

“Correlation between Serum Prednisolone and Serum Albumin level in Childhood with Nephrotic Syndrome: A study in tertiary care hospital in Bangladesh”

Abu Bakkir Siddique¹, Mohammed Hanif², Farid Ahmed³, Nazia Hossain⁴,
Maizbha Uddin⁵

1. Resident Medical Officer, Dhaka Shishu (Children) Hospital.

2. Professor & Head, Department of Paediatric Nephrology, Bangladesh Institute of Child Health, Dhaka (Shishu) Hospital.

3. Professor & Head, Department of General Paediatrics, Bangladesh Institute of Child Health, Dhaka (Shishu) Hospital.

4. Resident Medical Officer, Dhaka Shishu (Children) Hospital.

5. Assistant Professor, Department of Pharmacology, Dhaka University.

Corresponding Author: Dr Abu Bakkir Siddique

Abstract: Nephrotic syndrome, or nephrosis, is defined by the presence of nephrotic-range proteinuria, edema, hyperlipidemia, and hypoalbuminemia. While nephrotic-range proteinuria in adults is characterized by protein excretion of 3.5 g or more per day but in children it is defined as protein excretion of more than 40 mg/m²/h or a first-morning urine protein/creatinine of 2-3 mg/mg creatinine or greater. Prednisolone is a steroid medication used to treat certain types of allergies, inflammatory conditions, autoimmune disorders, and cancers, is very potent medication to treat children with nephrotic syndrome. The aim of this study was to evaluate the association between serum Prednisolone and serum albumin in childhood nephrotic syndrome. This prospective observational study was done in the department of Paediatric Nephrology & Kidney diseases, Dhaka Shishu (Children) Hospital, Sher - E - Bangla Nagar, Dhaka and Clinical Pharmacy & Pharmacology Dept. University of Dhaka from January 2014 to December 2014. Serum Prednisolone and serum Albumin were measured by enzymatic colorimetric method. The relationship between serum Prednisolone and serum Albumin was shown by Chi-square test and Paired 't' test. Serum prednisolone was measured in nephrotic syndrome during active phase & in remission and the average values were 2.088795 mic. mol/ml & 2.175277 mic. mol/ml respectively which was significantly high in remission of NS. This was not done previously in our country. Serum albumin was also measured in this study, average s. albumin level during active phase & in remission were 9.339318 gm/L & 20.4907 gm/L respectively which was significantly high in remission of NS.

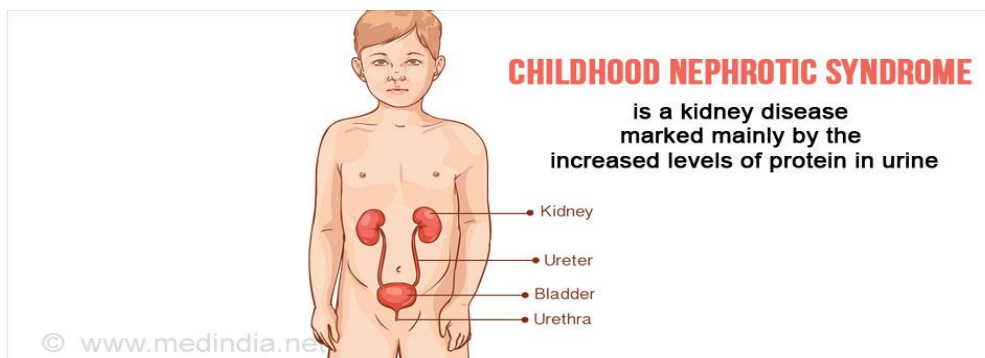
Key words: Nephrotic syndrome, Hypoalbuminemia, Serum Prednisolone, Serum Albumin

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I. Introduction

Nephrotic Syndrome is a disease primarily of Pediatric age group. The syndrome is characterized by heavy proteinuria > 40mg/ m²/ h, hypoalbuminaemia < 2.5 gm /dl, edema and hyperlipidemia.¹ Majority of affected children were steroid/prednisolone-sensitive minimal change disease. First-line drug for the treatment of idiopathic nephrotic syndrome is steroid/prednisolone therapy.² Ashypoalbuminaemia is one of the cardinal features, measurement of serum albumin level is important.¹ In children the most common presentation of glomerulonephritis is nephrotic syndrome. Histologically minimal change disease is the commonest 76.4%.³ In a retrospective study of all children in Nelson R Mandela School of Medicine, the commonest cause of chronic kidney disease (stage 2-5) was Nephrotic Syndrome comprising 30.9% in children < 5 years old & 40.8% in > 5 years old.⁴ In Nephrotic syndrome, renal failure may develop in some percentage. 30-40 % steroid resistant minimal change disease develops end stage renal disease by 5 years.⁵



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First-line drug in idiopathic nephrotic syndrome of childhood is prednisolone. The degree of therapeutic response and the side effects of prednisolone may show considerable inter individual variation among patients receiving standard daily doses. This variability can be explained to some extent by differences in severity of the disease. The volume of distribution and the plasma clearance of prednisolone are abnormally high during the active phase of nephrotic syndrome but tend to decrease as the disease improves.⁴ The protein binding of prednisolone is highly dependent on plasma protein levels which, in turn, are known to increase markedly within a few weeks of therapy in responsive patients.² Hypoalbuminaemia in children with the nephrotic syndrome is due to an increase in turnover of total body albumin, may be result of a combination of two factors: 1) an increase in the fractional rate of catabolism of albumin and 2) albuminuria.²

In children with ascites&anasarca, the fractional rate of albumin catabolism and the renal loss of albumin both are greatly increased. The deficiencies of albumin seen in the Plasma of children with nephrotic syndrome are due to an increased fractional rate of catabolism in association with renal losses. In nephrotic syndrome with hypoalbuminaemia, patient may present with severe edema/anasarca, severe respiratory distress and with complications as immunocompromised.² Sometimes hospital stay of patients with nephritic syndrome become prolonged due to complications like huge ascites, anasarca, deep vein thrombosis, respiratory distress etc.

Most of the Nephrotic syndrome patients are steroid responsive. Some response earlier, some take long duration and a few do not respond. Prednisolone is the drug of choice. Still it has some toxicity. On the other hand, hypoalbuminaemia one of the cardinal feature of NS, causes edema, ascites, anasarca, severe respiratory distress and some co-morbidities. Sometimes albumin transfusion becomes eminent. Bioavailability of serum prednisolone will be low, when serum albumin is low, as serum prednisolone bound with protein in serum which causes delayed recovery of patient with nephritic syndrome. So serum prednisolone& albumin needs to be measured during active phase and in remission to see relationship and their clinical outcome. Moreover, no study was done in our country by measuring serum prednisolone and albumin level in nephrotic syndrome.

So, this study was done to measure serum prednisolone level and serum albumin level in nephrotic syndrome during active phase and in remission and to observe their relationship with clinical outcome.

II. Objectives

General Objective:

1. To evaluate the correlation between serum prednisolone level and serum albumin level in children with idiopathic nephrotic syndrome.

Specific Objectives:

1. To estimate the serum prednisolone in children with nephrotic syndrome in Bangladesh.
2. To estimate serum albumin level in children with nephrotic syndrome in Bangladesh.

III. Method& Materials

A prospective observational study was done in the department of Paediatric Nephrology & kidney diseases, Dhaka Shishu (Children) Hospital, Sher - E - Bangla Nagar, Dhaka and Clinical Pharmacy & Pharmacology Dept. University of Dhaka from January 2014 to December 2014. Forty-four diagnosed nephrotic syndrome patients admitted in Dhaka Shishu Hospital were purposively included in this study whose age, 1-8 years, steroid responder & Idiopathic nephrotic syndrome were included. NS patients, age < 1 years and > 8 years. Steroid dependent & resistant nephrotic syndromes were excluded. Prior to commencement of the study ethical clearance was taken from the ethical clearance committee of BICH. Informed written consent from legal guardian was taken after proper counseling. Reassurance was given to the guardian regarding investigations.

First of all thorough history & elaborate clinical examination were noted on a questionnaire. Biochemical & other necessary investigations like CBC, Urine R/E, S. cholesterol, spot urine protein creatinine ratio, HBsAg, S. creatinine MT, USG of KUB, CXR, etc. were done. Two ml Blood was collected from the patient & centrifuged. Then Serum was collected & stored in refrigerator. Then serum Albumin & Serum Prednisolone were measured by chromatograph machine in active phase & in remission. S. albumin level was measured in the department of Biochemistry, Dhaka Shishu Hospital and S. Prednisolone was measured in the Dept. of Pharmacology, Dhaka University. Data were collected by using prescribed questionnaire, compiled and analyzed by using STRATA 12. Chi-square test and Paired ‘t’ test were used as the test for significance. P value of < 0.05 was considered statistically significant.

IV. Result

This study was a prospective observational study. Serum Prednisolone and Albumin level were measured in nephrotic syndrome patients during active phase and in remission & their relationships with clinical outcome were seen. The results in this study are given below.

Table 1: Mean age of the study participants in year (n=44)

	Mean age	S.E	CI
age	4.287356	0.180519	3.928497 4.646216

Mean age of patient was 4 years 3 months.

Figure 1: Sex distribution of the study participants (n=44)

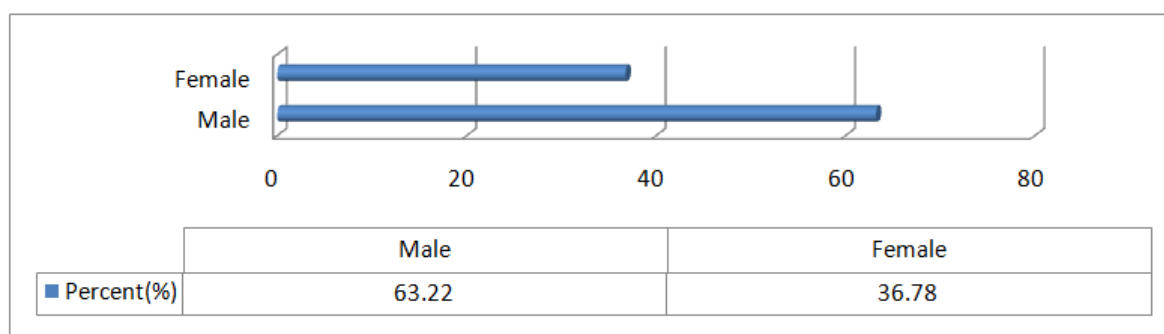
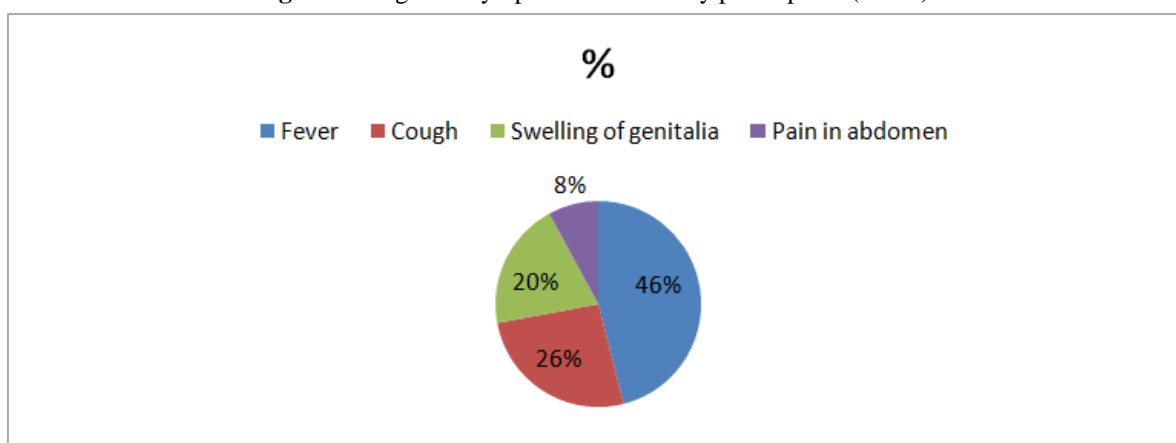


Figure 2: Signs & Symptoms of the study participants (n=44).



All patients presented with oedema, puffy face & ascites. Fever- 52.27%, cough - 29.55% , swelling of genitalia -22.73% and pain in abdomen - 9% among study participants.

Table 2: Distribution of signs & symptoms in remission among the study participants (n=44)

	Odema	Fever	swelling genitalia	of swelling abdomen	of pain in abdomen	cough	Puffy face
Present	0	0	0	0	0	0	0
Absent	43	43	43	43	43	43	43

All the patients in remission having no symptom like oedema, fever, swelling of genitalia, ascites, pain in abdomen, cough, puffy face etc.

Table 3: Serum Prednisolone level during active phase of NS and in remission (n=44)

Group	Obs	Mean	Std. Err.	Std. Dev.	[95% Conf. Interval]
Active phase	25	2.088795	0.008978	0.04489	2.070265 2.107324
In remission	16	2.175277	0.02928	0.117122	2.112868 2.237687
combined	41	2.122544	0.014123	0.090428	2.094001 2.151087
difference		-0.08648	0.030626		-0.15086 -0.0221

Ho: diff = 0	t = -2.8238
Ha: diff != 0	P = 0.0113

Serum prednisolone level is significantly high in remission (P value = 0.0113).

Table 4: Serum Albumin level during active phase of NS and in remission (n=44)

Group	Obs	Mean	Std. Err.	Std. Dev.	[95% Conf. Interval]
Active phase	44	9.339318	0.671417	4.453675	7.985277 10.69336
In remission	43	20.4907	1.177342	7.720348	18.11473 22.86667
combined	87	14.85092	0.900013	8.394765	13.06175 16.64009
difference		-11.1514	1.347467		-13.8305 -8.47225

Ho: diff = 0	t = -8.2758
Ha: diff != 0	P < 0.0000

Serum albumin is significantly high in remission (P value < 0.0000).

Table 5: Distribution of patients by relapse among study participants (n=44)

	no of patient	percentage	m.albumin in AP(gm/L)	m.albumin in Rem(gm/L)	m.pred.in AP (mic.mol/ml)	m.pred.in Rem (mic.mol/ml)
NS 1st attack	16	36.36	9.43	22.49	2.089	2.175
NS 1st relapse	12	27.27	9.33	20.40	2.082	2.173
NS 2nd relapse	10	22.73	9.33	20.40	2.082	2.173
FRNS	6	13.64	9.28	16.48	2.080	2.171

Above table shows that 16 were 1st attack NS, 12 were 1st relapse NS, 10 were 2nd relapse NS and 6 were FRNS among 44 study participants.

V. Discussion

This study was done in the in the department of paediatric nephrology & kidney diseases, Dhaka Shishu (Children) Hospital, Sher - E - Bangla Nagar, Dhaka and Clinical Pharmacy & Pharmacology Dept. University of Dhaka from January 2014 to December 2014 . In this study, serum prednisolone was measured in nephrotic syndrome during active phase & in remission and the average values were 2.088795 mic. mol/ml& 2.175277 mic.mol/ml respectively which was significantly high in remission of NS. This was not done previously in our country. Serum albumin was also measured in this study, average s. albumin level during active phase & in remission was 9.339318 gm/L & 20.4907 gm/L respectively which was significantly high in remission of NS. Another study done by Jorge J et al 1997 showed that serum albumin was 19.04 gm/L. So serum prednisolone has direct relation with serum albumin that is serum prednisolone increases when serum albumin is increased. In this study, 1st attack nephrotic syndrome was 36.36 %, 1st relapse nephrotic syndrome was 27.27 %, 2nd relapse nephrotic syndrome was 22.73 % and frequent relapse nephrotic syndrome was 13.64 %. Serum prednisolone & serum albumin levels were higher in 1st attack nephrotic syndrome than frequent relapse nephrotic syndrome. In age distribution, mean age of patient was 4 years 3 months and in

sex distribution, male is predominant 63.22 %. Clinical presentation of cases: oedema, puffy face & ascites were present in all patients of nephrotic syndrome. Fever, cough, swelling of genitalia and pain in abdomen were present in 52.27 %, 29.55 %, 22.73 % and 9 % of cases respectively. All the signs & symptoms were absent in remission of nephrotic syndrome.

VI. Limitations

The study showed a positive association between Serum prednisolone and Serum albumin. However, lower number of sample size and one single study place may not reflect the exact scenario of all around the country about Nephrotic Syndrome.

VII. Conclusion

Serum prednisolone and Serum albumin both were significantly increased in remission than active phase of Nephrotic Syndrome patients which ensures better clinical outcome of NS.

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