International Journal of Contemporary Pediatrics
Shankar NP et al. Int J Contemp Pediatr. 2020 Apr;7(4):790-794
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20201132

Original Research Article

Risk factors and clinical outcome of hypomagnesemic patients in pediatric intensive care

Poornima Shankar N., Kavya C., Varsha Monica Reddy*

Department of Pediatrics, KIMS Hospital and Research Centre, Bangalore, Karnataka, India

Received: 18 September 2019
Accepted: 03 February 2020

***Correspondence:**
Dr. Varsha Monica Reddy,
E-mail: drvarshareddy29@gmail.com

ABSTRACT

Background: Hypomagnesemia is a common finding in current medical practice, especially in critically ill patients. Magnesium ion plays a vital role in various metabolic processes in body and its deficiency leading to serious clinical consequences. Since hypomagnesemia is most often asymptomatic, it goes unsuspected and therefore undiagnosed. Hence, early detection of hypomagnesemia has prognostic and therapeutic implications. It is imperative to understand the various risk factors and their clinical outcome that is associated with hypomagnesemia.
Methods: This is an observational study done in a tertiary centre in Bangalore, India where-in 100 children who met the inclusion criteria, admitted to the PICU were recruited and prospectively studied. Serum Magnesium along with various clinical and biochemical parameters were correlated to enumerate the various risk factors associated with hypomagnesemia.
Results: In this study authors found the incidence of hypomagnesemia to be around 53%. Authors found higher incidence in age group of 1-5 yrs (40%) and least were in the age groups of <1 year and more than 10 years (19%) and there was no gender preponderance. Authors also evaluated the various risk factors associated with hypomagnesemia. There was significant association of hypocalcemia (60%) and hypokalemia (45.2%) with hypomagnesemia. Infections (33.9%) and neurological disorders (26.41%) seemed to collectively comprise around 60% of the hypomagnesemic group. All patients admitted secondary to sepsis and Traumatic Brain Injury (TBI) had hypomagnesemia proving to be a significant risk factor. Authors also found increased mortality among hypomagnesemic group. However, found no association between low serum magnesium and PICU stay.
Conclusions: There is high prevalence of hypomagnesemia in critically ill patients and is associated with a higher mortality. It is also commonly associated with infections, CNS disorders, respiratory diseases and metabolic derangements like hypokalaemia and hypocalcaemia. There is no association of Hypomagnesemia with duration of PICU stay.

Keywords: Clinical profile, Hypomagnesemia, Mortality, Risk factors

INTRODUCTION

Magnesium (Mg) is the second most abundant intracellular cation and fourth most abundant cation in the body, deemed forgotten because of its under-diagnosis and under-treatment in day to day practice. It has been implicated in the Pathophysiology of many diseases especially in critically ill patients. Magnesium plays a vital role in the active transport of calcium and potassium ions across cell membranes, a process that is important for nerve impulse conduction, muscle contraction, vasomotor tone, and normal heart rhythm.[1] It has been recognized as a cofactor for more than 300 enzymatic reactions. Magnesium is involved in important metabolic processes including ATP-dependent biochemical reactions, synthesis of DNA, RNA expression, cell signaling at muscle and nerve levels, and glucose and Blood Pressure (BP) control, among others.[2] Hypomagnesemia therefore can lead various clinical consequences and is most often unrecognized due to its clinical under-diagnosis.

Hypomagnesemia is a common entity in critically ill patients and is associated with high mortality.[3] The etiology of hypomagnesemia in critical illness is complex and may involve a number of mechanisms such as decreased intake, increased renal or gastrointestinal losses and altered intracellular extracellular distribution. Through the activation of neuroendocrine pathways, Mg deficiency induces a systemic stress response that has been implicated in the pathophysiology of many diseases and increase in the morbidity especially in critically ill patients. In this study, we have tried to enumerate the various risk factors associated with hypomagnesemia and related mortality.

METHODS

This prospective observational study was carried out in the PICU of pediatrics department in Kempegowda institute of medical sciences, Bangalore; from December 2017 to May 2018, after approval by the Institutional Ethics Committee. 100 patients aged between 1 month and 18 years were randomly recruited into the study. Neonates, Patients who received magnesium prior to transfer to Pediatric Intensive Care Unit, Patients who are on drugs interfering in the magnesium absorption with documented evidence, Patients who were diagnosed to have magnesium deficiency earlier, Patients with chronic renal failure and renal tubular acidosis were excluded from the study.

After a thorough history and physical examination, first set of samples were drawn immediately and processed within 6 hours. Routine laboratory investigations including complete blood picture, C-Reactive Protein (CRP), serum electrolytes, serum aminotransferases, Blood Urea Nitrogen (BUN), serum creatinine, as well as serum magnesium levels were measured using blood sample taken for routine examination at admission initially. Patients staying for 3 days or more are taken into consideration and again sera magnesium levels repeated between seventh and tenth day if PICU stay is extended. Two milliliters of whole blood will be collected by venipuncture under strict aseptic precaution and sent to biochemistry laboratory for assessment of serum magnesium levels which was done by calorimetric method.

Data was collected regarding age, gender, clinical diagnosis, serum magnesium level, medicines in use, nutritional state by weight for age, starvation time and mechanical ventilation and any other relevant parameters. Hypomagnesemia is defined as serum magnesium levels <1.8 mg/dl. Special emphasis was out on monitoring serum magnesium levels during the first 7 days of admission (within first 6 hrs of admission, after 3 days and after 7 days if the stay is more than that).

Statistical analysis

Data were entered in MS Office Excel and were analysed using Statistical Package for Social Sciences (SPSS) version 24.0. Descriptions of categorical variables like age category, gender, drug use, etc were done in frequency and percentage. Association of magnesium level and other categorical variables like gender, age, calcium status was done using Chi-square test. All tests were two tailed and p value <0.05 was considered statistically significant.

RESULTS

Analysis was performed on a total of 100 patients (Figure 1: Study flow chart). In the present study, out of 100 patients, majority were in age group of 1-5 yrs (40%) and least were in the age groups of <1 year and more than 10 years (19%) and age seemed to be a significant factor affecting calcium levels. Overall 53 (53%) were males and 47 (47%) were females, males being predominant with male to female ratio of 1.12:1, however had no statistically significant effect on serum magnesium levels. Various metabolic derangements were correlated between the two groups among which hypokalemia and hypocalcemia were significantly present in hypomagnesemic group.

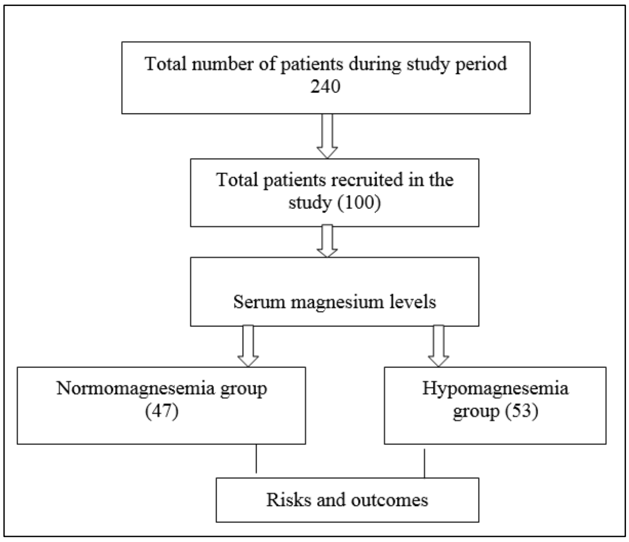

Figure 1: Study design.

Serum magnesium measurements were serially repeated to assess patients who subsequently developed hypomagnesemia during the course of PICU stay. Accordingly (Table 1), 48 (90.6%) of the patients were hypomagnesemic at admission, only 3 (4.7%) developed hypomagnesemia during 3 to 7 days of PICU stay and only 2 (3.8%) patients were found to be hypomagnesemic after first 7 days of PICU stay. These variations were found to be statistically insignificant as p value is not less than 0.05. Authors also assessed the effect of starvation and nutrition on hypomagnesemia. Patients were restricted oral intake due to various medical indications as part of their medical management. Authors also assessed the nutritional status of the children at admission and categorized them into grades of malnutrition as per Indian Academy of Pediatrics classification. There was no major variation in the distribution of these patients between hypomagnesemic and normomagnesemic groups. Therefore, found that nutritional status or starvation had no significant relation with the development of hypomagnesemia. However, 2 (3.8%) of severely malnourished patients developed hypomagnesemia in due course compared to normal patients.

Table 1: Association and risk factors of hypomagnesemia in PICU patients.

Category		Hypomagnesemia N (%)	Normal magnesium levels N (%)	p value#
Age	<1 year	10 (18.9)	9 (19.1)	0.02*
	1 to 5 years	14 (26.4)	26 (55.3)	
	6-9 years	13 (24.5)	6 (12.8)	
	≥10 years	16 (30.2)	6 (12.8)	
Gender	Male	29 (54.7)	24 (51.1)	0.71
	Female	24 (45.3)	23 (48.9)	
Metabolic profile	Hypocalcemia	32 (60.4)	12 (25.5)	0.001*
	Hyponatremia	12(22.6)	8(17.02)	0.34
	Hypokalemia	24(45.2)	12(25.53	0.005*
Picu stay	1-3 days	48 (90.6)	45 (95.7)	0.38
	3-7 days	3 (5.7)	2 (4.3)	
	>7 days	2 (3.8)	0	
Starvation	<3	43 (81.1)	41 (87.2)	0.25
	3-5	7 (13.2)	6 (12.8)	
	6-10	3 (5.7)	0	
Nutrition (% of expected weight)	50-60	2 (3.8)	3 (6.4)	0.52
	61-70	12 (22.6)	11 (23.4)	
	71-80	25 (47.2)	26 (55.3)	
	>80	14 (26.4)	7 (14.9)	
	Death	6 (11.3)	0	0.02*

Table 2: Occurrence and incidence of hypomagnesemia in admitted PICU patients with respect to their primary diagnosis category.

Diagnosis	Hypo-magnesemia (53)		Normal magnesium (47)	
	n	%	n	%
Infections	18	33.9	2	4.25
Septic shock	5	9.4	0	0
Respiratory	5	9.4	17	36.1
GIT	1	1.88	3	6.38
CNS	14	26.41	7	14.89
Poisoning	3	5.66	8	17.02
Traumatic Brain Injury	4	7.55	0	0
Pediatric surgery	1	1.88	1	2.12
Miscellaneous	3	5.66	7	14.89

Among the hypomagnesemic group (Table 2), patients with infections and patients with CNS abnormalities like meningitis, encephalitis, seizure disorder were the major risk categories comprising over 60% of the cases. The presence of infections seemed a significant risk factor for hypomagnesemia with 18 (33.9%) of them affected, while only 2 (4.25%) of these patients having normal magnesium levels. It was important to note that all patients presenting with septic shock and those admitted secondary to traumatic brain injury, 5 (9.4%) and 4 (7.55%) respectively, were found to have hypomagnesemia. There was significant association specifically between patients with dengue fever or bronchopneumonia and hypomagnesemia as p value <0.05. Among patients admitted for other respiratory ailments, 5 (9.4%) had low magnesium levels, however majority of them 17 (36.1%) had normal magnesium levels. The higher mortality in this study can be ascribed to higher incidences of other electrolyte deficiencies and multiorgan dysfunction in the hypomagnesemic group when compared with normomagnesemic group.

In this study, out of the 100 patients that were studied during their PICU stay, 6 patients succumbed all of whom belonged to hypomagnesemic group which was statistically significant.

DISCUSSION

Hypomagnesemia is a common entity especially in critically ill children. The incidence seems to highly variable across numerous studies, ranging from 14% to 61%.[4] In this study the incidence was high as 53%, which is similar to the incidence as shown in study by Singhi et al, who found a prevalence of 60%.[5] Male gender showed a preponderance to hypomagnesemia as compared to females as shown by several other studies as well.[5,6]

Electrolyte abnormalities are common among critically ill patients due to multifactorial etiopathogenesis such as multiorgan failure especially renal and cardiac secondary to decreased perfusion, activation of the vasopressin and renin-angiotensin-aldosterone system, adverse effects of multimodal treatments and importantly altered serum magnesium levels. Combined effect of Hypomagnesemia and secondary electrolyte abnormalities predisposes the myocardium to reperfusion injury by depleting endogenous antioxidants and recruiting inflammatory cells. Low magnesium levels have also been attributed to inciting Systemic Inflammatory Response Syndrome (SIRS) and organ dysfunction thereby increasing morbidity and mortality among PICU patients.

Hypocalcemia classically can occur secondary to hypomagnesemia, as it lowers parathyroid hormone secretion and also causes end-organ resistance to its action. Mg acts as a natural calcium antagonist by regulating calcium access into the cell and also causes Low plasma levels of calcitriol (1,25-dihydroxyvitamin D). This explains the high prevalence of hypocalcemia in hypomagnesemic patients. This study showed hypocalcemia accompanying 60.4% of the hypomagnesemic patients which was found to be statistically significant with a p value of 0.001. Studies have shown that even Mild hypomagnesemia (plasma magnesium concentration between 1.1 and 1.3 mEq/L) can lower the plasma calcium concentration.[7] Hypomagnesemia also predisposes to hypokalemia by enhancing its renal secretion in the loop of henle and cortical collecting tubule via ATP-inhibitable luminal potassium channels.[8] it can also occur secondary to vomiting/diarrhea/nasogastric suctioning or diuretic therapy. Rude et al, showed that hypomagnesemia not only predisposes to hypokalemia but is relatively refractory to isolated potassium supplementation until magnesium deficiency has been corrected.[9] In this study authors found almost half (45.2%) of the patients hypokalemic whereas only one-fourth (25.33%) of normomagnesemic group were hypokalemic. However, Patients with severe hypomagnesemia (serum Mg less than or equal to 1.0 mEq/dl) experienced hypokalemia more often.[10]

Most of the hypomagnesemic patients had a short PICU stay, which is also affected by various other factors like underlying disease, co-morbidities. Authors found no significant association between length of PICU stay and hypomagnesemia, which is in agreement with other studies by Limaye et al, and Hulst et al.[11,12] Authors also found no significant association between nutritional status at admission or number of days of starvation and serum magnesium levels.

Mg ion plays a vital role in immunological functions, including macrophage activation, adherence and bactericidal activity of granulocyte oxidative burst, lymphocyte proliferation and endotoxin binding to monocytes, increased cytokine concentration, consequently playing a major role in increased incidence of sepsis in hypomagnesemic patients.[11,13,14] Authors found significant association between infections and hypomagnesemia, with a incidence of 33.9% among those with hypomagnesemia, in contrast to only 4.25% in normomagnesemic group.

Magnesium ion has been studied in many molecular studies due to its potential neuroprotective role. Low magnesium levels may theoretically potentiate glutamatergic neurotransmission, leading to a supportive environment for excitotoxicity, which can lead to oxidative stress and neuronal cell death.[15] Authors found that the majority of the children with CNS disorders were found to be hypomagnesemic. This might also explain the presence of hypomagnesemia in all patients who were admitted secondary to traumatic brain injury. Low serum magnesium in TBI may also be related to the initial stress response of the severe head injury. Nayak et al, studied neurological outcome of TBI which correlated well with the serum magnesium concentration and appeared to be an independent prognostic marker in patients with severe TBI.[16]

Several studies have been done to correlate mortality and hypomagnesemia and have found to have varied results. While some of them have found positive correlation between mortality and hypomagnesemia, some have failed to find and relationship between the two. In this study all the patients who died had developed hypomagnesemia during the course, hence a significant association (p=0.02) was established between death and development of hypomagnesemia.

CONCLUSION

Authors have been able to find high prevalence of hypomagnesemia in critically ill patients and found to be associated with a higher mortality. It is also commonly associated with infections, CNS disorders and respiratory diseases and metabolic derangements like hypokalaemia and hypocalcaemia. There is no association of Hypomagnesemia with duration of PICU stay. Hypomagnesemia was also found in patients having hypocalcaemia.

ACKNOWLEDGEMENTS

Authors would like to thank Dr. Srinivasa S. and Dr. Yashoda H. T, Department of Pediatrics, KIMS, Bangalore, Karnataka, India.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Schwalfenberg GK, Genuis SJ. The importance of magnesium in clinical healthcare. Scientifica. 2017;2017.
2. Glasdam SM, Glasdam S, Peters GH. The importance of magnesium in the human body: a systematic literature review. Advan Clin Chem. 2016;73:169-93.
3. Tong GM, Rude RK. Magnesium deficiency in critical illness. J Intensive Care Med. 2005;20(1):3-17.
4. Hansen BA, Bruserud Ø. Hypomagnesemia in critically ill patients. J Inten Care. 2018 Dec 1;6(1):21.
5. Singhi SC, Singh J, Prasad R. Hypo-and Hypermagnesemia in an Indian Pediatric Intensive Care Unit. J Trop Pediatr. 2003 Apr 1;49(2):99-103.
6. Rubeiz GJ, Thill-Baharozian MA, Hardie DO, Carlson RW. Association of hypomagnesemia and mortality in acutely ill medical patients. Criti Care Med. 1993 Feb;21(2):203-9.
7. Fatemi S, Ryzen E, Flores J, Endres DB, Rude RK. Effect of experimental human magnesium depletion on parathyroid hormone secretion and 1, 25-dihydroxyvitamin D metabolism. J Clin Endocrinol Metab. 1991 Nov 1;73(5):1067-72.
8. Nichols CG, Ho K, Hebert S. Mg (2+)-dependent inward rectification of ROMK1 potassium channels expressed in Xenopus oocytes. J Physiol. 1994 May 1;476(3):399-409.
9. Rude RK, Oldham SB, Sharp Jr CF, Singer FR. Parathyroid hormone secretion in magnesium deficiency. J Clini Endocrinol Metab. 1978 Oct 1;47(4):800-6.
10. Chernow B, Bamberger S, Stoiko M, Vadnais M, Mills S, Hoellerich V, et al. Hypomagnesemia in patients in postoperative intensive care. Chest. 1989 Feb 1;95(2):391-7.
11. Limaye CS, Londhey VA, Nadkart MY, Borges NE. Hypomagnesemia in critically ill medical patients. J Assoc Physi Ind. 2011 Jan;59(1):19-22.
12. Hulst JM, van Goudoever JB, Zimmermann LJ, Tibboel D, Joosten KF. The role of initial monitoring of routine biochemical nutritional markers in critically ill children. J Nutrit Biochem. 2006 Jan 1;17(1):57-62.
13. Malpuech-Brugère C, Nowacki W, Daveau M, Gueux E, Linard C, Rock E, et al. Inflammatory response following acute magnesium deficiency in the rat. Biochim Biophys Acta. 2000 Jun 15;1501(2-3):91-8.
14. Chen M, Sun R, Hu B. The influence of serum magnesium level on the prognosis of critically ill patients. Zhonghua wei zhong bing ji jiu yi xue. 2015 Mar;27(3):213-7.
15. Castilho RF, Ward MW, Nicholls DG. Oxidative stress, mitochondrial function, and acute glutamate excitotoxicity in cultured cerebellar granule cells. J Neurochem. 1999 Apr 1;72(4):1394-401.
16. Nayak R, Attry S, Ghosh SN. Serum magnesium as a marker of neurological outcome in severe traumatic brain injury patients. Asian J Neurosurg. 2018 Jul;13(3):685.

Cite this article as: Shankar NP, Kavya C, Reddy VM. Risk factors and clinical outcome of hypomagnesemic patients in pediatric intensive care. Int J Contemp Pediatr 2020;7:790-4.