Calcium and magnesium abnormalities in critically ill children

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Abstract

Background: Critical illnesses are associated with several electrolyte derangements which are often not monitored in sick children and leads to increased morbidity and mortality.

Objectives: Primary objective of the study was to assess calcium and magnesium abnormalities in critically ill children presenting in pediatric intensive care unit.

Patients and methods: We conducted prospective observational study in patients aged between 1 month and 16 years old, who were hospitalized at Pediatric Intensive Care Unit (PICU) during the period between January 2019 to May 2020, to estimate magnesium & calcium abnormalities on admission.

Results: Out of 129 patients, 48.8% patients had hypocalcemia and 7.8% had hypomagnesemia while 20.2% had hypermagnesemia . Patients with hypocalcaemia had a higher PRISM score (P = 0.030), sepsis diagnoses (P = 0.192), need for mechanical ventilation (p=0.067) and mortality (p=0.124). While hypomagnesemia was significant with sepsis diagnosis (P = 0.024) and need for mechanical ventilation (P = 0.042).

Conclusion: Calcium and magnesium disturbances are frequent findings in critically ill pediatric patients and are often under estimated. So all critically ill children need to be monitored for these abnormalities in PICU.

Key words: Hypocalcemia; Hypomagnesemia; Hypermagnesemia; critically ill; Children.

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Introduction

Calcium and magnesium disturbances are common in patients admitted to pediatric intensive care units but routine monitoring and replacement of these electrolytes are often underemphasized.Ca is the most abundant mineral in the body, important for nerve excitability, skeletal muscle integrity, coagulation, cardiac contractility and cellular permeability. Hypocalcaemia is common abnormality in patients admitted in intensive care units. The prevalence of hypocalcemia varies significantly in various studies ranging from 34% to 68% (**Singhi et al., 2003; Naik et al., 2014; Naseem et al., 2019**). Magnesium is the fourth most abundant mineral in the body and is essential for optimal metabolic function. It acts as a cofactor for more than 300 enzymes, regulating a number of fundamental functions such as muscle contraction, neuromuscular conduction, glycemic control, myocardial contraction, and blood pressure. Various studies have reported the incidence of hypomagnesaemia 29.1% to 70% in critically ill-patients **(Beleidy et al.,2017; Deshmukh et al., 2000; Saleem et al.,2009)**.Thus their imbalance in either direction(hypo and hyper) can affect various cellular functions leading to significant morbidity and mortality**(Naseem et al., 2019)**. Hence early recognition of these imbalances and intervention to correct them is essential to avoid poor outcomes. The primary objective of this study was to determine the abnormalities of calcium and magnesium in critically ill children, and secondary objectives of the study were to find out mutual relationship between calcium and magnesium, and their correlation with PICU stay.

Patients and methods

Study design

It was a prospective observational study, included 129 patients aged 1 month to 16 years, who were hospitalized at Pediatric Intensive Care Unit, Vivekananda Polyclinic Institute of medical science, Lucknow India, during the period between January 2019 and May 2020.

Data collection

We included pediatric patients admitted to PICU, but excluded patients with history of chronic renal disorders, patients on renal replacement therapy, chronic diarrhea and patients who left against medical advice. Complete history, clinical examination, anthropometric measurements (weight, height, head circumference and mid upper arm circumference), demographic information, severity of illness using PRISM(Pediatric Risk of Mortality) III **(Pollack et al.,1996)**scores were noted at the time of admission. Organ failure was assessed according to pediatric organ dysfunction criteria **(Goldstein et al., 2005)**.All patients subsequently underwent complete laboratory assessments including; sepsis profile, blood gas analysis & blood chemistry. Serum total and ionic calcium (by Ion Selective Electrode Method) and magnesium (by Xylidyl Blue Method) levels were assessed in sample taken at the time of admission. Electrolytes were classified as normal, hypo or hyper according to reference ranges obtained from **Nelson textbook of pediatrics**, viz. Calcium (total): 8.8-10.8 mg/dL, Calcium (ionized): 4.8 to 4.92 mg/dL, Magnesium: 1.5-2.6 mg/dL. Duration of mechanical ventilation if needed, total duration of PICU stay and outcome (discharged or died) were recorded.

Ethics approval and consent for participation

This manuscript obtained ethical approval from the Institutional Ethics Committee of

Vivekananda Polyclinic Institute of medical science, Lucknow. After Ethical committee approval, written consent from the parents was taken.

Statistical analysis

The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 21.0 statistical Analysis Software. The values were represented in numerical values and percentages as Mean±SD. Chi-square test; Independent samples 't'test and Analysis of variance (ANOVA) tests were used to compare the data. A 'p' value less than 0.05 was considered to be statistically significant. Linear correlation was evaluated using Pearson's correlation coefficient.

Results

Out of total 164 admissions in PICU, 26 patients were excluded as per exclusion criteria while 9 didn't give consent. So total 129 patients were enrolled in study.

There were 43 (33.3%) females & 86 (66.7%) males, Majority of the patients were aged from 1-month to 5 -years 63.6% (n=82). 7.8% (n=10) were severely malnourished (**Table.1**). Average GCS at admission was 11.22±3.65 (Ranged from 3 to 15), organ failure was observed in 22 (17.1%) cases, Sepsis in 85(65.9%) cases and 28 (21.7%) cases required mechanical ventilation. Duration of PICU stay ranged from 1to18 days, mean duration being 4.34±3.13 days. Total 108(83.7%) patients were discharged while 21(16.27%) expired. 74.4% (n=96) of our study population presented with illness of more than 3 days duration of which 33.3% (n=43) presented after 7 days of onset of acute illness.

Table 1.Baseline Characteristics of Study Population

Findings	No.	%
Age		
• **1 m to 1 yr**	50	38.8
• **2-5 yr**	32	24.8
• **6-12 yr**	37	28.7
• **13-16 yr**	10	7.8
Gender		
• **Female**	43	33.3
• **Male**	86	66.7
Mean Height ±SD (Range) cm	95.52±34.34 (46-165)	
Mean Weight ±SD (Range) kg	15.87±12.74 (1.65-61.2)	
Mean Head circum ±SD (Range) cm	45.85±6.38 (30-59)	
Severely Malnourished	10	7.8
Mean Body temperature ±SD (Range) ºF	98.57±1.23 (96.0-105.0)	

At admission 48.8%were hypocalcemic and 51.2% normocalcemic while none was found to be hypercalcemic, 7.8%were hypomagnesemic, 72.1% normomagnesemic and20.2% were hypermagnesemic respectively. Mean calcium levels were 8.3±1.1(4.6-10.4) mg/dL, mean magnesium levels were 2.2±0.63(0.98-5.67)mg/dL and mean PRISM score was 7.91±6.04 (2-28) (**Table.2 and 3**)

Table 2. Baseline parameters of Study Population

Parameters	Min.	Max	Mean	SD
At admission (n=129)				
Ionized Calcium (mg/dl)	2.24	7.62	4.25	0.77
Total Calcium(mg/dl)	4.6	10.4	8.63	1.01
Magnesium(mg/dl)	0.98	5.67	2.21	0.61
Potassium(mmols/lt)	2.22	8.2	4.62	1.11
Phosphorus(mg/dl)	1.5	11.4	4.36	1.56
PRISM score	2	28	7.91	6.04

Table 3 .Baseline Electrolyte Levels (mg/dl)

Variables	**Below normal**		**Normal**		**Above normal**	
	No.	%	No.	%	No.	%
Ionized Calcium	114	88.4	8	6.2	7	5.4
Total Calcium	63	48.8	66	51.2	0	0.0
Magnesium	10	7.8	93	72.1	26	20.2

Hypocalcemia was found in 46.5% females and 50% males at admission, but association of baseline calcium levels with age, gender and nutritional status were not significant. Hypocalcemia was associated with patients presenting with longer duration of symptoms (more than 7 days)(p=0.037). Rate of organ failure (20.6% vs. 13.6%), mechanical ventilation (60.3% vs. 71.2%), mortality (12.5% vs. 4.0) and duration of PICU stay (4.40±3.43 days vs. 4.09±2.85 days) were also higher among cases with hypocalcemia as compared to those with normocalcemia, but the differences were not found to be significant statistically. PRISM score of patients with hypocalcemia at admission was significantly higher as compared to those with normocalcemia (9.10±6.86 vs. 6.79±4.93) (p=0.03), (**Table.4**)

Proportion of cases with hypomagnesemia were higher in age group 13-16 years (p=0.01). Gender and nutritional status were not found to be significantly associated with magnesium levels. Sepsis was observed in significantly higher proportion of cases with hypomagnesaemia as compared to normal and raised magnesium (90.0% vs. 68.8% and 46.2% respectively)(p=0.024).Requirement of mechanical ventilation was numerically higher among magnesium deficient and balanced levels as compared to hypermagnesemia (30.0% and22.6% vs. 15.4% respectively) (P = 0.589),Duration of PICU stay was maximum among cases with deficient magnesium (4.9±4.2 days), followed by normomagnesemic (4.31±3.21 days) and minimum among those with raised magnesium (3.73±2.39 days),but this difference was not found to be statistically significant (p=0.559). PRISM score of cases with normal magnesium levels was higher as compared to deficient and raised levels (8.41±6.44 vs. 6.40±4.90 and

6.73±4.71), but this difference was also not found to be significant statistically, (**Table.5**).

Table 4. Association of calcium with various parameters

Variables	Total (n=129)	Hypocalcemia (n=63)	Normocalcemia (n=66)	p-value
Age group No.(%)				
1mth-1yr	50(38.8%)	19(38%)	31(62%)	0.087
2yr-5yr	32(24.8%)	17(53.1%)	15(46.9%)	
6yr-12yr	37(28.7%)	19(51.4%)	18(48.6%)	
13yr-16yr	10(7.8%)	8(80%)	2(20%)	
Female No.(%)	43(33.3%)	20(46.5%)	23(53.3%)	0.709
Male No.(%)	86(66.7%)	43(50%)	43(50%)	
Duration of symptoms				
<3days	33	10(30.3%)	23(69.7%)	
3-7days	53	31(58.5%)	22(41.5%)	0.037
>7days	43	22(51.2%)	21(48.8%)	
GCS <12	77	32(50.8%)	45(68.2%)	0.044
Organ failure No.(%)	22 (17.1%)	13(20.6%)	9 (13.6%)	0.291
Sepsis No.(%)	85 (65.9 %)	38 (60.3%)	47 (71.2%)	0.192
Mechanical ventilation No.(%)	28 (21.7 %)	18 (28.6%)	10 (15.2%)	0.067
PICU stay mean(SD)		4.40 (3.43)	4.09 (2.85)	0.582
PRISM mean(SD)		9.10 (6.86)	6.79 (4.93)	0.030

Table 5. Association of magnesium with various parameters

Variables	Total (129)	Hypomagnesemia (n=10)	Normomagnesemiaa (n=93)	Hypermagnesemia (n=26)	p-value
Age group					
1mth-1yr	50(38.8%)	5(10%)	30(60%)	15(30%)	
2yr-5yr	32(24.8%)	2(6.3%)	26(81.3%)	4(12.5%)	0.01
6yr-12yr	37(28.7%)	0	30(81.1%)	7(18.9%)	
13yr-16yr	10(7.8%)	3(30%)	7(70%)	0	
FemaleNo.(%)	43(33.3%)	5(11.6%)	34(79.1%)	4(9.3%)	0.065
Male	86(66.7%)	5(5.8%)	59(68.6%)	22(25.6%)	
Duration of symptoms					
<3days	33	4(12.1%)	23(69.7%)	6(18.2%)	0.095
3-7days	53	5(9.4%)	33(62.3%)	15(28.3%)	
>7days	43	1(2.3%)	37(86%)	5(11.6%)	
GCS <12	77	5(50%)	55(59.1%)	17(65.4%)	0.686

Organ failure No.(%)	22 (17.1%)	1 (10.0%)	17 (18.3%)	4 (15.4%)	0.778
Sepsis No.(%)	85 (65.9 %)	9 (90.0%)	64 (68.8%)	12 (46.2%)	0.024
Mechanical ventilation No.(%)	28 (21.7 %)	3 (30.0%)	21 (22.6%)	4 (15.4%)	0.589
PICU stay mean(SD)	-	4.9 (4.2)	4.31 (3.21)	3.73 (2.39)	0.559
PRISM mean(SD)	-	6.40 (4.90)	8.41 (6.44)	6.73 (4.71)	0.327

Moderate level of significant correlation between total calcium and ionized calcium was observed (p value = <0.001 and r value = 0.668). Statistically significant correlation between total calcium and PRISM score was observed but level of correlation was weak (p value = 0.044 and r value = -0.178). But serum magnesium levels did not show any significant correlation with calcium, PRISM score and PICU stay, (**Table.6**).

Table 6.Correlation of electrolytes with GCS, Duration of Symptoms, PRISM score and Duration of PICU Stay (Pearson's Correlation)

Variables		**Total C**	**Mg**	**Dur of symptoms**	**GCS**	**PRISM score**	**PICU stay**
Ionized Ca	'r'	0.668	0.034	0.002	0.060	-0.193	0.004
	'p'	<0.001	0.699	0.984	0.501	0.029	0.968
Total Ca	'r'		-0.013	-0.024	-0.056	-0.178	-0.100
	'p'		0.882	0.788	0.526	0.044	0.258
Mg	'r'			-0.034	0.003	-0.026	-0.142
	'p'			0.699	0.970	0.768	0.107
Dur. of symp	'r'				-0.195	0.147	0.083
	'p'				0.027	0.097	0.348
GCS	'r'					-0.550	-0.401
	'p'					<0.001	<0.001
PRISM score	'r'						0.184
	'p'						0.037

Discussion

Critical illness affects the normal body metabolism and various physiological activities. It has a detrimental effect on homeostasis. While the focus of electrolyte

imbalances during critical illness is generally stressed on maintenance of sodium and potassium level, while role of other electrolytes particularly macro-minerals like calcium and magnesium are often underestimated and have not been studied extensively. In the present study, the calcium and magnesium abnormalities and their mutual relationship in 129 critically ill children was evaluated and their association with demographic profile, clinical characteristics and PICU stay were analyzed.

The incidence of hypocalcaemia was 48.8% in our study, in other studies incidence varies from34% to 57.6% **(Naseem et al., 2019; Haghbin et al., 2010)**. Similar findings were seen in a study of 100 critically ill children by **Singhi et al. (2003)** who found hypocalcaemia in 35 per cent of patients at admission. **Naik et al. (2014)** studied serum calcium levels in a prospective cohort of 320 children admitted to PICU and observed hypocalcemia in 47.5 percent of patients at the time of admission. Thus hypocalcemia is common in ill children presenting in PICU.

Although we did not find any association between hypocalcemia and sepsis, but in few studies, sepsis was found to be significantly associated with hypocalcaemia **(Beleidy et al.,2017; Deshmukh et al.,2000)**. **Buysse et al.(2001)** found as many as 68% children with septic shock were hypocalcaemic.

Our study found hypocalcemia to be significantly associated with higher PRISM score (0.030), showing poor outcome, but did not find a significant association of hypocalcemia with mechanical ventilation need, which was similar to result of **Filyk et al. (2019)**. Although, **Naseem et al.(2019)** reported electrolyte imbalance to be significantly associated with mortality, however, they could not find its association with morbidity, complications and duration of PICU stay, which were similar to our observation.

Hypomagnesemia was observed in only 7.8% of the study population at admission, while abnormally high levels of magnesium were seen in 20.2% of our patients. Various studies shows prevalence of hypomagnesemia ranging 29% (**Erdoğan and Menevşe et al., 2018**) to as many as 70% patients admitted to PICU **(Deshmukh et al.,2000)**. **Filyk et al.(2019**) reported it in as many as 70.4% of young children in ICU aged 1 to 36 months, but abnormally high levels of magnesium have reported in very few studies (7.3%), **Dandinavar et al., 2019)**. The possible reason for 20.2% hypermagnesemic cases in our study could be administration of magnesium sulphate in various modes prior to admission in our study population. 74.4% of our study population presented with illness of more than 3 days duration of which 33.3% presented after 7 days of onset of acute illness. Also, 37.2% of our patients presented with abnormal neurological signs and 29.5% with respiratory illness. Treatment of such illness often involves administration of inhaled or intravenous magnesium sulphate. The possibility of such patients being admitted to a nearby hospital for treatment prior to admission to our hospital cannot be ruled out and thus magnesium should be measured on admission before initiating therapy.

A significant association of hypomagnesemia was found with sepsis (p=0.024). **Saleem and Haque et al. (2009)**

also found hypomagnesemia to be significantly associated with increasing age and sepsis. Association of age and sepsis with hypomagnesemia has also been reported in few other studies (**Sadeghi-Bojd et al., 2019**; **Erdoğan and Menevşeet al., 2018;Singhi et al., 2003**).Magnesium levels did not show significant association with any of the other outcomes.

As far as relationship of magnesium levels with PICU outcomes is concerned, there are contradictory reports. **Erdoğan and Menevşe et al. (2018)** found that hypomagnesemia was significantly associated with higher PRISM score, duration of intensive care unit stay, need for mechanical ventilator and the number of days connected to mechanical ventilator as well as mortality rate. While **Saleem and Haque et al. (2009)** found higher mortality in normomagnesemic children as compared to hypomagnesemic children though it was not significant statistically, which was similar to our observation.Calcium and Magnesium levels did not show any significant correlation in our results.

Our study provides data regarding incidence of calcium as well as magnesium abnormalities in critically ill pediatric patients admitted to PICU in north India. Calcium and magnesium disturbances are quite frequent in PICU. Along with hypocalcemia and hypomagnesemia, hypermagnesemia is also common in sick children, so these electrolytes should be measured in all critically ill children to treat appropriately and reduce the risk of further deterioration of these macrominerals, which can help in reducing their impact on the outcome.

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Conflict of interest: None declared

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