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Original Research Article

Hypomagnesemia as a predictor of mortality in critically ill pediatric patients in picu using prism score

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ABSTRACT

Background: Magnesium is the fourth most abundant cation in the human body and the second most abundant intracellular cation after potassium. A potential relationship between low magnesium levels and increased mortality has been suggested in the literature. The objectives were to detect prevalence of hypomagnesemia in critically ill children, its association with sepsis and to correlate this with mortality.
Methods: This study was an observational study done on 100 children who met the inclusion criteria, admitted to the PICU of Kempegowda Institute of Medical Sciences, Bangalore, Karnataka, India. Patients under the study were managed and treated according to their clinical status and supportive traditional treatment.
Results: Prevalence of hypomagnesemia in critically ill pediatric patients was 53%. In this study, majority of the cases admitted to PICU were dengue (19%) and bronchopneumonia (15%) which were significantly associated with hypomagnesemia as p value was less than 0.05. As regard prognosis, Mg had an AUC of 0.576 for prediction of mortality whereas the AUC for PRISM score was 0.811. Logistic regression analysis showed that hypomagnesemia is a significant predictor for mortality among critically ill children (p value=0.028) and OR=3.180 (0.854-7.965).
Conclusions: Present study has found high prevalence of hypomagnesemia in critically ill patients. Hypomagnesemia was associated with a higher mortality rate in critically ill patients and commonly associated with infections and respiratory diseases. Hypomagnesemia indicated poor outcome and higher mortality rates in critically ill patients.

Keywords: Critically ill patients, Hypomagnesemia, PICU

INTRODUCTION

Magnesium is the fourth most abundant cation in the human body and the second most abundant intracellular cation after potassium. It serves as a cofactor in more than 300 enzymatic reactions mainly involving transfer of phosphate group, for example formation of ATP. Hypomagnesemia is a common finding in current medical practice, mainly in critically ill patients. A potential relationship between low magnesium levels and increased mortality has been suggested in the literature. Clinical manifestations of hypomagnesemia include neuromuscular, neurologic, psychiatric and cardiac disorders, which may considerably increase the morbidity of such patients. Hypomagnesemia is easily mistaken for potassium deficit or calcium deficit a condition with which it is often associated. It is difficult to correct hypokalemia or hypocalcemia secondary to hypomagnesemia unless magnesium is corrected.[1] Magnesium is important for the transfer, storage and use of energy and it regulates and catalyzes over 300 enzyme systems. Hypomagnesaemia can thus lead to various

metabolic abnormalities and clinical consequences, which are caused by an imbalance between the Gastrointestinal (GI) absorption and renal excretion of magnesium. The principal manifestation of hypomagnesemia is heart arrhythmias, which unless diagnosed and treated, can be lethal.[2] A healthy human adult have about 25 gm or 1000 mmoL magnesium, where approximately 60% stores in bones, 20% in muscles, 20% in soft tissues, 0.5% in erythrocytes, and 0.3% in serum.[3] About 70% of the plasma magnesium is ionized or complexed to filterable ions, while 20% is bound to proteins. Magnesium homeostasis in humans mainly involves the kidneys, small bowel, and bones.[4,5] GI absorption and renal excretion are the most important mechanisms for controlling and regulating the magnesium homeostasis. The cellular regulation of magnesium uptake and release occurs slowly, and healthy individuals need to ingest about 0.15-0.2 mmoL/kg/day to contain a normal magnesium status. The intestinal absorption of dietary magnesium depends on both intake and body magnesium status and occurs via passive and active pathways.[5] The passive absorption is driven by a favorable electrochemical gradient and occurs mainly paracellulary through leaky epithelia primarily located in the small intestine. Additionally, the process of passive absorption interacts with the levels and absorption of calcium.[6,7]

METHODS

For each patient, a complete diagnostic work-up was performed including thorough history and physical examination. Physical examination included recording heart rate, respiratory rate, blood pressure, and Glasgow coma scale. Laboratory work-up included random blood glucose, complete blood count, C-reactive protein, serum electrolytes including magnesium level, blood cultures, liver and kidney function tests, prothrombin and partial thromboplastin times. Cultures of other body fluids, like cerebrospinal fluid (CSF) and urine, were done when clinically required.

Chest radiograph, brain CT, and other laboratory or radiological investigations were performed when indicated. In addition, a severity score was calculated which was the Pediatric Risk of Mortality (PRISM) score.[2] PRISM score was automatically calculated within 24 hours of admission together with assessment of serum Mg^{2+}. Serum Mg level was determined using Calmagite

Colorimetric method. Patients were classified into groups based on this level as patients with serum magnesium <1.5 mg/dl were considered hypomagnesemic and were taken as cases while patients with level >1.5 mg/dl and less than 2.3 mg/dl were considered normomagnesemic and were taken as controls. Primary outcome measure was occurrence of death during PICU admission. Secondary outcome measures included length of PICU stay and need of mechanical ventilation.

RESULTS

As regard to serum magnesium level, author found that 53 of the 100 studied patients were hypomagnesemic and their magnesium level ranged from 0.8-1.4 mg/dl and 47 children were normomagnesemic and their level ranged from 1.5 mg/dl-2.3 mg/dl) (Table 1).

Table 1: Socio-demographic and clinical characteristics of the studied groups.

Demographic data		Hypomagnesemic group (n=59) Mean±SD	Normomagnesemic group (n=41) Mean±	Test of significance	P value
Age (years)		4.44±4.45	4.12±4.37	1118.5*	0.523
Range		45 days-15 years	45 days-15 years		
Sex	Male	39 (66.1%)	23 (56.1%)	1.028**	0.311
	Female	20 (33.9%)	18 (43.9%)		
BMI		7.85±3.38	7.27±2.74	1126*	0.558
Range		8.87-28.06	11.11-21.42		
Length of stay in the PICU (days)		10.16±9.03	6.04±6.43	823.500*	0.007
Range		1-35 days	1-30 days		
PRISM score		25.83±5.23	19.68±6.06	594.500*	<0.001
Range		13-33	13-30		
Mortality risk of according to PRISM score		61.90±21.41	35.87±26.34	595**	<0.001
Range		11%-88.6%	11%-77.2%		
Need for ventilation	Yes	45 (76.3)	15 (36.6)	15.87**	<0.001
	No	14 (23.7)	26 (63.4)		
Mortality	Died	34 (57.6)	12 (29.3)	7.83**	0.008
	Survived	25 (42.4)	29 (70.7)		

Table 2: Cut off point, area under the curve, sensitivity and specificity of magnesium, CRP and PRISM score in predicting mortality.

Test result variable(s)	AUC	p	Confidence interval		Cut off value	Sensitivity	Specificity
			Lower	Upper			
CRP	0.716	<0.001	0.600	0.833	51	85%	68%
Mg	0.576	0.049	0.318	0.675	1.25	61%	71%
Prism score	0.811	<0.001	0.705	0.918	25.50	81%	55%

Ages of hypo-magnesemic children ranged from 45 days to 15 years with mean (±SD) age of 4.44±4.45 years while the ages of children with normal level ranged from 45 days to 14 years with mean (±SD) age of 4.12±4.37 years. 29 patients (54.7%) of the hypomagnesemic group were males and 24 (45.3%) were females while in the normomagnesemic one 24 patients (51.1%) were males and 23 patients (48.9%) were females (Table 1). BMI ranged from 8.87 to 28.06 in the hypomagnesemic group with mean (±SD) of 7.85±3.38 while in the normomagnesemic one it ranged from 11.11 to 21.42 with mean (±SD) of 7.27±2.74 (Table 1). As regard to length of stay in the PICU, the mean duration of stay of patients with hypomagnesemia (±SD) was 10.16±9.03 days while that of patients with normal level (±SD) was 6.04±6.43 days (p value=0.007) (Table 1).

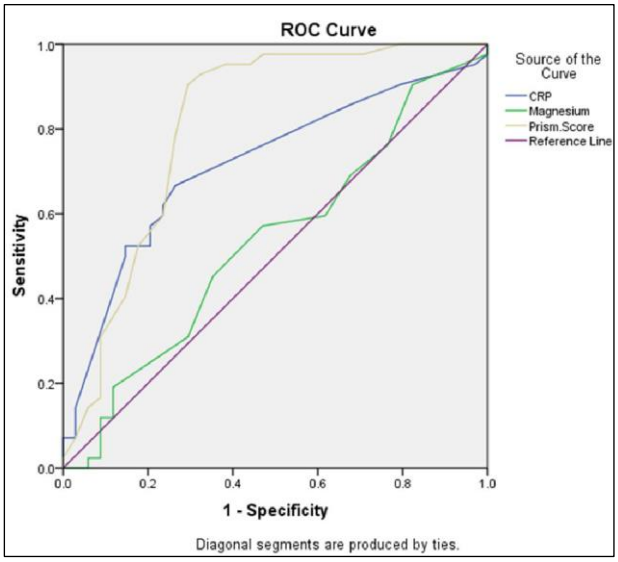

Figure 1: ROC curve of serum magnesium level, CRP and PRISM score for prediction of mortality in the studied patients.

Mean PRISM score in the hypomagnesemic group (±SD) was 25.83±5.23 with while mean PRISM score in the normomagnesemic one (±SD) was 19.68±6.06 with Table 1). As regard to need of ventilation, 76.3% of patients with hypomagnesemia needed ventilator support in comparison to only 36.6 % of patients with normal level (p value=<0.001). Mortality rate in the hypomagnesemic group was 57.6% while in the normomagnesemic one it was 29.3 % (p value=0.008) (Table 1).

Further analysis by ROC curve was performed to test the predictive power of Mg^{2+} along with other relevant factors for mortality. Mg^{2+} achieved an AUC of 0.576 (p=0.049). Best cut-off level for prediction of mortality in this study was 1.25 mg/dl with sensitivity of 61% and specificity of 71%. On the other hand, CRP and PRISM score can highly predict mortality with values of (AUC=0.716, p=<0.001) and (AUC=0.811, p=<0.001) respectively Table 2 and Figure 1.

DISCUSSION

Hypomagnesaemia can result in disturbances in nearly every organ system and can cause potentially fatal complications such as coronary artery vasospasm, ventricular arrhythmia, and even sudden death.[9] As regard to serum magnesium level, the prevalence of hypomagnesemia was high as 53 of the 100 studied patients were hypomagnesemic and their level ranged from 0.8-1.4 mg/dl and 47 were with normal level and their level ranged from 1.5-2.3 mg/dl. These results were in agreement with Kumar D et al, who found that the prevalence of hypomagnesaemia was 53% and that of normomagnesemia was 47%. In contrast, Soliman HD et al, study on 442 patients found that the prevalence of hypomagnesemia was much lower than normomagnesemia (14% to 18%).[11] This difference may be due to measurement of ionized magnesium in that study.

Ages of patients with hypomagnesemia ranged from 45 days to 15 years with mean age (±SD) of 4.44±4.45 years while ages of those with normal magnesium level ranged from 45 days to 14 years with mean age (±SD) of 4.12±4.37 years. 29 children (54.7%) of the hypomagnesemic group were males and 24 (45.3%) were females, while in the normomagnesemic one 24 children (51.1%) were males and 23 (48.9%) were females. Authors found no significant statistical difference between both hypomagnesemic and normomagnesemic groups as regard age, sex or anthropometric measures Table 1 and this was in agreement with studies done by Kumar D et al, Fatih D et al, Safavi M et al.[10,12,13]

Mean PRISM score in hypomagnesemic patients (±SD) was 25.83±5.23 while mean PRISM score in normomagnesemic patients (±SD) was 19.68±6.06. This difference was statistically significant, and this denotes presence of high association between disease severity and hypomagnesemia. Despite Soliman HM et al, have found lower incidence of hypomagnesemia in his studied group, they found that patients who developed ionized hypomagnesemia during their ICU stay had higher APACHE II score, longer ICU stay and higher mortality rate than other patients.[11] In contrast, Mir ZSH et al, did not find significant difference between hypomagnesemic and normomagnesemic patients as regard Acute Physiology and Chronic Health Evaluation (APACHE) which is a severity of disease classification system and one of several ICU scoring systems.[14] This may be due to the small size of that studied sample (only 70 patients). They found higher incidence of electrolyte disturbances, multiorgan dysfunction and mortality among the hypomagnesemic group irrespective of this insignificant ICU stay or APACHE-II score. The authors in that study explained this finding by a strong association between hypomagnesemia and sepsis, a common cause of death in ICU patients. On assessment of the Risk factors for mortality in this study, authors found that hypomagnesemia is a significant risk factor (P=0.003) and this was in agreement with the results of a systematic review done by Fairley J et al, as they searched MEDLINE, CENTRAL, and EMBASE databases from 1975 to July 2014 for English language articles excluding obstetric, non-intensive care unit based, and specific population (poisoning, cardiothoracic, and neurosurgery) studies.[15] They identified articles on magnesium measurement, associations, and therapy. They identified 34 relevant studies and they found that risk of mortality was significantly increased with hypomagnesemia (odds ratio, 1.85, 95% confidence interval, 1.31-2.60).

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