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Prevalence of Hypomagnesemia and Its Predictive Prognostic Value in Critically Ill Medical Patients

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ABSTRACT
Background: *Hypomagnesemia is the most under-diagnosed electrolyte abnormality in critically ill patients. Many studies have been done previously showing varied prevalence and increased association with mortality and morbidity in these patients.*

AIMS AND OBJECTIVES:*To find out the prevalence of hypomagnesemia in critically ill medical patients and to relate the serum magnesium levels with patients mortality and morbidityoutcome considering the length of ICU stay, need for ventilatory support, durationof ventilatory support, APACHE 2 and SOFA score, primary medical conditions and other electrolyte abnormalities associated with if any in critically ill patients admitted in a medical intensivecare unit.*

RESULTS: *the prevalence of hypomagnesemia in critically ill medical patients was 53%. The patients with hypomagnesemia had higher mortality (47.2% vs. 23.4%, p value 0.013), longer ICU (7.07±3.91 vs. 5.12±1.31 days, p value 0.002) and hospital stay (10.05±5.17 vs. 8.27±1.24 days, p value 0.024), higher APACHE2 (12.83±3.55 vs. 10.10±1.30, p value <0.001) and SOFA scoring (SOFA9.67±2.43 vs. 7.87±0.94, and maximum SOFA 13.83±4.02 vs. 9.25±1.45, p value <0.001 for both), more frequent need for mechanical ventilation (69.8% vs. 40.4%, p value 0.003) and longer duration of ventilatory assistance (3.60±4.16 vs. 1.87±2.39 days, p value 0.014), more frequently associated with sepsis (60.4% vs. 40.4%, p=0.046) and diabetes (49.1% vs. 21.3%, p = 0.004) and other electrolyte abnormalities like hypocalcemia (81.1% vs. 34.0%, p = <0.001), hypokalemia (81.1% vs. 51.1%, p = <0.001) and hyponatremia(62.3% vs. 40.4%, p = 0.029) in compared to patients with normal magnesium.Though associated the mortality did not correlated significantly (beta -0.042, t -0.373, sig. 0.710, 95% CI -0.202 and 0.138) with hypomagnesaemiain this study and the sepsis (beta -0.561, t -3.513, sig. 0.001, 95% CI -0.647 and -0.179) and the maximum SOFA score (beta -1.043, t -3.422, sig. 0.001, 95% CI -0.159 and -0.042) became evident as the strong predominant underlying factor for hypomagnesemia.*

KEY WORDS:*Hypomagnesemia, Critically ill patients, Ventilatory support*

I. INTRODUCTION

One of the most common and under diagnosed electrolyte disturbance in hospitalized patientsis hypomagnesaemia, especially in critically ill.Magnesium plays an important role in maintaining body homeostasis; acting as cofactor for most of the ATPase by forming ATP-magnesium complex. Magnesium deficiency has been associated with a number of clinicalmanifestations such as arrhythmias, cardiacinsufficiency, coronary vasospasm, sudden death, skeletal and respiratorymuscle weakness, bronchospasm, tetany, seizures, and other neuromuscularabnormalities and a number of electrolyte abnormalities, includinghypokalemia, hypocalcemia, hyponatremia, and hypophosphatemia[1, 3-6]. In current medical practice hypomagnesemia is the most under diagnosed as well as often overlooked electrolyte abnormality[2]. It should be searched systematically for its prognostic significance in critically ill patients.[10]Many studies have been done previously showing varied prevalence and increased association with mortality and morbidity in these patients.[7-9]We aim in this study to find out the prevalence of hypomagnesaemia in critically ill medical patients and to correlate the serum magnesium levels with patients mortality and morbidity outcome considering the length of ICU stay, need for ventilatory support, duration of ventilatory support, APACHE and SOFA score, primary medical conditions like sepsis and diabetes and other electrolyte abnormalities associated with, if any in critically ill patients admitted in our medical intensive care unit.

II. METHODOLOGY

We conducted a prospective observational study in our medical intensive care unit of a tertiary care hospital from July 2013 to December 2013. The study was approved by the Institutional Ethical Committee. Hundred patients admitted to the medical ICU for critical illness with vital instability requiring intensive care for more than at least 2 days with age more than 12 years were included after a written informed consent was obtained. Patients receiving magnesium supplementation prior to transfer to ICU were excluded from this study. A blood sample was collected for estimation of serum total magnesium level on the day of admission to ICU. A detailed history and thorough clinical examination were performed in every patient. Other biochemical and hematological investigations were done by standard laboratory method and also radiological investigations as indicated in every patient. On the day of admission APACHE 2 (acute physiology and chronic health evaluation) score was calculated according to standard scoring system. The SOFA score has been calculated everyday and the mean and maximum values were taken into account. Patients were followed up to assess their mortality and morbidity in the form of total ICU and hospital stay, need of mechanical ventilation and duration of ventilatory assistance, associated medical conditions like sepsis, diabetes and other electrolyte abnormalities. The study did not interfere with the patient management in the ICU. Serum total magnesium was measured by colorimetric method using Titan Yellow (described by Neill and Neely) [11]. The normal value of total serum magnesium was between 1.7 to 2.4 mg/dl.[2] Other routine laboratory investigations (normal ranges) included sodium (136 to 145 mEq/L), potassium (3.5 to 5.5 mEq/L), total serum calcium (8.2 to 10.6 mg/dl), total bilirubin (less than 1.2 mg/dl), creatinine (0.4 to 1.3 mg/dl) and glucose (less than 126 mg/dl for fasting and 200 mg/dl for random or post-prandial). Duration of ventilation was defined as the number of days with mechanical ventilation. Patients were classified into two groups according to their initial serum total magnesium level: hypomagnesemia (less than 1.3 mEq/L) and normomagnesemia (1.3 to 2.1 mEq/L).Finally all collected data were tabulated and analysed using standard statistical methods by SPSS version 20 for Windows. Qualitative data were analysed by chi-squre test, quantitative data by unpaired student t test, correlation by Pearson's correlation co-efficient test and multivariate regression analysis for individual risk assessments.

III. RESULTS

Table1:morbidity and mortality in patients with low and normal magnesium level

parameters	Low Mg	Normal Mg	Sig.
prevalence	53%	47%	-
Serum Mg level(mg/dl)	1.23±0.18	1.89±0.12	<0.001
Age of the patients	54.34±6.10	55.81±5.63	0.216
Gender (%)	Male 60.4%, Female 39.6%	Male 61.7%, Female 38.3%	0.892
APACHE 2 score	12.83±3.55	10.10±1.30	<0.001
SOFA score	9.67±2.43	7.87±0.94	<0.001
Max. SOFA score	13.83±4.02	9.25±1.45	<0.001
ICU stay(days)	7.07±3.91	5.12±1.31	0.002
Hospital stay(days)	10.05±5.17	8.27±1.24	0.024
Mortality (%)	47.2%	23.4%	0.013
Need of MV (%)	69.8%	40.4	0.003
MV Duration(days)	3.60±4.16	1.87±2.39	0.014
Sepsis (%)	60.4%	40.4%	0.046
Diabetes (%)	49.1%	21.3%	0.004
Hypocalcemia (%)	81.1%	34.0%	<0.001
Hypokalemia (%)	81.1%	51.1%	<0.001
Hyponatremia (%)	62.3%	40.4%	0.029

Our study comprising a 100 of critically ill medical patient and they are grouped into hypomagnesaemic and normomagnesemic according to their serum level of magnesium. The prevalence of hypomagnesaemia is 53% in this study. The mean level of serum magnesium was 1.23±0.18 mg/dl in hypomagnesaemic patients in compared to 1.89±0.12 mg/dl in normomagnesemic group of patients. Our studied population was age and sex matched.The mortality rate was significantly high in hypomagnesaemic patients (47.2%vs.23.4%; p value 0.013) and the magnesium level was also low in patients who died compared to who survived (1.37±0.41 vs. 1.63±0.31mg/dl; p value 0.001).Morbidity was also high in patients with low magnesium level in respect of APACHE 2 score (12.83±3.55vs.10.10±1.30; p value 0.001), SOFA score (9.67±2.43vs.7.87±0.94; p value 0.001) and maximum SOFA score (13.83±4.02vs.9.25±1.45; p value 0.001), ICU stay (7.07±3.91vs.5.12±1.31 days; p value 0.002) and total duration of hospitalization (10.05±5.17vs.8.27±1.24 days; p value 0.024), need of mechanical ventilation (69.8%vs.40.4%; p value 0.003) and average duration of mechanical ventilation (3.60±4.16vs.1.87±2.39 days; p value 0.014), associated medical condition like sepsis (60.4%vs.40.4%; p value

0.046) and diabetes (49.1%vs.21.3%; p value 0.004), and other associated electrolyte imbalance like hypocalcemia (81.1%vs.34.0%; p value 0.001), hypokalemia (81.1%vs.51.1%; p value 0.001) and hyponatremia (62.3%vs.40.4%; p value 0.029).The magnesium level was also low in patients who needed mechanical ventilation compared to whom not needed (1.45±0.4 vs. 1.66±0.28 mg/dl; p value 0.004), in patients who developed sepsis (1.46±0.41 vs. 1.62±0.29 mg/dl; p value 0.037)compared to whom developed not, in diabetics (1.33±0.37 vs. 1.65±0.31 mg/dl; p value 0.001) compared to non-diabetics, in hypocalcemic (1.44±0.37 vs. 1.67±0.32 mg/dl; p value 0.002) hypokalemic (1.48±0.38 vs. 1.66±0.29 mg/dl; p value 0.017) and hyponatremic (1.45±0.39 vs. 1.63±0.36 mg/dl; 0.020) patients compared to whom not having that respectively.

Table2:simple linear regression analysis considering serum magnesium as dependant variable

Dependant variable: serum Mg^{++} level	Standardized Coefficients	t	Sig.	95.0% Confidence Interval for B	
	Beta			Lower Bound	Upper Bound
(Constant)		5.197	.000	1.404	3.142
maxSOFA	-1.043	-3.422	.001	-.159	-.042
ICUstay	-.747	-.874	.385	-.289	.112
mortality	-.042	-.373	.710	-.202	.138
sepsis	-.561	-3.513	.001	-.647	-.179
hypokalemia	-.154	-.529	.598	-.574	.333

From simple linear regression analysisonly the associated sepsis and the maximum SOFA score were significantly correlated with low magnesium level. Though the mortality rate was associated significantly with low magnesium level it did not correlated significantly with hypomagnesaemia in this study.

IV. DISCUSSION

The prevalence of hypomagnesemia in our study was 53%. Various studies evaluated hypomagnesemia in critically ill patients previously ranging from 14% - 70%.[12-18] In our study a relatively higher mortality was observed among patients with hypomagnesemia compared to normomagnesemic patients. The relation between hypomagnesemia and mortality varies from study to study. Chernow et al.[8] (41% vs 13%), Rubiez et al.[14] (46% vs 25%), and Safavi et al.[18] (55% vs 35%) had found higher mortality whereas Guerin et al.[9] (18% vs 17%) had found no difference in mortality between hypomagnesaemic and normomagnesemic patients in their studies.The higher mortality in hypomagnesaemic patients can be explained by increased association of morbidities like more need and longer duration of ventilatory assistance, association of sepsis and diabetes, other electrolyte abnormalities like hypocalcemia and hypokalemia in compared to patients with normal magnesium levels.The length of ICU stay and total hospital duration both were longer in hypomagnesaemic patients. Soliman et al.[17] also observed longer duration of ICU stay in patients with low magnesium. They also found the length of ICU stay as an independent risk factor for hypomagnesemia development.

We observed a higher APACHE 2 score and SOFA score on admission and maximum SOFA score during ICU period among patients with low magnesium. Soliman et al.[17] found that those patients who develop ionized hypomagnesemia during their ICU stay had higher APACHE 2 score on admission. Guerin et al.[9] and Rubiez et al.[14] though did not found any difference between APACHE 2 score in patients with low and normal magnesium in their studies.Hypomagnesemia is known to cause muscle weakness and respiratory failure. This is an important factor causing difficulty in weaning the patients from the ventilator.[19]In the present study we also observed that hypomagnesaemic patients needed ventilatory support more frequently and for a longer duration. C S Limaye et al.[20] also observed the same in their study. Safavi et al.[18] found also the longer duration of ventilatory assistance (7.2 vs 4.7 days, p value <0.01) in patients with low magnesium. Fiaccordori et al.[21] observed that patients with low muscle magnesium were on ventilatory support for more number of days. Molloy et al.[22] observed improvement of respiratory muscle weakness in hypomagnesaemic patients on administering magnesium in their study. Munoz et al.[23] found that in neonatal ICU the hypomagnesaemic patients need ventilatory assistance more frequently compared to normomagnesemic patients.Hypomagnesemia has important role in sepsis, as there is increased release of endothelin and proinflammatory cytokines (TNF-alpha and IL-6). Harkema et al.[24] had administered ATP-MgCl2 to the animal models with sepsis and shock in order to restore cellular bioenergetics and observed improved organ function and better survival.

Salem et al.[25] observed that progressive magnesium deficiency and hypomagnesemia are strongly associated with increased mortality in experimental sepsis and magnesium replacement provides significant protection against endotoxin challenge. Sepsis is an independent risk factor for developing hypomagnesemia during ICU stay as observed by Soliman et al.[17] In our study we found that the incidence of sepsis was much more common in patients with low magnesium in compared to normal magnesium (p value). CS Limaye et al.[20] also observed increased association of sepsis as twice as common in hypomagnesaemic patients.In our study hypomagnesemia was more common in diabetic patients (p value). CS Limaye et al.[20] also observed the same in their study. Associated hypomagnesemia in diabetes may occur due to increased renal losses accompanying glycosuria.[26]There is strong relationship between hypomagnesemia and insulin resistance.[27] Magnesium supplementation is associated with decreased insulin requirements.Other electrolyte abnormalities are also commonly associated with hypomagnesemia. In our study we observed increased association of hypocalcemia, hypokalemia and hyponatremia in patients with hypomagnesemia compared to normomagnesemic patients. Whang et al.[5] and C S Limaye et al.[20] also observed increased association of hypokalemia and hypocalcemia in hypomagnesaemic patients. Hypokalemia and hypocalcemia are said to be the predictor of hypomagnesemia.[28] Even hypokalemia and hypocalcemia seen in hypomagnesaemic patient is relatively refractory to potassium and calcium supplementation until the magnesium deficiency is corrected.[29, 30]In our study it was also evident from simple linear regression analysis model that the underlying sepsis and organ failure are the predominant underlying factor for hypomagnesemia is significantly correlated with low magnesium level. Though the mortality rate was associated significantly with low magnesium level it did not correlated significantly with hypomagnesaemia in this study; further and larger studies are needed to conclude that.

V. SUMMARY

The prevalence of hypomagnesemia in critically ill medical patients is high and associated with increased rate of mortality and morbidity in compared to patients with normal magnesium. Hypomagnesemia associated with prolonged ICU stay and hospital stay, higher APACHE 2 and SOFA scoring, more frequent and more prolonged ventilatory support, frequently associated with sepsis and diabetes mellitus and electrolyte abnormalities like hypocalcemia, hypokalemia and hyponatremia. Sepsis and organ failure are the strong predominant underlying factor for hypomagnesemia.Though the mortality rate was associated significantly with low magnesium level it did not correlated significantly with hypomagnesaemia in this study.Further studies are required to evaluate whether hypomagnesemia directly leads to increased mortality and morbidity and the potential benefit of magnesium supplementation to prevent or correct hypomagnesemia to improve poor patient outcome in critically ill medical patients.

VI. CONCLUSIONS:

There was a high prevalence of hypomagnesemia in the critically ill medical patients. Hypomagnesaemiawas associated with a higher mortality rate;longer ICU and hospital stay, higher APACHE2 and SOFA scoring, the more frequent need for ventilatory support and with longer duration, and commonly associated with sepsis and diabetes mellitus, and other electrolyte abnormalities like hypocalcemia, hypokalemia and hyponatremia in compared to patients with normal magnesium.Sepsis and organ failure are the strong predominant underlying factor for hypomagnesemia.Though the mortality rate was associated significantly with low magnesium level it did not correlated significantly with hypomagnesaemia in this study.Further studies are required to evaluate whether hypomagnesemia directly leads to increased mortality and morbidity and the potential benefit of magnesium supplementation to prevent or correct hypomagnesemia to improve poor patient outcome in critically ill medical patients.

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