International Journal of Advances in Medicine
Khare AR et al. Int J Adv Med. 2020 Jan;7(1):155-160
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: http://dx.doi.org/10.18203/2349-3933.ijam20195663

Original Research Article

Evaluation of admission serum magnesium levels in patients with septic shock and its correlation with outcome

Akshay R. Khare, Vishwanath C. Patil*, Jignesh N. Shah, Shivakumar S. Iyer

Department of Critical Care Medicine, Bharati Vidyapeeth Deemed to be University Medical College and Hospital, Pune, Maharashtra, India

Received: 19 November 2019
Revised: 30 November 2019
Accepted: 11 December 2019

***Correspondence:**
Dr. Vishwanath C. Patil,
E-mail: vishwanath629@yahoo.com

ABSTRACT

Background: Admission hypomagnesemia has been linked with an increased risk of septic shock. The purpose of this study was to evaluate admission serum magnesium levels in patients with septic shock and to determine its correlation with the outcomes.
Methods: It was a prospective observational study. Total 50 patients fitting the Sepsis-3 definition between time period of June 2017 to November 2018 were included in the study. Patients with suspected infection were identified at the bedside with qSOFA. Admission serum magnesium levels was measured for all patients included. APACHE II scores were calculated at the end of 24 hours after admission. Routine standard of care treatment was provided to all patients. The patients were monitored for organ dysfunctions based on daily SOFA scores, ventilator free days, vasopressors free days, dialysis free days, length of intensive care unit stay, length of hospital stay. The data was analysed using Statistical Package for Social Sciences for MS Windows.
Results: In this study hypomagnesemia was prevalent in 18%, normomagnesemia in 62% and hypermagnesemia in 20% of total included patients. The mean vasopressor free days in Hypomagnesemia group (7.11±12.79 days) were higher than those in normomagnesemic patients (5.06±5.51 days) and hypermagnesemia patients (1.70±3.09 days). Out of total 50 patients 18 died and 32 recovered. 11 patients out of 32 who recovered had abnormal admission serum magnesium levels whereas 8 pts out of 18 who died had abnormal admission serum magnesium levels. SOFA score in hypomagnesemic patients admitted with septic shock compared with those of normomagnesemic and hypermagnesemic patients was statistically significant.
Conclusions: Author did not find any statistically significant correlation between admission magnesium levels in septic shock patients and outcomes although SOFA score was higher in hypomagnesemic patients admitted with septic shock compared with those of normomagnesemic and hypermagnesemic patients. Serum magnesium may not truly reflect body's magnesium status. RBC magnesium may need to be studied to see whether it is a more reliable biomarker.

Keywords: Hypomagnesemia, Septic shock, Sequential organ failure assessment

INTRODUCTION

The global burden of sepsis is substantial with an estimated 15 to 19 million cases per year; the vast majority of these cases occur in low-income countries.[1] Septic shock is the most common cause of mortality in critically ill patients with a mortality rate reported to be as high as 50%.[2] Magnesium (Mg) is the fourth most abundant cation in the body and the second most abundant intracellular cation after potassium. It acts as a cofactor for more than 300 enzymes regulating vital functions like muscle contraction, neuromuscular conduction, glycemic control, myocardial contraction,

blood pressure, energy production, active transmembrane transport for other ions, synthesis of nuclear materials and bone development.[3]

Admission hypomagnesemia (Sr.Mg <1.5 mg/dL) has been linked with an increased risk of septic shock. Mg has been known to play an important role in the regulation of immune systems and inflammatory response and the release of nitric oxide.[2]

Hypermagnesemia on the other hand can cause serious deleterious effects. Mg can block the synaptic transmission of nerve impulses and causes the initial loss of deep tendon reflexes, flaccid paralysis and apnea. It can also cause hypotension, bradycardia, prolonged QRS duration and complete heart block.[4]

Studies with magnesium (Mg) and Magnesium Sulphate (MgSO4) have shown a peripheral (predominantly arteriolar) vasodilator effect with preserved cardiac function, within a large safety margin, not only indirectly by an endothelium-dependent release of Nitric Oxide (NO) but also directly via its ability to induce endothelium- independent vasodilation by a direct action on vascular smooth muscle as a calcium competitor. In addition to vasodilatory effects, infusion of MgSO4 is also associated with other potential pro-microcirculatory effects, such as an increase in red blood cell deformability, reduction of platelet aggregation, anti-inflammatory effects and maintenance of endothelial integrity.[5]

In a study by Rubeiz et al, they found that the APACHE II scores were similar in ICU patients with hypomagnesemia versus patients without hypomagnesemia, however, the mortality was significantly higher in the hypomagnesemia group.[6,7]

Microcirculatory alterations have a critical role in sepsis and persist despite correction of systemic hemodynamic parameters. Mg is involved in both endothelium-dependent and non-endothelium-dependent vasodilatory pathways. As cell membrane calcium channels are Mg dependent and Mg seems to be a factor regulating sepsis-associated calcium entry, Mg is strongly correlated with calcium ion entry in septic shock.[8]

The purpose of this study was to evaluate admission serum magnesium levels in patients with septic shock (as per the Sepsis-3 definition) and to determine its correlation to the outcomes.[9]

Objective of the study was to assess Serum Magnesium levels in patients with septic shock admitted to intensive care unit and follow such patients for progression of organ failures with Sequential Organ Failure Assessment (SOFA) score.[10]

To compare admission APACHE II score with admission Serum Magnesium levels in patient with Septic shock to correlate admission Serum Magnesium levels in patient with septic shock with ICU and Hospital mortality. To correlate admission Serum Magnesium levels in patients with septic shock with length of stay in ICU, Hospital length of Stay, Dialysis free days, Vasopressor free days and Ventilator free days.

METHODS

The present study was conducted at the attached teaching hospital after approval of the institutional Ethics Committee.

Study design was a prospective observational study. All patients admitted to intensive care unit were screened for septic shock.[9]

Inclusion criteria

- All patients admitted to intensive care unit with signs of septic shock as per the Sepsis-3 definition.

Exclusion criteria

- Patients who have received magnesium prior to transfer to intensive care unit. E.g. patients on magnesium containing antacids
- Patients on aminoglycosides, amphotericin B, thiazides
- Patients with chronic kidney disease requiring dialysis
- Patients with malabsorption syndromes or those who have undergone intestinal resections
- Patients below 18 years age.

Total 50 patients fitting the Sepsis-3 definition between time period of June 2017 to November 2018 were included in the study

Methodology of study was carried out on a group of patients who fulfil the inclusion criteria.

Materials

- Monitoring equipment
- Serum Magnesium levels
- APACHE II scoring system[7]
- SOFA scores[10]

Written informed consent was obtained from all patients prior to inclusion into the study. Date and address were confirmed from all patients. Patients with suspected infection were identified at the bedside with qSOFA, i.e. alteration in mental status, systolic blood pressure ≤100 mm Hg, or respiratory rate ≥22/min.[11] Patients with septic shock were identified with a clinical construct of sepsis with persisting hypotension requiring vasopressors to maintain MAP ≥65 mm Hg and having a serum lactate level >2 mmol/L (18 mg/dL) despite adequate volume

resuscitation. Septic shock is a subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality.

Admission serum magnesium levels was measured for all patients included. Normal reference range for Serum Magnesium is 1.6 to 2.5 mg/dL. Hypomagnesemia is defined as serum magnesium <1.6 mg/dL, Hypermagnesemia is defined as serum magnesium >2.5 mg/dL. The Randox Xylidil Blue Colorimetric method was used for estimation of serum Magnesium levels in laboratory. APACHE II scores were calculated at the end of 24 hours after admission.

Routine standard of care treatment like resuscitation, cultures and antibiotics was provided to all patients. The patients were monitored for organ dysfunctions based on daily SOFA scores, ventilator free days, vasopressors free days, dialysis free days, length of intensive care unit stay, length of hospital stay.

Anticipated Risk Factors: No risks involved.

Data analysis

The data was statistically analyzed using Statistical Package for Social Sciences (IBM SPSS version 25) for MS Windows. The data on qualitative characteristics was presented in percentages. The data on quantitative characteristics was presented as Mean±Standard deviation (SD). On the basis of laboratory results the patients were divided into 3 groups Hypomagnesaemia, Normomagnesemia and Hypermagnesemia on admission. The statistical significance of difference in qualitative characteristics was tested using Chi-Square test. The statistical significance of inter-group difference of mean of quantitative variables was tested using unpaired 't' test. The statistical significance of intra-group difference of mean of quantitative variables was tested using Analysis of Variance (ANOVA), p-values less than 0.05 was considered to be statistically significant.

RESULTS

The study included 50 patients with the youngest patient being 18 years and the oldest 72 years. Baseline characteristics of study population are shown in table 1. On admission, 18% (09/50) patients had hypomagnesemia, 62% (31/50) had hypermagnesemia and 20% (10/20) had normal serum magnesium levels. The lowest serum magnesium value recorded was 0.9mg/dL while the highest value was 3.53 mg/dL. There was no statistically significant variation of age, gender amongst the groups. There was no statistically significant difference in admission magnesium levels among both diabetic and non-diabetic patients.

Table 1: Baseline characteristics of study population.

Study variable	Hypo Mg (N=9)	Normo Mg (N=31)	Hyper Mg (N = 10)	p value
Age (years)	48.22	49.26	51.60	0.83
Male	8	22	8	0.512
Female	1	9	2	
Diabetes	1	8	3	0.585
Mean Lactate	2.38±0.73	3.12±2.44	4.19±2.44	0.38
Mean P/F ratios	173.60±91.42	179.04±80.53	158.83±93.92	0.81
Mean SOFA	7.44±1.42	9.03±2.69	10.40±3.10	0.06
Mean APACHE II	14.67±3.57	17.5±6.64	17.90±6.30	0.43

Distribution of patients as per organ system involvement as per SOFA scores is shown in (Table 2). There was no statistically significant difference in the groups with respect to distribution of various organ involvements in septic shock patients. Need for ventilation and dialysis among different groups is depicted in table 3. There was no statistically significant difference in need for ventilation and dialysis across various magnesium levels. Co-relation between magnesium level and Vasopressors free days, Ventilator free days (ICU stay minus days on ventilator), Dialysis free days, ICU Length of Stay, Hospital Length of Stay is shown in table 4. The mean vasopressor free days in Hypomagnesemia group (7.11±12.79 days) were higher than those in normomagnesemic patients (5.06±5.51 days) and hypermagnesemia patients (1.70±3.09 days). When compared using the ANOVA test, the difference was statistically not significant. On applying the unpaired t test between the above groups, the mean vasopressor free days in Normomagnesemia group were 5.06±5.51 days and in the hypermagnesemia group were 1.70±3.09 days. This difference was statistically significant. The mean dialysis free days in the hypomagnesemia group were 14.43±12.70, in Normomagnesemia group were 14.45±14.04 days and in the hypermagnesemia group were 7.60±5.44 days. The difference was not statistically significant.

Table 2: Organ system involvement as per SOFA scores.

Organ system involvement		Hypo Mg (No of patients)	Normo Mg (No of patients)	Hyper Mg (No of patients)	Total	Chi sq	p value
CNS	Yes	3	10	0	13	4.396	0.111
	No	6	21	10	37		
Renal	Yes	2	15	3	20	2.510	0.285
	No	7	16	7	30		
CVS	Yes	9	31	10	50		
Liver	Yes	2	3	0	5	2.609	0.271
	No	7	28	10	45		
Lungs	Yes	5	15	5	25	0.143	0.931
	No	4	16	5	25		
Haematology	Yes	2	11	2	15	1.179	0.554
	No	7	20	8	35		
Total	Yes	23	85	20			
Total	No	31	101	40			

Table 3: Need for ventilation and dialysis.

Study variables	Hypo Mg		Normo Mg	Hyper Mg	Total	Chi sq	p value
Need for Ventilation	Yes	4	19	6	29	0.833	0.659
	No	5	12	4	21		
Need for dialysis	Yes	0	6	3	9	2.990	0.224
	No	9	25	7	41		
Total		9	31	10	50		

Out of total 50 patients 18 died and 32 recovered.[11] patients out of 32 who recovered had abnormal admission serum magnesium levels whereas 21 were normomagnesemic. 8/18 who died had abnormal admission serum magnesium levels and 10/18 who died were normomagnesemic. The p value was 0.481.

Table 4: Co-relation between magnesium level and vasopressors free days, ventilator free days (ICU stay minus days on ventilator), dialysis free days, ICU length of stay, hospital length of stay.

Variables	Group	Mean	SD	p value
Vasopressors free days (ICU Stay minus days on vasopressor)	Hypo Mg	7.11	12.79	0.24
	Normo Mg	5.06	5.51	
	Hyper Mg	1.70	3.09	
	Total	4.76	7.07	
Ventilator free days (ICU stayminus days on ventilator)	Hypo Mg	3.56	2.65	0.51
	Normo Mg	6.61	10.05	
	Hyper Mg	4.00	4.47	
	Total	5.54	8.28	
Dialysis free days	Hypo Mg	14.33	12.7	0.32
	Normo Mg	14.45	14.04	
	Hyper Mg	7.6	5.44	
	Total	13.06	12.65	
ICU length of Stay	Hypo Mg	10.67	12.90	0.58
	Normo Mg	10.03	7.39	
	Hyper Mg	7.10	6.51	
	Total	9.56	8.36	
Hospital length of Stay	Hypo Mg	14.33	12.70	
	Normo Mg	15.29	13.90	
	Hyper Mg	8.80	7.33	
	Total	13.82	12.69	

Table 5: Mortality outcomes.

		Abnormal Mg	Normal Mg	Total	P value
Mortality Outcome	Recovered	11	21	32	0.481
	Died	8	10	18	
	Total	19	31	50	
		42%	32%		

DISCUSSION

The aim of this study was to evaluate the admission serum magnesium levels in patients with septic shock and its correlation with outcome. In this study author did not find any statistically significant relation between distribution of age and gender across the study population.

This distribution of patients across these 3 groups was as follows: Hypomagnesemia 9/50(18%) Normomagnesemia in 31/50(62%) Hypermagnesemia in 10/20(20%) which was similar to study findings done by Soliman et al.[12] Author found a higher incidence of diabetes among the hypermagnesemic group as compared to the hypomagnesemic group. This finding is similar to those of Thongprayoon C et al.[2] Although the relationship between magnesium and diabetes has been studied and also found to be significant by other studies whether the relationship is causal is not clear.

Many studies have demonstrated a statistically significant relation between the incidence of hypomagnesemia and the occurrence of sepsis Limaye et al, 38% patients with hypomagnesemia were septic, Kumar et al, 34% patients with hypomagnesemia were septic.[13,14] In our study author looked at only septic shock patients and their correlation with magnesium and SOFA score. Authors did not find any literature on patients with septic shock where the causal relationship of magnesium with SOFA score has been studied.

The finding of this study of a longer duration of mechanical ventilation in the hypomagnesemic patients was similar to the studies done by Safavi et al, Limaye et al, and Gupta et al.[15,13,16]

The findings of this study were that the vasopressor free days were higher in hypomagnesemic patients than in hypermagnesemic patients. This suggests that vasopressors were required for a longer period in hypermagnesemic patients. This finding was similar to the observations of Celi et al.[17] Author did not come across any studies in a septic shock population correlating serum magnesium values with vasopressor free days.

In this study the mean baseline creatinine was also higher in the hypermagnesemic group (mean creatinine value 1.56 mg/dL) suggesting that there may be an underlying element of subclinical AKI in this subset. Authors did not find any studies looking at dialysis free days in septic shock patients with dysmagnesemia.

Although in this study the mean duration of ICU stay was higher in hypomagnesemia group than in hypermagnesemia group, this difference was not statistically significant. The studies done by Chernow et al, 1989 Limaye et al, 2011 they did not find any statistically significant correlation between length of ICU stay and magnesium levels.[18,13]

In this study This difference between hypomagnesemia and hypermagnesemia groups was not statistically significant. Of the 32 that survived, 11 patients (34%) had abnormal magnesium values. These results were not statistically significant.

Jiang Pan et al, 2017 performed a systematic review and meta-analysis to evaluate the association of serum magnesium level with prognosis of critically ill patients upon admission to the ICU.[10,19] studies comprising 1,122 cases and 630 controls were finally selected for analysis. The patients with hypomagnesemia had higher mortality rate (risk ratio [RR] 1.76; 95% Confidence Interval [CI] 1.54-2.00; $p<0.00001$).

In this study of 50 patients with septic shock hypomagnesemia was prevalent in 18%, normomagnesemia in 62% and hypermagnesemia in 20%.

Author found the following correlations to be statistically significant

- SOFA score in hypomagnesemic patients admitted with septic shock with those of normomagnesemic and hypermagnesemic patients was statistically significant (p value 0.027 and 0.018 respectively).
- Vasopressor free days between normomagnesemic and hypermagnesemic patients (p value 0.022).
- Dialysis free days between normomagnesemic and hypermagnesemic patients (p value 0.031).

There was no statistically significant correlation between the groups with respect to APACHE II score, need for mechanical ventilation and dialysis, ventilator free days, length of ICU stay, hospital length of stay and mortality.

CONCLUSION

Correlation between admission magnesium levels in septic shock patients and final outcomes were not statistically significant. Serum magnesium may not truly reflect body's magnesium status. RBC magnesium may be a more reliable biomarker. The findings of our study need to be looked at in a larger population.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Marik PE, Khangoora V, Rivera R, Hooper MH, Catravas J. Hydrocortisone, vitamin C, and thiamine for the treatment of severe sepsis and septic shock: a retrospective before-after study. Chest. 2017;151(6):1229-38.
2. Thongprayoon C, Cheungpasitporn W, Erickson SB. Admission hypomagnesemia linked to septic shock in patients with systemic inflammatory response syndrome. Renal Failure. 2015;37(9):1518-21.
3. Al Alawi AM, Majoni SW, Falhammar H. Magnesium and human health: perspectives and research directions. Int J Endocrinol. 2018.
4. Topf JM, Murray PT. Hypomagnesemia and hypermagnesemia. Rev Endocrine Metab Dis. 2003;4(2):195-206.
5. Pranskunas A, Vellinga NA, Pilvinis V, Koopmans M, Boerma EC. Microcirculatory changes during open label magnesium sulphate infusion in patients with severe sepsis and septic shock. BMC Anesthesiol. 2011;11(1):12.
6. Rubeiz GJ, Thill-Baharozian MA, Hardie DO, Carlson RW. Association of hypomagnesemia and mortality in acutely ill medical patients. Crit Care Med. 1993;21(2):203-9.
7. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. Critical Care Med. 1985;13(10):818-29.
8. Velissaris D, Karamouzos V, Pierrakos C, Aretha D, Karanikolas M. Hypomagnesemia in critically ill sepsis patients. J Clin Med Res. 2015;7(12):911.
9. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA. 2016;315(8):801-10.
10. Vincent JL, Moreno R, Takala J, Willatts S, De Mendonça A, Bruining H, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. Int Care Med. 1996 July;22(7):707-10.
11. Seymour CW, Liu VX, Iwashyna TJ, Brunkhorst FM, Rea TD, Scherag A, et al. Assessment of clinical criteria for sepsis: for the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016;315(8):762-74.
12. Soliman HM, Mercan D, Lobo SS, Mélot C, Vincent JL. Development of ionized hypomagnesemia is associated with higher mortality rates. Critical Care Med. 2003;31(4):1082-7.
13. Limaye CS, Londhey VA, Nadkart MY, Borges NE. Hypomagnesemia in critically ill medical patients. J Assoc Phys Ind. 2011;59(1):19-22.
14. Kumar S, Honmode A, Jain S, Bhagat V. Does magnesium matter in patients of Medical Intensive Care Unit: A study in rural Central India. Ind J Crit Care Med: Peer-Reviewed, Official Publication Indian Soc Critical Care Med. 2015;19(7):379.
15. Safavi M, Honarmand A. Admission hypomagnesemia--impact on mortality or morbidity in critically ill patients. Middle East J Anaesthesiol. 2007;19(3):645-60.
16. Gupta SS, Bindra GS, Batada V, Gupta AK. To study serum magnesium level and its correlation with prognostic significance in critically ill patients. J Ind Acad Clin Med. 2016;17(1):37.
17. Celi LA, Scott DJ, Lee J, Nelson R, Alper SL, Mukamal KJ, et al. Association of hypermagnesemia and blood pressure in the critically ill. J Hypertension. 2013;31(11):2136.
18. Chernow B, Bamberger S, Stoiko M, Vadnais M, Mills S, Hoellerich V, et al. Hypomagnesemia in patients in postoperative intensive care. Chest. 1989;95(2):391-7.
19. Jiang P, Lv Q, Lai T, Xu F. Does hypomagnesemia impact on the outcome of patients admitted to the intensive care unit? A systematic review and meta-analysis. Shock: Injury, Inflammation, Sepsis: Lab Clin Approaches. 2017;47(3):288-95.

Cite this article as: Khare AR, Patil VC, Shah JN, Iyer SS. Evaluation of admission serum magnesium levels in patients with septic shock and its correlation with outcome. Int J Adv Med 2020;7:155-60.