the glomeruli, antineutrophil cytoplasmic neutrophil (ANCA), Goodpasture syndrome, extramembranous or membranoproliferative glomerulonephritis, thrombotic microangiopathy, alloantibodies from enzyme replacement therapy, or nonsteroidal anti-inflammatory drug (NSAID) toxicity or gold salt
- c. Infections: human immunodeficiency virus (HIV), hepatitis B virus, hepatitis C, cytomegalovirus, parvovirus B1, preeclampsia, toxoplasmosis, amyloidosis, and paraproteinemia

The clinical picture that occurs is generally anamnesis in patients with nephrotic syndrome with frequent complaints, namely edema or swelling. Edema usually starts in the lower extremities, such as the legs, with high intravascular hydrostatic pressure. Apart from that, it can also occur in the periorbital and genital areas (scrotum) with low intravascular hydrostatic pressure. Other complaints include weight gain, weakness, and foamy urination. If the edema is severe and spreads, it can manifest as anasarca edema with swelling throughout the body. Other symptoms that appear as manifestations of diseases that cause secondary nephrotic syndrome include diabetes mellitus, lupus nephritis, history of drugs, history of malignancy, or amyloidosis. Ascites, pleural effusion, and symptoms of UTI may also be found in patients. Muehrcke's bands found on the nails may be associated with periods of hypoalbuminemia. The patient's history can reveal if nephrotic syndrome occurs due to systemic or secondary disease, for example, drugs or malignancy (Nilawati, 2016).

In the case that occurred, based on a physical examination on February 7, 2022, it was found that the patient's general condition appeared to be mildly ill. On examination of vital signs, blood pressure was 150/80 mmHg, pulse 80 times/minute, respiratory rate 19 times/minute, and axillary temperature was 36.50C. The head, neck, thorax, and abdomen were within normal limits on physical examination. On physical examination of the upper and lower extremities, weakness was found in the left limb; the acral was warm, dry, and red. There was edema in both legs. Complete blood laboratory results showed Hb = 9.2 g/dl and HCT = 28.8%. For triglyceride examination, the results were 163 mg/dl and LDL cholesterol 240 mg/dl. The results of a complete urine examination showed urine protein 3+. Creatinine examination resulted in 1.71 mg/dl. Serum electrolyte examination showed a potassium result of 2.49 mmol/L. For random blood sugar (GDA) tests, the results were 121 mg/dl. On chest x-ray examination, an enlarged cast or cardiomegaly is seen.

Based on the results of the history, physical examination, and supporting examinations that have been carried out, a diagnosis can be made for this patient, namely secondary nephrotic syndrome. Thus, what the patient needs to do is as follows.

1. Consult the patient with a specialist in internal medicine
2. Explain to patients that nephrotic syndrome is a chronic disease that can relapse and requires long-term monitoring
3. Explain to the patient that in severe conditions, there is a risk of complications from kidney failure, so the patient requires dialysis or a kidney transplant.
4. Educate patients on adequate rest, limiting heavy physical activity, low cholesterol, and low salt diet.
5. Educate patients to limit daily fluids to <1500 ml/day.

6. Patient education regarding the recommended daily diet is sufficient calories and protein (1 g/kg/day). On the other hand, if the diet is low in protein, protein energy malnutrition (MEP) will occur.
7. Educate patients on a low-salt diet (sodium <2400 mg/day). In patients with hypertension, sodium consumption is limited to <1500 mg/day.
8. Educate patients to continue taking medication regularly and check with an Internal Medicine Specialist for treatment evaluation.
9. We are educating the patient's family to remind the patient about the routine of taking medication and the Medication Monitor (PMO).
10. Educate patients to eat nutritious foods and always maintain cleanliness.
11. Explain to patients that consuming corticosteroids for the management of nephrotic syndrome can cause the patient to be immunocompromised.
12. We are educating patients and families to prevent nephrotic syndrome, such as regular check-ups with doctors, avoiding cigarette smoke, eating a balanced diet, getting adequate rest, and managing stress well (Rahman, 2021).
13. Educate patient family members about healthy lifestyles; drink at least 1 liter of water/day, reduce consumption of sweet drinks, limit consumption of foods that are too salty, and exercise diligently at least twice a week.

Efforts to prevent the secondary etiology of nephrotic syndrome can be carried out through the non-communicable disease program of the Ministry of Health of the Republic of Indonesia in the form of CREDIT, which is an acronym for

1. Check your health regularly
2. Get rid of cigarette smoke
3. Have regular physical activity
4. Balanced diet
5. Get enough rest
6. Manage stress

To control hypertension, you can do PATUH, which is an acronym for:

1. Check your health regularly and follow the doctor's recommendations
2. Treat the disease with appropriate and regular treatment
3. Stick to a diet with balanced nutrition
4. Strive for physical activity safely
5. Avoid cigarette smoke, alcohol, and carcinogenic substances.

Reducing the consumption of packaged drinks and controlling intake can also reduce the risk of developing diabetes, which can be a secondary etiologic of nephrotic syndrome. A low salt, protein, and fluid diet should also be attempted to prevent the disease from progressing.

CONCLUSION

Nephrotic Syndrome is a glomerular disease characterized by edema, massive proteinuria >3.5 grams /day, hypoalbuminemia <3.5 grams/day, hypercholesterolemia, and lipiduria. Nephrotic syndrome can be caused by primary and secondary glomerulonephritis due to infection, malignancy, connective tissue disease, drugs or toxins, and due to systemic disease. In this patient, the results of a physical examination on February 7, 2022, showed that there was edema in both extremities, the face was asymmetrical (the left lip dropped slightly), blood pressure reached 150/90, and the motor strength of the left extremity was reduced. Meanwhile, on supporting examinations, proteinuria and hypercholesterolemia were found. Where the results of the physical and supporting examinations support the diagnosis of secondary nephrotic syndrome due to a history of systemic disease (diabetes) in this patient. The management given is general management such as rest, low cholesterol, low salt, fluid restriction <1500ml, and protein diet. Treatment of edema with diuretics, treatment of proteinuria, treatment for hypertension and history of stroke, as well as causal treatment according to the etiology of nephrotic syndrome. The patient has had management planning and therapy by the treatment of nephrotic syndrome.

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