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THE RELATIONSHIP BETWEEN LIPID PROFILE AND THE INCIDENCE OF RELAPSING NEPHROTIC SYNDROME IN CHILDREN

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ABSTRACT
Nephrotic syndrome (NS) is one of the most common chronic kidney diseases in children, characterized by massive proteinuria, hypoalbuminemia, edema, and dyslipidemia. Relapse occurs in most cases and contributes to worsening the disease course. Dyslipidemia is suspected to influence relapse risk, but the specific relationship between lipid profile and relapsing NS remains unclear. Objective to analyze the association between total cholesterol, triglycerides, LDL, and HDL levels with relapse incidence in children with nephrotic syndrome. A retrospective study was conducted on 66 children aged 2–18 years with NS treated at H. Adam Malik General Hospital, Medan, in 2024. Subjects were divided into relapsing (n=54) and non-relapsing (n=12) groups. Data were obtained from medical records and analyzed using the Mann-Whitney test and Spearman correlation. Triglyceride (p=0.007), LDL (p=0.013), and HDL (p<0.001) levels differed significantly between the relapsing and non-relapsing groups. Total cholesterol showed no significant difference (p=0.164). The mean albumin level was significantly lower in the relapsing group (2.9 g/dL vs. 4.1 g/dL; p<0.001). A significant negative correlation was found between albumin and triglyceride levels (r=-0.326; p=0.008). Triglyceride, LDL, and HDL levels are significantly associated with relapse in pediatric nephrotic syndrome. Hypoalbuminemia is also an important risk factor. Lipid profile evaluation can serve as a useful indicator in monitoring and managing relapses.

Keywords: albumin; children; lipid profile; nephrotic syndrome; relapse

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INTRODUCTION

Nephrotic syndrome (NS) is a clinical condition characterized by massive proteinuria, which leads to hypoalbuminemia, hyperlipidemia, edema, and various other complications. Although approximately 94% of NS cases achieve remission in response to initial therapy, the relapse rate remains high, with 60–70% of patients in remission experiencing relapse (Kodner, 2009). Relapse in NS is defined as the presence of proteinuria ≥ +3 on urine dipstick for three consecutive days within one week after achieving remission (KDIGO, 2021). A meta-analysis conducted in Europe reported a relapse rate of 71.9%, while a study by the *International Pediatric Nephrology Association (IPNA)* found that approximately 85% of pediatric patients experience relapse, with 30–50% developing frequent relapses or becoming steroid-dependent (Veltkamp et al., 2021; IPNA, 2020). Data are still limited in Indonesia. However, a study conducted at Dr. Soetomo General Hospital in Surabaya reported that 99 out of 144 children with NS experienced relapse. Recurrent relapses increase the risk of various complications, including corticosteroid-related side effects, growth and developmental impairments, and opportunistic infections (Abeyagunawardena et al., 2022).

In addition to proteinuria and hypoalbuminemia, nephrotic syndrome (NS) also causes lipid metabolism disturbances, including elevated levels of triglycerides, total cholesterol, and low-density lipoprotein (LDL), along with decreased high-density lipoprotein (HDL). Hyperlipidemia is

thought to contribute to the risk of relapse through mechanisms involving altered lipoprotein synthesis and catabolism. Several studies have demonstrated a correlation between dyslipidemia and the frequency of relapse in NS patients (Tapia et al., 2023). In Indonesia, data on relapse of nephrotic syndrome (NS) and its associated risk factors remain limited. Therefore, this study aims to analyze the relationship between lipid profile levels (total cholesterol, triglycerides, LDL, HDL) and the incidence of relapse in children with nephrotic syndrome at H. Adam Malik General Hospital, Medan.

METHOD

This retrospective observational study conducted at H. Adam Malik General Hospital, Medan, in 2024. A consecutive sampling with total of 66 pediatric patients aged 2–18 years with confirmed nephrotic syndrome were included. Patients were classified into relapsing (n=54) and non-relapsing (n=12) groups based on medical record documentation. Inclusion criteria included complete lipid profile and albumin data. Exclusion criteria were secondary nephrotic syndrome and incomplete laboratory records. Data collected included demographic characteristics, serum lipid profile (total cholesterol, triglycerides, LDL, HDL), and albumin levels. Mann-Whitney test was used to compare lipid levels between groups, and Spearman's rank correlation test was used to evaluate the association between albumin and lipid levels. A p-value <0.05 was considered statistically significant.

RESULT

The study included a total of 66 pediatric subjects, consisting of 54 children (81%) diagnosed with relapsing nephrotic syndrome and 12 children (19%) with non-relapsing nephrotic syndrome. Several demographic characteristics of the study population are presented in Table 1. The majority of subjects were over 6 years of age (81.8%) and male (71.2%). On average, patients had elevated blood urea levels above the normal range, with a mean of 38.8±42.4 mg/dL. Serum creatinine levels were also mildly elevated, with a mean of 1.0±1.9 mg/dL. Most patients demonstrated proteinuria, with a mean protein level of 2.1±0.9.

Table 1.
Demographic Characteristics of the Study Population

Characteristic Demograpich	Total	Nefrotic Syndrome Relaps (n = 54)	Nefrotic Syndrome Non Relaps (n = 12)	*p value*
Age, n (%)				1,000†
≤6 Years Old	12 (18,2)	10 (83,3)	2 (16,7)	
>6 Years Old	54 (81,8)	44 (81,5)	10 (18,5)	
Gender, n (%)				0,484†
Boy	47 (71,2)	37 (68,6)	9 (83,3)	
Girl	19 (28,8)	17 (31,5)	2 (16,7)	
Ureum (*Mean*±SD)	38,8±42,4	40,7±46,4	30,3±12,8	0,829‡
Creatinine (*Mean*±SD)	1,0±1,9	1,1±2,1	0,5±0,2	0,383‡

*p<0,05, †: Uji Fisher Exact, ‡: Uji Mann Withney

The results of lipid profile analysis in this study are presented in Table 2, covering four components of the lipid profile: total cholesterol, triglycerides, LDL, and HDL. On average, patients showed elevated levels of total cholesterol (422.9±102.0 mg/dL), triglycerides (282.2±197.2 mg/dL), and LDL (318.1±85.4 mg/dL). Meanwhile, the mean HDL level remained within the normal range at 48.8±26.4 mg/dL. Among these four components, three lipid profile parameters—triglycerides, LDL, and HDL—were found to be associated with the incidence of relapsing nephrotic syndrome.

Based on total cholesterol levels, the relapsing group had a higher mean value (431.1±98.0 mg/dL) compared to the non-relapsing group (385.6±115.6 mg/dL), although the difference was not statistically significant (p>0.05). In contrast, a statistically significant difference was observed in triglyceride levels (p<0.05), with the relapsing group showing a higher mean (302.5±211.5 mg/dL) than the non-relapsing group (190.8±56.9 mg/dL).

There was also a significant difference in LDL levels between the two groups: the relapsing group had a higher mean LDL level (330.2±85.6 mg/dL) compared to the non-relapsing group (263.5±62.6 mg/dL). Additionally, a significant difference was found in HDL levels, with the relapsing group showing a lower mean HDL (45.6±27.8 mg/dL) than the non-relapsing group (63.1±11.4 mg/dL).

Table 2.
The Relationship Between Lipid Profile and the Incidence of Relapsing and Non-Relapsing Nephrotic Syndrome

Lipid profile	Total	Nefrotic Syndrome Relaps (n = 54)	Nefrotic Syndrome Non Relaps (n = 12)	*p value*
Cholesterol total (*Mean*±SD)	422,9±102,0	431,1±98,0	385,6±115,6	0,164†
Triglyserida (*Mean*±SD)	282,2±197,2	302,5±211,5	190,8±56,9	0,007*†
LDL (*Mean*±SD)	318,1±85,4	330,2±85,6	263,5±62,6	0,013*†
HDL (*Mean*±SD)	48,8±26,4	45,6±27,8	63,1±11,4	<0,001*†

*p<0,05, †: Uji Mann Whitney

DISCUSSION

This study involved a total of 66 patients, consisting of 54 children diagnosed with relapsing nephrotic syndrome and 12 in non-relapsing condition. Based on demographic characteristics, the majority of respondents were in the 10–14 year age group, and most were male. These findings are consistent with a study in Ethiopia, which reported a relapse incidence of 55.8% among children with nephrotic syndrome during the first six months of follow-up (Gashaw et al., 2022). Similarly, Tipparthy et al., (2023) reported that the most commonly affected age group in pediatric nephrotic syndrome was 6–9 years (42.5%), while Shanta et al. (2023) found that 66.7% of patients with nephrotic syndrome were male, indicating a consistent male predominance.

The results of this study demonstrate an increase in total cholesterol, triglycerides, and LDL levels, along with a decrease in HDL levels in the relapse group. However, only triglycerides, LDL, and HDL levels showed statistically significant differences. Although total cholesterol levels were higher in the relapse group, the difference was not statistically significant. This finding is consistent with a study conducted in India, which reported that the mean levels of cholesterol, triglycerides, and LDL were higher in patients experiencing relapse compared to those in remission (Krishanamurthy et al., 2018). A study in the United States also found that the lipid profiles of patients in relapse were above the 95th percentile with considerable variability, suggesting the possibility of a complex pathogenic mechanism (Merouani et al., 2003). Furthermore, Dowerah et al. (2023) reported that lipid levels remained elevated in patients with nephrotic syndrome during remission, indicating a long-term risk of vascular disease due to persistent hypercholesterolemia, even in the absence of relapse.

Dyslipidemia in nephrotic syndrome is caused by increased hepatic synthesis of lipoproteins in response to hypoalbuminemia and reduced oncotic pressure, decreased activity of lipases (LCAT, lipoprotein lipase), impaired expression of lipid-binding proteins such as apoE, apoC-II, apoC-III, and GPIHBP1, as well as elevated levels of PCSK9, which reduce hepatic LDL receptor availability. HDL metabolism is also affected due to urinary loss of LCAT and low albumin levels, both of which are essential for HDL formation (Hussain AS et al., 2013; Zilleruelo G et al., 1994; Lawang et al., 2008). This study confirms that relapse in nephrotic syndrome (NS) is associated with dyslipidemia, and that changes in HDL levels are reversible in the absence of relapse (Khan et al., 2020). Elevated triglyceride levels may also disrupt podocyte structure and increase the risk of proteinuria and relapse (Noone et al., 2018). However, several studies have suggested that lipid levels during the acute phase may not be predictive of relapse. Only triglyceride levels appear to

reflect chronic metabolic disturbances, being associated with relapse or the long-term effects of therapy (Merouani et al., 2003). Dyslipidemia may also accelerate glomerular damage and the progression of chronic kidney disease through atherosclerotic mechanisms (Lawang et al., 2008). Therefore, parental education on the importance of regular follow-up remains essential, even during remission. Routine total cholesterol testing should be complemented by a complete lipid profile, particularly in patients with steroid-resistant NS (Lawang et al., 2008). Statins are considered the first-line therapy, with alternatives including fibrates, nicotinic acid, and ezetimibe (Merouani et al., 2003).

CONCLUSION

Triglyceride, LDL, and HDL levels are significantly associated with the incidence of relapse in children with nephrotic syndrome. Hypoalbuminemia is also a contributing risk factor. Regular lipid profile monitoring may help predict and prevent relapses, aiding in better disease management.

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