EXPERIENCE WITH SERUM MAGNESIUM ESTIMATIONS IN CRITICALLY ILL PATIENTS ADMITTED IN HIGH DEPENDENCY UNIT OF A TERTIARY CARE HOSPITAL

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Abstract

Background: *Magnesium deficiency has been a common, but easily ignored, electrolyte abnormality. Studies on magnesium in our country are lacking. Here, we have estimated and correlated serum magnesium levels with outcomes and other electrolyte imbalance in critically ill patients with respect to the mortality, in hospital outcome and length of high dependency unit (HDU) stay.*

Methods: *A prospective, observational study was conducted in patients who had been admitted to the HDU. Patient's demographic profile, medical history, serum magnesium, calcium and electrolytes were enrolled on admission. Patients were divided into normomagnesemic, hypomagnesemic hypermagnesemic groups and compared for various parameters.*

Results: *Out of 60 critically ill-patients, 32 patients (53.33%) were hypomagnesemic, 20 patients (33.33%) were normomagnesemic and 8 patients (13.33%) were hypermagnesemic. The duration of stay of the patients in HDU, in hospital outcome and mortality showed significant variation between these groups. Associated electrolyte abnormalities in hypomagnesemic patients were hypokalemia (56.25%) and hypocalcemia (62.50%). Most of the hypomagnesemic patients were hypertensive (62.50% vs 40%) and was presented in drowsy state (50% vs 40%) compared to normomagnesemic group. Mortality of hypomagnesemic group was 37.50% while that of hypermagnesemic group was 25%. In hospital, arrythmia (18.75%) and convulsion (12.50%) developed in hypomagnesemic groups. Mean duration of length of stay in HDU was 7.45 days in hypomagnesemic, 6.83 days normomagnesemic, and 8.67 days in hypermagnesemic group.*

Conclusion: *Development of magnesium imbalance in critically ill patients is associated with bad prognosis. Monitoring of serum magnesium levels may have prognostic, perhaps therapeutic implication.*

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Introduction:

Magnesium is the fourth most abundant cation in the human body and the second most abundant intracellular cation after potassium. For some time, magnesium (Mg) has been considered the "fifth forgotten ion." However, for several years now the qualification "forgotten" is no longer relevant. Serum magnesium is currently receiving more attention from the medical community than in the past because of evidence that its deficiency contributes to a number of abnormal perturbations as it influences over 300 enzyme systems, including Na-K-ATPase mediated transport, and is essential for calcium homeostasis, nerve conduction, skeletal muscle activity, and maintenance of calcium and potassium homeostasis. Disorders of magnesium metabolism are among the most common electrolyte disturbances in hospitalized patients, especially in the critically ill elderly because

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of their low magnesium intake, diminished intestinal absorption, and increased urinary output (due to frequent use of diuretics and digitalis).[1,2] and are frequently unrecognized. It has been aptly said that "The eyes cannot see what the mind does not know." Hypomagnesemia is easily mistaken for potassium deficit, a condition with which it is often associated. Serum magnesium is a poor indicator of total body magnesium stores due to its major intracellular distribution and may be normal in the presence of total body magnesium depletion. Hypermagnesemia is found less commonly and is mostly iatrogenic or due to renal failure.

In this study, we have tried to correlate serum Mg levels with other electrolyte imbalance and observe outcome of the critically ill patients with respect to the length of stay, complications developed in hospital and the ultimate outcome (discharge/death).

Method:

This prospective observational study was carried out in the High dependency unit (HDU) of CMH, Dhaka; from June 2016 to November 2016. 60 (sixty) patients admitted to the HDU for critical illness were included in the study after a written informed consent was obtained. Patients were enrolled at random, and the selection bias was avoided by registering those patients who fulfilled the criteria for critical illness on the basis of a severity scoring system APACHE II (Acute Physiology and Chronic Health Evaluation). Patients who were stable, who had financial constraints and who had received magnesium prior to transfer to HDU were excluded from the study, as shown in the flow chart in Figure 1. A blood sample was collected for estimation of serum total magnesium levels on admission to HDU. Demographic data (age and sex), past medical history, medications administrated, and length of HDU stay were recorded for each patients. Other hematological, biochemical and radiological investigations were performed as indicated in every patient. APACHE score was calculated for each patient on the day of admission to HDU using APACHE II scoring system. The study did not interfere with the patient management in HDU. Serum total magnesium level was determined by colorimetric method. The normal value of serum total magnesium was between 1.6 to 2.3 mmol/l. The primary end point was mortality, and secondary end

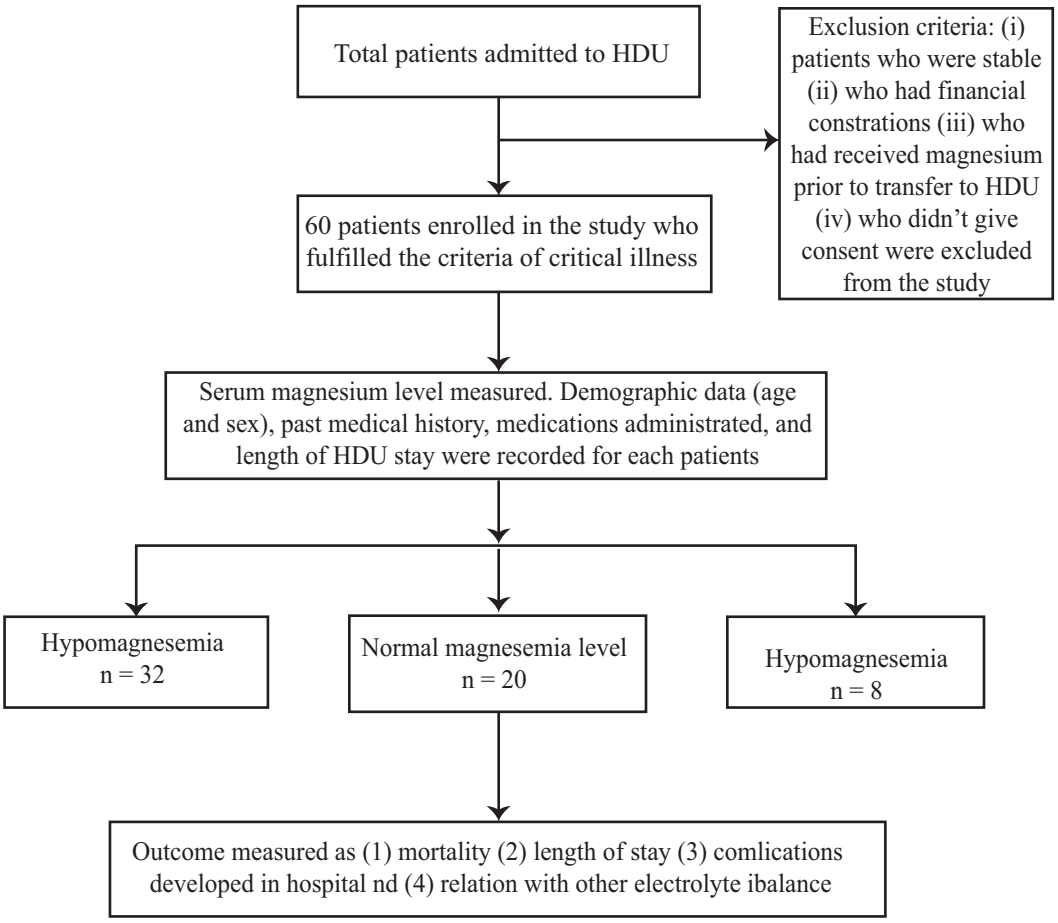

Fig.-1: *Flowchart showing enrolment of patients.*

point was in hospital outcome and length of high dependency unit (HDU) stay and relation with other electrolyte imbalance. Statistical analysis was performed using descriptive and inferential statistics. All data were expressed as mean ± standard deviation. Analysis was performed using the test statistics Student t test for the difference of means,Chi-square test and correlation. The software used in the analysis included SPSS version 22.

Result:

We studied 60 critically ill-patients and followed their clinical as well as biochemical parameters from the day of admission to HDU to the day of discharge from HDU or death. Septicemia, stroke, malignancy, respiratory failure, renal failure and patients with multiorgan dysfunction formed more than 50% of our study population. On admission, 53.33% (32/60) patients had hypomagnesemia, 13.33% (8/60) had hypermagnesemia and 33.33% (20/60) had normal serum magnesium levels. The lowest serum magnesium value recorded was 0.87mmol/l while the highest value was 3.32mmol/l. Among these patients, 36/60 (60%) were male patients and 24/60 (40%) were female patients. Mean age among study population was 63.3±18.14 years

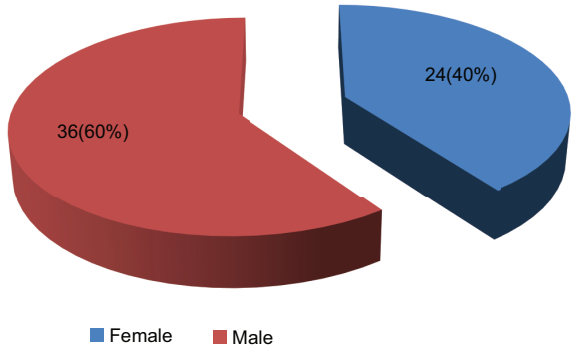

Fig.-2: *Sex distribution of the patient*

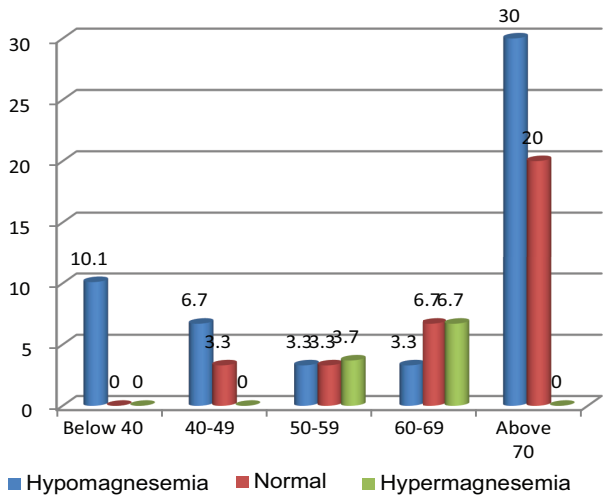

Fig.-3: *Relation of age and serum magnesium level*

The duration of stay of the patients in HDU, in hospital outcome and mortality showed significant variation between these groups. The range of duration of stay in MHDU varied from 2 day to 18 days with mean of 7.45 ± 3.94 days. The mean duration of stay in MHDU of patients with low serum magnesium was 7.45±4.39 days while that of patients with normal serum magnesium was 6.83±2.48 days and that of patients with high serum magnesium was 8.67±5.68 days.

Finding of the association between characteristics of study participants and hypomagnesemia is shown in Table 1.

Table-I

Comparison of patient characteristics between groups

Characteristics	Normal Mg N=20 33.33%	Hypo Mg N=32 53.33%	Hyper Mg N=8 13.33%
Sex			
Male	12(60%)	18(56.25%)	6(75%)
Female	8(40%)	14(43.75%)	2(25%)
C/F			
Vomiting	8(40%)	10(31.25%)	0(0.0%)
Unconscious	8(40%)	12(37.50%)	2(25%)
Convulsion	0(0.0%)	6(18.75%)	0(0.0%)
Drowsiness	8(40%)	16(50%)	4(50%)
Fever	6(30%)	14(43.75%)	2(25%)
Diagnosis			
CKD	6(30%)	12(37.50%)	0(0.0%)
IHD	8(40%)	6(18.75%)	2(25%)
DM	7(35%)	18(56.25%)	1(12.5%)
HTN	8(40%)	20(62.50%)	0(0.0%)
Stroke	2(10%)	14(43.75%)	0(0.0%)
Sepsis	4(20%)	6(18.75%)	2(25%)
Electrolyte imbalance			
Hyokalemia	6(30%)	18(56.25%)	6(75%)
Hypocalcemia	6(30%)	20(62.50%)	2(25%)
Hyponatremia	16(26.67%)	36(60%)	8(13.33%)
Outcome			
Arrythmia	2(10%)	6(18.75%)	2(25%)
Discharge	14(70%)	22(68.75%)	6(75%)
Death	4(20%)	12(37.50%)	2(25%)
LOS (days)			
Mean ± SD	6.83 ± 2.48	7.45 ± 3.94	8.67 ± 5.68

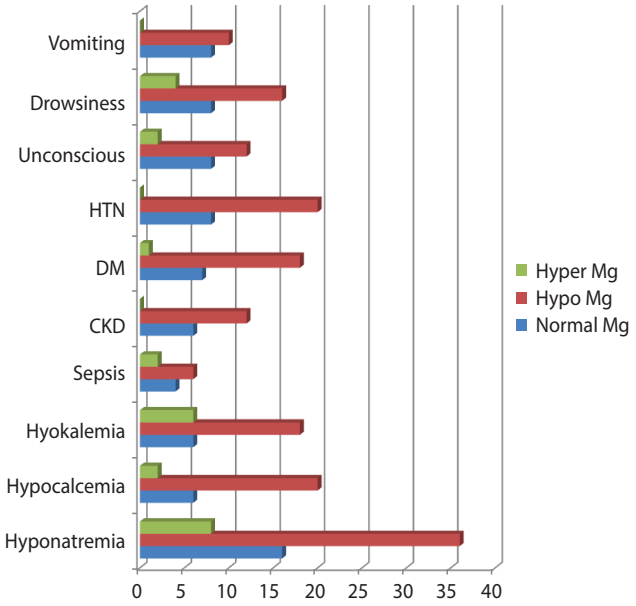

Fig.-4: *Comparison between groups according to clinical parameters and other electrolyte imbalance*

Of 32 patients with hypomagnesemia 20 (62.50%) also had hypocalcemia, 02 had hypercalcemia and 10 patients (31.25%) had normal calcium level. The incidence of hypocalcemia is significantly higher in patients with hypomagnesemia ($p<0.05$).

Thirty patients (50%) had documented hypokalemia on admission, of which 18(60%) had hypomagnesemia, 06 (20%) had normomagnesemia and 6 (20%) had hypermagnesemia which was statistically significant. Most of the hypomagnesemic patients were hypertensive (62.50% vs 40%) and was presented in drowsy state (50% vs 40%) compared to normo-magnesemic group.

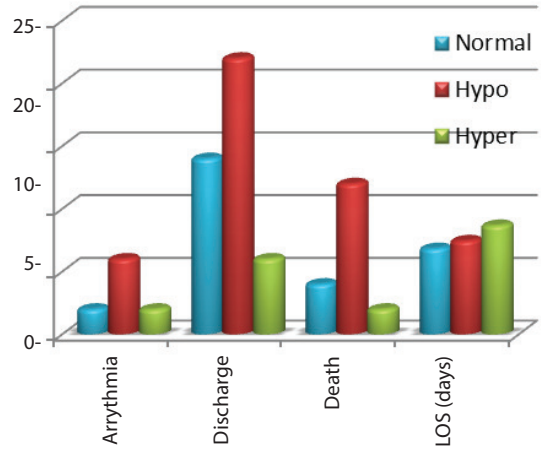

Fig.-5: *Distribution of patients according to Outcome*

Figure 5 showed that Mortality is higher in hyomagnesemic group, but LOS in HDU is higher in hypermagnesemic group.

In hospital, arrythmia (18.75%) and convulsion (12.50%) developed in hypomagnesemic groups. The cure/discharge rates from HDU were 14/20 (70%) for patients with normal magnesium and 22/32 (68.75%) for those with low magnesium, and the difference was not statistically significant. The mortality rate in hypomagnesemic group was 37.50% (12/32); whereas in normomagnesemic group was 20% (4/20). Significantly greater mortality rate was observed in hypomagnesemic patients as compared to normomagnesemic patients ($p<0.05$).Two patients, who died had hypermagnesemia.

Table-II

Prevalence of hypomagnesemia in critically ill patients in various studies.

Study	Year	No. of patients	Low Mg	High Mg	Normal Mg
Ryzen et al[6]	1985	94	51%	-	-
Chernow et al[7]	1989	193	61%	5%	34%
Reinhart et al[8]	1989	102	20%	9%	71%
Rubeiz et al[9]	1993	197	20%	7%	73%
Guerin et al[10]	1996	179	44%	6%	50%
Huijigen et al[11]	2000	115	14%	12%	74%
Deheinzelin et al[12]	2000	226	45.60%	-	54.40%
Soliman et al[13]	2003	422	18%	14%	68%
Safavi et al[14]	2007	100	51%	-	49%

Discussion:

Magnesium is mostly located in bone or within the cells. Assessment of magnesium status in either of these compartments in critical illness is impractical. The physician must therefore rely on determination of serum magnesium to determine if a patient is magnesium deficient.[3] Magnesium is the second most common intracellular cation. It plays an important role in homeostasis. Magnesium is the cofactor for most of the adenosine triphosphate (ATP) reactions because it is the ATP–magnesium complex that is bound to and hydrolyzed by the enzymes. Magnesium deficiency has been found to co-exist in up to 40% of patients with other electrolyte abnormalities. Many factors contribute to magnesium deficiency in critically ill patients; like impaired GI absorption, nasogastric suction, poor content of magnesium in feeding formulae or TPN solutions, administration of

drugs like diuretics, aminoglycosides, Amphotericin-B which cause renal wasting of magnesium[4,5]. Hypermagnesemia is reported less commonly and it is mostly due to renal failure or iatrogenic.

In our study of 60 critically ill-patients, 53.33% (32/60) patients had hypomagnesemia, 13.33% (8/60) had hypermagnesemia and 33.33% (20/60) had normal serum magnesium levels, signifying remarkable occurrence of hypomagnesemia in HDU patients.

Table II gives the prevalence of hypomagnesemia and hypermagnesemia in various studies carried out previously in critically ill patients all over the world and the results of this study. Most of the studies carried out previously have measured total serum magnesium. The prevalence of hypomagnesemia was in the range of 14% to 70%.[6-14]

Hypermagnesemia is found less commonly than hypomagnesemia. It is reported in the range of 4 to 14% in literature and in this study hypermagnesemia was seen in 13.33% of patients.The relationship between hyomagnesemia or hypermagnesemia and mortality rate varies from study to study. A higher mortality rate was detected in hypomagnesemic patients as compared to normomagnesemic patients by Chernow et al[7] (41% vs 13%), Rubiez et al[9] (46% vs 25%) and Safavi et al (55% vs 35%). Guerin et al had found no difference in ICU mortality between hypomagnesemic and normomagnesemic groups (18% vs 17%); but noted a higher mortality rate among hypermagnesemic patients.[10] Soliman et al observed that patients who develop ionized hypomagnesemia during their ICU stay have higher mortality rates.[13] In the current study the mortality rate in hypomagnesemic group was 37.50% which is significantly higher as compared to 20% in the normomagnesemic group and 25% in the hypermagnesemic group ($p< 0.05$).

The higher mortality rates in the hypomagnesemic patients can be explained by greater incidence of electrolyte abnormalities especially hypokalemia, hypocalcemia and cardiac arrhythmias in HDU patients.

In the study carried out by Soliman et al[13] there was no difference in the length of HDU stay among the three groups. But, In our study there was significant difference in length of ICU stay among 03 (three) groups.The mean duration of length of HDU stay was highest in hypermagnesemic group (8.67 ± 5.68 days), followed by hypomagnesemic group (7.45 ± 3.94 days) group and normomagnesemic group (6.83 ± 2.48 days). Magnesium plays an important role in sepsis .Hypomagnesemia is associated with increased release of endothelin and proinflammatory cytokines.[15] Salem et al[16] showed that progressive magnesium deficiency and hypomagnesemia are strongly associated with increased mortality in experimental sepsis and magnesium replacement provides significant protection against endotoxin challenge.

In the present study the there was no significant difference between incidence of sepsis between three groups. Hypomagnesemia has been known to be associated with diabetes mellitus. It is due to increased renal losses of magnesium that accompany glycosuria. There is a strong relationship between hypomagnesemia and insulin resistance[17]. Magnesium supplementation is associated with decreased insulin requirements.[18] In the present study hypomagnesemia is more common in diabetic patients (56.25% vs 35%) ($p<0.05$).

Hypomagnesemia is commonly associated with other electrolyte abnormalities. Whang et al[19] had found hypomagnesemia in 42% patients with hypokalemia, 29% patients with hypophosphatemia, 27% patients with hyponatremia and 22% patients with hypocalcemia. Hypokalemia and hypocalcemia are said to be the predictors of hypomagnesemia. Hypokalemia seen in hypomagnesemic patients is relatively refractory to potassium supplementation until magnesium deficiency is corrected.[20, 21]This is due to defective membrane ATPase activity and also because the renal potassium loss is increased in presence of hypomagnesemia. In this study half of the patients (50%) with hypokalemia also had low serum magnesium levels (18/30). Hypocalcemia is also commonly associated with hypomagnesemia. The mechanism involves defects in synthesis and release of parathyroid hormone (PTH) [22] as well as the end organ resistance to PTH.[23] Also the magnesium deficiency may directly act on bones to reduce calcium release independent of PTH.[24] As with hypokalemia, the hypocalcemia of magnesium depletion is difficult to correct unless magnesium deficits are corrected.[20] The present study also found increased incidence of hypocalcemia in hypomagnesemic patients than in normomagnesemic patients.

Conclusion:

Mg alterations have frequently been observed in critically ill elderly patients, as in this study, which have a high prevalence of hypomagnesemia. Physicians should be alert to the high incidence of hypomagnesemia in critically ill elderly patients and should consider a routine monitoring program, as hypomagensemia may be associated with adverse outcomes.

Limitations:

Our study has a limitation of smaller size of study population to comment on similar HDU stay. Although there was a high incidence of hypomagnesemia in the present study, its correction after magnesium supplementation was not included as a part of the study. The potential benefit of magnesium supplementation to prevent or correct hypomagnesemia in critically ill patients requires further study

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