Section: Community Medicine

Original Research Article

A STUDY ON SERUM MAGNESIUM IN PATIENTS ADMITTED IN MEDICAL CRITICAL CARE UNIT OF A TERTIARY CARE HOSPITAL

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Abstract

Background: Magnesium is the fourth most abundant cation in the human body and the second most common intracellular cation. It is an important cofactor of many enzyme systems in the body. Magnesium plays an important role in neuromuscular excitability and cardiac function[1]. Hypomagnesemia is one of the common electrolyte abnormalities in critically ill patients. But unfortunately, it is underdiagnosed in clinical practice. Magnesium plays an important role in sepsis. Hypomagnesemia is associated with increased release of endothelin and proinflammatory cytokines. Hypomagnesemia is associated with diabetes mellitus due to increased renal loss of Magnesium with glycosuria. The normal reference value of serum magnesium is 1.5 mg/dl to 2.5 mg/dl. Patients with magnesium levels less than 1.5 mg/dl were considered to have hypomagnesemia[2]. Hypomagnesemia leads to muscle weakness and respiratory failure, causing difficulty in weaning the patient from the ventilator and prolonged hospital stay. Analyse prognostic value of serum magnesium in patients admitted to critical care unit of a Tertiary Care Centre Hospital. **Materials and Methods:** This prospective observational study was conducted in acute medical care and respiratory Intensive care units in SVRRGGH, Tirupati. The study was conducted for a period of 1 year (From May 2020 to April 2021) on 150 subjects.This study population was analysed to estimate serum Magnesium level and to correlate serum magnesium level with variables like length of stay in critical care unit, need for ventilatory support, duration of ventilatory support and mortality. **Result:** A total of 150 patients admitted in critical care unit of our hospital were selected for study. Among 150 patients, 109 were males and 41 were females. The mean age (Years) in this study was 48.13±15.46. The mean (SD) of serum magnesium (mg/dL) was 1.99+/-0.79. The median (IQR) of serum magnesium (mg/dL) was 1.83. The serum magnesium (mg/dL) ranged from 0.24 - 4.24 in this study.44.7% of the participants had low serum magnesium. 30.7% of the participants had normal magnesium level. 24.7% of the participants had high magnesium level. The mean serum magnesium (mg/dL) was 1.99 ± 0.79.The mean (SD) of APACHE-II Score was 14.74+/-6.68. The median (IQR) of APACHE-II Score was 14.00 (10-20). The APACHE-II Score ranged from 0 – 30 in the present study. **Conclusion:** The mean serum magnesium level in this study is 1.99+0.79 mg%. 44.7% of patients had low serum magnesium levels. 30.7% of patients had normal magnesium levels. 24.7% of patients had high serum magnesium levels. APACHE II score was high in patients with low serum magnesium levels. Duration of ICU stay was longer in patients with low serum magnesium levels. There was no statistically significant association between serum magnesium level and need for ventilator in this study.

INTRODUCTION

Magnesium is an essential electrolyte that plays an important role in many enzyme systems of the body. Hypomagnesemia is common in hospitalised patients, which results in fatal complications if not treated properly. Hypomagnesemia may coexist with other electrolyte abnormalities like hypokalemia and hypocalcemia.[3]Recommended dietary allowance of the Magnesium is 400 to 420 mg daily for men and 310-320 mg for women. Pregnant women need 350-360mg, and lactating mothers need 310-320 mg daily.[2]Under normal conditions, 30% to 50% of dietary Magnesium is absorbed.The kidney is the primary site of Magnesium homeostasis. About 2.4g of Magnesium is filtered each day, and 100-120 mg is normally excreted in the urine.The normal reference range of serum Magnesium levels is 1.5 to 2.5 mg%.[2] In the body, Magnesium exists in four forms: a) Intracellular Magnesium b) Protein-bound Magnesium c) Magnesium bound to anions and d) Ionised Magnesium. Intracellular stores contribute to 99% of total body magnesium. Serum magnesium corresponds to 0.3% of total body magnesium. Ionised magnesium is the active form of Magnesium in the plasma. Intracellular Magnesium can be estimated using circulating RBC, mononuclear cells and skeletal muscle cells.

As Magnesium has a role in regulating smooth muscle tone, low magnesium levels can result in Bronchial airway constriction, Neuromuscular hyper excitability, Coronary vasospasm and seizure.[3]Hypokalemia with hypomagnesemia is relatively refractory to potassium correction until magnesium level is corrected as Magnesium is essential for membrane ATPase activity.[4]

Age, type of ICU admission (after elective surgery vs nonsurgical or after emergency surgery), chronic health problems and 12 physiologic variables (the worst value for each in the first 24 hours after ICU admission) are used to derive APACHE II score which is widely used in ICU to monitor the prognosis. This study was conducted to look for any association between serum magnesium levels and APACHE II score, need for ventilatory support, duration of ICU stay and mortality.

MATERIALSANDMETHODS

Study Design and Setting

This prospective observational study was conducted from May 2020 to April 2021, in the department of General Medicine of S V R R G General Hospital, Tirupati, Andhra Pradesh, India.Total 150 patients admitted in Acute medical care and respiratory intensive care units were included in the study. The study was approved by the institutional Scientific and Ethics Committee at Sri venkateswara Medical College, Tirupati, dated 01/02/2020, Lr.No.18/2020. Written informed consent was taken from all the participants/LAR at the time of enrollment.

Inclusion Criteria

Patients with age more than 18 years diagnosed with any medical illness and admitted in Acute Medical Care unit of Sri VenkateswaraRamnarainRuia Government General Hospital, Tirupati.

Exclusion Criteria

Patient who received Magnesium prior to transfer to Acute Medical Care or Respiratory intensive care unit.

Study Procedure

The study included patients admitted in AMC and RICU through OPD and emergency. Detailed history and clinical examination was performed and records were checked to confirm the presence of comorbidities such as Diabetes, Hypertension, Coronary Artery disease and other illnesses. Complete hemogram, Serum creatinine, serum electrolytes, liver function tests were done. During the hospital stay, patients were followed up with daily clinical examinations. Serum magnesium level in patients admitted to critical care unit was estimated and correlated with patient outcome regarding length of stay in the critical care unit, need for ventilatory support, duration of ventilatory support and mortality.

Analysis

The descriptive statistical analysis was performed to report the demographic variables. The data are reported as mean and standard deviation, as well as in percentage of the total population. One way Analysis of Variance (ANOVA) is performed to analyse the association between the variables. The significance is kept at 95% and a p-value less than 0.05 shows statistical significance. Post-hoc analysis is used to identify the significance level between the groups in a one-way ANOVA analysis. The data collected are analysed using IBM SPSS statistics version 20.0 (IBM Corp. Released 2011. IBM SPSS Version 20.0. Armonk, NY).

RESULTS

A total of 150 patients admitted in critical care unit of our hospital were selected for study. Among 150 patients, 109 were males and 41 were females. In the present study 72.7% patients are males and 27.3% are females. Male female ratio in the present study is 2.66.The mean Age (Years) in this study was 48.13±15.46. Majority of the patients belong to age group 41-50 year followed by 31-40 year and 51-60 year. Age ranged from 18 year to 89 year in this study.The means (SD) of serum magnesium (mg/dL) was 1.99+/-0.79. The median (IQR) of serum magnesium (mg/dL) was 1.83. The serum magnesium (mg/dL) ranged from 0.24 - 4.24 in this study.44.7% of the participants had low serum magnesium. 30.7% of the participants had normal magnesium level. 24.7% of the participants had high magnesium level. The mean serum magnesium

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(mg/dL) was 1.99 ± 0.79.Out of total 150 patients, 67 were in low serum magnesium group, 46 in normal serum magnesium group and 37 in high serum magnesium group. Majority of the patients in the present study belong to low serum magnesium group.

Shapiro-Wilk test was used to find correlation between serum magnesium level and APACHE II score. The mean (SD) of APACHE-II Score was 14.74+/-6.68. The median (IQR) of APACHE-II Score was 14.00 (10-20). The APACHE-II Score ranged from 0 – 30 in the present study. The mean Duration of Stay in ICU (Days) was 4.35±2.65.The median (IQR) duration of stay in ICU (Days) was 4.00 (2-5.75). The duration of stay in ICU (Days) ranged from 1 - 22.

In the present study 37 patients required ventilator which corresponds to 24.7% of study population. Mean duration of ventilator stay in the present study was 4.84+/-2.76 days. Duration of ventilator stay ranged from 2 to 18 days with most of the patients having ventilator stay of duration 3 to 6 days. In the present study, 106 patients survived and 44 patients expired. Mortality rate in this study was 29.3% and survival rate was 70.7%.

Kruskal Wallis test was used to make group comparisons of serum magnesium with APACHE II score. Patients with low serum magnesium had a mean APACHE II score of 17.5. Mean APACHE II score was 12.8 in patients with normal serum magnesium group and 12.2 in patients with high serum magnesium. The duration of ICU stay was longer in patients with low serum magnesium in this study. Among patients with low serum magnesium, 5 day was the median duration of stay in ICU. In patients with normal serum magnesium median duration of ICU stay was 2 days. Median duration of ICU stay was 2 days in patients with high serum magnesium.

Mean serum magnesium level in patients who needed ventilator support was 1.86+/-0.71 mg% in comparison with 2.03+/-0.81 mg% in patients who were not on ventilator support. There was no statistically significant association between need for ventilator and serum magnesium level in the present study (p value 0.35).The duration of ventilator stay was more in patients with low serum magnesium. The median duration of ventilator stay was 5 days in low serum magnesium group compared to 3 days in normal serum magnesium group and high serum magnesium group.

In the present study, there was a significantly higher mortality rate in patients with low serum magnesium level. Mortality rate was 56.7% in low serum magnesium group compared to 6.5% in normal serum magnesium group and 8.1% in high serum magnesium group.

Table 1: Association between S. Magnesium and Outcome using Chi-Square test

Outcome	Serum Magnesium				CHI Square Test	
	Low	WNL	High	Total	X^2	P Value
Expired	38(56.7%)	3(6.5%)	3(8.1%)	44(29.3%)	43.825	<0.001
Survived	29 (43.3%)	43 (93.5%)	34 (91.9%)	106 (70.7%)		
Total	67 (100.0%)	46 (100.0%)	37 (100.0%)	150 (100.0%)		

DISCUSSION

Magnesium is the second most common intracellular cation in the human body. Magnesium plays a significant role in homeostasis. Magnesium is a cofactor for adenosine triphosphate reactions. Disorders of magnesium metabolism are common in critically ill patients. The present study showed high prevalence of low serum magnesium in patients admitted in critical care unit. Study by Maria Paz Escuela et al,[5] C S Limaye et al,[6]and Dabbagh et al,[7] also showed high prevalence of low serum magnesium in critically ill patients. Factors that contribute to hypomagnesemia in critically ill patients are impaired gastrointestinal absorption, nasogastric suction,and malnutrition, drugs like diuretics, proton pump inhibitors and aminoglycosides.

In the present study, mean duration of ICU stay was more in patients with low serum magnesium. This is in consistent with study by Maria Paz Escuela et al,[5]Soliman et al,[8]Dabbagh et al,[7]and Kiran H S et al.[9] The Magnesium plays an important role in regulation of metabolism as in a) DNA and RNA synthesis b) Protein synthesis c) Transport of calcium and potassium ions. Low serum magnesium results in derangements in metabolism and induction of sepsis contributing to longer duration of stay in ICU. In study by Dabbagh et al,[7] duration of ICU stay was shorter in patients who received magnesium supplementation. In the present study duration of ventilator stay was also longer in patients with low serum magnesium which is consistent with study by C S Limaye et al,[6] and Dabbagh et al.[7] This can be explained by muscle weakness and respiratory failure caused by low serum magnesium level. Respiratory muscle weakness hampers weaning off of the ventilator.

The APACHE II score was higher in patients with low serum magnesium level in the present study which is consistent with study by Maria Paz Escuela,[5]Soliman et al,[8] and Dabbagh et al[7]. But in study by C S Limaye et al,[6] and Reinhart et al,[10] there was no significant association between APACHE II score and serum magnesium level. In the present study mortality rate was significantly higher in patients with low serum magnesium with a p value of<0.001. Higher mortality rate in patients with low serum magnesium can be attributed to sepsis and cardiac arrhythmia.[8] Low serum

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magnesium is an independent risk factor for sepsis. Low serum magnesium is associated with increased release of proinflammatory cytokines and reactive oxygen species which induce cascade of sepsis.[8] In study by Dabbagh et al,[7] mortality rate was lower in patients who received magnesium supplementation due to decrease in release of proinflammatory cytokines.

The maximum number of patients was in the age group of 41-50 years. 23% of patients were in the age group 41-50 years and 20.7% of patients were in the age group 31-40 years. In this study, the majority of patients were in their third or fourth decade of life. In the study by Maria Paz Escuela et al,[5] the mean age was 60.6+15.4, whereas in the study by Dabbagh et al,[7] mean age was 54+18.The male-female ratio in the present study was 2.66, and in the study by Maria Paz Escuela et al,[5] it was 2.1.

In the present study with a lab reference range of Magnesium 1.7 to 2.4 mg%, 44.7% of patients had low serum magnesium, 30.7% patients had normal serum magnesium and 24.7% patients had high serum magnesium levels. The distribution of serum magnesium in the present study is comparable with the study by Maria Paz Escuela et al.[5] In the study by Maria Paz Escuela et al,[5] 52.5% of patients had low serum magnesium, 34% patients had normal serum magnesium and 13.5% patients had high serum magnesium. In the study by C S Limaye et al,[6] 52% of patients had low serum magnesium, 41% patients had normal serum magnesium, and 7% had high serum magnesium. In the study by Dabbagh et al,[7] 60% of patients had low serum magnesium, 22% of patients had normal serum magnesium, and 18% had high serum magnesium. The study by Maria Paz Escuela et al,[5] C S Limaye et al,[6]Dabbagh et al,[7] and present study showed that majority of patients belong to the low serum magnesium group.

In this study, the mean duration of ICU stay was 4.35+2.65. The mean duration of stay in the low magnesium group was 5.94+1.81, in the normal magnesium group was 3.52+3.13 and in the high magnesium group was 2.49+1.33. Results in the present study were comparable with the study by Maria Paz Escuela et al,[5](mean duration of ICU stay was 4.1+2.65 in comparison with 6.4+7.4 days in patients with low serum magnesium).

Mean serum magnesium level in patients who needed ventilator support was 1.86+/-0.71 mg% in comparison with 2.03+/-0.81 mg% in patients who were not on ventilator support. There was a statistically significant association between magnesium level and the need for a ventilator in the study by Rahul Chowdaryet al.[11] The mean magnesium level in patients on the ventilator was 1.47 mg% in comparison with the mean magnesium level of 1.57 mg% in patients not on a ventilator. But in the present study, we could not find a statistically significant association between serum magnesium level and the need for a ventilator. This could be due to variations in criteria for mechanical ventilation and death of patient before keeping in ventilator.

In the present study, the mean duration of stay in ventilator was 4.84+2.76 days in comparison with 5.56+1.15 days in patients with low serum magnesium, which was statistically significant. The study by C S Limaye et al,[6](mean duration of ICU stay was 2.15+1.12 days in comparison with 4.27+2.12 days in patients with low serum magnesium) and Dabbagh et al,[7](mean duration of ICU stay was 6.5+2.64 days in comparison with 19.5+3.82 days in patients with low serum magnesium levels) also showed increased duration of ventilator stay in patients with low serum magnesium levels. Increased duration of ventilator stay in patients with low serum magnesium can be attributed to muscle weakness. Respiratory muscle weakness is one of the important factors causing difficulty in weaning off the ventilator.

In the present study, APACHE II score in patients with normal magnesium levels was 12.83+6.57 in comparison with 17.48+6.04 in patients with low magnesium levels. The result in the present study was comparable with the study by Maria Paz Escuela et al,[5](APACHE II score in patients with normal magnesium levels was 13.7+7.12 in comparison with 16.4+8.6 in patients with low serum magnesium levels). In the study by Soliman et al,[8] APACHE II score in patients with normal serum magnesium levels was 9.4+3.8 in comparison with 12.2+5.5 in patients with low serum magnesium levels. The present study and previous studies showed an inverse relationship between APACHE II score and serum magnesium level. APACHE II Score is a commonly used severity of illness scoring system in ICU. A higher APACHE II score suggests a high risk for mortality. Similarly, serum magnesium level can also be taken as a predictor of mortality.

In the present study mortality rate in patients with low serum magnesium was 56.7%, in patients with normal serum magnesium was 6.5%, and in patients with high serum magnesium was 8.1%. This study showed a significant association between serum magnesium level and mortality rate. The mortality rate was higher in patients with low serum magnesium. The finding in our study was comparable with the study by C S Limaye et al,[6]in which the mortality rate in the low serum magnesium group was 57.7%, and the mean mortality rate was 31.7%. In the study by Maria Paz Escuela et al,[5] mean mortality rate was 20.5%, and in patients with low serum magnesium group was 38.5%. In the study by C S Limaye et al,[6] mean mortality rate was 31.7% in comparison with 57.7% in patients with low serum magnesium.The present and previous studies showed a higher mortality rate in patients with low serum magnesium compared to patients with normal serum magnesium. Data from previous studies were not available for comparing mortality in patients with high serum magnesium level.

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Sepsis is a leading cause of mortality in patients admitted to the critical care unit. Magnesium plays an important role in the pathogenesis of sepsis. Magnesium modulates immunological functions such as macrophage activation, lymphocyte proliferation and generation of reactive oxygen species. In the study by Humphrey et al,[12] there was a significant relation between Magnesium and inflammatory cytokine production. Magnesium deficiency can increase interleukin 1, tumour necrosis factor-alpha, substance P and calcitonin gene-related peptide.[13] These findings from previous studies explain a higher mortality rate in patients with low serum magnesium levels.

Limitations in the Study

- Magnesium level within the first 24 hours of admission only was measured. Follow up magnesium level was not measured.
- Total serum magnesium only was measured. The ionised magnesium level was not considered in the present study.
- No follow up of patients after discharge from hospital.
- The study was an observational, non-interventional study. The effect of magnesium supplementation was not studied.

CONCLUSION

The mean serum magnesium level in this study is 1.99+0.79 mg%. 44.7% of patients had low serum magnesium levels. 30.7% of patients had normal magnesium levels. 24.7% of patients had high serum magnesium levels. APACHE II score was high in patients with low serum magnesium levels. Duration of ICU stay was longer in patients with low serum magnesium levels. There was no statistically significant association between serum magnesium level and need for ventilator in this study.

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