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Comparison of Clinical & Laboratory Profile Between Nephrotic & Healthy Children: Study in a Tertiary Care Hospital of Bangladesh

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Abstract

Introduction: *The nephrotic syndrome is caused by increased permeability across the glomerular filtration barrier. It is classically characterized by nephrotic range proteinuria, hypoalbuminemia, and edema. This study aimed to analyze the clinical and laboratory profile of children with nephrotic syndrome (NS).*

Methods: *This cross-sectional study was conducted at the Department of Paediatric Nephrology, National Institute of Kidney Diseases & Urology, Sher-E-Bangla Nagar, Dhaka, and the Department of Biochemistry and Molecular Biology, Dhaka Shishu Hospital, Dhaka, between December 2019 and June 2021. The study population included 60 children with nephrotic syndrome (Group A) and 60 age-matched healthy children (Group B) as controls. After obtaining informed written consent and ethical clearance, detailed history, clinical examination, and relevant investigations were performed on the participants. Statistical analysis was conducted using SPSS 24, with a significance set at a p-value of <0.05. The study ensured ethical considerations, confidentiality, and the participant's right to withdraw from the study.*

Result: *The mean age of all study children was 6.44±3.29 years (range: 2-12 years). The highest percentage of patients from both group A and group B were aged less than 6 years (55% and 51.67% respectively). However, there were no significant differences between the two groups of children regarding both mean age and age group distribution (p-value>0.05). A male was the predominant gender in both group A and group B (63.33 and 60%, respectively) without any significant difference between groups (p-value =0.701). Moreover, height, weight, BMI, pulse, SBP, DBP, and temperature do not significantly vary between groups. However, nephrotic children had significantly higher mean total platelet count (4.45±1.69 vs 3.24±1.58 lacs/mm^3) than healthy children. Besides, serum albumin was significantly lower among Group A compared to Group B (2.09±0.75 vs 4.25±0.52 mg/dL, p<0.001). No proteinuria was found in Group B and proteinuria ranges between 1+ to 4+ in Group A.*

Conclusion: *This study concluded that the mean age of all study children was 6.44±3.29 years (range: 2-12 years), along with male preponderance. Patients mostly lived in rural areas. There was no statistically significant finding between the two groups in terms of BMI, BP, and pulse. However, nephrotic children had significantly higher mean total platelet count (4.45±1.69 vs 3.24±1.58 lacs/mm^3) than healthy children. Besides, serum albumin was significantly lower among Group A compared to Group B (2.09±0.75 vs 4.25±0.52 mg/dL, p<0.001). No proteinuria was found in Group B and proteinuria ranges between 1+ to 4+ in Group A.*

Keywords: *Nephrotic Syndrome, Albumin, Dyslipidemia*

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I. INTRODUCTION

Nephrotic syndrome is the most common childhood kidney disease. Nephrotic syndrome (NS) is defined by massive proteinuria & hypoalbuminemia with resulting edema & hyperlipidemia (Boyer et al. 2017).[1] The incidence of idiopathic nephrotic syndrome (INS) is 1·15–16·9 per 100,000 children, which varies with ethnicity and region (Downie et al. 2017).[2] South Asian children are thought to have the highest incidence (Banh et al. 2016).[3] Complications due to the disease itself include infections, thromboembolism, cardiovascular diseases, hypovolemic crisis, anemia, and acute renal failure (Park and Shin 2011).[4] Thromboembolism is a significant complication of nephrotic syndrome in both adult and children which usually present early in the disease course. It complicates about 3% of children with nephrotic syndrome (Kerlin, Ayoob, and Smoyer 2012) [5] and the risk is higher among children with membranous nephropathy and membranoproliferative glomerulonephritis (Hârza et al. 2013). [6] The occurrence of deep vein thrombosis (DVT) among nephrotic children is associated with triglyceride levels greater than 300 mg/dL (Candelaria and Belangero 2011).[7] Nephrotic syndrome-induced dyslipidemia in children can be persistent or intermittent. Hyperlipidemia may persist in nearly half of the nephrotic syndrome patients at remission (Mérouani et al. 2003). The persistence and severity of lipid changes can be associated with the duration of the disease and the frequency of relapses. The pathology of nephrotic hyperlipidemia is complex and multifactorial. [8] Although both nephrotic range proteinuria and hypoalbuminemia are required for the diagnosis of nephrotic syndrome, edema is the most common presenting symptom in most cases. Periorbital edema is typically noted first and is often misdiagnosed as a manifestation of allergy. The edema is gravity-dependent, so throughout the day, periorbital edema decreases while edema of the lower extremities increases. Edema increases gradually and becomes detectable when fluid retention exceeds 3 to 5 percent of body weight. Hypertension is infrequent in patients with minimal change disease. However, it is common in patients with glomerulonephritis, who may also have nephrotic syndrome and hypertension. For patients with glomerulonephritis, hypertensive encephalopathy is an uncommon but serious complication. Gross hematuria is rare in idiopathic nephrotic syndrome, although microscopic hematuria is seen in 20% of cases. In contrast, gross hematuria is most often seen in patients with glomerulonephritis (e.g., postinfectious glomerulonephritis or membranoproliferative glomerulonephritis). Despite the marked increase in extracellular fluid volume, some children with nephrotic syndrome present with or develop signs of a decrease in effective circulating volume, such as tachycardia, hypotension, peripheral vasoconstriction, oliguria, and decreased GFR. Nephrotic range proteinuria is usually defined as >50 mg/kg/day or 40 mg/hr/m^2 in a 24-hour urine collection. In children, early morning 'spot' urine protein to creatinine ratio is often used to quantify proteinuria because it may be difficult to perform a 24-hour urine collection. The plasma albumin level is typically less than 3 g/dL (30 g/L) and may be less than 1 g/dL (10 g/L). Plasma protein levels are also markedly reduced due to hypoalbuminemia, often less than 5 g/dL (50 g/L). Hemoglobin and hematocrit may be increased in children with nephrotic syndrome, particularly MCD, as a result of plasma volume contraction. Thrombocytosis is common and platelet counts may reach 500,000 to 1 million counts/microL. Hemoconcentration and thrombocytosis may contribute to hypercoagulability and thrombotic complications. [9]

II. OBJECTIVE

General Objective

- To compare the clinical and laboratory profile of healthy children & children with nephrotic syndrome.

Specific Objectives

- To see the age and sex distribution of the respondents.
- To see the urinary findings between the two groups.

III. METHODS

This cross-sectional study was conducted at the Department of Paediatric Nephrology, National Institute of Kidney Diseases & Urology, Sher-E-Bangla Nagar, Dhaka, and the Department of Biochemistry and Molecular Biology, Dhaka Shishu Hospital, Dhaka, between December 2019 and June 2021. The study population included 60 children with nephrotic syndrome (Group A) and 60 age-matched healthy children (Group B) as controls. The purposive sampling method was used in this study. After obtaining informed written consent and ethical clearance, detailed history, clinical examination, and relevant investigations were performed on the participants. Blood samples were collected from fasting subjects, and serum was separated for subsequent estimation of high-sensitivity C-reactive protein (hs-CRP) and lipid levels. Hs-CRP was measured by immunofluorescence assay, while serum total cholesterol, triglycerides, high-density lipoprotein (HDL), and low-density lipoprotein (LDL) were measured by enzymatic methods. Statistical analysis was conducted using SPSS 24, with a significance set at a p-value of <0.05. The study ensured ethical considerations, confidentiality, and the participant's right to withdraw from the study.

Inclusion criteria:

- Group A: Children with nephrotic syndrome aged between 2-12 years, having no sign of acute infection, no hypertension, and hyperglycemia.
- Group B: age-matched healthy children not having signs of acute infection, no hypertension and hyperglycemia.

Exclusion criteria:

- Children with aged < 2 years and >12 years (atypical presentation of NS)
- A nephrotic syndrome due to secondary causes.

IV. RESULTS

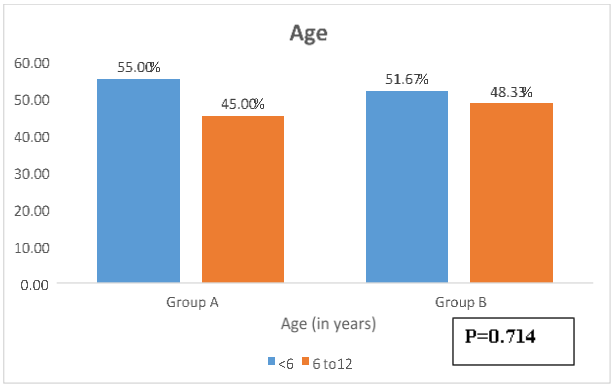

Figure 1: Distribution of study children according to Age (n=120).

The mean age of all study children was 6.44±3.29 years (range: 2-12 years). The highest percentage of patients from both group A and group B were aged less than 6 years (55% and 51.67% respectively). However, there were no significant differences between the two groups of children regarding both mean age and age group distribution (p-value>0.05).

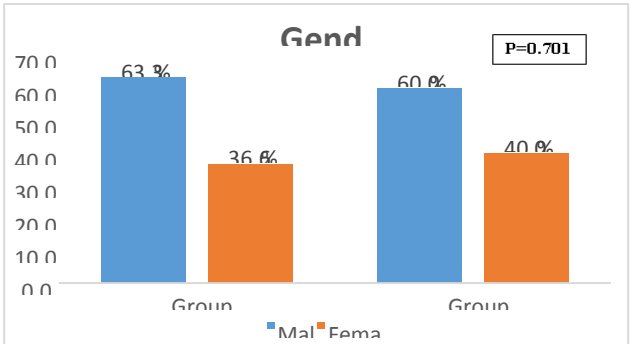

Figure 2: Gender distribution of study children (n=120).

A male was the predominant gender in both group A and group B (63.33 and 60%, respectively) without any significant difference between groups (p-value =0.701).

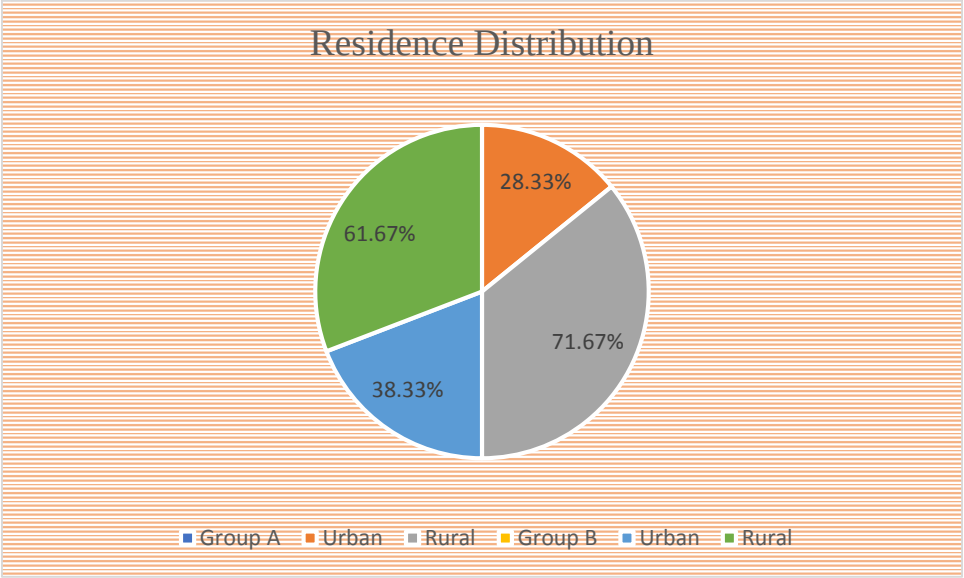

Figure 3: Residence distribution of the study children (n=120).

Table 1: Distribution of study children according to clinical findings (n=120).

Variables	Group B (n=60)	GroupA (n=60)	p-value*
	Mean±SD	Mean±SD	
Height (cm)	111.19±17.09	111.61±19.67	0.901
Weight (kg)	22.14±7.69	22.88±9.69	0.643
BMI (Kg/m^2)	17.45±2.47	17.57±2.57	0.785
Pulse (bpm)	78.07±7.20	78.10±6.62	0.979
SBP (mmHg)	98.83±8.75	99.33±8.05	0.745
DBP (mmHg)	98.83±8.75	62.08±5.77	0.511
Temperature (^{o}F)	98.40±0.14	98.35±0.27	0.213

Table 1 shows that height, weight, BMI, pulse, SBP, DBP, and temperature do not significantly vary between groups.

Table 2: Distribution of NS patients according to type & treatment of nephrotic syndrome (n=60).

Variable	Frequency	Percentage
Type of nephrotic syndrome (NS)		
Minimal change disease (MCD)	55	91.67
Other than MCD (FSGS and MPGN)	5	8.33
Number of episodes		
Initial episode	14	23.3
Infrequent relapse NS	24	40
Frequent relapse NS	10	16.7
Steroid dependent NS	9	15
Steroid resistant NS	3	5
Treatment history		
Corticosteroid alone	43	71.67
Corticosteroid plus other immunosuppressive (Mycophenolate	17	28.33

Table 2 shows that Minimal change disease (MCD) was found in 55 cases (91.67%); among the rest (8.33%) other than MCD patients 3 patients had focal segmental glomerulosclerosis (FSGS) and 2 patients membranoproliferative glomerulonephritis (MPGN). The initial episode of NS was found in 23.3% of cases, while 40.0% of cases had infrequent relapse NS and 16.7% had frequent relapse NS. Nine cases (15%) reported steroid-

dependent NS, while three (5%) had steroid-resistant NS. Maximum NS children (71.67%) were being treated with corticosteroid only, while seventeen cases (28.33%) were treated with Corticosteroid plus other medications (Mycophenolate mofetil, Tacrolimus, and Cyclosporin).

Table 3: Distribution of study children according to laboratory parameters (n=120).

Variables	Group B (n=60) Mean±SD	Group A (n=60) Mean±SD	p-value
Haemoglobin (g/dL)	11.68±1.06	12.14±1.58	0.064
WBC total count (x103/mm3)	10.62±13.12	11.17±2.76	0.753
Neutrophil (%)	55.42±13.13	59.22±12.12	0.102
Lymphocyte (%)	32.70±10.16	31.22±10.46	0.432
Eosinophil (%)	7.17±6.53	5.20±3.40	0.051
Platelet count (lacs/mm3)	3.24±1.58	4.45±1.69	<0.001
S. albumin (mg/dL)	4.25±0.52	2.09±0.75	<0.001
S. creatinine (mg/dL)	0.57±0.14	0.56±0.14	0.691
RBS (mmol/L)	4.48±0.74	4.71±0.83	0.104
24-hour urinary total protein	-	6.92±7.65	-

Table 3 shows that nephrotic children had significantly higher mean total platelet count (4.45±1.69 vs 3.24±1.58 lacs/mm^3) than healthy children. Besides, serum albumin was significantly lower among Group A compared to Group B (2.09±0.75 vs 4.25±0.52 mg/dL, p<0.001).

Table 4: Urine examination findings of study children (n=120).

Variables	**Group B**	**Group A**	**p-value***
	(n=60)	**(n=60)**	
	No. (%)	**No. (%)**	
Urinary albumin			<0.001
Nil	60(100)	11(18.33)	
+	0(0)	3(5)	
++	0(0)	16(26.67)	
+++	0(0)	29(48.33)	
++++	0(0)	1(1.67)	
Urine RBC (/HPF)			0.333
Nil	58(96.67)	55(91.67)	
0-1	2(3.33)	2(3.33)	
1-2	0(0)	3(5)	
Urine plus cell(/HPF)			0.006
Nil	1(1.67)	2(3.33)	
0-1	3(5)	2(3.33)	
1-2	52(86.67)	36(60)	
2-3	1(1.67)	9(15)	
2-4	2(3.33)	7(11.67)	
4-6	1(1.67)	4(6.67)	
Urine Culture			
Growth	0(0)	0(0)	
No growth	60(100)	60(100)	

Table 4 shows the urine examination findings of the study children. No proteinuria was found in Group B and proteinuria ranges between 1+ to 4+ in Group A.

V. DISCUSSION

As per the predetermined data sheet after careful history taking, clinical examination, and appropriate investigations fulfilling the inclusion and exclusion criteria, a total of 120 children (aged between 2-12 years)

were included in this study, irrespective of their gender, race, ethnic group, and age. Study children were categorized into group A, (n=60) and group B (n=60). Group A: children with nephrotic syndrome and Group B: age-matched healthy children. The mean age of all study children was 6.44±3.29 years (range: 2- 12 years). The highest percentage of children from both group A and group B were aged less than 6 years (55% and 51.67% respectively). Our study showed that male was the predominant gender in both the NS and healthy group (63.33 and 60%, respectively). However, there were no significant differences between the two groups of children regarding both age and gender distribution. Previous studies also reported similar age-gender distribution among children with nephrotic syndrome Patel et al. (2017); [10] Wasilewska et al. (2007);[11] Hossain (2016); [12] Esezobor, Solarin, and Gbadegesin (2020). [13] In the present study, minimal change disease (MCD) was found in 55 cases (91.67%), among the rest (8.33%) other than MCD patients three patients had focal segmental glomerulosclerosis (FSGS) and two patients had membranoproliferative glomerulonephritis (MPGN). This finding is not similar to a previous study done by Begum et al.(2017) [14] where MesPGN was the most common histological finding followed by MCD. This may be due to not including nephrotic syndrome due to secondary causes and most of our patients were not biopsy-proven MCD, but rather from clinical and some laboratory parameters. In this study, Group A and Group B had no significant differences in clinical findings. Nephrotic children had a significantly higher mean of total platelet count (4.45±1.69 vs 3.24±1.58 lacs/mm^3) and lower albumin level (2.09±0.75 vs 4.25±0.52 mg/dL, $p<0.001$) than healthy children. Similar to our study, Wasilewska et al. (2007) [11] found increased platelet counts and reduced albumin levels in their nephrotic patients compared to the control. Atherosclerosis along with hyperreactive platelets increases the risk of thrombosis among these children with hypoalbuminemia which can be further aggravated by dyslipidemia (Jackson and Calkin, 2007). [15] We found that 18% of patients were in remission of proteinuria during the study but their lipid profiles were higher similar to proteinuric patients. Comparable to our study Mérouani et al. (2003) found that hyperlipidemia persisted in nearly half of their nephrotic syndrome patients at remission. [8] Regarding urine examination, no proteinuria was found in Group B, and proteinuria ranges between 1+ to 4+ in Group A in the current study. Similarly, Albar H et al. showed in their study that, the prevalent laboratory findings were microscopic hematuria (50.7%), massive proteinuria (100%), hypoalbuminemia (100%), hypercholesterolemia (100%), and elevated serum creatinine (9.9%), which was quite similar to the present study. [16]

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.

VI. CONCLUSION

This study concluded that the mean age of all study children was 6.44±3.29 years (range: 2-12 years), along with male preponderance. Patients mostly lived in rural areas. There was no statistically significant finding between the two groups in terms of BMI, BP, and pulse. However, nephrotic children had significantly higher mean total platelet count (4.45±1.69 vs 3.24±1.58 lacs/mm^3) than healthy children. Besides, serum albumin was significantly lower among Group A compared to Group B (2.09±0.75 vs 4.25±0.52 mg/dL, $p<0.001$). No proteinuria was found in Group B and proteinuria ranges between 1+ to 4+ in Group A.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

VII. RECOMMENDATION

This study recommends that, to identify NS proper history, clinical and laboratory variables; such as quantification of proteinuria by protein/creatinine ratio (UPCR) in either a first morning (AM) urine or 24-h urine sample should be checked at least once before defining a patient as NS and/or starting alternative immunosuppression. Moreover, further studies should be conducted involving a large sample size and multiple centers in this regard.

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