

Correlation between Serum Magnesium and Calcium Level in Children with Idiopathic Nephrotic Syndrome during Nephrosis

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Abstract

Background: Biochemical alteration is a common phenomenon in all kidney disease including nephrotic syndrome (NS).

Objective: To evaluate the magnesium (Mg) level in patients with nephrotic syndrome and its relation to calcium.

Methods: In this observational cross sectional study, we measured serum magnesium and serum calcium levels in children with nephrotic syndrome. It was conducted in the Department of Pediatrics, Dhaka Shishu (children) Hospital, Dhaka, from January 2015 to June 2015. A total of fifty four diagnosed cases of nephrotic syndrome were divided into initial episode, first relapse, infrequent relapse and frequent relapse. Mean level of serum magnesium and calcium of all four groups were then compared.

Results: The mean level of serum magnesium during initial episode was 2.28 ± 0.36 mg/dl and it was 2.04 ± 0.29 , 2.06 ± 0.29 and 1.76 ± 0.32 mg/dl during first relapse, infrequent relapse and frequent relapse respectively. The mean serum magnesium level in different patterns of nephrotic syndrome was found to be statistically significant. Hypomagnesemia was mostly found in frequent relapse nephrotic syndrome patients. The mean level of serum calcium during initial episode was 2.01 ± 0.16 and it was 1.98 ± 0.17 , 2.06 ± 0.13 and 2.05 ± 0.15 during first relapse, infrequent relapse and frequent relapse respectively. The mean serum calcium level in different patterns of nephrotic syndrome was found to be statistically insignificant. There was no significant correlation between calcium level with magnesium level ($r = -0.08$, $p = 0.28$).

Conclusion: Hypomagnesemia is commonly found in frequent relapse nephrotic syndrome. There was no significant correlation between calcium with magnesium level.

Key words: Nephrotic syndrome, magnesium, calcium.

Introduction

Nephrotic syndrome patients frequently have abnormalities in calcium metabolism that manifest as hypocalcemia. Hypocalcemia is initially attributed to hypoalbuminemia but it may also relate to a low level of ionized calcium.¹ Magnesium is needed for more than 300 biochemical reactions in the body. It

helps maintain normal muscle and nerve function, keeps heart rhythm steady, supports a healthy immune system, and keeps bone strong.^{2,3} Nephrotic syndrome (NS) is a clinical entity characterized by massive loss of urinary protein (primarily albuminuria) leading to hypoproteinemia resulting in edema.^{4,5}

If the serum ionized calcium level declines below normal, clinical symptoms like neuromuscular irritability including tetany as manifested by chvostek's sign or Trousseau's sign. Patients with nephrotic syndrome (NS) lose 25-hydroxyvitamin D3 (25OHD3) in the urine and have low blood levels of this metabolite.⁶ The most frequent causes of hypomagnesemia in children are reduced intake, impaired intestinal absorption, renal loss and genetic disease. Severe hypomagnesemia induces secondary hypocalcemia in most experimental animals except

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rats. Furthermore, severe hypomagnesemia induces functional hypoparathyroidism.⁷

Magnesium supplement and testing may be ordered as a follow up to chronically low level of calcium and potassium and when a person has symptoms that may be due to magnesium deficiency such as muscle weakness, twitching, cramping, confusion, cardiac arrhythmia and seizure.^{8,9} A particular long list of prescription medications have been shown to reduce the body's supply of magnesium. Several types of diuretics, loop diuretics like frusemide, antibiotic, corticosteroids and immuno-suppressant drug cyclosporine.² So Magnesium level should be checked as a part of evaluation of the severity of the kidney problems. Proper supplementation of magnesium can properly manage the disease as they are altered in nephrotic syndrome. For these reasons the serum magnesium level in patients with idiopathic nephrotic syndrome is an important issue.

Materials and Methods

An observational cross sectional study was conducted in the Department of pediatrics Dhaka Shishu Hospital, Dhaka, from January 2015 to June 2015. A total of 54 diagnosed cases of nephrotic syndrome admitted in this hospital were included in this study. NS with associated illnesses such as diarrhoea, severe vomiting and those who already have metabolic disturbances and seizure were excluded from this study. Those who are taking calcium and vitamin D were also excluded. Written informed consent was taken from each parent at the commencement of the study. Prior permission was taken for this study from the Ethical Committee of Dhaka Shishu Hospital, Dhaka, Bangladesh. This article was based on dissertation for FCPS (pediatrics).

All necessary investigations, diagnostic and infection screening like CBC, urine R/M/E, urine C/S, serum albumin, cholesterol, spot protein creatinine ratio, Hbs Ag. On admission, 2 ml of blood was collected from each patient. Samples were centrifuged and stored in a refrigerator. Serum magnesium and calcium levels were assessed.

The 54 study children were then divided into 4 groups initial episode (n=15), first relapse- those presented with first relapse after completion of steroid therapy of initial episode (n=12), infrequent relapse- those presented with infrequent relapse following completion of steroid therapy of first relapse (n=13), frequent relapse- those had history of more than or equal to 4 relapse during the last year (n=14).

The magnesium was measured by Magnesium (MG) method, that was used on the Dimension (R) clinical

chemistry system. It is an in vitro diagnostic test intended for the quantitative determination of magnesium in human serum, plasma and urine. The magnesium method is a modification of the methylthymolblue (MTB) complexometric procedure described by Connerty, Lau and Briggs. The barium salt of ethylenebis (oxyethylenenitrilo) tetraacetic acid (Ba-EGTA) is used to reduce interference due to calcium which also reacts with MTB. Expected Values, Serum Magnesium normal value was considered 1.8-2.4 mg/dl, hypomagnesemia <1.8, hypermagnesemia >2.4mg/dl

Serum Calcium was labelled as mildly low 2-2.1mmol/l, moderately low 1.9-2.0mmol/l, severely low <1.9. The calcium was measured by calcium (CA) method. The CA method used on the Dimension® clinical chemistry system is an in vitro diagnostic test intended for the quantitative determination of calcium in human serum and plasma. Serum Calcium level, mildly low 2-2.1mmol/l, moderately low 1.9-2.0mmol/l, severely low <1.9. Data were processed and analysed using software SPSS (Statistical Package for Social Sciences) version 22. The test statistics used to analyze the data were descriptive statistics, correlation coefficient and student t test. Level of significance was set at 0.05 and p < 0.05 was considered significant.

Results

In this study, a total of 54 nephrotic syndrome children were included. Among them 25 were under 5yr, 29 were older than 5 yr. Mean age 5.51 (±2.56) year. Male to female ratio is 2.6:1. The study children were evaluated clinically for deficiency signs and symptoms of magnesium and calcium, but none of them showed any clinical signs and symptoms.

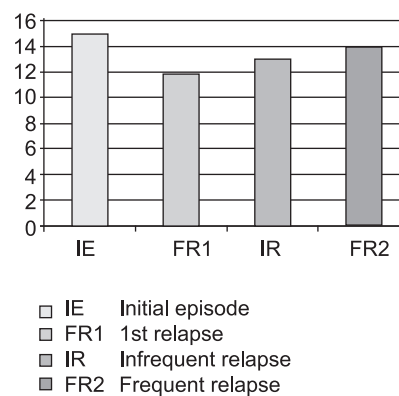


Fig.-1: Distribution of patients by type of attack

Among nephrotic syndrome cases 15(27.8%) patients were in initial episode, 12(22.2%) were in 1st relapse, 13(24.1%) were in infrequent relapse and 14(25.9%) were in frequent relapse nephrotic syndrome.

24.1 percent of the patients had hypomagnesemia (< 1.8 mg/dl) and 13.0% had hypermagnesemia (> 2.4 mg/dl). The rest of the cases had magnesium level within normal range (1.8 – 2.4 mg/dl) (Table-I).

Table-I

Serum magnesium and calcium level of the study population

Magnesium level	Number	Calcium level	Number
<1.8	13(24%)	<1.9	13(24%)
1.8-2.4	34(63%)	1.9-2.0	15(28%)
>2.4	7(13%)	2.0-2.1	26(48%)
total	54(100%)	total	54(100%)

The mean level of serum magnesium during initial attack was 2.28±0.36mg/dl, and it was 2.04±0.29mg/dl during first relapse, 2.06±0.29mg/dl during infrequent relapse and 1.76±0.32mg/dl during frequent relapse. The difference found among the mean level of serum magnesium level in different pattern of nephrotic syndrome by ANOVA test (one way) is statistically significant (P <0.01) [Table-II].

Table-II

Magnesium status in different states of nephrotic syndrome (n=54)

Type of Attack	Magnesium Level (mg/dl) [Mean±SD]	*P value
Initial episode (n=15)	2.28±0.36	<0.01
1st relapse (n=12)	2.04±0.29	
Infrequent relapse (n=13)	2.06±0.29	
Frequent relapse (n=14)	1.76±0.32	

*ANOVA Test

The mean level of serum calcium during initial attack was 2.01±0.16mmol/l, and it was 1.98±0.17mmol/l during first relapse, 2.06±0.13mmol/l during infrequent relapse and 2.05±0.15mmol/l during frequent relapse. The difference found among the mean level of serum calcium level in different pattern of nephrotic syndrome by ANOVA test (one way) is statistically insignificant (P >0.01) [Table-III].

Table-III

Calcium status in different states of nephrotic syndrome (n=54)

Type of Attack	Calcium Level (mmol/L) [Mean±SD]	*P Value
Initial episode (n=15)	2.01±0.16	>0.05
1st relapse (n=12)	1.98±0.17	
Infrequent relapse (n=13)	2.06±0.13	
Frequent relapse (n=14)	2.05±0.15	

*ANOVA Test

Among the patients with severely low (< 1.9 mmol/l) calcium level, about 30.75% of them had less than 1.8 mg/dl magnesium level, 30.75% of them had mg level at 1.8-2.4 and about 38.5% had mg level at greater than 2.4. Among the patients with Moderately Low Calcium level, 13% had mg level at < 1.8 mg/dl, 53.3% had mg level at 1.8-2.4 mg/dl and 33.7% of the patients had mg level greater than 2.4 mg/dl. Among the patients with mild calcium level, 23% of them had mg level at <1.8 mg/dl, 61.5% of them had mg level at 1.8-2.4 mg/dl and 15.5% had mg level greater than 2.4 mg/dl. The p level at 0.28 shows no significant correlation between mg level and calcium level (Table-IV).

Table-IV

Association between calcium level with magnesium level

Calcium level (mmol/l)	Magnesium level (mg/dl)			Total	p value
	< 1.8	1.8-2.4	> 2.4		
Severe (<1.9)	4 (30.75%)	4 (30.75%)	5 (38.5%)	13 (100%)	0.28
Moderate (1.9 - 2)	2 (13%)	8 (53.3%)	5 (33.7%)	15 (100%)	
Mild (2 – 2.1)	6 (23%)	16 (61.5%)	4 (15.5%)	26 (100%)	
Total	12	28	14	54	

*Chi-square test

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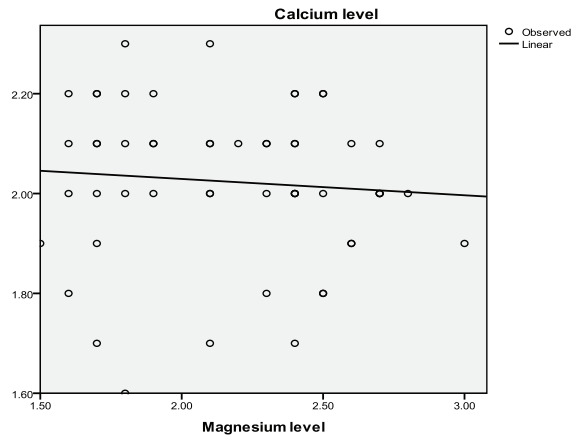


Fig.-2: Correlations of serum magnesium with calcium in children with nephrotic syndrome.

Magnesium is low in most cases of frequent relapse nephrotic syndrome patients. There was no significant correlation between calcium level with magnesium level ($r = -0.08$, $p = 0.28$).

Discussion

Some studies reported normal serum calcium levels in NS patients.¹⁰⁻¹² In study of Winata et al¹³ showed that the calcium level of NS children was lower than that in healthy children. The Hossain A et al¹⁴ study also support Winata et al. study they found ionized calcium level of NS children was lower than that in healthy children. 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 al¹⁵ observed that the ionized calcium in nephrotic syndrome children decrease after having proteinurea for more than two months. Choi et al¹⁶ also found a very weak positive correlation between the duration of disease and ionized calcium level from their 14 nephrotic syndrome samples. Garniasih et al¹⁷ found positive correlation 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.

There is however, meagre information available concerning magnesium metabolism in the nephrotic syndrome. Kobayashi A¹⁸ study revealed that serum magnesium level was significantly reduced in the untreated condition of the disease. Serum magnesium

level was gradually elevated to the normal range as the disease improved.

Prasad et al¹⁹ described that in the nephrotic syndrome the total magnesium was some what lower than normal, probably because of hypoprotinaemia and that the percentage of ultrafiltrable magnesium was increased in some patients associated with hypoalbuminaemia.

In one of the first cases of primary hyperaldosteronism reported, a very low serum magnesium.²⁰

Present study reveals that, hypomagnesemia is mostly found in frequent relapse nephrotic syndrome cases. This may be partly due to secondary hyperaldosteronism which is thought to develop in nephrotics with generalized oedema and partly due to loss of protein.

Our study also shows there is no significant association between calcium level with magnesium level ($p > 0.05$).

Conclusion

Hypomagnesemia is mostly found in frequent relapse nephrotic syndrome cases. There was no significant association between calcium level with magnesium level.

Recommendation

Further study should be done to look for any renal structural abnormality particularly tubular problem in those patients. Further multicentred randomized study should be under taken.

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