Section: Pediatrics

Original Research Article

A STUDY ON PLASMA LIPID PROFILE IN CHILDREN WITH NEPHROTIC SYNDROME DURING REMISSION AND ITS RELATION TO RELAPSE OF IDIOPATHIC NEPHROTIC SYNDROME

Nimisha Sidhardhan[1], Vidhya Sivakumaran[2], Menaka Palanisamy[3], Viknesh Raj Raajkumar[4], Jeevithan Shanmugam[5]

[1]Assistant Surgeon, Government Lawley Hospital, Coonoor, Nilgiris
[2]Assistant Professor in Pediatrics, Coimbatore Medical College, Coimbatore
[3]Assistant Professor in Pediatrics, Coimbatore Medical College, Coimbatore
[4]Assistant Surgeon, Government UPHC, Lalpet, Ranipet
[5]Professor in Community Medicine, KMCH Institute of Health Sciences and Research, Coimbatore

Received : 07/12/2023
Received in revised form : 30/01/2024
Accepted : 15/02/2024

Keywords:
Nephrotic syndrome, Pediatric patients, Dyslipidemia, Relapse.

Corresponding Author:
Dr. Viknesh Raj Raajkumar,
Email: iamvikneshraj@gmail.com

DOI: 10.47009/jamp.2024.6.1.378

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2024; 6 (1); 1909-1913

Abstract

Background: Nephrotic syndrome, primarily affecting children, presents with heavy proteinuria, hypoalbuminemia, edema, and hyperlipidemia. Dyslipidemia persists even during remission, potentially increasing cardiovascular risk. This study aims to compare lipid profiles in initial and relapsing nephrotic syndrome episodes among pediatric patients. **Materials and Methods:** A prospective observational study was conducted from June 2021 to May 2022 in a tertiary care hospital. Children aged 2-12 years with nephrotic syndrome were included. Socio-demographic data, clinical examinations, and lipid profiles were collected. Lipid levels were measured using standard methods, and associations were analyzed using descriptive statistics and Chi-square/Independent sample T tests. **Result:** Among 81 participants, 48.15% were aged 6-9 years, and 67.9% were male. Pedal edema, facial puffiness, and abdominal distension were common symptoms. 85.19% had a history of relapse, with 53.08% experiencing frequent relapses. Significant differences in lipid profiles were noted between groups with and without relapses. Serum cholesterol, triglycerides, and LDL increased with each relapse episode, while HDL decreased. **Conclusion:** Dyslipidemia is a prevalent complication of nephrotic syndrome, persisting even in remission. Proactive monitoring and interventions are crucial to mitigate cardiovascular risk and improve long-term outcomes.

INTRODUCTION

Nephrotic syndrome, characterized by heavy proteinuria, hypoalbuminemia, edema, and hyperlipidemia, primarily affects children and is significantly more common in this demographic compared to adults. Among children, minimal change disease (MCD) constitutes over 90% of idiopathic nephrotic syndrome instances, showcasing its prevalence in this population.[1–3] Children with nephrotic syndrome experience significant alterations in lipoprotein metabolism, leading to elevated levels of various lipoproteins such as VLDL, IDL, LDL, and Lpa.

These changes result from increased hepatic synthesis and decreased plasma catabolism of lipoproteins. The severity of hyperlipidemia often corresponds to the extent of hypoalbuminemia, and recent studies indicate that lipid abnormalities can persist even during clinical remission, with the duration and frequency of relapses influencing their persistence and severity.[2–7]

Hyperlipidemia, often observed during the active phase of nephrotic syndrome, tends to resolve with the reduction of proteinuria.

However, in some cases, particularly in frequently relapsing nephrotic syndrome, hyperlipidemia may persist, increasing the risk of atherosclerosis and progressive renal injury later in life. Therefore, diligent monitoring of lipid levels during nephrotic syndrome remission is crucial, especially for identifying high-risk patients prone to cardiovascular complications.[2,6,7]

Given the impact of lipid levels on coronary artery disease (CAD) risk later in life, understanding the spectrum of dyslipidaemia in initial and relapsing

ISSN (O): 2687-5365; ISSN (P): 2753-6556

nephrotic syndrome episodes becomes crucial.[2–7] Thus, this study aims to compare the lipid profiles between first-time nephrotic syndrome cases and subsequent relapses in pediatric patients, shedding light on potential patterns and implications for disease management and long-term outcomes.

MATERIALS AND METHODS

This prospective observational study was conducted within the Pediatric ward and Pediatric nephrology OPD of a tertiary care hospital in western Tamil Nadu from June 2021 to May 2022. Proper approval from the Institutional Human Ethical Committee was obtained before commencement. Children aged 2 to 12 years exhibiting typical features of nephrotic syndrome, as well as children with known history of nephrotic syndrome that achieved remission after completing a steroid course, were eligible for inclusion in the study.

Exclusion criteria encompassed children with minimal change disease, known cases of Diabetes mellitus, hypothyroidism, familial hypercholesterolemia, and edema due to causes such as congestive cardiac failure, protein-energy malnutrition, and chronic liver disease. The legally accepted representatives of eligible children in the pediatric OPD/Ward/Paediatric Nephrology OP/Ward were approached by the primary investigator, who provided detailed explanations about the study's objectives, necessity, patient rights, and ethical considerations. Information sheets were provided, allowing ample time and privacy for the representatives to comprehend the study's nature. Informed consent was obtained from the legally acceptable representatives, with oral/written assent acquired depending on the child's age.

A total of 81 children were followed throughout the study period. Children presenting with Nephrotic range proteinuria (40 mg/m2/h or > 1000 mg/m2/day; spot Up/Uc 2 mg/mg; 3-4+ by dipstick); hypoalbuminemia (albumin < 3.0 g/dL); and edema were classified as having the first or initial episode of nephrotic syndrome. Remission was defined as urine albumin nil or trace (or proteinuria <4 mg/m2/hr) in an early morning urinary sample for three consecutive days. Relapse was determined by urinary albumin 3+/4+ (or proteinuria 40 mg/m2/hr) in an early morning urinary sample for three consecutive days in a patient who had previously achieved remission. Frequent relapse was defined as two or more relapses in the initial six months or four or more relapses in any 12 months. Data collection involved a pretested questionnaire covering socio-demographic characteristics, clinical examination, and lipid profile (Serum Cholesterol, HDL, LDL, Triglycerides) variables.

The principal investigator recorded socio-demographic characteristics and clinical examination findings through detailed history-taking and thorough clinical examinations. For lipid profile analysis, early morning fasting blood samples were obtained, with serum total cholesterol, triglycerides, LDL cholesterol, VLDL cholesterol, and HDL cholesterol measured using standard methods. The blood samples taken were processed almost immediately, for further evaluation of Total cholesterol (TC), triglycerides (TGL), and HDL using specific enzymatic methodsIn Olympus auto analyzer. LDL was calculated using Fredrickson – Freidwald formula; (LDL= Total cholesterol – HDL- TGL/5).and VLDL was calculated using the formula VLDL = TGL/5. Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents was used to determine the cut off values.[8]

Descriptive statistics such as frequency/percentages or mean ± SD were employed, and associations between the previous relapse and frequent relapse groups with those who did not experience such events were assessed using Chi-square/Independent sample T tests. A significance level of $p<0.05$ was considered statistically significant.

RESULTS

In the study, 48.15% of participants fell within the age range of 6 to 9 years, while 43.21% were between 10 and 12 years. A smaller portion, 8.64%, was under five years of age.

Among the participants, nearly two-thirds (67.9%) were male children, with the remaining 32.1% being female children. A significant portion, 53.09%, was diagnosed between 2 and 4 years of age, while 40.74% were diagnosed between 5 and 7 years old. All children had a minimum duration of two years follow-up from the first diagnosis. Approximately 84% were dependent on steroids, while 16% showed resistance to steroid treatment.

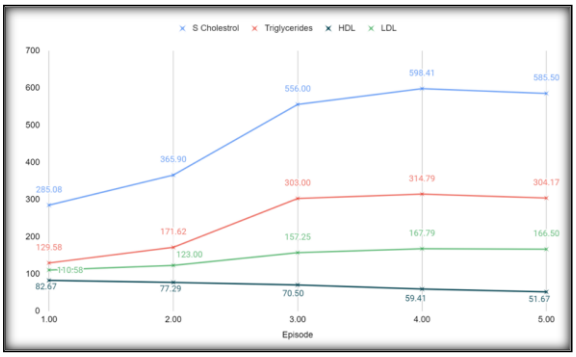

Figure 1: Mean Lipid Profile values at each relapse time

[Table 1 & 2] delineates the clinical symptoms observed among the participants. Pedal edema and facial puffiness were universally present, with 99% experiencing remission. Additionally, 88.88% exhibited abdominal distension, and a similar percentage (85.19%) had a history of previous relapse. Notably, of those who experienced relapses, 53.08% reported frequent episodes of nephrotic

ISSN (O): 2687-5365; ISSN (P): 2753-6556

syndrome relapse, indicating a substantial recurrence rate.

[Table 3] delves into the mean lipid profile values among participants with and without previous relapses, as well as those with frequent relapses versus those without.

Significant differences were observed across all measured parameters (Serum cholesterol, TGL, HDL, LDL) between the groups except for HDL between previous relapse episode and new episode, highlighting the potential impact of relapse history on lipid profile values. The Serum cholesterol, Triglycerides and LDL level increases for each relapse episode. Concurrently the HDL values reduce for each relapse episode. [Figure 1]

Table 1: Sociodemographic variables of study population

Parameter	N	%
Age(in years)		
2-5	7	8.64
6-9	39	48.15
10-12	35	43.21
Sex		
Male	55	67.90
Female	26	32.10
Age at first Diagnosis(in years)		
2-4	43	53.09
5-7	33	40.74
8-10	5	6.17
Clinical status		
Steroid dependant	68	83.95
Steroid resistant	13	16.05

Table 2: Clinical symptoms of study population

Symptom	Present		Absent	
	N	%	N	%
Pedal oedema	81	100	0	0
Facial puffiness	81	100	0	0
Abdominal Distension	72	88.88	9	11.12
Oliguria	72	88.88	9	11.12
Haematuria	1	1.23	80	98.77
Fever	10	12.34	71	87.66
Hypertension	5	6.17	76	93.83
Remission after first episode	80	98.77	1	1.23
History of previous relapse	69	85.19	12	14.82
History of frequent relapse episodes	43	53.08	38	46.92

Table 3: Comparison of mean Lipid profile values between Previous relapse/frequent relapse

PARAMETERS	Present		Absent		MD	t Value	P Value
	M	SD	M	SD			
Previous relapse episode							
Sr. Cholesterol	521.57	118.32	285.33	39.98	236.23	6.817	<0.001
TGL	268.33	76.92	132.92	20.11	135.43	6.035	<0.001
HDL	67.81	25.77	69.17	30.37	-1.355	90.164	0.87
LDL	152.52	32.72	112.33	16.09	40.19	4.152	<0.001
Frequent relapse episode							
Sr. Cholesterol	580.98	76.45	334.21	54.52	246.69	15.651	<0.001
TGL	30.5.94	40.55	155.29	51.44	150.65	14.646	<0.001
HDL	61.70	22.33	78.19	29.27	46.49	-2.864	<0.001
LDL	163.4	31.38	119.42	15.19	43.98	7.281	<0.001

DISCUSSION

In the study, majority were less than 9 years of age and more than two-thirds were males. 84% were dependent on steroids. All participants had pedal oedema and facial puffiness. More than four fifth had abdominal distension and history of previous relapse. More than half had frequent episodes of nephrotic syndrome relapse. These results were consistent with the findings of studies done by other researchers.[4,6,9–12]

The lipid profile was higher in all the study population. The lipid profile of those who had previous and frequent relapse/remission was considerably still higher than first episode and less episode. The lipid profile increases with each episode of nephrotic syndrome. The studies were consistent with the results of other studies.[1–7,9,11]

Dyslipidemia, characterized by abnormal lipid metabolism, is a nearly universal complication of persistent nephrotic syndrome, particularly in children.

In patients with nephrotic syndrome, dyslipidemia arises due to altered lipid and lipoprotein metabolism, leading to increased levels of various lipoproteins such as VLDL, IDL, LDL, and Lpa.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

The severity of dyslipidemia tends to correlate with the magnitude of proteinuria, a hallmark feature of nephrotic syndrome. Persistent dyslipidemia is a characteristic feature of the disease, even during remission, with its persistence and severity associated with the duration and frequency of relapses. The mechanism underlying are as follows

1. Increased Lipid Synthesis: Nephrotic syndrome leads to increased hepatic synthesis of lipids, including cholesterol and triglycerides. The exact mechanisms behind this increase are not fully understood, but it is believed to be related to changes in liver function triggered by the nephrotic state.

2. Decreased Lipid Clearance: Nephrotic syndrome also results in diminished plasma catabolism of lipoproteins, leading to reduced clearance of lipids from the bloodstream. This impairment in lipid clearance contributes to the elevated levels of cholesterol, triglycerides, and other lipoproteins observed in patients with nephrotic syndrome.

3. Loss of Proteins: The excessive loss of proteins, particularly albumin, through the urine (proteinuria) in nephrotic syndrome disrupts normal lipid metabolism. Albumin plays a crucial role in lipid transport and metabolism, and its loss contributes to dysregulation of lipid levels in the bloodstream.

4. Hormonal Imbalance: Hormonal changes associated with nephrotic syndrome, including alterations in the renin-angiotensin-aldosterone system and increased secretion of lipoprotein lipase inhibitors, further exacerbate dyslipidemia.

5. Podocyte Injury and Glomerular Dysfunction: The primary pathology of nephrotic syndrome involves injury to podocytes and the glomeruli. Podocytes are essential for maintaining the integrity of the glomerular filtration barrier. Dysfunction or injury to podocytes disrupts normal lipid metabolism within the kidney and contributes to dyslipidemia.

Overall, the complex interplay of factors, including increased lipid synthesis, impaired lipid clearance, protein loss, hormonal imbalances, and glomerular dysfunction, collectively contribute to the development of dyslipidemia in nephrotic syndrome. Understanding these underlying mechanisms is crucial for developing effective strategies to manage dyslipidemia and reduce associated cardiovascular risks in patients with nephrotic syndrome.

The consequences of dyslipidemia in nephrotic syndrome are far-reaching. They include an increased risk of atherosclerosis, myocardial infarction, stroke, and other cardiovascular events. Additionally, dyslipidemia contributes to the progression of renal injury, exacerbating glomerulosclerosis and proximal tubular cell injury. The impact of dyslipidemia on kidney function and cardiovascular health underscores the importance of proactive management and treatment.

To mitigate the risks associated with dyslipidemia in nephrotic syndrome, close monitoring of lipid levels during both active disease and remission phases is essential. Early identification of dyslipidemia allows for timely intervention and management strategies to reduce cardiovascular risk. Lifestyle modifications, including a heart-healthy diet, regular physical activity, and weight management, play a crucial role in preventing heart problems. Moreover, targeted pharmacological interventions, such as lipid-lowering medications, may be necessary to normalize lipid levels and reduce the risk of cardiovascular complications in patients with nephrotic syndrome.[13–20]

CONCLUSION

Dyslipidaemia is a prevalent and significant complication of nephrotic syndrome, contributing to cardiovascular morbidity and renal disease progression. Proactive monitoring, lifestyle modifications, and appropriate medical interventions are paramount to mitigate the adverse effects of dyslipidemia and improve long-term health outcomes in patients with nephrotic syndrome.

REFERENCES

1. V S, L L. A study of Serum lipids among children suffering from nephrotic syndrome. MedPulse International Journal of Pediatrics. 2019;9(1):33–5.
2. Chavan DrS, Salunkhe DrS, Singh DrA, Agarkhedkar DrS, Sodal DrS, Jadhav DrR. Lipid profile in children with Nephrotic syndrome. Pediatric Review: International Journal of Pediatric Research. 2018 Jun 30;5(6):314–9.
3. Mérouani A, Lévy E, Mongeau JG, Robitaille P, Lambert M, Delvin EE. Hyperlipidemic profiles during remission in childhood idiopathic nephrotic syndrome. Clin Biochem. 2003 Oct;36(7):571–4.
4. Upadhyay DrMR, Beriha DrSS, Pradhan DrSK. A comparative study of lipid profile in first attack versus relapse cases of idiopathic nephrotic syndrome in children. Pediatric Review: International Journal of Pediatric Research. 2018 Dec 31;5(12):636–41.
5. Mihajlović M, Stefanović A, Paripović D, Peco-Antić A, Simachew YM, Antonić T, et al. Lipoproteins and cholesterol homeostasis in paediatric nephrotic syndrome patients. Biochem Med (Zagreb). 2022 Jun 15;32(2):224–33.
6. B. S, B. M, Joseph N. Comparative study of lipid profile abnormalities in first episode and relapse cases of childhood nephrotic syndrome. Int J Contemp Pediatrics. 2016;1297–300.
7. Dowerah P, Gogoi A, Shira CD, Sarkar B, Mazumdar S. A Study of Dyslipidemia and Its Clinical Implications in Childhood Nephrotic Syndrome. Cureus. 2023 Oct 21;
8. Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents: Summary Report. Pediatrics. 2011 Dec 1;128(Supplement_5):S213–56.
9. Kabir MH AKDPMMCMCM. Relation between plasma lipids and relapse of idiopathic nephrotic syndrome in children. BIRDEM Med J. 2020;10(2):97–102.
10. Koushal Kumar SSNG. Prevalence of Different Clinical Variants of Nephrotic Syndrome in Children 1–18 Years of Age in Tertiary Care Hospital of North India. Int J Sci Study. 2020 Jan;7(10):121–4.
11. Subasakthi A SPASAH. Plasma Lipid Profile - Prognostic Factor in Nephrotic Syndrome – A Prospective Study. Annals of International Medical and Dental Research. 2017;3(3):28–32.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

12. Tipparthy S, Tanneru S, Thomas SRJ, Thanda P. Clinical and demographic profile of nephrotic syndrome in a rural tertiary care center. Int J Contemp Pediatrics. 2023 Feb 23;10(3):349–52.
13. Heaf JG. [Hyperlipidemia in nephrotic syndrome]. Ugeskr Laeger. 1991 Aug 26;153(35):2414–6.
14. Warwick GL, Caslake MJ, Boulton-Jones JM, Dagen M, Packard CJ, Shepherd J. Low-density lipoprotein metabolism in the nephrotic syndrome. Metabolism. 1990 Feb;39(2):187–92.
15. O'Donnell MP. Mechanisms and clinical importance of hypertriglyceridemia in the nephrotic syndrome. Kidney Int. 2001 Jan;59(1):380–2.
16. 1Moorhead JF, El-Nahas M, Chan MK, Varghese Z. Lipid Nephrotoxicity in Chronic Progressive Glomerular and Tubulo-Interstitial Disease. The Lancet. 1982 Dec;320(8311):1309–11.
17. Vaziri ND. Disorders of lipid metabolism in nephrotic syndrome: mechanisms and consequences. Kidney Int. 2016 Jul;90(1):41–52.
18. Al-Azzawi H, Obi O, Safi J, Song M. Nephrotic syndrome-induced thromboembolism in adults. Int J Crit Illn Inj Sci. 2016;6(2):85.
19. Agrawal S, Zaritsky JJ, Fornoni A, Smoyer WE. Dyslipidaemia in nephrotic syndrome: mechanisms and treatment. Nat Rev Nephrol. 2018 Jan 27;14(1):57–70.
20. Kumar AA. Robbins and Cotran Pathologic basis of Disease. 10th ed. Singh Manoj, Kumar Vinay, editors. New Delhi: Elsevier; 2020.

ISSN (O): 2687-5365; ISSN (P): 2753-6556