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CORRELATION BETWEEN IONIZED CALCIUM AND SERUM ALBUMIN LEVEL AND IN IDIOPATHIC NEPHROTIC SYNDROME IN CHILDREN

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ABSTRACT

Background: Nephrotic syndrome frequently have abnormalities in calcium metabolism that manifest as hypocalcaemia. The serum ionized calcium level depends on the severity and duration of proteinuria.

Methods: The aim of this study was to assess the correlation between serum albumin level and ionized calcium in children with idiopathic nephrotic syndrome. An analytic study with cross sectional comparative design was applied to nephrotic syndrome and healthy children between 2-8 years old in the

Department of Pediatrics, Jawaharlal nehru Medical College Hospital. A total of 120 subjects were recruited, 60 nephrotic syndrome as cases and 60 healthy children as controls. The mean serum albumin and serum ionized calcium levels of cases and controls were estimated respectively. Pearson's correlation test was done to see the correlation.

Results: Mean serum albumin level of cases and controls were 1.98±0.38 g/dl and 4.57±0.25 g/dl, respectively (p<.001) and mean serum ionized calcium of cases and controls were 1.13±0.08 mmol/L and 2.34±0.05 mmol/L respectively (p<.001). Pearson's correlation test between serum albumin and serum ionized calcium level of cases were significant (P<0.05).

Conclusion: There was a positive correlation between serum albumin level and ionized calcium in idiopathic nephrotic syndrome, that is lower the serum albumin level, the lower will be the serum ionized calcium and higher the albumin level, higher will be calcium level.

KEYWORDS :

Introduction

Nephrotic syndrome is a clinical condition and biochemical abnormalities characterized by massive proteinuria, hypoalbu minemia, and hyperlipidemia and generalized edema. 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/M2/per day or spot urinary protein to creatinine ratio exceeding 2. The proteinuria in childhood nephrotic syndrome is relatively selective, constitute primarily by albumin [1]. The decreased albumin level in nephrotic syndrome children is due to damaged glomerular filtration membrane in the renal cortex. Consequently, the negative charge on the glomerular capillary endothelium is lost. Furthermore the nature of size-selectivity in the glomerular capillary endothelium becomes disrupted [2].

Estimate on the annual incidence of nephrotic syndrome range from 2-7 per 100000 children and prevalence from 12-16 per 100000 [3]. There is epidemiological evidence of a higher incidence of nephrotic syndrome in children from Asia [4]. 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 [5,6].

Approximately 90% of children with nephrotic syndrome have idiopathic nephrotic syndrome. Idiopathic nephrotic syndrome is associated with primary glomerular disease without an identifiable causative disease or drug. Idiopathic nephrotic syndrome includes multiple histologic types: minimal change disease, mesangial proliferation, focal segmental glomerulosclerosis, membranous nephropathy, and membrano proliferative glomerulonephritis [7]. 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 preprotein. 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 [8].

Total calcium in human body is in three form, eg. ionized, bound to protein and complexed with anions. They are in equilibrium with each other. Only the serum ionized calcium has been reported to be physiologically active. If the serum ionized calcium level declines below normal, nervous system progressively becomes sensitive and provokes clinical symptoms. Patients with nephrotic syndrome (NS) lose 25-hydroxyvitamin D3 (25OHD3) in the urine and have low blood levels of this metabolite. This abnormality may be responsible for the hypocalcaemia, i.e. low ionized calcium. The mechanism of the hypocalcaemia is not evident. It is possible that the low value of 25OHD results in low blood levels of other vitamin D metabolites, such as 1,25-dihydroxyvitamin D [1,25-(OH)2D] and 24,25-(OH)2D3; a deficiency of these compounds may cause defective intestinal absorption of calcium (alpha) and resistance to the calcemic action of parathyroid hormone (PTH), resulting in hypocalcemia [9].

Hypocalcemia may manifest with tetany, carpopedal spasm, laryngospasm and seizures. These complications must be treated immediately with 2 ml/kg of 10% calcium gluconate intravenously. This must be administered slowly under cardiac monitoring. Initially intravenous calcium boluses can be given 6 hourly. Thereafter, oral calcium supplementation should be provided at 40-60 mg/kg/day [10]. A previous study showed that there was a positive relationship between serum ionized calcium and serum albumin level in nephrotic syndrome children [11]. The purpose of this study was to create awareness that hypoalbuminemia is accompanied by hypocalcemia owing to loss of albumin and vitamin D in urine and to reduce hypocalcemia related complications like tetany, seizure, carpopedal spasm and laryngospasm.

PURPOSE OF THE STUDY

Calcium remain in human body as ionized, bound to albumin and other calcium binding protein. Albumin and vitamin D metabolite are lost in urine. The loss of albumin and Vit D in urine is accompanied by hypoalbuminemia and hypocalcemia. Calcium and albumin are in equilibrium with each other. A reduction in total serum calcium can result from a decrease in albumin secondary to nephrotic syndrome. Thus nervous system will progressively become sensitive and provokes clinical symptoms. There is scanty data to see the correlation between serum albumin and serum ionized calcium in nephrotic syndrome. The rationale of this study is to shed some light that low serum albumin may be accompanied with low serum calcium and serious hypocalcemic effect that should be treated early even before steroid therapy

METIREALS AND METHOD

The objective of the study was to evaluate the correlation between serum albumin level and ionized calcium in children with idiopathic nephrotic syndrome. It was a cross sectional study carried out in the department of Paediatris Jawahar lal Medical College Hospital, Bhagapur during July 2015 to December2016. A total of 60 cases and

60 controls were enrolled by simple random sampling in this study. Study population was 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 calcium supplements 8-12 hours before the study. (c) Those who had taken blood/fresh frozen plasma/albumin transfusion. (d) Patient with liver disease. (e) Patient with acid base disorder (f) Patient with severe malnutrition. (h) Nephrotic syndrome with acute renal failure.

Procedures and Data analysis

After admission 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 control. Serum Ionized calcium level, serum albumin level were measured in cases. The controls were examined for serum ionized calcium and serum albumin level in addition with blood grouping. Serum ionized calcium was examined by Anatron Analyte 100 Electrolyte analyzer in the laboratory of a private diagnostic centre. Data were collected by a preformed structured questionnaire and was processed, calculated and analyzed using computer software. Unpair t test was done to compare the mean difference of serum ionized calcium level between cases and controls. Pearson's correlation test was performed to evaluate the relationship between serum ionized calcium and serum albumin level in cases. The statistical analysis was performed using the Statistical Package for Social Service (SPSS) version 16.0 for Windows.

A total of 120 children comprising 60 nephrotic syndrome children & 60 healthy children were recruited to this study. The mean albumin level in cases (1.98±0.38) g/dL was lower than controls (4.57±0.25) g/dL, (P value<0.05) (Table 1). The mean ionized calcium level in cases (1.13±0.08) mmol/L was lower than controls (2.34± 0.05) mmol/L, (P value<0.05) (Table 2). Shows the albumin level of cases are significantly lower (p<0.05) than the control (Table 3). Shows serum ionized calcium level of cases are significantly (P<0.05) lower than the control **. Correlation is significant at the 0.01 level (2-tailed) (Table 4). Shows that there is positive correlation {(r = 0.45) and (P-value<0.01)} between albumin level and ionized calcium of 60 nephrotic syndrome child, that is significant (Figure 1).

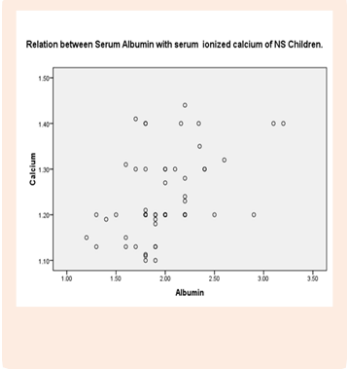

Table 1: Baseline characteristics of cases and controls (n=120).

Characteristics		Case (n=60)	Control (n=60)
Sex	Male (%)	41(68)	32(53)
	Female (%)	19(32)	28(47)
Weight (kg)		17.28 (±5.53)	13.37 (±5.10)
Height (cm)		100.93(±16.0)	97.72 (±14.9)
Decreased urine output (%)		60(100)	00 (00)
Puffiness of face (%)		60(100)	00 (00)
Generalized edema (%)		60(100)	00 (00)
Serum albumin level (gm/dL)		1.98±.38	4.57±.25
Serum ionized calcium (mmol/L)		1.13±.08	2.34±.05

Table 2: Difference between albumin level between case and control.

Albumin Level	No	Mean ± SD	
Case	60	1.98 ± 0.38	
Control	60	4.57 ± 0.25	
95% CI of Mean Difference	t-Value	Df	P Value
(-2.72 to -2.46)	40.12	59	0.00

Table 3: Difference between ionized calcium level between case and control

Ionized Calcium Level	No	Mean ± SD	
Case	60	1.13 ± 0.08	
Control	60	2.34 ± 0.05	
95% CI of Mean Difference	t-Value	Df.	P Value
(-0.14 to -0.08)	8.14	59	0.00

Table 4: Correlation between serum Albumin with serum ionized calcium of case.

CORRELATION	ALBUMIN	CALCIUM
ALBUMIN		
Pearson correlation	1	449
Significance (2-tailed)		000
N	60	60
CALCIUM		
Pearson correlation	449	1
Significance(2-tailed)	000	
N	60	60

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 glomerulo sclerosis, or mesangial proliferation on light microscopy and effacement of foot process on electron microscopy [12]. Nephrotic syndrome frequently has abnormalities in calcium metabolism that manifest as hypocalcemia and reduced intestinal absorption of calcium. Hypocalcemia is initially attributed to hypoalbuminemia but it may also relate to a low level of ionized calcium. The ionized calcium level depends on the severity and duration of proteinuria [13].

In this study we have found that the albumin level of cases and controls were 1.98(±0.38) mg/dl and 4.57±0.25 mg/dl respectively and it is significantly (p<0.05)) lower than control which is universal. The study showed that the ionized calcium level of NS children was lower than that in healthy children (p<0.05)). This may be due to the decrease in ionized calcium in NS children occurs subsequently during the course of diseases associated with timing of proteinuria. Hooft et al. [14] observed that the ionized calcium in nephrotic syndrome children decrease after having proteinurea for more than two months

In this study we have found a positive correlation (r = 0.45 and P-value<0.01) between serum ionized calcium level and serum albumin of nephrotic syndrome. This means that lower the albumin, lower will be the ionized calcium levels. Viola Irene et al. [13] found that there is positive correlation between serum albumin and serum ionized calcium which support our study. Choi et al. [11] also found a very weak positive correlation between the duration of disease and ionized calcium level from their 14 nephrotic syndrome samples. Garniasih [15] found an association between serum albumin level and total serum calcium in children. There was 50% of ionized calcium in total serum calcium, so when the total serum calcium level decreased then the ionized calcium level also decreased [16].

Limitation of the study

As there is scanty data available to see the correlation between serum albumin and serum ionized calcium in nephrotic syndrome, data back from 1960-1981 is used to support the study

CONCLUSION

There is a positive correlation between serum albumin level and ionized calcium in idiopathic nephrotic syndrome and this study showed that lower the serum albumin level, lower will be serum ionized calcium level.

Recommendatioin

In the diagnosis nephrotic syndrome along with serum albumin and serum cholesterol measurement, serum ionized calcium should be measured to detect hypocalcemia and to prevent hypocalcemic complications.

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