

Serum Cholesterol Levels in Children with Nephrotic Syndrome and Association to Different Patterns of Disease

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Abstract: ***Background:** Nephrotic syndrome (NS) is a common kidney disorder in children, marked by significant proteinuria, hypoalbuminemia, edema, and hyperlipidemia. Hyperlipidemia, specifically elevated serum cholesterol levels, is noteworthy for its role in disease progression and related complications. Understanding serum cholesterol variations across different NS patterns is essential for optimizing treatment and improving patient outcomes. **Methods:** A single - center, observational, analytical cross - sectional study was conducted at Indira Gandhi Institute of Medical Sciences (IGIMS) from July 2022 to July 2024. Children aged 1 - 14 years diagnosed with nephrotic syndrome were recruited from both inpatient and outpatient departments. The sample size was determined to be 369, based on a 60% prevalence rate of metabolic bone disease in NS, with a 95% confidence level and a 5% allowable error. A total of 370 patients were included. Data on age, disease pattern, and serum cholesterol levels were collected. Blood samples were analyzed for serum cholesterol, UP ratio, albumin, and proteinuria. Statistical analysis was performed using non - parametric tests due to the non - normal distribution of serum cholesterol levels. **Results:** The mean age of participants was 6.02 ± 3.33 years. The distribution of disease patterns was: first episode (39.2%), first relapse (18.3%), IFRNS (15.3%), and FRNS (27.2%). The overall mean serum cholesterol level was 469.62 ± 144.82 mg/dL. Mean serum cholesterol levels were 460.99 ± 142.96 mg/dL in the first episode group, 488.21 ± 140.11 mg/dL in the first relapse group, 449.73 ± 157.64 mg/dL in the IFRNS group, and 478.33 ± 143.08 mg/dL in the FRNS group. No significant differences in serum cholesterol levels were found between the groups ($\chi^2 = 4.964$, $p = 0.174$). **Conclusions:** Hypercholesterolemia is prevalent in children with nephrotic syndrome across all disease patterns. The lack of significant variation in serum cholesterol levels between different patterns of NS suggests that lipid abnormalities are a common feature irrespective of the disease pattern. Further research is needed to explore the mechanisms underlying lipid abnormalities to develop tailored treatment strategies.*

Keywords: nephrotic syndrome, Vitamin D, Cholesterol, Pediatric nephrotic syndrome

1. Introduction

Nephrotic syndrome (NS) is a prevalent kidney disorder in children, characterized by significant proteinuria, hypoalbuminemia, edema, and hyperlipidemia. Among these features, hyperlipidemia, particularly elevated serum cholesterol levels, has garnered considerable attention due to its potential role in disease progression and associated complications. [1] Serum Cholesterol levels were earlier used as a defining criterion for nephrotic syndrome. However, the definition has now changed, and high levels of Serum cholesterol remain a supportive finding. [2] Understanding how serum cholesterol levels vary across different patterns of nephrotic syndrome - such as first episode, first relapse, infrequent relapsing nephrotic syndrome (IFRNS), and frequent relapsing nephrotic syndrome (FRNS) - is crucial for tailoring treatment strategies and improving patient outcomes.

Dyslipidemia led to various complications of nephrotic syndrome, like thromboembolism and atherosclerosis. [3] Previous studies have established lipid abnormalities as a hallmark of NS, but the severity and clinical implications of these abnormalities can differ based on the disease pattern. For instance, children experiencing frequent relapses or exhibiting infrequent relapses often present with more pronounced hypercholesterolemia compared to those in their first episode of NS. These variations highlight the need for pattern - specific approaches to managing hyperlipidemia in NS patients.

2. Materials and Methods

A single - center, observational, individual - based, analytical cross - sectional (prevalence) study was conducted in the Department of Pediatrics at Indira Gandhi Institute of Medical Sciences (IGIMS) over a duration of two years, from July 2022 to July 2024. Following ethical clearance, recruitment, data collection, analysis, compilation, and presentation were carried out. Subjects were recruited from both the Indoor Patient Department (IPD) and the Outdoor Patient Department (OPD) of the Pediatrics Department at IGIMS. The study included children aged 1 - 14 years diagnosed with nephrotic syndrome. Based on previous studies, the prevalence of metabolic bone disease (MBD) in nephrotic syndrome is approximately 60%. With a confidence level (Z) of 95% and an allowable error of 5%, the sample size was calculated to be 369, which was confirmed using Epi Info Software (CDC). 400 Patients who met the inclusion criteria and did not fall under any exclusion criteria were informed about the study, and written informed consent was obtained from guardians and parents, with assent obtained from the subjects wherever applicable. Patient particulars were recorded. Detailed history was obtained from the informant, usually the guardians, and surrogate consent was obtained when necessary. Specific points of interest included age of onset of disease, pattern of disease (first episode, first relapse, infrequent relapsing, or frequent relapsing). A thorough clinical examination was performed for each patient, and all positive findings were recorded. Blood and urine investigations were conducted to confirm and document the disease status (active, relapse, or remission). Only active were included. Blood samples were collected under aseptic conditions and tested for parameters such as serum

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cholesterol, UP: Uc ratio, albumin, and proteinuria. Patients with deficiencies or biochemical abnormalities were treated with appropriate supplementation therapy. Participation in this study did not affect or delay the diagnosis or treatment of nephrotic syndrome. The inclusion criteria were children aged 1 - 14 years diagnosed with nephrotic syndrome with normal creatinine levels, while the exclusion criteria included children with congenital nephrotic syndrome, secondary nephrotic syndrome, osteogenesis imperfecta, or juvenile osteoporosis.

3. Results

A total of 370 patients were included in the study. The mean age of the participants was 6.02 ± 3.33 years. Among the participants, 144 (39.2%) were in the First Episode pattern group, 67 (18.3%) were in the First Relapse pattern group, 56 (15.3%) were in the IFRNS pattern group, and 100 (27.2%) were in the FRNS pattern group.

Clinical Details	Mean \pm SD Median (IQR) Min - Max OR N (%)
Age (Years)	6.02 \pm 3.33 6.00 (3.00 - 8.00) 1.00 - 14.00
Age Group	
1 to 5 Years	184 (49.7%)
6 to 10 Years	137 (37.0%)
11 to 14 Years	49 (13.2%)
Gender	
Male	263 (71.1%)
Female	107 (28.9%)
Duration of Illness (Years)	1.66 \pm 1.78 1.00 (0.50 - 2.00) 0.50 - 14.00
Pattern	
First Episode	144 (39.2%)
First Relapse	67 (18.3%)
IFRNS	56 (15.3%)
FRNS	100 (27.2%)

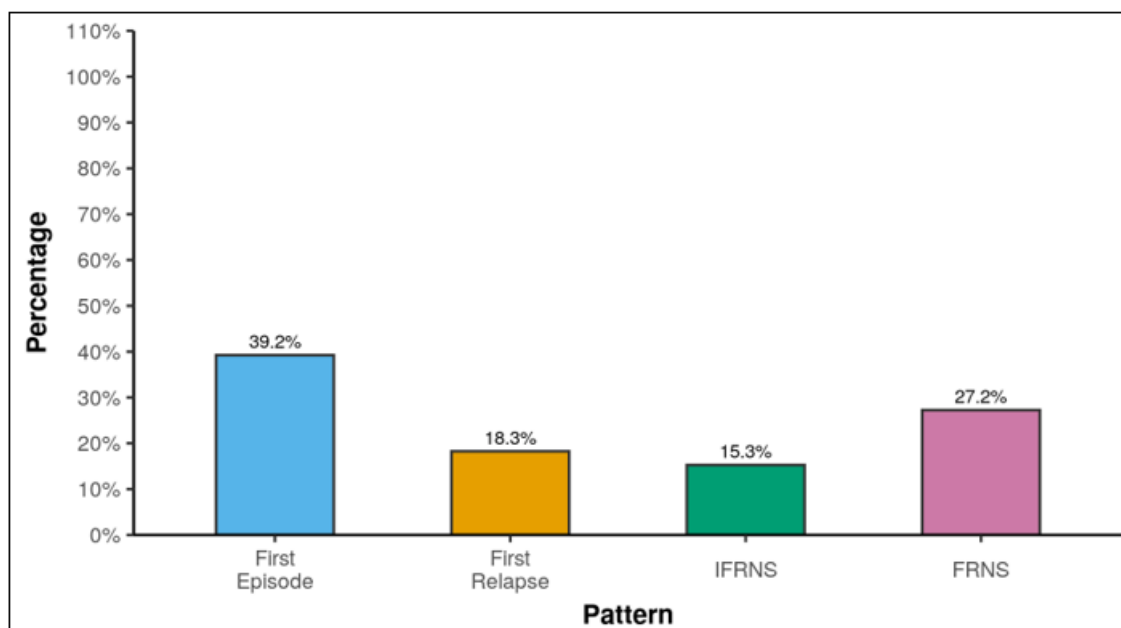


Figure 1: Distribution of subjects according to pattern of disease

The overall mean serum cholesterol level was 469.62 ± 144.82 mg/dL, with a median of 450.50 mg/dL (IQR 360 - 560). Serum cholesterol levels ranged from 162 to 937 mg/dL.

The data's skewness was 0.58, indicating a positive skew, while the kurtosis was 0.01, suggesting a normal distribution.

The Shapiro - Wilk test was significant ($p < 0.001$), indicating that the data was not normally distributed. Given that only one of the three criteria (skewness, kurtosis, Shapiro - Wilk test) suggested normality, it was concluded that the data did not follow a normal distribution and was unimodal.

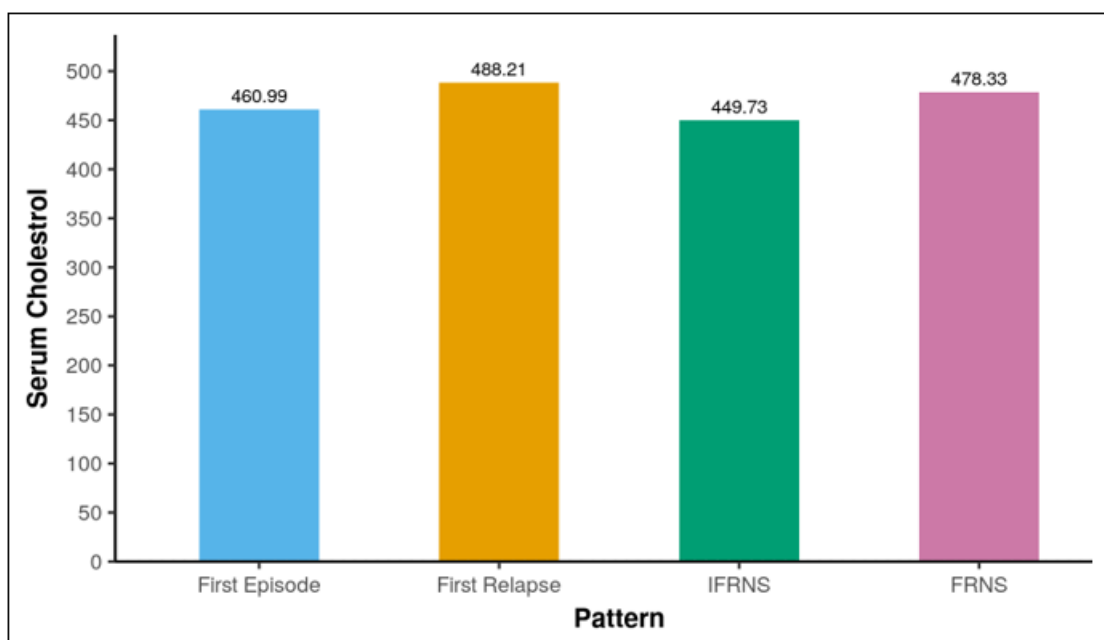
Serum Cholesterol	Pattern				Kruskal Wallis Test	
	First Episode	First Relapse	IFRNS	FRNS	χ^2	p value
Mean (SD)	460.99 (142.96)	488.21 (140.11)	449.73 (157.64)	478.33 (143.08)	4.964	0.174
Median (IQR)	444.5 (352 - 556)	482 (389.5 - 580.5)	413 (349.25 - 532.5)	451 (371 - 570.5)		
Min - Max	164 - 937	182 - 937	200 - 890	162 - 830		

Pairwise Comparison of Subcategories of Pattern	Adjusted P Value
First Episode - First Relapse	0.475
First Episode - FRNS	0.878
First Relapse - FRNS	0.985
First Episode - IFRNS	0.980
First Relapse - IFRNS	0.268
FRNS - IFRNS	0.587

Post - Hoc pairwise tests for Kruskal - Wallis test performed using Dunn Test method with Sidak correction.

Due to the non - normal distribution of serum cholesterol levels in the four subgroups of the pattern variable, non - parametric tests (Kruskal - Wallis Test) were used for group comparisons. The mean serum cholesterol levels were 460.99 ± 142.96 mg/dL in the First Episode group, 488.21 ± 140.11 mg/dL in the First Relapse group, 449.73 ± 157.64 mg/dL in

the IFRNS group, and 478.33 ± 143.08 mg/dL in the FRNS group. The median serum cholesterol levels were 444.5 mg/dL (IQR 352 - 556) in the First Episode group, 482 mg/dL (IQR 389.5 - 580.5) in the First Relapse group, 413 mg/dL (IQR 349.25 - 532.5) in the IFRNS group, and 451 mg/dL (IQR 371 - 570.5) in the FRNS group.



The serum cholesterol levels ranged from 164 to 937 mg/dL in the First Episode group, 182 to 937 mg/dL in the First Relapse group, 200 to 890 mg/dL in the IFRNS group, and 162 to 830 mg/dL in the FRNS group. There was no significant difference in serum cholesterol levels between the groups ($\chi^2 = 4.964$, $p = 0.174$). The strength of association, measured by Kendall's Tau, was 0.03, indicating little to no association.

4. Discussion

Our study evaluated serum cholesterol levels in 370 children with nephrotic syndrome, categorized into first episode (39.2%), first relapse (18.3%), IFRNS (15.3%), and FRNS (27.2%). The mean serum cholesterol level was 469.62 ± 144.82 mg/dL, ranging from 162 to 937 mg/dL, with no significant differences between the groups.

Comparing our findings with the study by Chavan S et al., which included 50 children, we found that their age distribution was primarily 2 - 8 years, with a male predominance (56% males). [4] Chavan S et al. reported 46% of cases in relapse, 40% in remission, and 14% newly diagnosed, with 78.25% of relapsers being frequent relapsers. They found that 50% had elevated total cholesterol levels.

Our study aligns with Chavan S et al. in showing prevalent hypercholesterolemia in nephrotic syndrome. However, while Chavan S et al. categorized cholesterol elevation by relapse status, our study did not find significant cholesterol differences across disease patterns, indicating that hypercholesterolemia is a common feature irrespective of the disease pattern.

Comparing our findings with Upadhyay et al., who studied 55 children, we see some key differences and similarities. [5] Upadhyay et al. reported that in the first attack group (30 cases), 53% were male, and in the relapse group (25 cases), 60% were male. Most children in both groups were between 1 - 5 years old. They found that the total serum cholesterol level was higher in relapse cases (470 ± 116 mg/dL) compared to the first attack group. Additionally, serum triglycerides (TG), low - density lipoprotein (LDL), and very - low - density lipoprotein (VLDL) levels were higher in the relapse group, while high - density lipoprotein (HDL) was lower. Serum albumin was low in all cases, with very low levels (<1.0 g/dL) in 16% of relapse cases.

In contrast, our study did not find significant differences in serum cholesterol levels across different disease patterns, including first episode, first relapse, IFRNS, and FRNS.

While Upadhyay et al. found higher cholesterol levels in relapse cases, our results suggest that hypercholesterolemia is a common feature across all patterns of nephrotic syndrome without significant variation.

In conclusion, our study aligns with Upadhyay et al. in confirming the presence of hypercholesterolemia in children with nephrotic syndrome. However, our findings suggest that serum cholesterol levels do not significantly differ between disease patterns, emphasizing the need for consistent monitoring and management of lipid abnormalities in all children with nephrotic syndrome, regardless of their disease pattern. Further research could explore the underlying mechanisms driving these lipid abnormalities to better tailor treatment strategies.

5. Conclusion

This study evaluated serum cholesterol levels in 370 children with nephrotic syndrome, categorized into first episode, first relapse, IFRNS, and FRNS. We found that hypercholesterolemia is prevalent in all disease patterns, with no significant differences in cholesterol levels between the groups. Our findings emphasize that lipid abnormalities are a common feature in nephrotic syndrome, irrespective of the disease pattern. Consistent monitoring and management of serum cholesterol levels are crucial in all children with nephrotic syndrome. Further research is needed to understand the underlying mechanisms and to develop tailored treatment strategies for managing hypercholesterolemia in this population.

Conflict of Interest

None.

References

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