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Original Article

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Prognostic Value of Biochemical and Hematological Parameters in Children with Nephrotic Syndrome

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Abstract

Background: Nephrotic syndrome causes a great morbidity and mortality among the children. **Objective:** The purpose of the present study was to compare the biochemical and hematological parameters and their prognostic value in steroid resistant (SRNS), frequent relapse and steroid dependent (FRNS+SDNS) and infrequent relapse (IFRNS) groups. **Methodology:** A prospective study of 43 children with idiopathic nephrotic syndrome (INS) selected randomly out of 480 children admitted with the disease at Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka from January 2003 to January 2005. There were 24 steroid sensitive nephrotic syndrome (SSNS) and 19 steroid resistant nephrotic syndrome (SRNS), of SSNS group 13 were infrequent relapse (IFRNS) and 11 were frequent relapse steroid dependent (FRNS+SDNS). **Result:** SRNS has low serum total protein (STP), albumin and hemoglobin compared to SSNS ($P<0.01$, $P<0.001$). SRNS also has high cholesterol, creatinine and urinary total protein (UTP) than SSNS ($P<0.01$, $P<0.001$). Higher difference was observed between SRNS and IFRNS ($P<0.001$). High serum cholesterol, UTP and low hemoglobin were found in FRNS+SDNS compared to IFRNS ($P<0.01$, $P<0.05$). **Conclusion:** STP, albumin, creatinine were equally low in SRNS and FRNS+SDNS. [J Shaheed Suhrawardy Med Coll, 2013;5(2):95-98]

Keywords: Biochemical parameters, hematological parameters, nephrotic syndrome

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Introduction

Nephrotic syndrome is characterized by massive proteinuria (urinary total protein >1gm/m2/day or urinary spot protein creatinine ratio of >200 mg/mmol), Hypoalbuminemia (serum albumin <2.5gm/dl), edema and hypercholesterolemia (serum cholesterol >250 mg/dl)[1]. Clinical and biochemical features of nephrotic syndrome result from heavy proteinuria with consequent hypoalbuminemia and edema[2].

Estimate of annual incidence of nephrotic syndrome is 2-7 per 100,000 children and the prevalence is 12-16 per 100,000 children. There is epidemiological evidence of higher incidence of nephrotic syndrome of children from South Asia and Africa[2-5]. Primary or idiopathic nephrotic syndrome is commonly seen in 95% of patients[6], 80% of whom show histological features of minimal change nephrotic syndrome (MCNS) and have good prognosis[7-8]. Although recurrence is common in nephrotic syndrome, 90-95% of children with MCNS are responsive to steroid therapy with complete clinical and biochemical remission and have excellent long term prognosis[2,6,7,9]. Steroid sensitive nephrotic syndrome (SSNS) comprises 80-90% of nephrotic syndrome and rest 10-20% nephrotic syndrome is steroid resistant (SRNS)[10]. Hypertension, hematuria,

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anemia, persistent hypocomplementimia with persistent raised serum creatinine and high cholesterol, unfavorable age (<2 years and >8 years) are regarded as bad prognostic features[1,2,7,10]. So, it is importancte to correlate the biochemical and hematological parameters with the prognosis of the disease.

The objectives of the study were to compare the biochemical and hematological parameters and their prognostic value in steroid resistant (SRNS), frequent relapse and steroid dependent (FRNS+SDNS) and infrequent relapse (IFRNS) groups.

Methodology

This observational prospective study was carried out in the pediatric nephrology unit of the Department of Pediatrics of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh from January, 2003 to January, 2005. The hospital is a tertiary referral hospital with diagnostic and treatment facilities. A total of 480 children with primary nephrotic syndrome were admitted in BSMMU during the study period. Forty three (43) children were randomly selected who were aged 1-15 years. Among them 19 had steroid resistant nephrotic syndrome (SRNS) labeled as Group-B and 24 were steroid sensitive nephrotic syndrome (SSNS) and was labeled as Group A, in SSNS 11 children had FRNS+SDNS (Group A1) and 13 had IFRNS syndrome in Group A2. Among 19 children with SRNS, the histological reports on biopsy were mesangial proliferative glomerulonephritis (7 children), MCNS (3 children) focal segmental glomerulosclerosis (5 children), membrano proliferative glomerulonephritis (2 children), and membranous glomerulonephritis (2 children). Higher number of SRNS was due to tertiary referral nature of the hospital. Children below one year and above fifteen years and those with congenital nephrotic syndrome, nephrotic syndrome secondary to systematic disease like systematic lupus erythematosis, hepatitis B, Henoch Schonlein purpura, falciparum malaria, lymphoma and amylodosis were excluded from the study. Those with severe protein energy malnutrition or Down's syndrome were also excluded. Parents and guardians of the enrolled children were informed about the purpose and procedure of the study and written consent was obtained at the enrollment. They were given the choice to withdraw from the study at any point of time during the course of study. Data was collected by pre-tested semi structured questionnaire. The study was approved by Ethical Review Committee of BSMMU.

Laboratory Investigations: Urinary Total Protein (UTP) was measured by auto analyzer (RA 50 chemistry analyzer). Five ml of venous blood sample was collected for estimation of serum albumin, total protein, cholesterol, creatinine, blood urea, and blood count including hemoglobin and ESR. Cut off value of low serum albumin was <2.5gm/dl, low STP<6.00 gm/dl, high cholesterol>250 mg/dl, high serum creatinine >0.6 mg/dl and UTP>1gm/m^2/day. Mantoux test (MT) and Bacillus calmette-Guernie (BCG) acceleration tests were performed when indicated. Antinuclear antibody (ANA) and anti DNA double stranded antibody (anti ds-DNA) were measured by enzyme-linked immunosorbent assay (ELISA) in the children when indicated to rule out systematic disease. HbsAg was tested by screening and ELISA. Chest X-ray and Ultrasonography of the kidneys, ureters and bladder were performed for all the patients. Renal biopsy was done for SRNS patients, NS with atypical presentation and before giving 3rd line drug.

Study Definition: SSNS was defined as responding to steroid therapy within 4 weeks after initiation of the therapy[2,3]. IFRNS was defined as less than 4 relapses within 1 year or less than 2 relapses within 6 months after initial responsive episodes. FRNS was defined as more than 4 relapses in one year and more than 2 relapses within 6 months after initial responsive episode. Remission was defined as protein free urine for 3 consecutive days and relapse was defined as proteinuria (urine albumin 3+ or more) for three consecutive days after responsive episode[2,3]. The occurrence of 2 consecutive relapses during alternate day prednisolone therapy or within 2 weeks of its discontinuation was defined as SDNS[2,3]. No remission after 4 weeks of standard prednisolone the therapy at 60 mg/m^2/day was defined as SRNS[2,3].

Statistical analysis: Statistical analysis was performed by using SPSS. ANOVA was used to compare the difference in means. Chi square test was used to compare between the groups.

Results

Table 1 shows means (± SD) of serum total protein (STP). The mean (± SD) serum total protein was significantly low in SRNS than both groups of SSNS (P<0.01 and <0.001). Higher difference was observed between SRNS and IFRNS (P<0.001). However the difference between FRNS+SDNS and IFRNS was not statistically significant. ANOVA Test.

Table 1: Comparison of serum total protein (STP) of steroid resistant and steroid sensitive groups

Parameters STP (g/dl)	No(n)	Mean ± SD	Range	95% CI		P value
				Lower bound	Upper bound	
SRNS (B)	19	3.22±0.86	1.80-5.40	2.81	3.93	B Vs A_1 <0.01**
FRNS+SDNS (A_1)	11	4.18±0.57	3.50-5.10	3.80	4.57	B Vs A_2 <0.001***
IFRNS (A_2)	13	4.58±0.85	3.30-6.00	4.07	5.09	A_1Vs A_2 >0.10^{ns}

Group Identification: Group B: Steroid resistant; Group A1: FRNS+SDNS (steroid sensitive); Group A2: IFRNS (steroid sensitive)

Table 2 shows the mean (± SD) of serum albumin levels were significantly lower in SRNS than FRNS+SDNS and IFRNS group (P<0.01). There was no difference between FRNS+SDNS and IFRNS. Anova Test.

Table 2: Comparison of serum albumin (g/dl) parameters of steroid resistant and steroid sensitive groups

Parameters serum albumin (g/dl)	No(n)	Mean ±SD	Range	95% CI		P value
				Lower bound	Upper bound	
SRNS (B)	19	1.24± 0.40	0.80-2.10	1.04	1.44	B Vs A_1 <0.01**
FRNS+SDNS (A_1)	11	1.76±0.35	1.00-2.10	1.53	2.00	B Vs A_2 <0.001***
IFRNS (A_2)	13	1.81± 0.45	0.80-2.40	1.53	2.08	A_1Vs A_2 >0.10^{ns}

Table 3 shows serum cholesterol was higher in SRNS and FRNS+SDNS compared to IFRNS (P<0.001, <0.01). It did not differ between SRNS and FRNS+SDNS. ANOVA Test.

Table 3: Comparison of serum cholesterol (mg%) parameters of steroid resistant and steroid sensitive groups

Parameters Serum cholesterol (mg%)	No(n)	Mean ± SD	Range	95% CI		P value
				Lower bound	Upper bound	
SRNS (B)	19	503.50±58.33	360-648	475.36		B Vs A_1 >0.05^{ns}
FRNS+SDNS(A_1)	11	430.50±83.10	305-619	374.63		B Vs A_2 <0.001***
IFRNS (A_2)	13	304.50± 0.16	200-485	256.10		A_1Vs A_2 <0.01**

Table 4 shows serum creatinine mean (± SD) was higher in SRNS than FRNS+SDNS (P<0.001) and IFRNS (P<0.001). No difference was observed between subgroup of SSNS.

Table 4: Comparison of serum creatinine (mg%) parameters of steroid resistant and steroid sensitive groups

Parameters Serum creatinine (mg%)	No (n)	Mean ± SD	Range	95% CI		P value
				Lower bound	Upper bound	
SRNS (B)	19	1.05±0.32	0.60-0.80	0.60	1.70	B Vs A_1 <0.001***
FRNS+SDNS (A_1)	11	0.66±0.07	0.60-0.80	0.60	0.80	B Vs A_2 <0.001***
IFRNS (A_2)	13	0.65±0.00	0.60-0.80	0.60	0.71	A_1Vs A_2 >0.50^{ns}

Table 5 urinary total protein (UTP) was higher in SRNS than FRNS+SDNS and IFRNS (P<0.001). The difference between SRNS+SDNS and IFRNS was also significant (P<0.05).

Table 5: Comparison of urinary total protein (g/dl) of steroid resistant and steroid sensitive groups

Parameters Urinary total protein (g/dl)	No(n)	Mean ±SD	Range	95% CI		P value
				Lower bound	Upper bound	
SRNS (B)	19	5.78±1.68	2.73-9.38	4.96	6.60	B Vs A_1 <0.001***
FRNS+SDNS (A_1)	11	3.63±0.85	2.10-5.55	3.06	4.21	B Vs A_2 <0.001***
IFRNS (A_2)	13	2.80±1.12	1.50-5.22	2.12	3.48	A_1Vs A_2 >0.05*

Table 6 shows that no difference was observed between SRNS and FRNS+SDNS. The mean (± SD) hemoglobin in SRNS and FRNS+SDNS were lower than IFRNS (P<0.01 and <0.05).

Table 6: Comparison of hemoglobin (%) of steroid resistant and steroid sensitive groups

Parameters Hemoglobin (%)	No(n)	Mean ± SD	Range	95% CI		P value
				Lower bound	Upper bound	
SRNS (B)	19	9.63±1.95	6.36-14.50	8.69	10.57	B Vs A_1 <0.10^{ns}
FRNS+SDNS (A_1)	11	10.84±1.33	8.70-13.00	9.95	11.73	B Vs A_2 <0.01**
IFRNS (A_2)	13	12.45±2.21	8.30-15.00	11.1	13.78	A_1Vs A_2 >0.05*

Discussion

Ninety five percent nephrotic syndromes are idiopathic (INS) and 80% of idiopathic childhood nephrotic syndromes are MCNS. Presence of hypertension, gross hematuria and impaired renal function indicate significant glomerular lesion[9,11].

In this study, significantly low serum total protein, low albumin, high urinary total protein, high cholesterol, urinary total protein and low hemoglobin were noted in SRNS compared to SSNS. Also significantly high cholesterol and low hemoglobin were noted in this study group of FRNS+SDNS compared to IFRNS. These findings are in corollary with standard text books[2,8,12]. Low serum total protein and albumin can be due to long standing proteinuria which was either due to the disease as in SRNS type or late treatment[2,10]. Very high cholesterol and low hemoglobin usually mean non minimal lesion NS[2,10]. However volume contraction can give rise to high hemoglobin and high hematocrit level[10]. Raised serum creatinine in SRNS, FRNS+SDNS groups in this study was consistent with previous studies[2,10]. Tarashish et al[13] observed end stage renal disease in 5% and 20% of SSNS and SRNS respectively, similar type of finding with raised serum creatinine in this study was positively correlated with poor outcome.

Gulati et al[14] had seen no significant differences among various subgroups which biochemical parameters like blood urea nitrogen, serum creatinine, serum total protein, albumin, and cholesterol were compared. Their observation as poor response was associated with age of onset more than 8 years, male sex, hypertension, microscopic hematuria and presence of non-minimal nephrotic syndrome lesions on histopathology.

Srivastava[15] observed proteinuria with associated microscopic hematuria were more likely a manifestation of significant renal lesion. Constantinescu and Mendoza[16] observed poor association with hematuria. MCNS has occasional gross hematuria[17] and transient hypertension[18].

Begum[19] observed hypertension, hematuria and renal impairment significantly higher in SRNS. Singh et al[20] found hematuria heavy proteinuria, azotemia and hypertension in idiopathic focal segmental glomerulosclerosis. Other studies also has seen different prognostic markers. Caridi et al[21] found no different in outcome of NS in patients with single mutation of nephrin and podocin genes. Ezrin-a cytoskelaton linking protein a patent maker of podocyte injury has been low in nephrotic syndrome with unfavorable prognosis[22]. Misra et al[23] and Roy et al[24] has seen decreased serum IgG level as predictive marker for unfavorable prognosis of nephrotic syndrome in children.

Conclusion

Steroid resistant nephritic syndrome (SRNS) had low serum total protein (STP), albumin and hemoglobin compared to steroid sensitive nephrotic syndrome (SSNS). Steroid resistant nephrotic syndrome also had high cholesterol, creatinine and urinary total protein (UTP) than

steroid sensitive nephrotic syndrome. FRNS+SDNS had high cholesterol, UTP and low hemoglobin than IFRNS. So low serum total protein (STP), albumin, hemoglobin and high cholesterol, creatinine, urinary total protein (UTP) are prognostic features in children with idiopathic nephrotic syndrome. Further large scale, multicenter study would be helpful.

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