Original Article

Occurrence and Effect of Hypomagnesemia in Patients Suffering from Guillain-Barre Syndrome in Intensive Care Unit

AKM Ferdous Rahman[1],Syed Tariq Reza[1], Muhammad Asaduzzaman[1], Kamrun Satter[2], Salma Akter[3], Md. Salim[1], M. Abdur Rahman[4]

[1]Anesthesiologist, DMCH, [2]Senior Consultant, Comilla General Hospital, [3]Medical Officer, Mugda Medical College Hospital, [4]Professor & Head, ICU, Bangladesh Medical College Hospital, Dhaka

Corresponding Author: E-mail: ferdous_cmc@yahoo.com

Abstract

Background: *Predicting patient outcome is an important component of patient care in the critical care units. It has a vital importance to the intensivists. Because it allows the planning of early aggressive therapeutic interventions, optimum resource allocation and appropriate counseling of the family as well as the patient. So the intensivists have developed a number of prognostication tools for the patient admitted to ICU for above purpose. The two widely adopted systems to predict mortality are the Acute Physiology Assessment Chronic Health Evaluation (APACHE2) & Simplified Acute Physiology Score(SAP).Though useful, these tools are complex & require input of a large number of variables derived from patients history, physical examination & initial laboratory data. In several studies, it has been shown that serum magnesium level has great effect on mortality & morbidity in critically ill patient. But there is no study to observe the effect of hypomagnesium on the outcome of GBS in ICU.*

Methods and materials: *A prospective observational study in the intensive care unit of DMCH from January 2014 to December 2015. Thirty patients admitted to the ICU with suspected GBS requiring intensive care for more than at least 2 days with age more than 18 years were included. A blood sample was collected for estimation of serum total magnesium level on the day of admission to ICU. Finally all collected data were tabulated and analysed using standard statistical methods by SPSS version 17 for Windows. The Chi-square test was applied to correlate hypomagnesemia & normomagnesemia with the outcome.*

Result: *Total numbers of patients were thirty. 40% of patient had been suffering from hypomagnesemia. 40% patient needed mechanical ventilation.The mean length of mechanical ventilation days were higher in hypomagnesemic patients than normomagnesemic with were 17.66±8.40 vs 12.05±3.68 days. The mean length of ICU stay were 20.50(±9.48) days in hypomagnesemia and 14.22(±3.33) days in normomagnesemics. 33.33% patient had hyponatremia,58.33% patient had hypokalemia,50% patient had hypocalcemia. 50% patients with hypomagnesemia had sepsis. :Mortality rate in hypomagnesemic patients were 80% that were 20% in normomagnesemia.*

Conclusion: *Hypomagnesemia has played a pivotal role in prediction of mortality and morbidity in GBS. So hypomagnesemia can be used as a prediction tool for patient suffering from GBS in ICU.*

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Introduction:

Magnesium is the fourth most abundant cat-ion in the human body and the second most abundant intracellular cat-ion after potassium. Magnesium (Mg) is pivotal in the transfer, storage, and utilization of energy as it regulates and catalyzes more than 300 enzyme systems. Al-Ghamdi et al, Altura et al. Magnesium deficiency has been associated with a number of clinical manifestations such as atrial and ventricular arrhythmias, cardiac insufficiency, coronary spasm, sudden death, skeletal and respiratory muscle weakness, bronchospasm, tetany, seizures, and other neuromuscular abnormalities and a number of electrolyte abnormalities, including hypokalemia, hypocalcaemia, hyponatremia, and hypophosphatemia. Al-Ghamdi et al, Sanders et al, Fawcett et al, Whang et al, Speich M et al. Hypomagnesaemia is one of the most common electrolyte disturbances in hospitalized patients, especially in the critically ill. The Prevalence of hypomagnesaemia (measuring total serum magnesium) has a wide range (11% to 61%), and considerable controversy exists regarding its effects on morbidity and mortality. Reinhart et al, Chernow et al, Guerin et al. The severity of hypomagnesaemia can be assessed using subjective clinical evaluation and biochemical markers of organ dysfunction. Prevalence of Hypermagnesaemia varies from 5.7% to 9.3%. Drueke TB et al. The highest serum magnesium concentrations reported so far is 13.4 mmol/L in a 78 years old woman who swallowed water from the Dead Sea.Huey et al, Oren et al. severe hypermagnesaemia in fact that seems to be a feature in patients who drown in the Dead Sea. Oren et al. Hypermagnesaemia commonly occurs due to the excessive administration of magnesium salts or magnesium-containing drugs, especially in patients with reduced renal function. Hypermagnesaemia may rarely be due to redistribution from cells. Swaminathan et al. Disorders of magnesium metabolism are common in hospital patients and are frequently unrecognized. Low magnesium intake may be a contributor to many diseases including diabetes, cardiovascular disease and osteoporosis. Common complications of hypomagnesaemia include cardiac arrhythmias, and hypocalcaemia. Hypermagnesaemia, though less frequent, can also lead to cardiovascular and neuromuscular manifestations. Early recognition of disordered magnesium metabolism and correction of the electrolyte imbalance is necessary to avoid these complications. Swaminathan et al. The aim of this study was to evaluate the relationship between levels of magnesium and length of ICU stay, electrolyte disturbance and mortality rate of patient suffering from GBS in ICU.

Methods:

A prospective observational study in the intensive care unit of DMCH from January 2014 to December 2015. The study was approved by the Institutional Ethical Committee & permission was taken from ICU in-charge. Thirty patients admitted to the ICU with suspected GBS requiring intensive care for more than at least 2 days with age more than 18 years were included after a written informed consent was obtained. Patients receiving magnesium supplementation prior to transfer to ICU were excluded from this study. Accidental death like accidental extubation, ventilator failure or any iatrogenic insult, alternative diagnosis later on, unwilling to continue treatment in DMC, ICU also excluded from 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 investigations were done by standard laboratory method and also radiological investigations as indicated in every patient by the ICU doctor. When GBS was diagnosed clinically, blood for s. magnessium level was sent by investigator The study did not interfere with the patient management in the ICU. Patients were followed up to assess their mortality and morbidity in the form of total ICU stay, need of mechanical ventilation and duration of ventilatory assistance, associated medical conditions like sepsis, electrolyte abnormalities.. 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.Two 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 from intubation to extubation. Length of ICU stay was defined as number of days from admission to ICU & release from HDU. 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 17 for Windows. The Chi-square test was applied to correlate hypomagnesemia & normomagnesemia with the outcome.

Results

Tabel-I *Distribution of the patients by age*

Age group (years)	Hypo magnesium	Normo magnesium	Total	P value
< 20 years	02(16.7)	03(15.79)	05(16.7)	0.44
21-30 years	06(50.0)	06(31.58)	12(40.0)	
31-40 years	01(8.33)	06(31.58)	07(23.3)	
> 40 years	03(25.0)	03(15.79)	06(20.0)	
Total	12(100)	18(100)	30(100)	
Mean ±SD	28.67(±10.52)	29.61(±8.36)	29.23(±9.12)	

Table-I shows in case of hypomagnesaemia mean age was 28.67(±10.52) years and 29.61(±8.36) years in case of normomagnesemia.

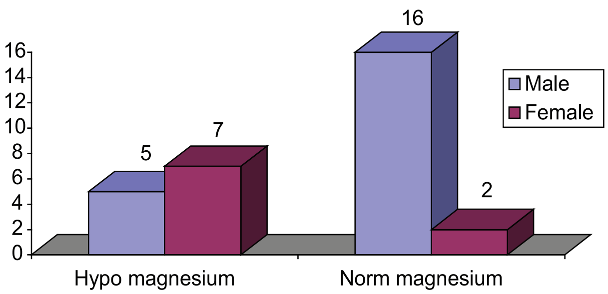

Fig 1 *Distribution of thepatients by sex and hypo and norm magnesium*

Figure shows hypomagnesaemia had female preponderance which was 58.33%.

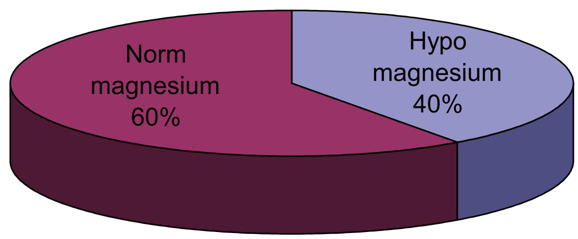

Fig 2 *Distribution of magnesium level of the study population*

Table-II *Association between need for ventilator support with hypo and norm magnesium*

Need for ventilator support	Hypo magnesium	Norm magnesium	Total	P value
Yes	07(63.63%)	04(36.36%)	11(100%)	0.06
No	05(26.31%)	14(73.68%)	19(100%)	
Total	12(40%)	18(60%)	30(100%)	

Need for mechanical ventilation was not significant.

Table-III *Mean duration of ventilator support and length of stay in ICU according to hypo magnesium & normomagnesium.*

	Hypomagnesium	Normomagnesium	P value
Duration of ventilator support	17.66(±8.40)	12.05(±3.68)	0.01
Length of stay in ICU	20.50(±9.48)	14.22(±3.33)	0.01

The mean length of mechanical ventilation days is higher in hypomagnesemic patients than normomagnesemic with was (17.66±8.40 vs 12.05±3.68) days. The mean mechanical ventilation days was inversely correlated with serum magnesium level (p 0.01).

The mean length of ICU stay was 20.50(±9.48) days in hypomagnesemia. The length of ICU stay was inversely correlated with serum magnesium level (p=0.01).

Table-IV *Relation between electrolytes imbalance with hypo magnesium and norm magnesium*

Electrolytes	Hypo magnesium	Norm magnesium	Total	P value
Hyponatremia	04(33.33%)	04(22.22%)	08	0.67
Hypokalemia	07(58.33%)	01(5.55%)	08	0.002
Hypocalcemia	06(50%)	02(11.11%)	08	0.03
Normal	01(8.33%)	13(72.22%)	14	0.002
Total	12	18	30	

Table 4 shows the mean potassium and calcium level were significantly different between hypomagnesemia and normomagnesemia group but sodium level was not significantly different.

Table -V *Distribution of patients with sepsis diagnosis.*

Sepsis	Hypo magnesium	Norm magnesium	Total	P value
Yes	06(50%)	00(0%)	06(20%)	**0.002**
No	06(50%)	18(100%)	18(80%)	
Total	12(100%)	18(100%)	30(100%)	

Table-V shows significant association of sepsis with hypomagnesemia, 50% patients with hypomagnesemia had sepsis.(p <0.05).

Table-VI *Association between mortality with hypo and norm magnesium*

Mortality	Hypo magnesium	Norm magnesium	Total	P value
Death	04(33.33%)	01(5.55%)	05(16.67%)	**0.04**
Discharge	08(66.67%)	17(94.44%)	25(83.33%)	
Total	12(100%)	18(100%)	30(100%)	

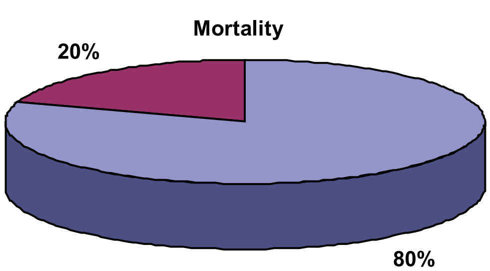

Figure 3 shows there was significantly increased mortality rate in hypomagnesemic patients compared to normomagnesemia (80% vs 20% p<0.001).

Discussion

In the study, in case of hypomagnesaemia mean age was 28.67(±10.52) years and 29.61(±8.36) years in case of normomagnesemia. Hypomagnesaemia had female preponderance which was 58.33%. In study of Mousavi et al showed the mean age of patients was 60.54±2.06 yrs. (range, 15-97 yrs) in critically ill patient. There were 252 males (55.7%) and 121 (44.3%) females. In our study, 40% (12/30) patients were hypomagnesemic, 60% (18/30) were normomagnesemic, suggesting frequent occurrence of low Mg in ICU patients suffering from GBS. Limaye CS et al studied serum magnesium levels in critically ill , On admission to MICU 52% patients had hypomagnesemia, 7% patients had hypermagnesemia and 41% patients had normomagnesemia. It has been observed in some studies, which had measured ionized Mg, the prevalence of hypomagnesemia was much lower (14% and 18%, respectively) than the studies, which had measured total serum or RBC Mg (20–70%).

The primary endpoints of this study were serum Mg level and mortality of patients suffering from GBS. Secondary outcome measures were need for ventilator support, duration of ventilator support, the associated electrolyte disturbances and length of ICU stay &other co-morbidities(sepsis).In the study,33.33% hypomagnesemic pt developed hyponatremia & 22.22% normomagnesemic pt developed hyponatremia which were not statistically significant but Percentage of patient developing hypokalemia & hypocalcemia in two group were statistically significant. Mg deficiency along with other electrolyte abnormalities has been found to coexist in up to 40% of patients. Many factors contribute to hypomagnesemia in GBS patients such as decreased absorption caused by impaired gastrointestinal activity, malnutrition, renal wasting of various drugs (e.g., digitalis, gentamicin, loop diuretics, etc.),hypokalemia, and hypocalcemia.

Hypomagnesemia also leads to muscle weakness and respiratory failure, causing difficulty in weaning the patient from the ventilator. In the current study, it has been seen that 58.33% patients with hypomagnesemia needed ventilatory support & 22.22% normomagnesemic patient needed ventilator support.Hypomagnesemic patient required a longer duration of mechanical ventilation(17.66±8.40) vs (12.05±3.68) . Fiaccadori *et al.*, had observed that patients with low muscle Mg were on ventilatory support for more number of days.[131] Safavi and Honarmand et al had found that in patients with hypomagnesemia the duration of mechanical ventilation was longer (7.2 vs. 4.7 days, $P < 0.01$).[114] Prolonged ventilation is not just due to muscle weakness causing difficulty to wean. Hypormagnesemia is characteristically associated with neuromuscular blockade and muscle weakness and therefore also prolonged ventilation time. Safavi M et al.

In the study carried out by Soliman *et al.*, there was no difference in the length of ICU stay among the hypo, as well as normomagnesium groups. However, the patients who developed hypomagnesemia during their ICU stay had a longer duration of stay in the ICU. In the study conducted by Limaye *et al.*, also there was no difference in the length of ICU stays among hypomagnesemic versus normomagnesemic patients.In the present study, we have a significant difference in the length of ICU stay in hypomagnesemic and a normomagnesemic group of patients 20.50±9.48 days vs. 14.22±3.33 days.

Mg plays an important role in sepsis. Hypomagnesemia is associated with increased release of endothelin and proinflammatory cytokines(Lee JW,Marino P et al).This was strongly associated with increased mortality in experimental sepsis, and Mg replacement provides significant protection against endotoxin challenge. This effect was due to the down-regulation of the release of inflammatory cytokines (tumor necrosis factor-alpha, interleukin-6).(Buckley MS,Haque A et al)Sepsis was an independent risk factor for developing hypomagnesemia during ICU stay as found by Soliman *et al.*In the study conducted by Limaye *et al.*, the incidence of sepsis was twice as more common in hypomagnesemic patients as compared to normomagnesem patients ($P < 0.05$). Similarly, in the present study, the incidence of sepsis was twice as common in hypomagnesemic patents as in normomagnesemic patients.

Various studies have shown varying relationship between hypomagnesemia and mortality/ morbidity rates. A higher mortality rate was detected in hypomagnesemia patients when compared with normomagnesemic patients by Limaye *et al.*, (57% vs. 31%), Safavi and Honarmand (55% vs. 35%), and Rubeiz *et al.*, (46% vs. 25%).There was no significant difference in ICU mortality between hypomagnesemic and normomagnesemic groups (18% vs. 17%), but noted a higher mortality rate among hypermagnesemic patients by Guérin *et al.*our study revealed the mortality rate in hypomagnesemic group 33.33%, which was significantly higher as compared to 5.55% in the normomagnesemic group. The higher mortality in this study can be ascribed to a greater incidence of electrolyte abnormalities especially hypokalemia and cardiac arrhythmias and a strong association of hypomagnesemia with sepsis and malnutrition.

Conclusion

Magnesium alterations have frequently been observed in patients suffering from GBS in ICU. In this study, there is a high prevalence of hypomagnesemia in GBS patients, which were associated with adverse outcomes. Physicians should be alert to the high incidence of hypomagensemia in GBS patients and should consider their routine monitoring.

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