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Original Article

Comparative Study of Lipid Profile Abnormalities in Initial Attack and Relapse Cases of Childhood Nephrotic Syndrome

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Shamima Farzana[1*], A F M Azizur Rahman Siddique[2], Ferdousi Hasnat[3], Rasheda Akther[4], Most. Monira Begum[5], Taslima Sultana[6], Arif Rabbany[7], Vikarun-nesa[8], S M Sorowar Kamal[9]

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*Corresponding Author

ABSTRACT

Introduction: *Nephrotic syndrome (NS) is a common pediatric kidney disorder characterized by proteinuria, hypoalbuminemia, edema, and hyperlipidemia. It often presents as either an initial attack or a relapse, with varying clinical and biochemical features. This study investigates the differences in lipid profiles between children experiencing an initial attack and those with relapses of NS.* ***Methods & Materials:*** *This prospective analytic study was carried out in the Department of Pediatrics, Dhaka Medical College Hospital (DMCH) and Dhaka, from November 2015 to October 2017. A total of 60 children with nephrotic syndrome were studied, divided into two groups of 30 each. Group I included children with an initial attack, while Group II consisted of children presenting with first or subsequent relapses. Statistical analysis was done using the statistical package for social science (SPSS-22) program.* ***Result:*** *The study shows that puffy face, edema, and ascites were present in 100% of nephrotic syndrome (NS) cases, while genital swelling was more frequent in relapses (60% vs. 13.3%, p = 0.001). On admission, relapse cases had higher cholesterol (539.7 vs. 388.8 mg/dl), triglycerides (367.0 vs. 275.2 mg/dl), and LDL (414.5 vs. 284.9 mg/dl) compared to initial attacks (p < 0.001). During remission, these lipid levels improved but remained significantly higher in relapses, with HDL showing no significant difference.* ***Conclusion:*** *This study highlights significant lipid profile differences between initial attacks and relapses in childhood nephrotic syndrome. Relapse cases showed higher cholesterol, triglycerides, and LDL levels during active phases and remission compared to initial attacks.*

Keywords: *Lipid Profile, Nephrotic Syndrome, Initial Attack, Relapse Cases*

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1. *Junior Consultant, Department of Paediatrics, Kurmitola General Hospital, Dhaka, Bangladesh*
2. *Junior Consultant, Department of Surgery, Kurmitola General Hospital, Dhaka, Bangladesh*
3. *Associate Professor, Department of Paediatrics, Dhaka Medical College Hospital, Dhaka, Bangladesh*
4. *Junior Consultant, Department of Paediatrics, Kurmitola General Hospital, Dhaka, Bangladesh*
5. *Assistant Professor, Department of Paediatrics, Tangail Medical College, Tangail, Bangladesh*
6. *Junior Consultant, Department of Paediatrics, Sarkari Karmochari Hospital, Dhaka, Bangladesh*
7. *Junior Consultant, Department of Paediatrics, Mymensingh Medical College Hospital, Mymensingh*
8. *Junior Consultant, Department of Paediatrics, Kurmitola General Hospital, Dhaka, Bangladesh*
9. *Junior Consultant, Department of Radiology & Imaging, National Gastroliver Institute & Hospital, Dhaka, Bangladesh*

INTRODUCTION

Nephrotic syndrome (NS) is a common kidney disorder in children, characterized by significant proteinuria, hypoalbuminemia, edema, and hyperlipidemia. It is a heterogeneous condition with varying etiologies, most commonly classified as primary (idiopathic) and secondary (resulting from systemic diseases or infections) [1]. The management and prognosis of childhood nephrotic syndrome largely depend on the frequency of relapses, the response to steroids, and the complications associated with the disease, including lipid profile abnormalities [2]. The lipid abnormalities observed in nephrotic syndrome are a well-established feature of the disease and can be identified at the time of initial diagnosis and during relapses. These abnormalities typically include elevated serum total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL-C), and very low-density lipoprotein cholesterol (VLDL-C), accompanied by reduced levels of high-density lipoprotein cholesterol (HDL-C) [3]. These lipid alterations have been attributed to several mechanisms, including enhanced hepatic lipogenesis due to hypoalbuminemia and the increased activity of lipoprotein lipase, which leads to the mobilization of fatty acids into the liver [4]. The hyperlipidemia observed in nephrotic syndrome is significant not only for its association with cardiovascular risks but also for its potential role in exacerbating renal injury [5]. A comparative analysis of lipid profile abnormalities between the initial attack and relapse cases of nephrotic syndrome may provide valuable insights into the pathophysiological differences and help in optimizing therapeutic strategies. While both the initial and relapse phases of nephrotic syndrome are characterized by hyperlipidemia, the degree of lipid abnormalities and their association with disease activity may differ. Studies have suggested that the degree of hyperlipidemia in relapse cases may be more pronounced, with a higher risk of complications such as thromboembolic events, which are common in nephrotic syndrome [6]. The relationship between lipid abnormalities and long-term renal outcomes has

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been a subject of ongoing research. Elevated lipid levels are believed to contribute to glomerulosclerosis and tubulointerstitial fibrosis, which may worsen renal function over time [7]. The exact mechanisms through which lipids exacerbate kidney damage in nephrotic syndrome remain under investigation, but studies suggest that lipid accumulation in renal tissues can induce inflammation and oxidative stress, promoting kidney injury [8]. Furthermore, the lipid abnormalities in nephrotic syndrome are considered a risk factor for the development of cardiovascular diseases later in life, as children with nephrotic syndrome often maintain dyslipidemia even after remission [9]. While the role of lipid abnormalities in childhood nephrotic syndrome has been well documented, there is a limited body of research comparing the lipid profiles between the initial attack and relapse phases. Understanding whether lipid abnormalities are more pronounced or persistent during relapse phases could inform clinical decisions, especially in the management of children with frequent relapses. Additionally, therapeutic interventions such as statins and other lipid-lowering agents have been suggested to improve lipid profiles and reduce cardiovascular risk in nephrotic syndrome [10]. This study aims to compare lipid profile abnormalities between initial attack and relapse cases of childhood nephrotic syndrome. By analyzing serum levels of total cholesterol, triglycerides, LDL-C, and HDL-C, the study seeks to identify whether lipid abnormalities are more severe or persist longer during the relapse phase of nephrotic syndrome.

METHODS & MATERIALS

This prospective analytic study was carried out in the Department of Pediatrics, Dhaka Medical College Hospital (DMCH) and Dhaka, from November 2015 to October 2017. Children with a diagnosis of nephrotic syndrome admitted in the pediatric nephrology in DMCH were included in this study by purposive sampling technique. A total of 60 patients were studied. Two groups among cases were studied to evaluate any lipid profile variation. Each group included 30 children. In group I, 30 children were selected purposively who were diagnosed with initial attack nephrotic syndrome. At the same time, 30 children in group-II were also selected purposively who attend this department either with 1st or subsequent relapse. After the selection of cases in either group, the serum lipid profile (total cholesterol, triglycerides, LDL, HDL) was measured. Data were collected by structured questionnaires. Statistical analysis was done using the statistical package for social science (SPSS-22) program. Contingency table test, Independent sample T-test, and Chi-square test were used to compare variables between the two groups. A P-value of ≤ 0 .05 was considered as the level of significance. Permission was taken for this study from the Ethical Review Committee (ERC) of Dhaka Medical College & Hospital, Dhaka, Bangladesh. Written consent was obtained from either of the parents.

Inclusion criteria:

- Children diagnosed with nephrotic syndrome are either initial attacks or relapse cases.
- Age at presentation from 2 years to 8 years.
- Either sex was included.

Exclusion criteria:

- Gross hematuria
- Hypertension
- Impaired renal function test
- Hypocomplementemia
- Secondary nephrotic syndrome.
- Patients with prior H/O diabetes mellitus, hypothyroidism, familial hypercholesterolemia.
- Steroid-resistant and steroid-dependent case.

RESULTS

Table – I: Clinical presentation between initial attack and relapse cases (*n*=60)

Clinical parameters	Initial attack (n=30)		Relapse (n=30)		P value
	No	%	No	%	
Puffy face	30	100.0	30	100.0	1.000
Edema	30	100.0	30	100.0	1.000
Genital swelling	4	13.3	18	60.0	0.001*
Ascitis	30	100.0	30	100.0	1.000

Chi-square test, *= significant

Table I shows clinical presentations of NS like puffy face, edema, ascites were present in 100% of patients of both groups, which was statistically insignificant. Four patients (13.3%) of the initial attack and eighteen patients (60%) of the relapse group presented with genital swelling and the difference was statistically significant (p<0.05).

Table – II: Comparison of lipid profile on admission and during remission in initial attack of nephrotic syndrome (group-I) (*n*=30)

Lipid profile	On admission (n=30) Mean ± SD	During remission (n=30) Mean ±SD	t-value	p-value
Cholesterol (mg/dl)	388.8 ± 65.6	288.1 ± 45.8	17.38	<0.001*
Triglyceride (mg/dl)	275.2 ± 63.7	185.7 ± 60.5	12.94	<0.001*
LDL (mg/dl)	284.9 ± 56.5	192.2 ± 41.8	15.10	<0.001*
HDL (mg/dl)	47.4 ± 16.8	54.5 ± 13.3	1.815	0.075is

Data were expressed as mean ± SD.

P value reached from the Paired t-test, *= significant, is= Insignificant.

Table II shows that the mean values of cholesterol (388.8 ± 65.6mg/dl), triglyceride (275.2 ± 63.7mg/dl), LDL (284.9 ± 56.5mg/dl) of initial attack of NS on admission were significantly elevated (p-value <0.05), compared to the mean values of cholesterol (288.1 ± 45.8 mg/dl), triglyceride (185.7 ± 60.5mg/dl), LDL (192.2 ± 41.8 mg/dl) during remission. The

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mean value of HDL of the initial attack of NS on admission was (47.4 ± 16.8 mg/dl), while in remission it was (54.5 ± 13.3 mg/dl). The p-value (0.075) was insignificant.

Table – III: Comparison of lipid profile on admission and during remission in relapse cases (*n*= 30)

Lipid profile	On admission (n=30) Mean ± SD	During remission (n=30) Mean ± SD	t-value	p-value
Cholesterol	539.7 ± 95.4	445.3 ± 95.4	6.936	<0.001*
Triglyceride	367.0 ± 105.5	290.6 ± 84.3	5.055	<0.001*
LDL	414.5 ± 83.2	337.0 ± 105.5	5.01	<0.001*
HDL	55.2 ± 20.3	58.5 ± 19.9	-1.533	0.136[is]

Data were expressed as mean ± SD.
P value reached from the Paired t-test, *= significant, is = insignificant.

Table III shows that the mean values of cholesterol (539.7 ± 95.4 mg/dl), triglyceride (367.0 ± 105.5 mg/dl), LDL (414.5 ± 83.2 mg/dl) of relapse cases of NS on admission were significantly elevated (p-value < 0.05), compared to the mean values of cholesterol (445.3 ± 95.4 mg/dl), triglyceride (290.6 ± 84.3 mg/dl), LDL (337.0 ± 105.5 mg/dl) during remission. Whereas the mean value of HDL of relapse cases on admission was (55.2 ± 20.3 mg/dl), compared to the mean value of HDL (58.5 ± 19.9 mg/dl) during remission. The p-value (0.136) was insignificant.

Table – IV: Comparison of lipid profile on admission between initial attack and relapse cases (*n*= 60)

Lipid profile	Relapse (n=30) Mean ± SD	Initial attack (n=30) Mean ± SD	t-value	p-value
Cholesterol	539.7 ± 95.4	388.8 ± 65.6	7.111	<0.001*
Triglyceride	367.0 ± 105.5	275.2 ± 63.7	4.080	<0.001*
LDL	414.5 ± 83.2	284.9 ± 56.5	7.049	<0.001*
HDL	55.2 ± 20.3	47.4 ± 16.8	1.616	0.111[is]

Data were expressed as mean ± SD.
Unpaired t-test, *= significant, is = insignificant

Tale IV shows that the mean values of cholesterol (539.7 ± 95.4 mg/dl), triglyceride (367.0 ± 105.5 mg/dl), LDL (414.5 ± 83.2 mg/dl) of relapse cases of NS were significantly elevated (p value < 0.05), compared to the mean values of cholesterol (388.8 ± 65.6mg/dl), triglyceride (275.2 ± 63.7 mg/dl) LDL (284.9 ± 56.5 mg/dl) of initial attack cases of NS on admission. Whereas the mean value of HDL of relapse cases on admission was (55.2 ± 20.3 mg/dl), compared to the mean value of HDL (47.4 ± 16.8 mg/dl) of initial attack cases of NS. P-value (0.111) was insignificant.

Table – V: Comparison of lipid profile during remission in nephrotic syndrome between initial attack and relapse cases

Lipid profile	Initial attack (n=30) Mean ± SD	Relapse (n=30) Mean ± SD	p-value
Cholesterol	288.1 ± 45.8	445.3 ± 95.4	<0.001*
Triglyceride	185.7 ± 60.5	290.6 ± 84.3	<0.001*
LDL	195.2 ± 41.8	336.6 ± 103.1	<0.001*
HDL	54.5 ± 13.3	58.5 ± 19.9	0.360[is]

Unpaired t-test, *= significant, is= insignificant

Table V shows that the mean values of cholesterol (445.3 ± 95.4 mg/dl), triglyceride (290.6 ± 84.3 mg/dl), LDL (336.6 ± 103.1 mg/dl) of relapse cases of NS were significantly elevated (p-value < 0.05), compared to the mean values of cholesterol (288.1 ± 45.8 mg/dl), triglyceride (185.7 ± 60.5 mg/dl), LDL (195.2 ±41.8 mg/dl) of initial attack cases of NS during remission. Whereas the mean value of HDL of relapse cases during remission was (58.5 ± 19.9mg/dl) compared to the mean value of HDL (54.5 ± 13.3mg/dl) of initial attack cases of NS. P-value (0.360) was insignificant.

DISCUSSION

Nephrotic syndrome (NS) in children is a disorder characterized by heavy proteinuria, hypoalbuminemia, edema, and hyperlipidemia. The management and outcome of NS are influenced by multiple factors, including the frequency of relapses and the presence of associated complications, such as lipid abnormalities. One of the major clinical manifestations observed in this study was the presence of puffy face, edema, and ascites in 100% of both the initial attack and relapse groups. These findings are consistent with the classical clinical features of nephrotic syndrome and are well documented in previous studies [11,12]. The presence of genital swelling, however, was significantly more common in the relapse group (60%) compared to the initial attack group (13.3%), with a p-value of 0.001, highlighting a possible correlation between relapse episodes and the severity of edema. Genital swelling has been reported in various studies as a prominent feature of nephrotic syndrome, especially during relapses, possibly due to the altered distribution of fluid in the body [3,5]. In terms of lipid profile abnormalities, this study reveals several important findings. In the initial attack cases, there were significantly elevated levels of cholesterol, triglycerides, and LDL-C compared to the values during remission. The mean cholesterol level during the initial attack was 388.8 ± 65.6 mg/dl, which decreased significantly to 288.1 ± 45.8 mg/dl during remission, with a p-value of <0.001. Similar trends were observed for triglycerides and LDL-C. These findings are consistent with earlier studies, which have shown that hyperlipidemia is a hallmark of nephrotic syndrome and is often at its peak during the active phase of the disease [10]. Elevated lipid levels are believed to be the result of altered lipid metabolism due to

hypoalbuminemia, which leads to an increased hepatic synthesis of lipoproteins [13]. In contrast, the HDL-C levels did not show a statistically significant change, which is in agreement with some reports indicating that HDL levels tend to be less affected by the nephrotic state. In relapse cases, the lipid abnormalities were even more pronounced. On admission, cholesterol levels in the relapse group were 539.7 ± 95.4 mg/dl, significantly higher than the 388.8 ± 65.6 mg/dl observed in the initial attack group. Similarly, triglycerides (367.0 ± 105.5 mg/dl vs. 275.2 ± 63.7 mg/dl) and LDL-C (414.5 ± 83.2 mg/dl vs. 284.9 ± 56.5 mg/dl) were significantly elevated in relapse cases compared to the initial attack cases. These findings support the hypothesis that relapse episodes of nephrotic syndrome are associated with more severe lipid disturbances [6]. Elevated lipid levels during relapses could be attributed to several factors, including prolonged or repeated corticosteroid use, which is known to induce hyperlipidemia, as well as the increased hepatic production of lipids in response to the nephrotic state [14]. The mean lipid levels were still higher in the relapse group during remission, the differences were statistically significant only for cholesterol, triglycerides, and LDL-C, with p-values of <0.001. This suggests that while lipid abnormalities may persist after remission in relapse cases, they are not as elevated as during the active phase. However, the sustained elevation of lipid levels during remission in the relapse group emphasizes the potential long-term risks associated with recurrent nephrotic syndrome, such as cardiovascular complications [15]. The mean HDL-C levels in both groups during remission were similar and showed no significant difference, suggesting that the reduction in HDL-C levels observed during the active phase of nephrotic syndrome tends to normalize during remission. This finding is in line with studies suggesting that HDL levels tend to recover once the nephrotic state resolves [16]. The results of this study also have implications for treatment strategies in nephrotic syndrome. Lipid-lowering therapies, such as statins, have been suggested for the management of hyperlipidemia in nephrotic syndrome, particularly in patients with persistent dyslipidemia and those at high risk for cardiovascular diseases. In this study, the more severe lipid abnormalities observed in the relapse cases highlight the need for closer monitoring of lipid levels in children with frequent relapses, as they may benefit from earlier intervention with lipid-lowering agents. Furthermore, lifestyle modifications, including dietary interventions and physical activity, could be considered as adjunctive treatments to improve lipid profiles in these children [17].

Limitations of The Study

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community. Moreover, VLDL could not be assessed because of non – availability.

CONCLUSION

This study highlights significant differences in lipid profile abnormalities between initial attacks and relapse cases of childhood nephrotic syndrome. Lipid profiles during the active phases revealed higher levels of cholesterol, triglycerides, and LDL in relapse cases compared to initial attacks, with these abnormalities persisting during remission.

RECOMMENDATION

Given the significant lipid abnormalities observed in both initial attacks and relapse cases of childhood nephrotic syndrome, particularly in relapse cases, it is recommended that regular lipid profile monitoring be integrated into the clinical management of these patients. Early intervention strategies, including dietary modifications, lipid-lowering therapies, and comprehensive follow-up during remission, should be prioritized to minimize the risk of long-term cardiovascular complications. Further multicenter prospective studies with larger sample and long term follow up will validate the findings of the present study.

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