

Erythrocyte Sedimentation Rate in Children with Idiopathic Nephrotic Syndrome and its Correlation with Serum Albumin

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Abstract

Background: The erythrocyte sedimentation rate is a simple, inexpensive screening test. Elevation of ESR in various forms of renal disease is a widely known clinical observation. In nephrotic syndrome patients elevation of ESR occurs due to increased fibrinogen level.

Methods: The aim of this cross sectional comparative study was to estimate ESR of nephrotic syndrome and to assess the relationship of it with serum albumin level and was conducted in Department of Pediatric Nephrology, Comilla Medical College Hospital from January 2013 to December 2013. A total of 60 cases and 60 controls were included in this study. ESR was measured by using the Westergren method. Serum albumin was measured by enzymatic colorimetric method. The relationship between ESR and serum albumin was measured by Pearson's correlation.

Results: Mean ESR of cases and controls were 102 ± 5.53 mm and 35 ± 6.73 mm in first hour respectively ($p < .05$). Mean serum albumin level of cases and controls were $1.88 \pm .37$ g/dl and $4.91 \pm .41$ g/dl, respectively ($p < .05$). Pearson's correlation test between ESR and serum albumin level of cases were significant ($P < 0.05$).

Conclusion: Blood ESR is raised in idiopathic nephrotic syndrome and it has negative correlation with serum albumin.

Recommendation: To diagnose nephrotic syndrome blood ESR should be measured along with other biochemical parameter.

Introduction

Nephrotic syndrome is characterized by massive proteinuria, hypoalbuminemia and edema. Hypercholesterolemia is almost always present [1]. It is a chronic disorder, characterized by alterations of permeability at the glomerular capillary wall, resulting in its inability to restrict the urinary loss of protein. Nephrotic range proteinuria is defined as proteinuria exceeding 1000 mg/per day or spot urinary protein to creatinine ratio exceeding 2. The proteinuria in childhood nephrotic syndrome is relatively selective, constitute primarily by albumin. Estimate on the annual incidence of nephrotic syndrome range from 2-7 per 100000 children and prevalence from 12-16 per 1000000. There is epidemiological evidence of a higher incidence of nephrotic syndrome in children from Asia [2]. The condition is primary in 95 percent cases. An underlying disorder that might be identified in less than 5 percent cases includes systemic lupus erythematosus, Henoch Schonlein Purpura, amyloidosis and infection with HIV, parvovirus B19 and hepatitis B and C viruses [1, 3, 4]. More than 80 per cent patients with nephrotic syndrome show minimal change disease (MCD) characterized by normal histology on light microscopy. The remaining is contributed by focal segmental glomerulosclerosis (FSGS) and mesangioproliferative glomerulonephritis. MCD and FSGS are often considered to represent the same pathophysiological process. Membranous nephropathy and membranoproliferative conditions uncommon in children [5 - 7].

There is indirect evidence that immunological mechanism may be involved in the pathogenesis of MCNS. The remission that occasionally follows measles, presence of allergy in some cases and response to immunoactive agents suggest an underlying immune dysfunction. Several studies shows diminished cellular immunity, low serum IgG and occasional abnormalities of T- lymphocyte cell subsets. An increase in serum levels of soluble interleukin-2 receptor, IL-8 tumor necrosis factor- α and vascular permeability has been reported. Others have shown up regulation of the gene for IL-4 and IL-13 in peripheral blood lymphocytes and glomeruli obtained from patients with nephrotic syndrome [1].

The mechanism of edema formation in nephrotic syndrome is incompletely understood, it seems likely that in most instances, massive urinary protein loss leads to hypoalbuminemia, which causes decreased plasma oncotic pressure and transudation of fluid from the intravascular compartment to the interstitial space. The reduction in intravascular volume decreases renal perfusion pressure, activating rennin-angiotensin-aldosterone system, which stimulates tubular reabsorption of sodium. The reduced intravascular volume also stimulates the release of ADH, which enhances the reabsorption of water from collecting duct. Nephrotic Syndrome is a hypercoagulable state resulting from multiple factors, vascular stasis, and an increase in hepatic production of fibrinogen and other clotting factors, decreased serum levels of anticoagulant proteins, increased plasma platelet production and increased platelet aggregation [8]. In the nephrotic state, serum lipid levels are elevated for two reasons. Hypoalbuminemia stimulates generalized hepatic protein synthesis including synthesis of lipoproteins. In addition, lipid catabolism is diminished as a result of reduced plasma levels of lipoprotein lipase related to increased urinary loss of this enzyme [8].

In idiopathic nephrotic syndrome urinalysis reveals 3+ or 4+ proteinuria, and microscopic hematuria in 20% of children. Spot protein: creatinine ratio exceeds 2.0 and urinary protein excretion exceeds 40 mg/m²/hr. The serum creatinine value is usually normal. The serum albumin level is < 2.5 g/dl and serum cholesterol and triglyceride levels are elevated. Serum complement levels are normal. A renal biopsy is not routinely performed if the patient fits the standard clinical picture of MCNS [8].

Albumin is the major protein of human plasma and makes up approximately 60% of the plasma protein. Some 40% of albumin is present in the plasma, and the other 60% is present in the extracellular space. The liver produces about 12g of albumin per day, representing about 25% of total hepatic protein synthesis and half of its secreted protein. Albumin is initially synthesized as a preproprotein. Its signal peptide is removed as it passes into the cisternae of the rough endoplasmic reticulum, and a hexapeptide at the resulting amino terminal is subsequently cleaved off further along the secretory pathway [9].

Sedimentation of red cells occurs when anticoagulated blood is allowed to settle. The rate at which the red cells fall is known as the erythrocyte sedimentation rate (ESR). ESR mainly depends on four factors; (1) The size of the rouleau, (2) Plasma factors, (3) The shape and number of red cells, (4) Technical and mechanical factors. ESR primarily depends on the rouleau formation. The size of the rouleaux depends on the presence of certain factors in the plasma, specially its fibrinogen and globulin content. Normally red cells tend to remain separate from each other, because they are negatively charged. As a result they repel one another. Fibrinogen neutralizes the charges on the red cells and makes the red cells sticky. Therefore, when the fibrinogen concentration increases in the plasma, the repelling force on the red cells is removed, this facilitates rouleau formation. Increased viscosity of blood decreases ESR (e.g.-Polycythemia) and decreased viscosity causes increased ESR (e.g -Anemia). A change in the shape of red cells also opposes rouleaux formation. Increase in temperature decreases the viscosity of blood and cause increase in ESR. ESR is the index of inflammatory activity in the body. It increases with an increase in the rate of inflammation and decreases with a decline in inflammatory activity. Thus ESR gives a clue regarding the progress of the disease and response of the disease to treatment [10].

Cheah and Ransome reported that nephrotic syndrome patient have higher ESR [11]. But there is scanty data to see the extent of ESR which may be influenced by fibrinogen level. The purpose of this study is to evaluate the extent of rise of ESR in nephrotic syndrome children during attack and disease progression.

Patients and Method

The objective of this study was to estimate the blood ESR and evaluate the correlation between blood ESR and serum albumin in children with idiopathic nephrotic syndrome. It was a cross sectional comparative study carried out in the Department of Paediatric Nephrology, Comilla Medical College Hospital, and Comilla during January 2013 to December 2013. A total of 60 cases and 60 controls were enrolled by simple random sampling in this study. Study populations were all children aging from 2 years to 8 years irrespective of sex with the following inclusion and exclusion criteria.

Inclusion criteria:

(a) Nephrotic syndrome age from 2 years to 8 years. (b) Child and parents were willing to give consent and blood sample.

Exclusion criteria:

(a) Age less than 2 year and more than 8 years. (b) Those who had taken blood/fresh frozen plasma/albumin transfusion. (c) Patient with Liver disease. (d) Patient with infection (e) Patient with severe Malnutrition.

Procedures

Nephrotic syndrome was diagnosed by history who has generalized edema, scanty micturition, massive proteinuria, hypoalbuminemia and hypercholesterolemia. Massive proteinuria was diagnosed who has morning spot urinary protein creatinine ratio more than 2, hypoalbuminemia was diagnosed serum albumin level less than 2.5 gm/dl and hypercholesterolemia was considered who has serum cholesterol more than 220 mg/dl. Infected cases were excluded who has raised CRP. Every case satisfying the selection criteria was enrolled in the study. Children of 2-8 years old attended as relative of patient in the pediatric outpatient and inpatient department of whom blood grouping was done at free of cost were included as control. With all aseptic precaution blood was taken both from cases and controls. Serum albumin was measured by enzymatic colorimetric method (ERBA CHEM 7 ANALYZER). ESR was measured by using the Westergren tube in the Pediatric ward of Comilla Medical College Hospital. Data were collected by a preformed structured questionnaire.

Data Analysis and Interpretation

Data were processed, calculated and analyzed using computer software. Unpaired t test was done to see the difference of mean ESR level between cases and controls. Pearson's correlation test done see the relation between serum albumin and ESR of cases. The statistical analysis was performed using the Statistical Product and Service Solutions version 16.0 for Windows.

Results

Table I: Characteristics of case and control.

Characteristics		NS children (n=60)	Healthy children (n=60)	P value
Age	2- 4 years(%)	29(48)	27(45)	-
	5-8 years(%)	31(52)	33(55)	-
Sex	Male (%)	41(68)	32 (53)	-
	Female (%)	19 (32)	28 (47)	-
Weight in kg (\pm SD)		17.27 (\pm 5.54)	13.36 (\pm 5.11)	-
Height in cm(\pm SD)		100.83(\pm 16.00)	97.71 (\pm 14.80)	-
Swelling of the body (%)		60(100)	00 (00)	-
Scanty micturition (%)		60(100)	00 (00)	-
Puffiness of face (%)		60(100)	00 (00)	-
Generalized edema (%)		60(100)	00 (00)	-
Serum albumin in gm/dl(\pm SD)		1.88(\pm .37)	4.91(\pm .41)	<0.05
Serum cholesterol in gm/dl(\pm SD)		240(\pm 07)	150(\pm 04)	<0.05
Blood CRP(mg/L) (\pm SD)		4(\pm .03)	3.5(\pm .07)	>0.05

A total of 120 children comprising 60 nephrotic syndrome children & 60 healthy children were recruited to this study. The mean albumin level in cases 1.88(\pm .37) g/dL was lower than controls 4.91(\pm .41) g/dL, (P value<0.05). The mean cholesterol level in cases and controls were 240(\pm 07) mg/dl and 190(\pm 04) mg/dl, (P value<0.05) respectively. Mean blood CRP of both cases and controls were 4(\pm .03) mg/L and 3.5(\pm .07) mg/L respectively.

Table II: Difference between ESR level between case and control.

Blood ESR	No	Mean \pm SD	P value
Case	60	102 \pm 5.53	<0.05
Control	60	35 \pm 6.73	

Table II shows the albumin level of cases are significantly lower (p<0.05) than the control.

Table III: Correlation between serum albumin with blood ESR of cases.

Correlations		Albumin	Blood_ESR
Albumin	Pearson's Correlation	1	-.226
	Sig. (2-tailed)		.083
	N	60	60
Blood_ESR	Pearson's Correlation	-.226	1
	Sig. (2-tailed)	.083	
	N	60	60

Table III shows negative correlation ($r = -0.226$) and since $P\text{-value}=0.04$ at 5% level of significance.

Figure: Relation between Serum Albumin with blood ESR of NS Children

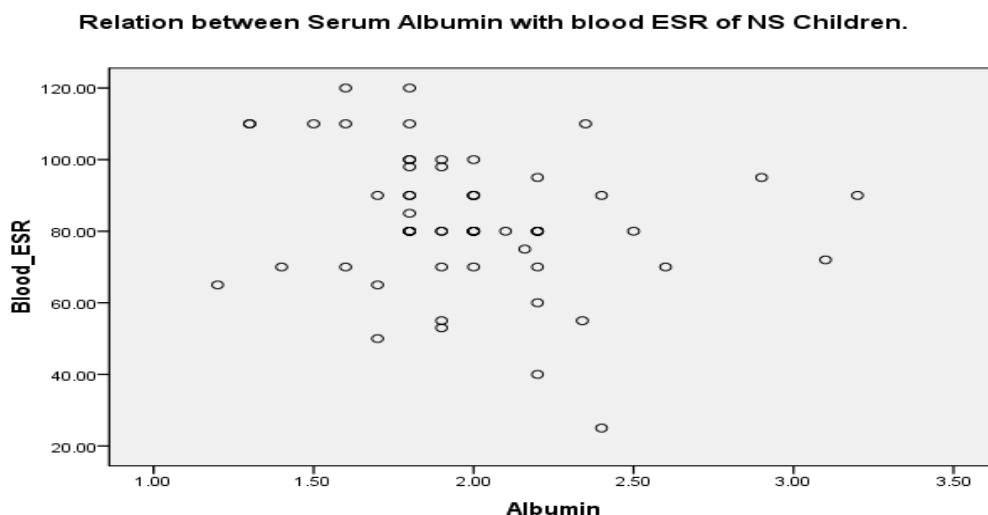


Figure shows there is negative correlation between blood ESR and serum albumin.

Discussion

Nephrotic syndrome is an important chronic disease in children is characterized by the association of the clinical features with renal biopsy findings of minimal changes, focal segmental glomerulosclerosis, or mesangial proliferation on light microscopy and effacement of foot process on electron microscopy [12].

Elevation of ESR in various forms of renal disease is a widely known clinical observation. A number of descriptive studies have been published looking particularly at the incidence of marked ESR elevations in patients with renal disease. None of these studies however has

systemically surveyed ESR values in a group of renal patients [13, 14].

In this study we have found that the mean ESR level of cases is 102 ± 5.53 mm/1st hour level of cases which is significantly ($p < 0.05$) higher than control. Ozane et al. [15] suggested that the increased level of ESR in nephrotic syndrome due to increased fibrinogen level which is in confrontation of our study.

We have found a negative correlation ($r = -0.226$ and $P\text{-value} < 0.05$) between blood ESR level and serum albumin of nephrotic syndrome. This means that lower the albumin, higher will be ESR level. S Eustace et al. [16] found that there is negative correlation between blood ESR and serum albumin which support our study.

Conclusion

Blood ESR is raised in idiopathic nephrotic syndrome and it has negative correlation with serum albumin that is lower the serum albumin level, higher will be blood ESR level.

Recommendation

To diagnose nephrotic syndrome blood ESR should be measured along with other biochemical parameter.

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