



Blood Pressure Differences in Nephrotic Syndrome Patients with Steroid Resistant Nephrotic Syndrome Patients and Steroid Sensitive Nephrotic Syndrome

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Abstract

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BACKGROUND: Syndrome nephrotic is the most common kidney disease found in pediatric kidney disease, classification based on clinical response to steroids or histopathological characteristics. Increased blood pressure in steroid-resistant nephrotic syndrome (NS) is still a complication to be aware of in cases of NS.

AIM: The aim of the study was to determine the differences in systolic and diastolic blood pressure in patients with steroid-sensitive NS and steroid-resistant NS.

METHODS: Analytical correctional study in 50 children with NS divided into 25 Steroid Resistant NS (SRNS) groups and 25 steroid sensitive NS (SSNS) people who met inclusion and exclusion criteria to assess systolic and diastolic blood pressure in each group in pediatric nephrology division of the general hospital of Haji Adam Malik Medan.

RESULTS: There is a difference in systolic blood pressure in the SRNS and SSNS groups which mean $p = 0.024$ and there is no difference in diastolic blood pressure in the SRNS group with SSNS $p = 0.358$. If linked levels of proteinuria to blood pressure, systolic and diastolic in both groups found no significant link $p > 0.05$ high blood pressure with the degree of proteinuria in both group.

CONCLUSION: There are differences in systolic blood pressure in the SRNS and SSNS groups.

Introduction

Hypertension that occurs in nephrotic syndrome (NS) is an event that will cause a poor prognosis in cases of NS both in the Steroid Resistant NS (SRNS) group and in the steroid sensitive NS (SSNS) group [1]. According to a 2011 study in Bangladesh found, more hypertension incidence was found in SRNS compared to the SSNS group [2]. However, in another study in Manado, the average systolic and diastolic blood pressure was higher in the SSNS group than in the SRNS group [3].

NS is most commonly found in boys (with a male ratio: female 1.5–2:1) where most sufferers are children from the Asian continent [4]. According to the response to steroids, SN can be classified into two, namely, SSNS and SRNS [1]. Syndrome nephrotic sensitive steroid cover 80–90% syndrome while the rest is SRNS [2].

Proteinuria is one of the signs of NS [1]. Proteinuria is a condition in which the selectivity of glomerulus is disrupted so that proteins can be found in the urine [5]. A 2006 study of 29 children found a link between proteinuria and hypertension in 14 children [6].

Research in Indonesia 2019 on 484 schoolchildren aged 12–14 without symptoms found incidence of hypertension 12.9% and proteinuria 7.42% [7].

Hypertension that occurs in children aged <1 year and > 8 year in children with renal impairment causes a poor prognosis [8]. Hypertension is more common in SRNS than SSNS ($p > 0.05$), steroid therapy is associated with the incidence of hypertension in an SN treatment regimen ($p < 0.01$) [2]. Patient SSNS has a higher average systolic and diastolic blood pressure than SRNS, but this hypertension event is not statistically meaningfully related to SRNS and SSNS [3]. Almost the same research was also conducted by Mamesah *et al.* at RSUP Prof Dr. R. D. Kandou Manado. They found that SRNS patients had a higher average systolic and diastolic blood pressure than SSNS, and this incidence of hypertension was not associated with the incidence of SRNS and SSNS [9].

There were differences in blood pressure in both the SRNS and SSNS groups from several studies to see the difference in blood pressure of SSNS and SRNS sufferers at The General Hospital of Haji Center Adam Malik Medan.

Methods

This study is a correctional study conducted in NS patients treated in the nephrology division from July 2020 to September 2020. The size of the samples in this researcher was calculated based on a categorical formula of no pairs. Calculations were carried out using a 95% confident interval with a sample count of at least 22 patients. Informed consent obtained from all participants involved in the study, inclusion criteria are NS patients aged 1–18 years; patients have been getting steroid treatment for 4 weeks. Exclusion criteria are patients with acute or chronic renal failure, patients with chronic diseases such as severe malnutrition, pulmonary tuberculosis and malignancy.

Characteristic data of study subjects such as clinical manifestations and demographic data, physical examination and anthropometry collected during outpatient, blood pressure examination conducted using sphygmomanometer, and proteinuria check by Sysmex XN 1000.

Data analysis

Univariate analysis was conducted to obtain the spread of characteristics of the research sample. Normal distributed numerical data is presented in standard mean and deviation, in addition to being presented in maximum or minimum values. Categorical data are shown in percentages and frequencies. Chi-Square test was to assess gender characteristic differences, Mann–Whitney test to assess differences in systolic and diastolic blood pressure. The Wallis–Kruskal test was used to compare degree of proteinuria in both groups. Proteinuria's relationship with blood pressure was assessed with the Kruskal–Wallis test. Data processing was conducted using Statistical Package for Social Sciences for Windows (SPSS) version 24.0, 2016 with a $p < 0.05$ significance level and a 95% confident interval.

Ethical considerations

This study was approved by Health Research Ethics Committee Medical Faculty, Universitas Sumatera Utara.

Results

In this study, each group of 25 SRNS and 25 SSNS children who met the criteria for inclusion and exclusion were involved in this study. Characteristic data

showed that the distribution of male children was highest in the SRNS group of 18 (72%) and the distribution of many female children in the SSNS group 17 (68%) from this data there is a meaningful difference with $p = 0.005$. Median age in the SRNS group was 10 years and in the SSNS group of 12.5 years with a minimum age of almost the same in both groups. In systolic blood pressure values were found to be cyclical differences in both groups with a value of $p = 0.024$ ($p < 0.05$), where in the SSNS group it was found to be a higher systolic median than in the SRNS group. In the diastolic blood pressure value, there was no significant difference in both groups with a value of $p = 0.354$ ($p > 0.05$) with the median equal at 70 mmHg.

Table 1: Subject characteristics

Subject characteristics	SRNS (n = 25)	SSNS (n = 25)	p
Gender, n (%)			0.005 ^a
Male	18 (72)	8 (32)	
Female	7 (28)	17 (68)	
Age, mean (SD), years	10 (8.4–17.8)	12.5 (3.1–17.8)	0.432 ^b
Body weight, mean (SD), kg	32.92 (16.12)	39.30 (16.81)	0.178 ^c
Body height, mean (SD), cm	131.40 (28.35)	136.76 (22.19)	0.460 ^c
Blood pressure			
Systolic, median (min-max) mmHg	100 (90–140)	110 (100–170)	0.024
Diastolic, median (min-max) mmHg	70 (60–100)	70 (60–100)	0.358
Proteinuria, n (%)			0.092 ^d
Negative	11 (44)	12 (48)	
+1	11 (44)	4 (16)	
+2	3 (12)	8 (32)	
+3	0	1 (4)	

^aChi-square, ^bMann–Whitney, ^cT Independent, ^dKruskal–Wallis, SRNS: Steroid-resistant nephrotic syndrome, SSNS: Steroid sensitive nephrotic syndrome.

The basic characteristic data of research subjects are shown in Table 1 and Figures 1 and 2.

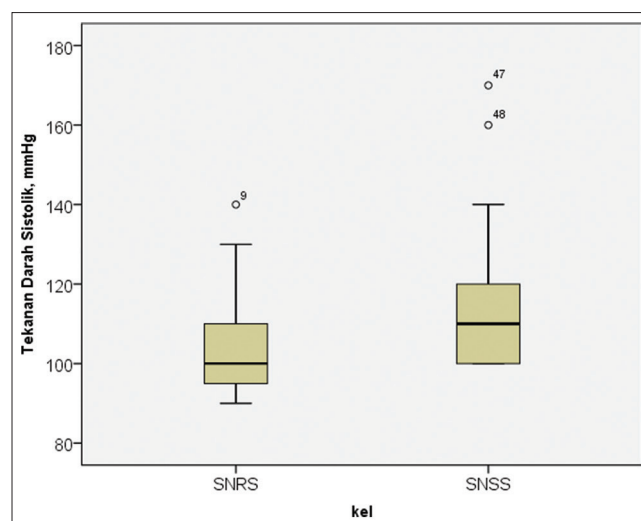


Figure 1: Systolic blood pressure boxplot chart in steroid-resistant nephrotic syndrome (NS) and steroid sensitive NS groups

There was no correlation between proteinuria levels and median blood pressure and systolic blood pressure in both the SSNS and SRNS groups. In the SSNS group proteinuria negative and +2 found the median systolic and diastolic values were higher than others $p = 0.597$ and SRSS $p = 0.088$ but meaningless. In the SRNS group had a median systolic value equal to all three degrees of proteinuria. At diastolic values, the SRNS group found higher median values in proteinuria +1 and +2 compared to proteinuria negative. The correlation proteinuria

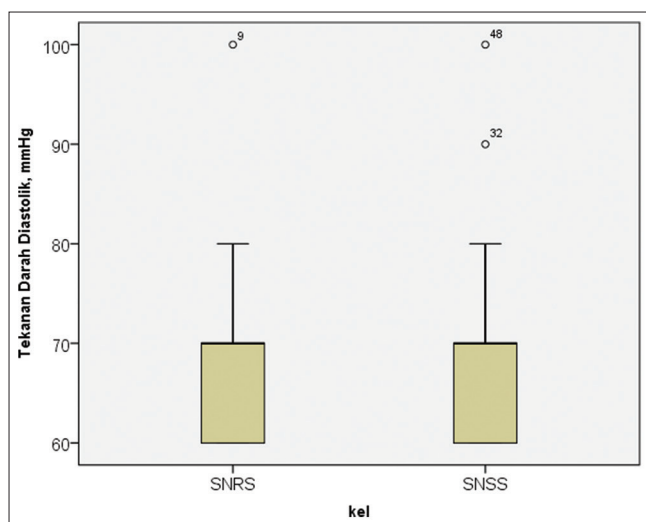


Figure 2: Diastolic blood pressure boxplot chart in steroid-resistant nephrotic syndrome (NS) and steroid sensitive NS groups

and blood pressure in SRNS and SSNS are shown in Table 2.

Table 2: Proteinuria's relationship with blood pressure in the SRNS and SSNS groups

SSNS groups	n	Systolic BP, Median (range), mmHg	p	Diastolic BP, Median (range), mmHg	p
SRNS					
Proteinuria					
Negative	11	100 (90–130)	0,556	60 (60–80)	0,528
+1	11	100 (90–140)		70 (60–100)	
+2	3	100 (90–100)		70 (60–70)	
SSNS					
Proteinuria					
Negative	12	110 (100–170)	0,597	70 (60–90)	0,088
+1	4	105 (100–130)		60 (60–70)	
+2	8	110 (100–160)		70 (70–100)	
+3	1	100		70	

SRNS: Steroid-resistant nephrotic syndrome, SSNS: Steroid sensitive nephrotic syndrome.

Discussion

NS in children is the most commonly found disease of the child's kidneys [10], [11]. NS is a clinical syndrome with symptoms of massive proteinuria (≥ 40 mg/m² LPB/h or protein/creatinine ratio in urine > 2 mg/mg or dipstick $\geq 2+$), hypoalbuminemia ≤ 2.5 g/dL, edema, and can be accompanied by hypercholesterolemia [2]. NS incidence in children in the United States and the United Kingdom is 2–4 new cases per 100,000 children per year [4]. In developing, the incidence is higher. In Indonesia, it is reported to be 6/100,000 per year in children under the age of 14 [1].

In this study, we divided NS patients into two groups with the same proportion to reduce bias, the proportion of male gender in the SRNS group was more than in the female gender, but in the SSNS group it was found that the female gender proportion was more than the proportion of male sex. This is directly proportional to the prevalence of NS in children from the Asian

continent where the prevalence of males is 1.5–2:1 of females [3].

Diagnosis of NS in patients under 1 year and above 8 years of NS should be performed renal biopsy before obtaining immunosuppressive therapy including steroids, because at this age the incidence of NS is an idiopathic type [8]. About 50% of children affected by NS are 1 year 6 months to 5 years old; 75% are younger than 10 years old [11], [12]. This was different in our study where the median age in this study was found at age 10 in the SRNS group and the average age of 12.5 years in the SSNS group.

The incidence of hypertension in children is about 20% caused by kidney disease [9]. Hypertension can be found in disease condition or in the course of NS disease due to steroid toxicity [1]. Corticosteroids can cause hypertension through the effects of coracoid minerals is by deflating the retention of sodium and water in the kidneys, expanding plasma volume and ultimately increasing blood pressure [13]. Etiology hypertension in NS is multifactor, that is, related to renal and non-renal intrinsic factors and the serviceman with extrinsic/environmental factors [14]. The underfill hypothesis states that sodium retention in NS is mainly due to reduced circulation volume due to fluid shift from intravascular to interstitial compartments due to reduced plasma oncotic pressure by hypoalbuminemia. This change activates the retention of sodium and water in the kidneys. While the overfill hypothesis states that the retention of sodium reflects the absence of intrinsic defects in the kidneys in dealing with sodium, which, in turn, leads to an expansion of volume [15]. In new, in our study, there was a higher increase in systolic blood pressure in the SSNS group compared to the significant SRNS group, but there was no difference in diastolic blood pressure in the SRNS and SSNS groups. This compares with a 2011 study in Bangladesh in which there were more hypertension events found in the SRNS group than SSNS ($p > 0.05$) [2] and in line with research in Indonesia 2016 where blood pressure found in the SSNS group was higher than the SRNS group but not statistically meaningful [3]. Another study by Mamesah 2019 found the average systolic and diastolic blood pressure of the SRNS group compared to the SSNS group [9]. Other studies that support our study have a high prevalence of hypertension in the SRNS and SSNS groups where the prevalence of hypertension in different patient populations with SNs ranges from 8% to 59.1% [14]. Research by Kontchou 2009 mentioned the discovery of 65% prevalence of hypertension in the SSNS group [16].

In our study assessed the relationship of proteinuria degrees with high systolic and diastolic blood pressure found no meaningful relationship in both groups ($p > 0.05$). This is incompatible with a 2006 study by Seeman that found a link between proteinuria and hypertension in 14 healthy children with abnormal kidney ultrasound results [6]. Research in Indonesia

on 494 children in 2019 also found the incidence of hypertension and proteinuria in schoolchildren 12–14 years without symptom [7].

Conclusion

There were significant differences in systolic blood pressure in both the SRNS and SSNS groups with higher systolic blood pressure medians in the SSNS group and no difference in diastolic blood pressure in both groups. The high prevalence of the SSNS group emphasizes that blood pressure monitoring in NS patients requires strict treatment to monitor further complications.

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