Published by iambr.info/AMBR
Open Access Original Work

Magnesium, calcium and phosphorus in the intensive care unit: Do we need to monitor?

Chepsy C Philip[1], Mary John[1], John Abraham[2]

To cite: Philip CC, John M, Abraham J. Magnesium, calcium and phosphorus in the intensive care unit: Do we need to monitor? *Arch Med Biomed Res.* 2014;1(3):96-102.

Publication history
Received: May 11, 2014
Revised: August 08, 2014
Accepted: August 22, 2014

Correspondence to
Chepsy C Philip;
chepsyphilip@gmail.com

ABSTRACT
Magnesium, calcium and phosphorus are important electrolytes involved in the regulation of homeostasis. However the utility in monitoring them in critically ill patients is still unclear. We therefore undertook a prospective, non-interventional, single center study in the intensive care unit of a tertiary care hospital in northwestern India to determine the incidence and clinical presentation of magnesium, phosphorus, and calcium abnormalities in patients admitted to the intensive care unit (ICU). Ionized calcium, serum calcium, magnesium, and phosphorus along with arterial blood gases (ABG) were measured on admission with clinical features recorded in an approved format in 300 consecutive patients admitted to the ICU over a period of two years. Thereafter, ionized calcium, serum phosphorus, serum magnesium, and ABG were monitored every alternate day. Hypocalcemia was the commonest electrolyte abnormality seen in 165 (55%) patients followed by hyperphosphatemia seen in 74 (24.67%) and hypophosphatemia seen in 72 (24%) patients. Hypocalcemia with renal failure was seen in 52 (31%) patients (P = 0.009). Hypophosphatemia and hypomagnesemia were commoner with respiratory failure i.e. 23 (31.95%) and 13 (27.66%) patients, respectively. An association of liver disease with hypomagnesemia was noted in our study, $P < 0.05$. Arrhythmias associated with electrolyte abnormalities were the most common clinical observation, seen in 69 (41.81%) patients with hypocalcemia, 20 (42.55%) with hypomagnesaemia, and 29 (40.27%) with hypophosphatemia. Hypocalcemia, hypomagnesemia, and hyperphosphatemia are not infrequent in patients admitted to the intensive care unit. There is a need to monitor these electrolytes to enable early detection.

KEY WORDS: ***Calcium; Intensive care unit; Magnesium; Phosphorus***

INTRODUCTION
Disorders of magnesium, calcium and phosphorus are common in patients admitted to intensive care units (ICU)[1]. However, routine monitoring and replacement of these ions are still underemphasized[2]. Magnesium is the second most abundant intracellular cation after potassium and plays an important role in cellular metabolism and homeostasis[3,4]. Hypomagnesemia may be caused by redistribution or magnesium depletion due to decreased intake or increased loss by osmotic, loop, and thiazide diuretics. Acidosis may increase the extracellular magnesium

concentration due to redistribution, and hemolysis may spuriously elevate the plasma magnesium level. It is often caused by excessive administration of magnesium salts[5].

Calcium and phosphorus are recognized to be responsible for much of the structural integrity of the bony skeleton and also to participate in several diverse processes, such as enzyme activation, cell division, blood coagulation, and membrane stability[6]. Hypocalcemia caused by critical illness is usually multifactorial (e.g. hypoalbuminemia, metabolic or respiratory acidosis, hypomagnesemia, renal failure, massive blood transfusions) although calcium loss due to increased tissue sequestration of calcium may be the predominant cause in patients with pancreatitis, septicemia, burns, or toxic shock[5]. Tetany is the commonest symptom associated with an acute reduction in plasma ionized calcium. The characteristic clinical features of these electrolyte disorders present as neurological and cardiac manifestations. Available data suggest adverse outcomes with these electrolyte abnormalities, hence it might be prudent that routine surveillance be done, and conditions treated wherever possible.

The aims of this study are to assess the prevalence of magnesium, phosphorus and calcium abnormalities in patients admitted to the ICU and to study the clinical presentation of these patients in relation to the abnormalities of magnesium, phosphorus and calcium.

MATERIALS AND METHODS

The study was conducted from 2007 till 2009 and was approved by the institutional ethics committee. A total of 300 patients were eligible for the study. During the study period the Arterial Blood Gas analyzer could not be used for a period of 60 days. Patients admitted at these times were not included in the analyses. Prospective surveillance and blood sampling were performed on admission to the ICU and every alternate day thereafter as part of the standard protocol. Serum magnesium, calcium, and phosphorus were analyzed by calorimetric method. Ionized calcium was measured with ion specific electrodes.

The surveillance being performed as part of standard routine clinical workup with no additional investigation, no additional consent was sought. All patients admitted in the ICU were included in the analyses except in the scenario mentioned earlier. Descriptive statistics were derived using Excel and statistical software SPSS; with parametric and non-parametric tests applied for comparison.

All patients were followed up till the day of discharge from the ICU and interventions noted. Normal values were defined as per the institutional reference ranges, namely - serum magnesium: 1.7-2.6 mg/dl, serum phosphorus: 2.5-4.5 mg/dL, serum calcium: 8.5-10.8 mg/dL and ionized calcium: 1.1-1.3 mmol/dL.

RESULTS

A total of 300 patients admitted into the intensive care unit were included in this study. Majority of the patients admitted in this multidisciplinary intensive care unit were under medical specialties i.e. 226 (75.34%) patients (**Figure 1**). Respiratory failure was the most common diagnosis seen in 81 (27%) patients followed by renal failure in 79 (26.33%) patients.

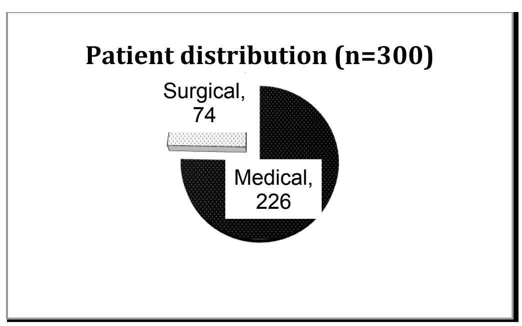

Figure 1: Patient distribution by broad specialty category

Hypocalcemia was the commonest electrolyte abnormality seen in 165 (55%) patients followed by hyperphosphatemia seen in 74 (24.67%) patients and hypophosphatemia seen in 72 (24%) patients. Hypomagnesemia was more common than hypermagnesemia i.e. 47 (15.67%) and 30 (10%) patients, respectively. Hypocalcemia was seen in 165 (55%) patients compared to only 7 (2.33%) patients with hypercalcemia. Hyperphosphatemia was commoner than hypophosphatemia i.e. 74 (24.67%) vs. 72 (24%) patients. Hypocalcemia with renal failure was seen in 52 (31%) patients, which was statistically significant (P = 0.009). Hypophosphatemia and hypomagnesemia were commoner in patients with respiratory failure i.e. 23 (31.95%) and 13 (27.66%) patients, respectively. In those patients with hypocalcemia, renal failure was the most common diagnosis i.e. 15 (31.51%) patients. This was followed by respiratory failure in 45 (27.28%) patients. Among patients with hypophosphatemia, respiratory failure was the most common diagnosis seen in 23 (31.95%) patients, followed by sepsis seen in 18 (25%) patients. In those patients with hypomagnesemia, respiratory failure and renal failure were the most common diagnosis seen in 13 (27.66%) patients each (**Table 1 and 2**). The association of CNS disorders with hypercalcemia was statistically significant i.e. P value < 0.05. In patients with hyperphosphatemia, renal failure was the most common diagnosis seen in 32 (43.24%) patients, followed by sepsis seen in 21 (23.38%) patients (**Table 2**). When the diagnosis were compared against hypo and hyper electrolyte abnormalities, the results obtained showed a statistically significant relation with hypocalcemia (P value 0.038) and hypophosphatemia (P value 0.023) i.e. occurrence of hypocalcemia and hypophosphatemia was significantly associated with the diagnosis (**Table 2**).

Table 1: Frequency of electrolyte abnormalities

Diagnosis	Hypocalcemia (n=165)	P	Hypophosphatemia (n=72)	P	Hypomagnesemia (n=47)	P
	N (%)		N (%)		N (%)	
Sepsis	39 (23.6)	0.434	18 (25.0)	0.964	11 (23.4)	0.832
Respiratory failure	45 (27.3)	0.134	23 (31.9)	0.944	13 (27.7)	0.332
CNS disorder	23 (13.9)	0.124	15 (20.8)	0.187	09 (19.2)	0.737
Liver disease	06 (3.6)	0.148	05 (7.0)	0.323	01 (2.1)	0.140
Renal failure	52 (31.5)	0.009	11 (15.3)	0.326	13 (27.7)	0.1

Table 2: Incidence of electrolyte abnormalities in broad diagnosis groups

Diagnosis	Ionised Calcium (N)		Serum Phosphorus (N)		Serum Magnesium (N)	
	< 1.1 (mmol/dl)	> 1.3 (mmol/dl)	< 2.5 (mg/dl)	> 4.5 (mg/dl)	< 1.7 (mg/dl)	> 2.6 (mg/dl)
Renal failure (n=119)	52	01	11	32	13	10
Sepsis (n=100)	39	02	18	21	11	09
Respiratory failure (n=100)	45	01	23	14	13	04
Neurological disorder (n=100)	23	02	15	04	09	02
Liver disease (n=21)	06	01	05	03	01	05
P value	0.038		0.023		0.09	

In those who were ventilated, hypocalcemia was the most common electrolyte abnormality seen in 144 (87.27%) patients (**Figure 2**).

Arrhythmias associated with electrolyte abnormalities were the most common clinical observation. This was seen in 69 (41.81%) patients with hypocalcemia, 20 (42.55%) patients with hypomagnesemia, and 29 (40.27%) patients with hypophosphatemia (**Table 3**). Diuretics had been used in 69 (41.81%) patients with hypocalcemia, 20 (42.55%) with hypomagnesemia and 29 (40.27%) patients with hypophosphatemia. The association of use of antacids with hypocalcemia was statistically significant ($P < 0.05$). Use of blood and blood products were noted in 56 (33.93%) patients with hypocalcemia, 27 (37.5%) patients with hypophosphatemia, and 14 (29.78%) patients with hypomagnesemia (**Table 4**).

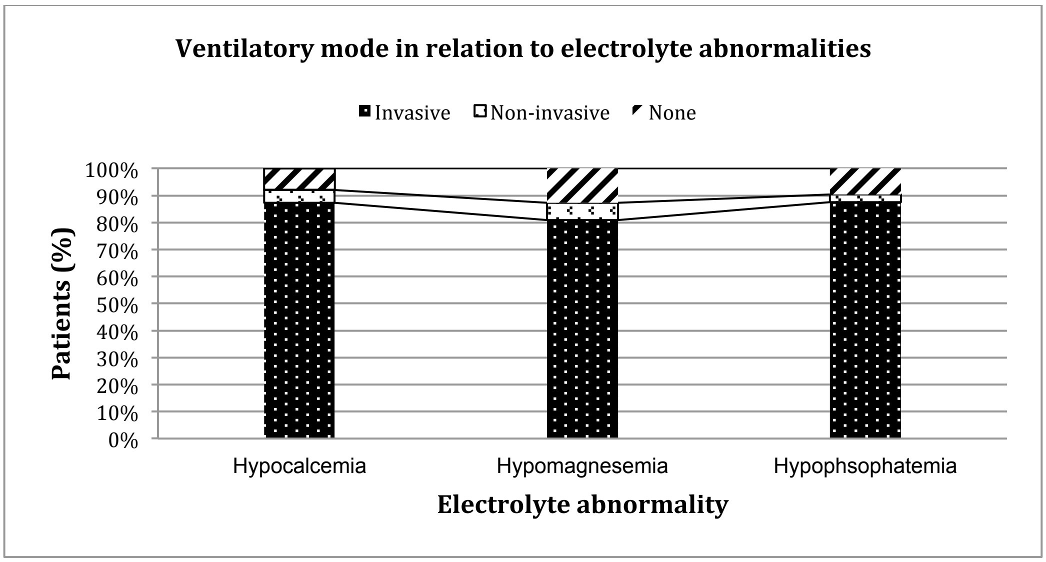

Figure 2: Frequency of ventilator support

Table 3: Frequency of Clinical observations

Signs	Hypocalcemia	Hypophosphatemia	Hypomagnesemia
	N (%)	N (%)	N (%)
Arrhythmia	69 (41.81)	20 (42.55)	29 (40.27)
Chvostek's	07 (4.24)	04 (8.51)	03 (4.16)
Trousseau's	07 (4.24)	04 (8.51)	03 (4.16)

Table 4: Effect of interventions

Therapeutic Agents *	Hypocalcemia	P	Hypophosphatemia	P	Hypomagnesemia	P
	N (%)		N (%)		N (%)	
Transfusion	56 (34.0)	0.312	27 (37.5)	0.308	14 (29.8)	0.190
Diuretics	69 (41.8)	0.745	29 (40.3)	0.931	20 (42.6)	0.669
Muscle relaxants	35 (21.2)	0.948	16 (22.2)	0.261	08 (17.0)	0.238
Antacids	83 (50.3)	0.004	08 (11.1)	0.004	03 (6.4)	0.189
Laxatives	17 (10.3)	0.885	08 (11.1)	0.203	03 (6.4)	0.189
Dialysis	28 (17.0)	0.510	11 (15.3)	0.475	09 (19.1)	0.298
*Multiple therapeutic agents possible in a patient.						

DISCUSSION

This study documents the incidence and effects of abnormalities in calcium, magnesium, and phosphorus in the intensive care unit (ICU). We noted a majority of patients being admitted under medical specialties similar to Hästbacka; who noted that 61% of the patients were admitted under medical specialties and 39% were admitted under surgical specialties[10]. Men are more commonly admitted to Intensive care units than women, and were more commonly represented in cohort studies and clinical trials involving critical care conditions such as acute lung injury and sepsis[11].

There appeared to be sex differences in critical care as noted in (**Figure 3**). These are consistent with observations that older women may receive less aggressive care at the end of life[12].

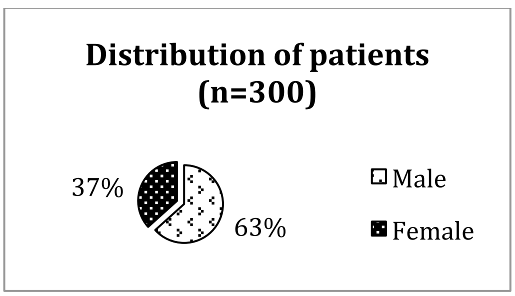

Figure 3: Distribution of patients by sex

Respiratory failure was the most common diagnosis among the patients admitted to our ICU. The diagnosis of respiratory failure included patients with COPD, pneumonia, bronchial asthma, ARDS, and pulmonary tuberculosis. Hypomagnesemia was more common than hypermagnesemia. Earlier studies have noted that 12.3% and 18% of their patients respectively, admitted to the ICU had hypomagnesemia[13].

Recent reports suggest an incidence of hypocalcemia roughly similar to our study[10,14]. Hypercalcemia has a lower incidence amongst the critically ill with only few case reports described. A similar low incidence of hypercalcemia has been noted in the West[15]. Our study showed the lowest incidence of hypercalcemia.

There are many reasons for disorders of magnesium, phosphorus, and calcium. Many of these factors may be present simultaneously in ICU patients[5]. A large number of patients with hypocalcemia had renal failure; hypophosphatemia, and hypomagnesemia were seen in a large number of patients with respiratory failure. The association of hypocalcemia with renal failure was statistically significant (P value 0.009). The high incidence among patients with respiratory disease in our study can be attributed to the underlying respiratory alkalosis. Similarly, in a hospital-based study, all patients with acute renal failure had hypocalcemia[16]. Hypophosphatemia secondary to phosphorus redistribution is commonly caused by respiratory alkalosis and re-feeding of malnourished patients[17].

Respiratory and renal failures were the most common diagnoses in the patients with hypomagnesemia seen in our study. The high incidence of hypomagnesemia seen in our patients could be attributed to the organ failure and high incidence of mechanical ventilation in these patients; with resulting acidosis leading to intracellular shifting of magnesium. These observations are supported by various studies and case reports[18]. The association of CNS disorders with hypercalcemia (P value 0.043) and liver diseases with hypermagnesemia (P value 0.044) was statistically significant in our study. The causal or predictor role is still to be seen.

Renal failure was the most common diagnosis seen in our study amongst patients with hyperphosphatemia. Hyperphosphatemia is also associated with non-recovery (72% vs. 24%) in critically ill patients[19].

Phosphorus and magnesium deficiencies are associated with respiratory muscle fatigue and are common causes of failure to wean off a patient from the ventilator. In our study, hypocalcemia was the most common electrolyte abnormality seen in patients who required mechanical ventilation. This was followed by hypophosphatemia and hypomagnesemia. It has been observed that normal duration of conventional mechanical ventilation in patients with low serum phosphorus levels is longer (10.5 ± 5.2 vs. 7.1 ± 2.8)[20].

In our study, arrhythmias were the most frequently observed cardiac observation. Similar observations have been noted in other studies[18]. It has also been observed that Atrioventricular Nodal Reentrant Tachycardia (ANRT) and Atrioventricular Reciprocating Tachycardia (ART) were induced in patients with hypomagnesemia[21]. In our study, Chvostek's and Trousseau's sign were observed in only few patients.

Diuretics decrease the renal threshold for magnesium re-absorption in addition to wasting of phosphorus and calcium[22]. In our study, the diuretic use could be the possible cause in abnormalities of hypocalcemia, hypomagnesemia, and hypophosphatemia. We also observed hypocalcemia following transfusions. Hypercalcemia after transfusion can be mediated by the citrate content of transfused blood or by a large volume of fluid administration and hypoalbuminemia, which might also explain the hypomagnesemia and hypophosphatemia[16].

Limitations

One limitation of this study is the lack of homogeneity in the study population. There were no exclusion criteria for patients with known electrolyte disorders or on long standing medications. Also, the primary diagnosis leading to admission to the ICU was not considered. Also, the restrictive diagnostic criterion applied in our study is not completely representative of the study population. The majority of patients admitted to ICU's have a combination of these diagnoses. We do acknowledge that timing of intervention could also affect the associations observed. Many patients received corrective interventions between samplings thus possibly masking the magnitude of our findings.

A properly structured prospective study with strict exclusion and inclusion criteria and detailing of the interventions is required to truly reflect the magnitude of the associations.

CONCLUSION

There are very few studies of disorders of calcium, magnesium, and phosphorus among adult critically ill patients. Disorders of calcium, magnesium, and phosphorus are prevalent in the intensive care unit and need to be frequently monitored. Our study is a prospective observational study with limitations in terms of power of the study and criteria used for patient selection into the ICU. These abnormalities in our observation are possibly associated with arrhythmias, blood transfusions, and diuretic use and may have a bearing on the clinical outcome. A multicentric study with stringent patient selection and longer follow up will possibly serve in understanding the role of these electrolytes.

Author affiliations

[1]Department of Internal Medicine, Christian Medical College, Ludhiana, Punjab 141011, India
[2]Department of Anesthesia and Critical Care, Christian Medical College, Ludhiana, Punjab 141011, India

REFERENCES

1. Worthley LI, Baker SB. The essentials of calcium, magnesium and phosphate metabolism: part I. Physiology. *Crit Care Resusc*. 2002;4(4):301-6.
2. Baker SB, Worthley LI. The essentials of calcium, magnesium and phosphate metabolism: part II. Disorders. *Crit Care Resusc*. 2002;4(4):307-15.

3. Huijgen HJ, Soesan M, Sanders R, Mairuhu WM, Kesecioglu J, Sanders GT. Magnesium Levels in Critically Ill Patients What Should We Measure? *Am J Clin Pathol*. 2000;114(5):688-95.
4. Swaminathan R. Magnesium metabolism and its disorders. *Clin Biochem Rev*. 2003;24(2):47-66.
5. Moe SM. Disorders involving calcium, phosphorus, and magnesium. *Prim Care*. 2008;35(2):215-37.
6. Ross AC, Taylor CL, Yaktine AL, Del Valle HB. Dietary reference intakes for calcium and vitamin D. *National Academies Press (US)*. 2011.
7. Geerse DA, Bindels AJ, Kuiper MA, Roos AN, Spronk PE, Schultz MJ. Treatment of hypophosphatemia in the intensive care unit: a review. *Crit Care*. 2010;14(4):R147.
8. Delmez JA, Slatopolsky E.. Hyperphosphatemia: its consequences and treatment in patients with chronic renal disease. *Am J Kidney Dis*. 1992;19(4):303-17.
9. Fine A, Patterson J. Severe hyperphosphatemia following phosphate administration for bowel preparation in patients with renal failure: two cases and a review of the literature. *Am J Kidney Dis*. 1997;29(1):103-5.
10. Hästbacka J1, Pettilä V. Prevalence and predictive value of ionized hypocalcemia among critically ill patients. *Acta Anaesthesiol Scand*. 2003;47(10):1264-9.
11. Fowler RA, Filate W, Hartleib M, Frost DW, Lazongas C, Hladunewich M. Sex and critical illness. *Curr Opin Crit Care*. 2009;15(5):442-9.
12. Wright AA, Zhang B, Ray A, Mack JW, Trice E, Balboni T, et al. Associations between end-of-life discussions, patient mental health, medical care near death, and caregiver bereavement adjustment. *JAMA*. 2008;300(14):1665-73.
13. Booth JV, Phillips-Bute B, McCants CB, Podgoreanu MV, Smith PK, Mathew JP, et al. Low serum magnesium level predicts major adverse cardiac events after coronary artery bypass graft surgery. *Am Heart J*. 2003;145(6):1108-13.
14. Vincent JL, Abraham E, Annane D, Bernard G, Rivers E, Van den Berghe G. Reducing mortality in sepsis: new directions. *Crit Care*. 2002;6 Suppl 3:S1-18..
15. Rubeiz GJ, Thill-Baharozian M, Hardie D, Carlson RW. Association of hypomagnesemia and mortality in acutely ill medical patients. *Crit Care Med*. 1993;21(2):203-9.
16. Zivin JR, Gooley T, Zager RA, Ryan MJ. Hypocalcemia: a pervasive metabolic abnormality in the critically ill. *Am J Kidney Dis*. 2001;37(4):689-98.
17. Parrillo JE, Dellinger RP. Critical Care Medicine: Principles of Diagnosis and Management in the Adult (Expert Consult-Online and Print). 4th Ed. Elsevier Saunders. Philadelphia. 2014.
18. England MR, Gordon G, Salem M, Chernow B. Magnesium administration and dysrhythmias after cardiac surgery: a placebo-controlled, double-blind, randomized trial. *JAMA*. 1992;268(17):2395-402.
19. Baquerizo A, Anselmo D, Shackleton C, Chen T-W, Cao C, Weaver M, et al. Phosphorus ans an early predictive factor in patients with acute liver failure1. *Transplantation*. 2003;75(12):2007-14.
20. Brunelli SM, Goldfarb S. Hypophosphatemia: clinical consequences and management. *J Am Soc Nephrol*. 2007;18(7):1999-2003.
21. Monico EP, Bachman D, Anthony RG. Hypomagnesemia. *Am J Emerg Med*. 1997;15(4):441-2.
22. Favus MJ, Bushinsky DA, Lemann J Jr. Regulation of calcium, magnesium and phosphate metabolism. In: *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism*. 6th Ed. American Society for Bone and Mineral Research. 2006.76-83.