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A Prospective Observational Study of Serum Magnesium Levels in Critically Ill Patients

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Abstract:
Introduction: *Magnesium is fourth most common cat ion in the body and second most common intracellular cat ion after potassium, yet its deficiency in critically ill patients is frequently overlooked. Various studies have reported the incidence of hypomagnesemia up to 65% in critically ill-patients.*
Materials and Methods: *This observational study was conducted in the Department of Medicine, M.G.M Medical College, Jamshedpur among the critically ill patients admitted in MICU and ICCU from January 2018 to December 2018. Ethical clearance was obtained and the study was initiated. Patients were selected based on the inclusion criteria. Written informed consent was taken from all the patients. A complete history, physical examination and systemic examination was done in all the patients. Amongst patients who fulfilled the inclusion criteria, 5 mL of venous blood was taken at the time of hospital admission for blood investigations and other routine examinations. Patient's baseline information was recorded at admission including age, sex, blood pressure (in mmHg), and random glucose level at admission (in mg/dL).*
Results: *At admission, the incidence of hypomagnesaemia was 52.6%;27.3% patients had hypermagnesaemia, while 20% patients had normomagnesaemia. A significantly higher APACHE II Score was recorded in subjects with hypomagnesaemia compared to those with normomagnesaemia. Hyponatraemia was seen in 76% patients, while 29.4% patients had hypocalcaemia and 44.2% had hypokalaemia. Length of ICU stay was found to be significantly higher in subjects with hypomagnesaemia compared to those with normomagnesaemia and hypermagnesaemia ($p<0.0001$). Mortality was higher in patients with hypomagnesaemia (80%), while that in the hypermagnesaemia group had 53.8% mortality.*
Conclusion: *This study revealed the prevalence of dysmagnesaemia in the critically ill population of ICU and highlighted the role of magnesium monitoring. This study also showed that hypomagnesaemia was associated with higher APACHE II score, longer ICU stay and greater mortality.*
Key Words: *Magnesium; Hypomagnesaemia; Critical Illness; Mortality; Dysmagnesaemia.*

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I. Introduction

Magnesium is fourth most common cat ion in the body and second most common intracellular cat ion after potassium, yet its deficiency in critically ill patients is frequently overlooked. Various studies have reported the incidence of hypomagnesemia up to 65% in critically ill-patients.[1] Although many paradigms have been explored to minimize the mortality in critical care units, magnesium loss has been scarcely addressed; in this respect leading to inconclusive results.[2] Serum magnesium monitoring may have prognostic and perhaps therapeutic implications because critically ill-patients are predisposed to both symptomatic or asymptomatic magnesium deficiency that can lead to some important clinical consequences (such as hypokalemia, cardiac arrhythmias, hypocalcemia, neurotoxicity and psychiatric problems), ultimately increasing the morbidity and mortality.[3] There is a paucity of data in Indian literature, addressing this common, but under diagnosed electrolyte deficiency. Present study was undertaken against this backdrop at a tertiary care teaching hospital to assess the magnitude of magnesium deficiency and its influence on the outcome of critically ill-patients so that baseline reference data for insight and management of the problem in routine cases in our intensive care units (ICUs) is formed.[4]

II. Materials And Methods

This observational study was conducted in the Department of Medicine, M.G.M Medical College, Jamshedpur among the critically ill patients admitted in MICU and ICCU from January 2018 to December 2018. Ethical clearance was obtained and the study was initiated. Patients were selected based on the inclusion criteria. Written informed consent was taken from all the patients. A complete history, physical examination and systemic examination was done in all the patients. Amongst patients who fulfilled the inclusion criteria, 5 mL of

venous blood was taken at the time of hospital admission for blood investigations and other routine examinations. Patient's baseline information was recorded at admission including age, sex, blood pressure (in mmHg), and random glucose level at admission (in mg/dL). The blood sample collected was used for investigations like complete blood count, serum electrolytes, serum calcium, renal function tests, liver function tests and serum magnesium. APACHE II score was calculated on the day of admission to MICU/ICCU. Arterial blood sample of 2mLwas collected in all patients for ABG analysis. Duration of stay in the ICU was recorded. The study did not interfere with the patient management in the ICU.

Statistical Analysis: SPSS Software for Windows™ Ver. 17, IBM™ Corp NY and Microsoft Excel™ 2007, Microsoft® Inc.USA was used to perform the statistical analysis. Analysis was done by using description and inferential statistics. All the data were expressed in mean ± standard deviation (SD). The analysis was performed by using Student's t-test for the difference of means, Chi-square test and correlation. ANOVA followed by Tukey's HSD test was used to test the significance of difference between more than two parameters in parametric data.

Methodology: At alkaline pH, magnesium reacts with Xylidyl blue to form a red coloured compound. This method developed originally by Mann and Yoe, is based upon the formation of a water soluble red-purple chelate of magnesium and Xylidyl blue. The intensity of the developed colour is proportional to the serum magnesium concentration. Sample was mixed with the reagent and incubated at 25° C for 5 minutes. The coloured complex formed by magnesium with the monoreagent was read on a colorimeter in 1mLcuvettes. The absorbance of the sample (AT) and Standard (AS) was measured against Blank at 505 nm. The results were expressed in mg/dL. The reference range of serum magnesium for this study was between 1.7-2.4 mg/dL. Serum magnesium less than 1.7 was considered to be hypomagnesaemia and more than 2.4 was considered to be hypermagnesaemia.

III. Results

This prospective study included 95 patients admitted in the intensive care unit. Out of these 95 subjects, 30.5% patients were in the age group </=30 yrs., 15.8% in the age group of 41-50 and 6.3% in the age group of >70 yrs. Figure 1 shows that majority of the study population suffered from cerebrovascular accidents (18.8%) (including infarct and haemorrhage) followed by COPD with acute exacerbation (12.5%). The least common diagnoses included Diabetes with Diabetic Ketoacidosis (1%) and hanging with Hypoxic Encephalopathy (1%) with 1 patient each in both.

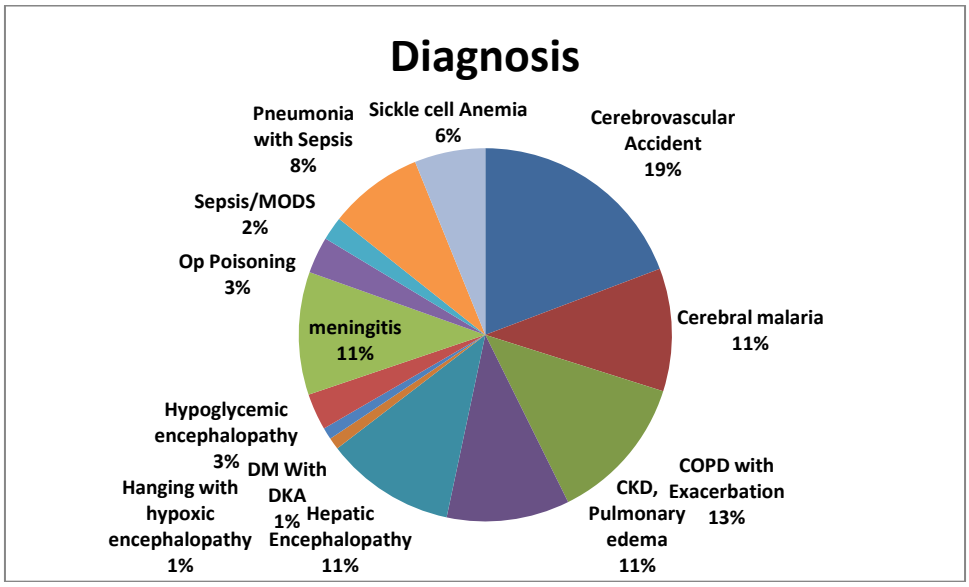

Figure 1: Diagnoses of Patients admitted in the Intensive Care Unit

Out of the total 95 subjects 52.63% patients had hypomagnesaemia, 27.37% had hypermagnesaemia and 20% had normomagnesaemia. Average serum magnesium recorded was 1.95mg/dL. In our study, 73 patients had hyponatraemia (Na <135mmol/L) and 22 patients had normal sodium levels. No significant difference was recorded in the three groups, viz. Hypomagnesaemia, Normomagnesaemia and Hypermagnesaemia. 42 patients of the study population had hypokalaemia (K+<3.5mmol/L), while 50 patients had normal potassium and 3 had hyperkalaemia (K+>5.5mmol/L). No significant difference was recorded in the

three groups, viz. Hypomagnesaemia, Normomagnesaemia and Hypermagnesaemia.43 patients (45.2%) had hypocalcaemia and 52 patients (54.7%) had normal serum calcium levels. Mean serum calcium was 8.76 mg/dL. Lowest serum calcium recorded was 8mg/dL. 28 patients with Hypomagnesaemia had Hypocalcaemia as well.

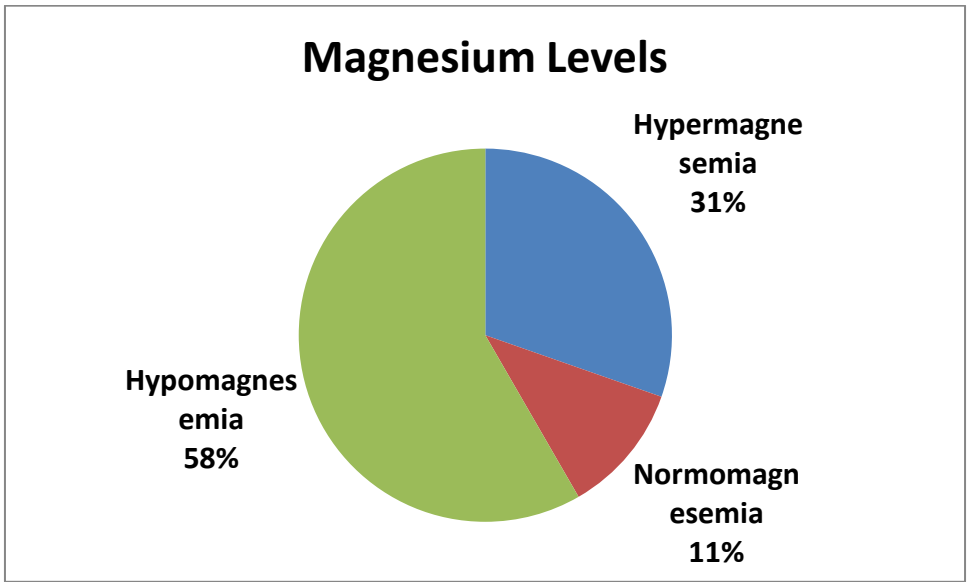

Figure 2: Serum Magnesium levels in patients

A significantly higher APACHE II Score was recorded in subjects with hypomagnesaemia compared to those with normomagnesaemia ($p<0.0001$). Length of ICU stay was an important outcome variable that was chosen for this study as it depends on multiple factors including electrolyte homeostasis. Length of ICU stay was found to be significantly higher in subjects with hypomagnesaemia compared to those with normomagnesaemia ($p<0.0001$) and hypermagnesae-mia ($p<0.0001$).

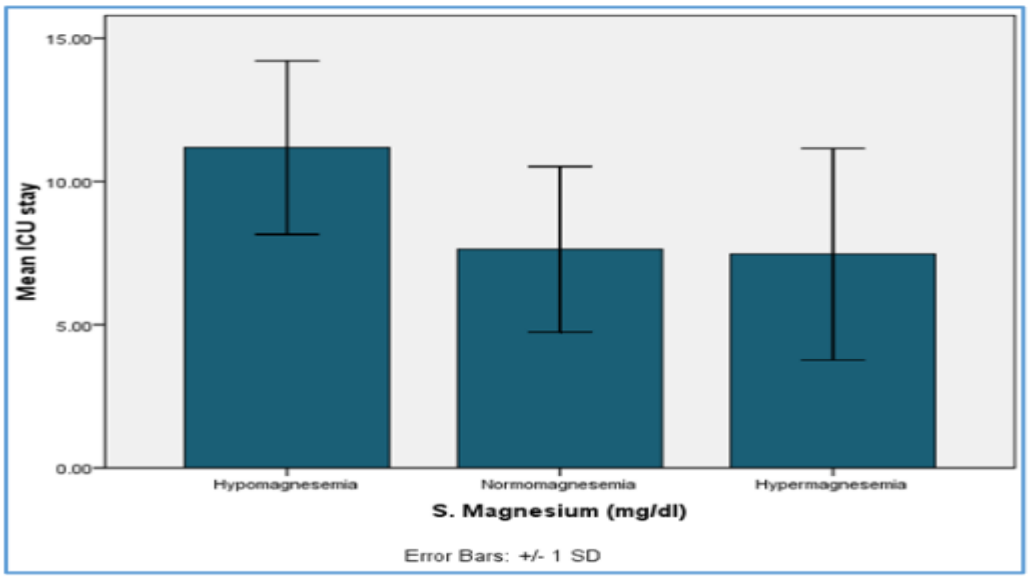

Figure 3. ICU Stay and association with Serum Magnesium Levels

Higher frequency of mortality in subjects was found to exist ($p=0.002$) with hypomagnesaemia and hypermagnesaemia. 34 patients (35.7%) survived, while 61 patients (64.21%) succumbed to their illnesses. Amongst the hypomagnesaemia group mortality reached to an astounding 80%, while that in the hypermagnesaemia group had 53.8% mortality. 36.8% patients with normomagnesaemia succumbed to their illnesses.

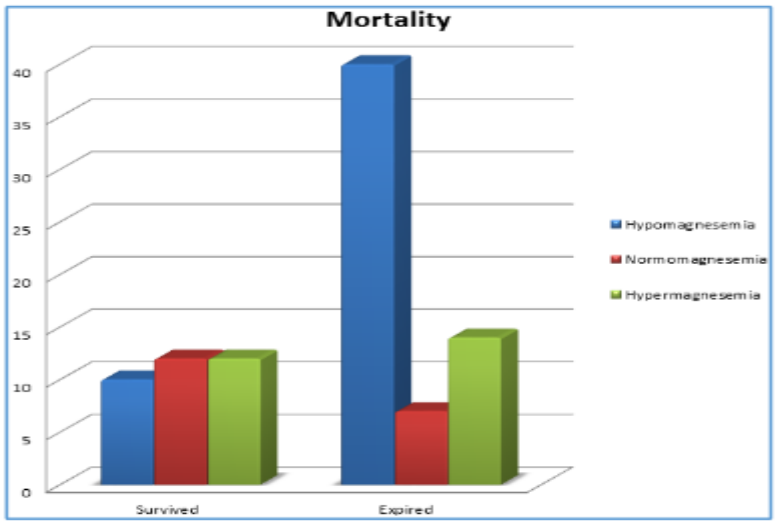

Figure 4. Association of Mortality with Serum Magnesium Levels

IV. Discussion

The significance of magnesium and its relationship to the origin of life has been traced to the formation of chlorophyll with magnesium at the centre of the molecule, and its interaction with Adenosine Triphosphate (ATP). Aerobic organisms then use the oxygen to release the energy stored in organic nutrients (including carbohydrates), and this energy is stored as Adenosine Triphosphate (ATP). The release of energy from ATP requires magnesium, which is an essential cofactor for the ATPase enzymes that hydrolyse ATP.[5] Therefore, magnesium is essential for providing us with energy and for allowing us to utilise this energy to sustain life. It also maintains neuromuscular excitability and it is important for maintenance of cardiac function. By regulating enzymes controlling intracellular calcium, Mg affects smooth muscle vasoconstriction.

In this study, the prevalence of Hypomagnesaemia was found to be 52.6% (50 subjects). 27.37% (26 subjects) had hypermagnesaemia, while 20% (19) of the subjects were normomagnesaemic.[6] An observational study on 102 medical ICU patients by Reinhart et al showed that hypomagnesaemia was present in 20% of patients, while hypermagnesaemia was present in 9% of patients, and of all ions Mg had the highest prevalence of abnormal values. Another prospective observational study on 100 ICU patients by Limaye et al showed that on ICU admission, 52% of patients had hypomagnesaemia, 41% had normal serum Mg levels and 7% had hypermagnesaemia. Chernow et al9measured serum Mg levels in blood samples from 193 ICU patients and found that 117 of 193 (61%) had hypomagnesaemia on ICU admission.[7] Subhraprakash pramanik et al in a study of 100 critically ill patients found the prevalence of hypomagnesaemia as 53%.[8]

The mean level of serum magnesium was 1.23±0.18 mg/dL in hypomagnesaemic patients compared to 1.89±0.12 mg/dL in normomagnesaemic group of patients. A significantly higher APACHE II Score was found using Tukey's HSD test in subjects with hypomagnesaemia compared to those with normomagnesaemia ($p<0.0001$). The mean APACHE II score was 22.93.[9] Highest APACHE II score recorded was 27, while the lowest score was 19. A similar result was obtained by Sunil Kumar et al in their study with the mean APACHE II score between hypomagnesaemic and normomagnesaemic group was 21.82±5.90 and 19.26±4.37. Safavi M et al showed in their study that Hypomagnesaemic patients had more severe organ dysfunction and higher APACHE II score than the other patients. This may be explained by a strong association of hypomagnesaemia with sepsis and septic shock, common cause of death in the ICU patient. This may be explained by a strong association of hypomagnesaemia with sepsis and septic shock, a common cause of death in the ICU patients.[10]

V. Conclusion

This study revealed the prevalence of dysmagnesaemia in the critically ill population of ICU. This study highlights the role of magnesium monitoring in critical illness. It adds to the scarce Indian data with regards to the magnesium homeostasis in ICUs. This study also showed that hypomagnesaemia was associated with higher APACHE II score and longer ICU stay. A significant proportion of the mortality was seen in both hypomagnesaemic group and hypermagnesaemic group. Hypomagnesaemia should be identified and corrected, because it is associated with increased adverse events and high mortality in critically ill patients. Physicians should maintain a high index of suspicion for hypomagnesaemia and the need for Mg replacement therapy.

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