Original Article

DOI: 10.17354/ijss/2015/486

Serum Magnesium Levels in Critically Ill Patients: A Prospective Study

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Abstract

Background: Though the importance of magnesium is known, it is not a usually recognized electrolyte abnormality in clinical practice. The prevalence of hypomagnesemia may be high in critically ill patients.

Materials and Methods: It was a prospective, observational study. A total of 150 consecutive critically ill patients admitted to the intensive care units of JSS Hospital, Mysore under the Department of General Medicine fulfilling inclusion and exclusion criteria were studied. Serum magnesium levels along with other relevant investigations were done within first 24 h of hospital admission. The hospitalization details and progress of the patients were recorded. Patients were followed up until the end points, i.e., discharge by the treating physician, discharge against medical advice or in-hospital death, and discharge for a referral.

Results: On admission 94 out of 150 (i.e., 63%) had normomagnesemia, 45 out of 150 patients (i.e., 30%) had hypomagnesemia, 11 out of 150 (i.e., 7%) had hypermagnesemia. The patients with hypomagnesemia "compared with" patients with normomagnesemia, had higher mortality rate (51% vs. 36%), higher APACHE II score on admission (24.13 vs. 22.47), need of ventilator support was more frequent (35% vs. 17%), a more frequent hypocalcemia (49% vs. 31%), a more frequent hypoalbuminemia (62% vs. 51%), and a more frequent septicemia (47% vs. 21%). Patients with diabetes (49% vs. 21%), hypertension (53% vs. 30%), and alcoholics (33% vs. 19%) had hypomagnesemia more frequently. There was no association of hypomagnesemia with arrhythmia, neurological manifestations, duration of stay, potassium disturbances, other electrolyte abnormalities creatinine levels, metabolic acidosis, inotropic use type of diet and anemia.

Conclusion: This study highlights the magnitude of hypomagnesemia in critically ill patients. Hypomagnesemia was associated with a higher APACHE II score on admission, increased mortality, increased need of ventilator support, hypocalcemia, hypoalbuminemia, and septicemia. There was an association of hypomagnesemia with diabetes and hypertension.

Key words: Critical illness, Hypomagnesemia, Magnesium

INTRODUCTION

Magnesium being the fourth most populous cation in the human body, and the second most populous intracellular cation next to potassium; it plays an essential physiological role in many functions of the body.[1] Hypomagnesemia may have serious implications in critically ill patients.[2]

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Month of Submission : 09-2015
Month of Peer Review : 09-2015
Month of Acceptance : 09-2015
Month of Publishing : 10-2015

Magnesium deficiency has a dubious credit of being the most unrecognized electrolyte disorder in routine clinical practice.[3] Though the importance of magnesium has been observed in ill patients, magnesium has been dubbed as the "forgotten cation."[4,5] Hence, we set out with an objective of studying serum magnesium levels in critically ill patients. This study was conducted over a period of 2-years in a teaching tertiary care referral hospital at Mysore, Karnataka state, South India.

METHODOLOGY

It was a prospective observational study (descriptive non-interventional study). Institutional Ethics Committee

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Approval was obtained. APACHE score was calculated for each patient on the day of admission to intensive care unit (ICU) using APACHE II scoring system. Critically ill adult patients above the age of 18 years admitted in ICUs with APACHE II score of 18 or more were included. The study included 150 patients admitted in ICUs under the Department of General Internal Medicine over a period of 2-years. Written Informed consent was obtained for all cases. Patients were excluded from the study; if they had received blood products, magnesium or calcium infusions before sampling. Inclusion in the study would not affect the routine patient care in the ICU. Serum Magnesium levels within the first 24 h of admission into the ICU were taken. Samples of venous blood (4.5 ml) were collected from every patient within the first 24 h of admission. Serum magnesium levels were assayed in JSS hospital laboratory by xylidyl blue colorimetric method using IMOLA auto analyzer with the normal range of serum magnesium being 1.7-2.7 mg/dL. The following data were noted: Age, gender, presenting symptoms and signs, diagnosis, relevant investigation reports, treatment and intravenous fluids used, duration of stay in ICU and any complications thereof, any new developments in ICU, use of mechanical ventilation, and its duration and mortality in the ICU, etc. Patients were followed up until discharge (from ICU) or death. All the patients enrolled were studied considering the following parameters: Length of stay in ICU, need for ventilator support, duration of ventilator support, APACHE score and mortality.

Statistical Methods

Quantitative data is represented as mean ± standard deviation. To assess the association among variables the Chi-square test, *t*-test, ANOVA were used. Differences were considered statistically significant if $P < 0.05$. Statistical analysis was performed using SPSS version 16.0 for Microsoft windows.

RESULTS

Out of the total 150 patients, a total of 93 patients were males and 57 were females. Out of total 150 patients 94 patients, i.e., 62.66% had normomagnesemia, 45 patients, i.e., 30% of total cases had hypomagnesemia (Figure 1). The lowest serum magnesium value was 1.0 mg/dL, and the highest was 4.2 mg/dL with mean being 2.018 mg/dL. Out of total 150 cases, cases with hypermagnesemia were only 11, i.e., 7.33% and statistically not significant. Hence, hypermagnesemia is not included in the discussion henceforth. Out of the total 45 patients with hypomagnesemia, a total of 29 patients were males and 16 were females. In total 150 critically ill cases the mean APACHE II score was 22.97 ± 4.06, mean APACHE II score in patients recovered and discharged was 21.13 ± 2.88, in those who died 25.00 ± 4.50, in discharged against medical advice 22.84 ± 3.17, in discharged at request cases 19.00 ± 1.41, in hypomagnesemia cases 24.13 ± 4.14, in hypomagnesemia cases with death as outcome 25.91 ± 3.82, in hypermagnesemia cases 25.82 ± 12.24. Hypomagnesemia was associated with increased mortality and a higher APACHE II score ($P = 0.02$) (Figure 2). The range of duration of stay in critical care unit varied from 1 to 36 days with mean of 7.90 days. The mean duration of stay of patients with low serum magnesium was 7.15 ± 6.04 days in ICUs while that of patients with normal serum magnesium was 8.31 ± 7.72 days and that of patients with high serum magnesium was 7.45 ± 5.97 days. The difference was not statistically significant ($P > 0.65$). Out of total 150 patients 21.33% (32 out of 150) needed ventilator support. 35.5% (16 out of 45) patients with hypomagnesemia needed mechanical ventilator support, while only 10.66% (16 out of 94) of the normomagnesemic group needed ventilatory support and no patients of hypermagnesemia needed ventilator support. Hypomagnesemia was associated with increased ventilator requirement ($P < 0.009$). Hypomagnesemia was associated with increased incidence of hypocalcemia ($P = 0.031$). There was no significant association between hypomagnesemia and other electrolytes (both potassium and sodium). There was a significant association of hypomagnesemia with hypoalbuminemia ($P = 0.03$). There was an association between sepsis and hypomagnesemia ($P = 0.015$). There was an association between hypomagnesemia in critically ill patients and diabetes and/or hypertension. The present study does not show any relation of hypomagnesemia with inotropic use, increased creatinine values, presence of metabolic acidosis or anemia. There was an increasing trend of alcoholics having hypomagnesemia, even though it was not statistically significant ($P = 0.08$). There was no association of hypomagnesemia with arrhythmia or neurological complications. There was no association of hypomagnesemia with either diet or smoking.

DISCUSSION

Hypomagnesemia is a common finding in critically ill patients. The prevalence of hypomagnesemia in critically ill patients in different studies range from 20% to 65%.[4-13] In the present study, 30% of the patients had hypomagnesemia. The majority of the studies done earlier as well as the present study have made use of only total serum magnesium levels, whereas ionized magnesium levels should be measured ideally which gives a better idea of associations since it is the ionized magnesium which is metabolically active.[11] Hypermagnesemia is less common compared to hypomagnesemia, ranging

from 4% to 14% in different studies.[4-13] In the present study, 7.33% of patients had hypermagnesemia. The association between hypomagnesemia and mortality varies between different studies.[4-13] A higher mortality rate was detected in hypomagnesemic patients as compared to normomagnesemic patients by Chernow *et al.*[5] (41% vs. 13%), Rubeiz *et al.*[7] (46% vs. 25%), Safavi and Honarmand.[12] (55% vs. 35%), and Limaye *et al.*[13] (57.7% vs. 31.7%). Guérin *et al.*[8] had found no difference in mortality in ICU patients between hypomagnesemic and normomagnesemic groups (18% vs. 17%); In the current study, the mortality rate in hypomagnesemic group was 51.1% (Figure 3) which is significantly higher as compared to 36.2% in the normomagnesemic group and 27.3% in the hypermagnesemic group. Whether this increased mortality is due to hypomagnesemia or due to a combination of other electrolyte abnormalities like hypocalcemia, hypoalbuminemia, increased incidence of septicemia, and more risk factors such as diabetes and hypertension or due to the severity of the underlying illness itself is difficult to ascertain. In this study, there is an increased mean APACHE II score in hypomagnesemia and hypermagnesemia group compared with normomagnesemia with a mean of 24.13 in hypomagnesemia group and 22.97 in normomagnesemia group. It shows that hypomagnesemia is associated with increased mortality and a high APACHE II score ($P = 0.022$). Safavi and Honarmand.[12] also showed increased APACHE II score in hypomagnesemia cases (14.16 vs. 10.80). Limaye *et al.*[13] had found no difference in APACHE II score (14.52 vs. 15.75) in ICU patients between hypomagnesemic and normomagnesemic group. Safavi and Honarmand.[12] showed that ICU stay (9.16 vs. 5.71 days) and total hospital stay (15.29 vs. 12.81 days) are higher in hypomagnesemia group. Limaye *et al.*[13] did not find statistically significant difference. Safavi and Honarmand.[12] and Limaye *et al.*[13] also showed statistically significant difference in need of ventilator support ($P < 0.05$). Hypomagnesemia was associated with increased ventilator requirement ($P < 0.009$) in the current study. The present study shows that hypomagnesemia is associated with increased incidence of hypocalcemia. ($P = 0.031$). Safavi and Honarmand.[12] and Limaye *et al.*[13] also showed similar association. The present study does not show any association with potassium abnormalities the reason for which is difficult to explain. Limaye *et al.*[13] also did not find any association whereas Safavi and Honarmand.[12] showed greater incidence of hypokalemia ($P < 0.05$). There was an increased incidence of sepsis in patients with hypomagnesemia in the present study. ($P = -0.015$) Safavi and Honarmand.[12] and Limaye *et al.*[13] also showed increased incidence of septicemia in hypomagnesemia patients. The present study shows association of hypomagnesemia in critically ill patients with diabetes and hypertension which concurs with Safavi and Honarmand.[12] and Limaye *et al.*[13] Even though the literature shows increased incidence of hypomagnesemia in alcoholics, it is not statistically significant in the present study. There is an increasing trend of alcoholics having hypomagnesemia, even though it is not statistically significant. ($P = 0.08$). Limaye *et al.*[13] also did not find any association.

There are no clear-cut guidelines for the correction of hypomagnesemia. According to Kevin J. Martin *et al.*[14] in cases of severe (<1 mEq/L in the serum) and symptomatic hypomagnesemia, correction is recommended. In asymptomatic patients with relatively mild reductions in serum Mg++ (between 1.0 and 1.5 mEq/L, the significance of hypomagnesemia and hence the need of treatment is not clear.

This study does not show any relation with arrhythmia, neurological manifestations, duration of stay, potassium

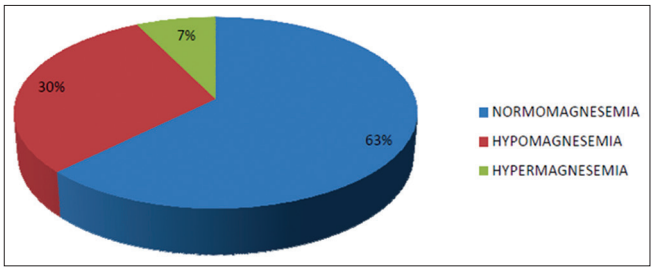

Figure 1: Magnitude of magnesium disturbances

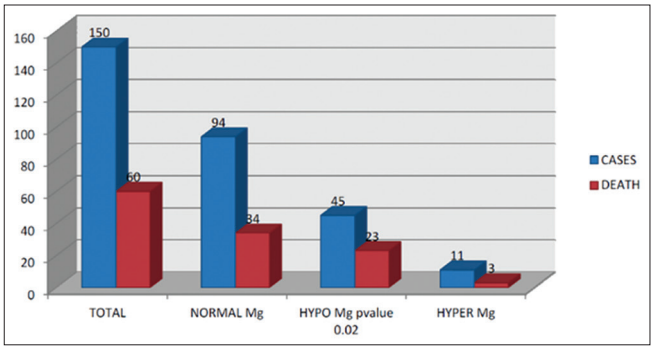

Figure 2: Magnesium and mortality

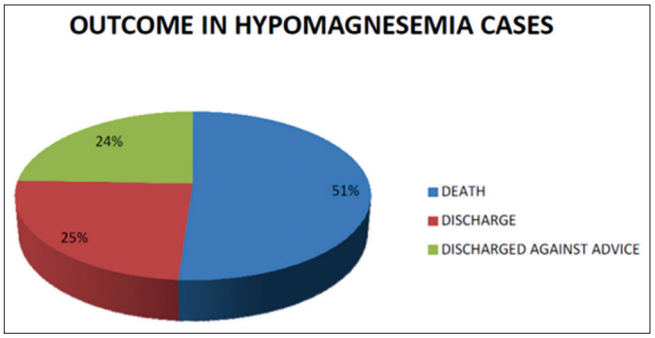

Figure 3: Outcome in hypomagnesemia

disturbances, other electrolyte abnormalities, creatinine levels, metabolic acidosis, inotropic use, type of diet, and anemia. Whether hypomagnesemia in critically ill is a significant abnormality in itself contributing to the causality of complications, which needs to be corrected or is it just an insignificant association without any implications is difficult to ascertain.

Limitations of this Study

- Total serum magnesium instead of ionized magnesium is measured
- Magnesium levels within first 24 h of admission were only done. Follow-up magnesium levels were not done
- Lack of clear-cut guidelines for treatment of magnesium abnormalities
- This is a descriptive non-interventional study. A large multicentric, randomized, double-blind, interventional, trial for magnesium supplementation in critically ill patients with hypomagnesemia is required in future to evolve a consensus/guidelines for treatment of hypomagnesemia in critically ill.

CONCLUSION

This study highlights the magnitude of magnesium disturbances on admission in critically ill patients admitted to ICUs under Department of General Medicine of JSS Hospital, Mysore. Hypomagnesemia is associated with high APACHE II score and high mortality. Patients with hypomagnesemia who died had a higher APACHE II score which shows that hypomagnesemia is associated with increased mortality. Patients with hypomagnesemia required ventilator support more frequently. Hypomagnesemia had statistically significant association with the following·hypocalcemia, hypoalbuminemia, septicemia, diabetes, and hypertension. This study does not show any relation with arrhythmia, neurological manifestations, duration of stay, potassium

disturbances, other electrolyte abnormalities, creatinine levels, metabolic acidosis, inotropic use, type of diet, and anemia. Whether hypomagnesemia in critically ill is a significant abnormality in itself contributing to the causality of complications, which needs to be corrected or is it just an insignificant association without any implications is difficult to ascertain.

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How to cite this article: Kiran HS, Sriramachandrudu A, Murthy KAS, Gowdappa HB. Serum Magnesium Levels in Critically Ill Patients: A Prospective Study. Int J Sci Stud 2015;3(7):241-244.

Source of Support: Nil, **Conflict of Interest:** None declared.