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SERUM MAGNESIUM AS A PROGNOSTIC FACTOR IN CRITICALLY ILL PATIENTS AND ITS CORRELATION WITH APACHE 2 SCORE

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Corresponding Author:
Dr. Radha T.R
Email: dr.tr.radha@gmail.com

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Roopa[1], Radha T R[2], Sujeesh H S[3]

[1]Junior Resident, Department of General Medicine, Government Medical College Kottayam, Kerala, India
[2]Professor, Department of General Medicine, Government Medical College Kottayam, Kerala, India
[3]Assistant professor, Department of General Medicine, Government Medical College Kottayam, Kerala, India

Abstract

Background: Magnesium is the fourth most common cation in the human body and second most abundant intracellular cation after potassium. More importantly patients who develop magnesium deficiency in ICU have mortality rates 2 to 3 times higher and prolonged hospitalization compared to those who are magnesium sufficient. **Materials and Methods:** A total of 206 patients admitted to medical ICU who fulfilled inclusion and exclusion criteria were considered during this study. Patients were classified into three groups based on initial magnesium levels: Hypomagnesemia <1.6 mEq/L, Normomagnesemia 1.6 to 2.5 mEq/L, Hypermagnesemia >2.5 mEq/L. The following parameters were studied during the course of ICU stay, APACHE 2 score, ventilator need duration of mechanical ventilation length of ICU stay and mortality. **Result:** Among the 206 patients admitted in ICU majority of patients were between 40 and 49 years of age among which 62% patients were males. The mean APACHE 2 score was 14. APACHE 2 score decreased by 3.64 days for each unit increase in magnesium. Mean duration of ICU stay of the patients was 5.21 days. ICU stay decreased by 1.24 days for each unit increase in magnesium. Majority of patients didn't require ventilator support during the stay in ICU. There was 33% decrease in requirement of ventilator support for every 0.1 mEq /L increase in serum magnesium levels. **Conclusion:** The need for invasive ventilation and duration of invasive ventilation were significantly higher among the patients with hypomagnesemia compared to the patients with normal magnesium levels (p-value <0.05). Mortality was higher in the cases than in the controls (p-value <0.05).

INTRODUCTION

Hypomagnesemia can potentially cause fatal complications including ventricular arrhythmia, coronary artery spasm, and sudden death. It also associates with increased mortality and prolonged hospitalization. Magnesium is an essential element in maintaining critical functions like cardiac membrane potential, intracellular signalling, and it also serves as a cofactor for several enzymes involved in protein and DNA synthesis.[1]

The incidence of hypomagnesemia is reported to be 2% in the general population, 10e20% in hospitalized patients, 50e60% in intensive care unit (ICU) patients, 30e80% in persons with alcoholism, and 25% in outpatients with diabetes.[2]

Magnesium is an essential element within the human body, and takes part in many biochemical reactions. The potential clinical importance of this ion began to emerge as early as the 1960s.[3] This metal interacts with the human body both as an ion, and as a fundamental cofactor in numerous enzymatic reactions that regulate metabolism and protein synthesis, and maintain cellular integrity.[4]

Both hypermagnesemia and hypomagnesemia are known to induce physiological alterations that contribute to the development of various diseases. Moreover, the therapeutic potential of magnesium sulfate ($MgSO_4$) has been explored in critical care conditions, such as ischemic and hemorrhagic stroke head trauma, arrhythmias, asthmatic status, and preeclampsia.[5,6]

Magnesium is often known as the "forgotten electrolyte". This is because, even though alterations in level are common, the diagnosis, clinical implications, and treatment are often overlooked.[7]

The incidence of abnormalities of Magnesium occurring in critically ill patients in ICU is 65%.[8]

Hypomagnesemia is caused by conditions like inadequate dietary magnesium intake and gastrointestinal and renal disorders and correlates with increased morbidity and mortality in hospitalized patients and correlates with prolonged duration of ICU stay, increased need and time of requirement of mechanical ventilation (MV), increased incidence of sepsis and other electrolyte disturbances (hypocalcemia and hypokalemia).9 On the other hand, hypermagnesemia occurs less frequently and is seen in 5% of hospitalized patients. 10It occurs as a result of impaired renal magnesium excretion, iatrogenic administration of magnesium in antacids, enemas, or parenteral nutrition, diabetic ketoacidosis etc., and may have serious implications.

MATERIALS AND METHODS

It was a Prospective Observational study conducted at Medical Intensive Care Unit, Government Medical College, Kottayam from January 2019 to December 2019. Patients admitted to medical intensive care unit in Government Medical College Kottayam were the study population.

Sample size

According to study conducted by SS Sen et al,[11]

p=16

Sample size N=zα2(pq)/d2

p=16

q=84

d=5

N=3.84×16×84 /5×5=206

Inclusion Criteria

Patients suffering from various medical conditions admitted in Medical ICU are included.

Exclusion Criteria

- Patients with following associated conditions which can be a separate risk factor for electrolyte imbalance were excluded.
- Patients receiving magnesium supplement earlier.
- Patients on diuretics, aminoglycosides
- Patients having undergone GI surgery
- Patients having chronic diarrhea /malabsorption syndrome, pancreatitis
- Patients below 18 years of age will be excluded.
- Sampling technique
- Consecutive cases eligible for the study were taken.

Methodology

206 consecutive patients admitted to the Medical Intensive Care Unit were studied. Serum magnesium levels were measured and also APACHE 2 score was calculated at the time of admission to ICU. Based upon the serum magnesium levels patients were classified into hypomagnesemia, normomagnesemia and hypermagnesemia groups. These patients were followed up and outcome analysis was done based on four parameters: Need for ventilator support, duration of ventilator support duration of ICU stay and mortality.

Ethical Consideration: The study was conducted in this institution after obtaining due ethical clearance from the Institutional Review Board of Government Medical College, Kottayam and Department of General Medicine, Government Medical College,Kottayam . Informed written consent was obtained in the vernacular from patients meeting eligibility criteria and who were subsequently enrolled in the study.

Data management and statistical analysis: The data was coded and entered in Microsoft Excel and statistical analysis were done using SPSS software. Associations between various factors were assessed using chi square test for qualitative variables. Appropriate non parametric were applied wherever required. The level of statistical significance was taken as p value less than. All the continuous variables like age, electrolyte parameters & APACHE 2 score are summarized as mean with SD or median with IQR depending on the distribution. Categorical variables are summarized as proportions. Association between electrolyte levels and duration of icu stay and duration of ventilator support with Magnesium levels was assessed using poisson regression and negative binomial regression.

RESULTS

As per [Table 1] age of participants ranged from 15 to 86. With majority of patients between 40 to 49 years of age. Mean age of patients was 44.7 ± 15.9 years. Most of the patients were males (128, 62.1%). The median (IQR) APACHE2 Score of the patients was 14 (10, 17). Majority of patients [193 (93.7%)] included in the study had APACHE 2 score ≤ 25 indicating better prognosis.

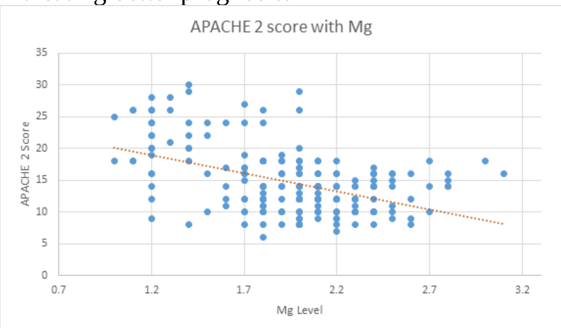

Figure 1: Scatter plot between APACHE 2 Score and Mg level with best-fit line

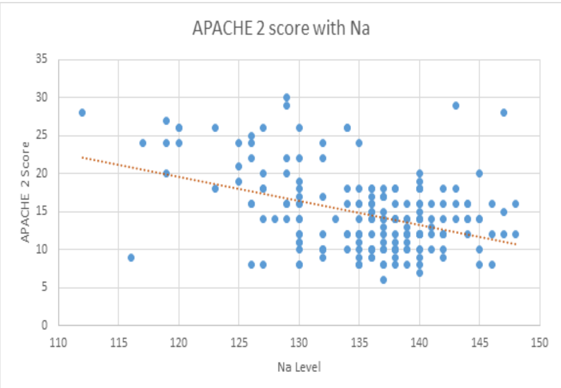

Figure 2: Scatter plot between APACHE 2 Score and Na level with best-fit line

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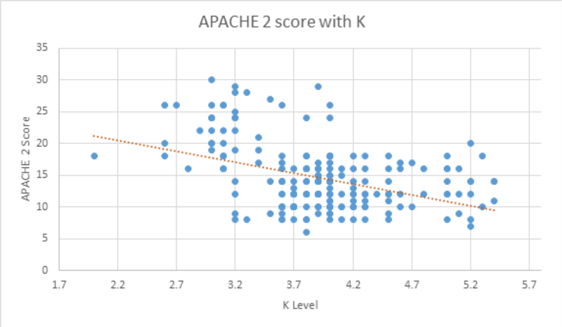

Figure 3: Scatter plot between APACHE 2 Score and K level with best-fit line

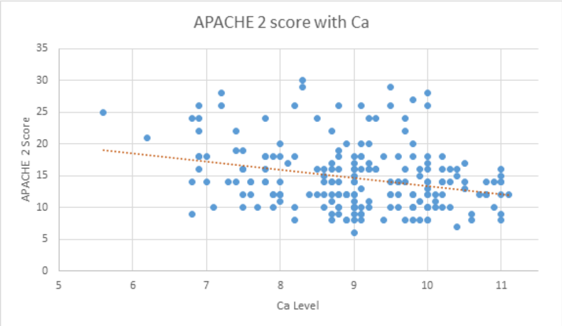

Figure 4: Scatter plot between APACHE 2 Score and Ca level with best-fit line

As per [Table 2 and Figure 1-4] multiple linear regression analysis done to predict the APACHE2 score based on electrolyte levels at admission. A significant regression equation was found (F(4, 201) = 19.46), with an R2 of 0.28. The predicted APACHE2 Score is equal to 48.15 – 3.08 x Mg level – 0.13 x Na level – 1.18 x K level -0.61 x Ca level, where the levels are measured in mEq/l. APACHE2 score decreased by 3.08, 0.13, 1.18 and 0.61 for each unit increase in Mg, Na, K and Ca levels respectively. Mg level, Na level and Ca level were found to be significant predictors independently.

As per [Table 3] majority (155, 75.24%) of patients did not require a ventilator support during the stay in ICU. Hypomagnesemia was associated significantly with need of ventilator with chi square value 96.3 and p value <.001. There is an increased need for ventilation in those with hypomagnesemia compared to those with normal levels of magnesium. (88.9% vs 11.2%). Odds ratio was estimated through binomial regression to be 63.6 (95% CI [20.2 to 199.5]) with p value <.001. Those with hypomagnesemia are 62.6 times more likely to be ventilated compared to those with normal magnesium levels. The proportion of patients needing Ventilator support ≥ 5 days was highest in patients with hypomagnesemia and lowest in patients with hypermagnesemia the difference was statistically significant with Fisher's exact p value <.001.

As per [Table 4] negative binomial regression analysis was done to predict the duration of ventilator support based on electrolyte levels at admission. A significant regression equation was found (Likelihood Ratio Chi square = 36.25), with an R2 of 0.0623. The predicted duration of ventilator requirement is equal to 5.86 – 1.53 x Mg level – 0.002 x Na level – 0.59 x K level – 0.05 x Ca level, where the levels are measured in meq/l. Duration of ventilator support decreased by 1.53 days for each unit increase in Mg and only Mg level was found to be a significant predictor in the adjusted analysis.

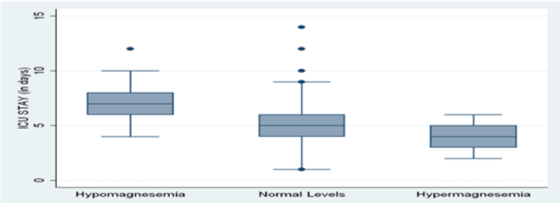

Figure 5: Box plot showing ICU stay with different levels of magnesium

Duration of ICU stay is significantly higher in those with hypomagnesemia with p value <.001. On an average, those with hypomagnesemia stayed in ICU for an extra 2 days compared to those with normal magnesium levels.

As per [Table 5] Poisson regression analysis adjusted with other electrolyte levels was done to predict the duration of ICU stay based on Magnesium levels at admission. Robust standard errors for the parameter estimates were obtained. A significant regression equation was found (Chi Square = 41.55), with an R2 of 0.03. The predicted ICU stay is equal to 3.48 – 0.22 x Mg level – 0.01 x Na level – 0.001 x K level - 0.02 x Ca level, where the levels are measured in mEq/l. ICU stay decreased by 0.22 days, 0.01 days, 0.001 days & 0.02 days for each unit increase in Mg, Na, K & Ca levels respectively. Both Mg & Na level were found to be significant predictors in the adjusted analysis. ICU stay of patients ranged from 1 to 14 days with a mean of 5.21 ± 2.1 days.

As per [Table 6] there was significant difference of all electrolyte levels at admission between the patients who expired from ICU and those who were shifted out to ward with those with higher parameters having good prognosis. The differences were statistically significant with p value < .001.

Table 1: Age and Gender-wise Categories

Interval	N	%
10 – 19	9	4.4
20 – 29	31	15.0
30 – 39	36	17.5
40 – 49	51	24.8
50 – 59	38	18.4
60 – 69	26	12.6
70 – 79	10	4.8

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80 – 89	5	2.4
	206	100

Table 2: Association between APACHE 2 score and electrolyte levels (results of multiple linear regression)

Predictor	Coefficient	CI	p value
Mg	-3.08	-4.99, -1.16	.002
Na	-0.13	-0.25, -0.01	.04
K	-1.18	-2.50, 0.13	.08
Ca	-0.61	-1.20, -0.02	.04

Table 3: Hypomagnesemia and Duration of Ventilator support

Magnesium level	Mg level < 1.6	Mg level ≥ 1.6	p value
Ventilator days	5.5 ± 1.5	4.1 ± 1.8	.004

Table 4: Association between duration of Ventilator support and Magnesium levels

Predictor	Coefficient	CI	p value
Mg	-1.53	-2.56, -0.50	.004
Na	-0.002	-.06, 0.06	.954
K	-0.59	-1.28, 0.10	.096
Ca	-0.05	-0.32, 0.22	.718

Table 5: Association between duration of ICU stay and electrolyte levels (results of multiple linear regression)

Predictor	Coefficient	CI	p value
Mg	-0.22	-0.35, -0.07	.003
Na	-0.01	-0.02, -0.001	.03
K	-0.001	-0.09, 0.08	.988
Ca	-.02	-0.07, 0.03	.467

Table 6: Final status of the patient and electrolyte levels at admission

	Final status		
	Expired	**Shifted to ward**	**p value**
Mg levels at admission	1.35 ± 0.25	2.04 ± 0.36	< .001
Na Levels at admission	128.61 ± 6.6	136.64 ± 5.84	< .001
K Levels at admission	3.17 ± 0.30	4.04 ± 0.57	< .001
Ca levels at admission	8.05 ± 1.15	9.18 ± 1.03	<.001

Table 7: Prevalence of hypomagnesemia among patients admitted to ICU (in previous studies)

Study	Year	No.of patients	Prevalence
Chernow et al,[13]	2007	100	51%
Fairley et al,[14]	2003	422	18%
Baker et al,[15]	1996	179	44%
Griffitth et al,[16]	2000	226	45%
Huijigen et al,[17]	2000	115	14%
Rubiez et al,[18]	1993	197	20%

DISCUSSION

A total of 206 patients who satisfied the inclusion criteria were included in my study. In this study the majority of patients were in the age group 40 to 49 years. The mean age of patients in my study was 44. Out of 206 patients 128 were males and 78 were females i.e. most of the patients were males (62.1%). The mean magnesium levels of patients admitted to ICU was 1.95. Among the study population (206),36 patients (17.4%) had hypomagnesemia. In comparison with the previous studies.

The mean APACHE 2 score of patients in my study was 14. According to study conducted by Siddique S Khan et al,[19] in the Intensive Care Unit (ICU) of the Aga Khan University Hospital, Karachi, mean APACHE-II score recorded in this study was 20.84. Thus the duration of ICU stay decreased by 0.22 days for each unit increase in serum magnesium levels.

In my study out of 206 patients ,51 required ventilator support. Among the 51 patients who required ventilator support, 32 had hypomagnesemia. Majority of patients (75.24%) did not require ventilator support during ICU stay. Also when comparing the serum magnesium levels with that of requirement of ventilator support it is found that there is a 30% decrease in need for ventilator support for every 0.1 mEq/l increase in serum magnesium levels.

In the study conducted by C S Lismaye et al,[20] it was found that patients with hypomagnesemia needed ventilator support more frequently and for a longer duration. In a study conducted by Soliman et al,[21] it was found that patients with low magnesium were on ventilator support for more number of days.

In my study majority of patients (86.41%) survived. The mortality was 13.59%. Comparing the serum magnesium levels with outcome of the patients there was 33% decreased chance of mortality for every 0.1 mEq/l increase in serum magnesium levels. A higher mortality rate was detected in hypomagnesemic patients as compared to normomagnesemic patients in study conducted by Rubiez et al,[18] (46% vs 25%)

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and Safavi et al (55% vs 35%).[12] The relationship between hypomagnesemia and mortality rate varies from study to study.

CONCLUSION

This study highlights the role of magnesium monitoring in critical illness and its value for favourable outcome. It adds to the scarce Indian data regarding magnesium homeostasis in ICUs. The need for invasive ventilation and duration of invasive ventilation were significantly higher among the patients with hypomagnesemia compared to the patients with normal magnesium levels (p-value <0.05). Mortality was higher in the cases than in the controls (p-value <0.05). Development of hypomagnesemia during an ICU stay is associated with a worse prognosis. It is often associated with the development of sepsis. Monitoring of magnesium levels may have prognostic, and perhaps therapeutic, implications.

REFERENCES

1. Herroeder S, Schönherr ME, Hert SGD, Hollmann MW. Magnesium—essentials for anesthesiologists. Anesthesiology 2011;114:971 93.
2. Guerrera MP, Volpe SL, Mao JJ. Therapeutic uses of magnesium. Am Fam Physician 2009;80:157e62
3. Wacker, W.E.C.; Parisi, A.F. Magnesium Metabolism. N. Engl. J. Med. 1968, 278, 712–717.
4. Yunes, P.; Mojtaba, M.; Atabak, N.; Mohammad, R.G.; Mohammad, A.; Mohammad, S. et al. The role of magnesium sulfate in the intensive care unit. EXCLI J. 2017, 16, 464–482.
5. Mazur, A.; Maier, J.A.M.; Rock, E.; Gueux, E.; Nowacki, W.; Rayssiguier, Y etal. Magnesium and the inflammatory response: Potential physiopathological implications. Arch. Biochem. Biophys. 2007, 458, 48–56.
6. Cascella, M.; Vaqar, S. Hypermagnesemia. In StatPearls; StatPearls Publishing: Treasure Island, FL, USA, 2023.
7. Hansen, B.-A.; Bruserud, Ø. Hypomagnesemia in critically ill patients. J. Intensive Care 2018, 6, 21.
8. Van Laecke, S. Hypomagnesemia and hypermagnesemia. Acta Clin. Belg. 2019, 74, 41–47.
9. Muir, K.W.; Lees, K.R.; Ford, I.; Davis, S. Intravenous Magnesium Efficacy in Stroke (IMAGES) Study Investigators. Magnesium for acute stroke (Intravenous Magnesium Efficacy in Stroke trial): Randomised controlled trial. Lancet 2004, 363, 439–445.
10. Saver, J.L.; Starkman, S.; Eckstein, M.; Stratton, S.J.; Pratt, F.D.; Hamilton, S.; Conwit, R.; Liebeskind, D.S.; Sung, G.; Kramer, I.; et al. Prehospital Use of Magnesium Sulfate as Neuroprotection in Acute Stroke. N. Engl. J. Med. 2015, 372, 528–536.
11. Sen, A.P.; Gulati, A. Use of magnesium in traumatic brain injury. Neurotherapeutics 2010, 7, 91–99.
12. Safavi M, Honarmand A. Admission hypomagnesemia - Impact on mortality or morbidity in critically ill patients. Middle East J Anesthesiol. 2007;19:645–60.
13. Chernow B, Bamberger S, Stoiko M, Vadnais M, Mills S, Hoellerich V, et al. Hypomagnesemia in patients in postoperative intensive care. Chest. 1989;95:391–7.
14. Fairley, J.L.; Zhang, L.; Glassford, N.J.; Bellomo, R. Magnesium status and magnesium therapy in cardiac surgery: A systematic review and meta-analysis focusing on arrhythmia prevention. J. Crit. Care 2017, 42, 69–77.
15. Baker, W.L. Treating arrhythmias with adjunctive magnesium: Identifying future research directions. Eur. Heart J. Cardiovasc. Pharmacother. 2017, 3, 108–117.
16. Griffiths, B.; Kew, K.M. Intravenous magnesium sulfate for treating children with acute asthma in the emergency department. Cochrane Database Syst. Rev. 2016, 4, CD011050.
17. Huijgen HJ, Soesan M, Sanders R, Mairuhu WM, Kesecioglu J, Sanders GT. Magnesium levels in critically ill patients. What should we measure? Am J Clin Pathol. 2000;114(5):688–695.
18. Rubeiz GJ, Thill-Baharozian M, Hardie D, Carlson RW. Association of hypomagnesemia and mortality in acutely ill medical patients. Crit Care Med. 1993;21:203–9. [PubMed] [Google Scholar]
19. Said Khan SM, Aly WW. Magnesium levels among critically ill elderly patients-mortality and morbidity correlations. Advances in aging research. 2014;3(1):12
20. C S Limaye 1, V A Londhey, M Y Nadkart, N E Borges. Hypomagnesemia in critically ill medical patients; J Assoc Physicians India2011 Jan:59:19-22.
21. Soliman HM, Mercan D, Lobo SS, Mélot C, Vincent JL. Development of ionized hypomagnesemia is associated with higher mortality rates. Crit Care Med. 2003;31:1082–1087. [PubMed] [Google Scholar]