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Section A-Research paper

SERUMMAGNESIUMLEVELS AT ADMISSION AND ITS RELATION WITHMORBIDITY AND MORTALITY IN INTENSIVE CAREPATIENTS

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Abstract

Background: Hypomagnesemia in patients with critical illnesses ranged from 20% to 60% in various studies conducted throughout the world. It is among the most typical electrolyte problem that goes undiagnosed in severely unwell patients. Low magnesium levels can be utilised as a determinant of the severity and prognosis of patients who are critically ill.

Objectives: Theobjectivesofthestudyaretocorrelatehypomagnesemia with the clinical and other biochemical parameters and also clinical outcome inthosepatients.

Materials and Method: A total of 78 subjects were enrolled in the study. Serum magnesium, calcium, sodium, creatinine and blood urea were evaluated. Results obtained were analyzed using SPSS 20.0 version and the association was tested using independentt-test. A p value less than 0.05 was considered significant.

Results: Among the study population, 37patientshad hypomagnesemiaand41 patients had normal serum magnesium level. Among the 37 patients who had hypomagnesemia, 51.35% were females and 48.65% were males. The mean APACHE score was high in patients with hypomagnesemia. The 'p' value of APACHE II was less than 0.05 showed that there was significant difference between these two groups. Comparison of serum magnesium level with serum potassium, serum calcium, sepsis and diabetes also showed statistical significance. The need for ventilation and mortality was high in patients with hypomagnesemia compared to normomagnesemia patients 26 vs 17 and 21 vs 11 respectively.

Conclusion: Hypomagnesemia significantly correlated with diabetes mellitus, sepsis, hypokalemia, hypocalcemia, APACHE II score, length of ICU stays, need for mechanical ventilation, and death rate.

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Keywords:APACHE score, Hypokalemia, hypomagnesemia, Sepsis, Ventilatorysupport

Introduction

Magnesium is the fourth most commonelement followingiron,oxygenandsiliconinearthcrust.It was discovered for the first time in 1755 by Joseph Black.[1] Magnesium was originally isolated in 1808 by Sir Humphry Davy. Magnesium ranks as the eleventh most prevalent element in the human body by mass.[2]Around 1000 mmol (22–26 g) of magnesium ions are present in the human body, and 60% of these ions mix with calcium ions in the bone to form a complex. Free serum ionized magnesium levels should be between 1.7 and 2.4 mg/dL (1.2-1.75 mEq/L / 0.6-0.9 mmol/L) in healthy individuals. It is a crucial cofactor in over 300 enzymatic processes, including the production of nucleic acids. It acts as an activator for the majority of phosphate group transfer enzymes.[3] The creation of bones and teeth, neuromuscular and cardiac excitability, calcium ion channel gating, ion flux across membranes, and improved glucose tolerance are all facilitated by magnesium.[4] Magnesium can chelate anions such as ATP and functions as a physiological antagonists of calcium in cells. Magnesium serves as a mediator for numerous enzymatic processes in the human body.[4,5] Due to its ability to transport other ions across membranes, it exerts indirect control over several crucial organ systems, including the cardiovascular system, and influences how well they function. Additionally, magnesium mediates the vasoconstriction of smooth muscle.[6]In hospitalized patients, especially those who are seriously ill, an abnormal level of magnesium in their serum is identified. The key clinical manifestations of hypomagnesemia are cardiovascular abnormalities like hypertension, torsade de pointes and ventricular fibrillation and metabolic abnormalities like hypokalemia and hypocalcemia; and neuromuscular symptoms like muscle weakness, tremors, seizures, and paresthesias.[7]In critically ill patients, low magnesium levels may have a significant role in determining the severity and overall prognosis.[8] As a result, it can be considered a key prognostic marker with other substances and other electrolytes that are regularly checked in intensive care units. Studies have demonstrated that hypomagnesemia in critically ill patients has been linked to unfavorable outcomes. The present study was carried out to determine the prevalence of hypomagnesemia in patients admitted to critical care units and to correlate it with patient outcomes because magnesium is crucial for numerous physiological processes and the maintenance of normal homeostasis.

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Materials and Methods

Study design: Prospective observational study

Study settings: This study was conducted in Department of general medicine, Sree Mookambika Institute of Medical Sciences, Kulasekharam, Tamil Nadu.

Study Period: The study was conducted during the period of January 2019 toAugust2020 (18 months).

Inclusion criteria

The patients with below conditions were included in the study

- CardiacFailure
- RespiratoryFailure
- Chronic kidney disease (CKD)
- Cirrhosis, Pneumonia
- Pulmonaryedema
- Poisoning
- Sepsis
- Cerebrovascularaccident (CVA)
- Statusepilepticus and DiabeticKetoacidosis (DKA)

Exclusion criteria

- Patientswhoreceivedbloodtransfusionpriorto admission and patients on magnesium sulphate.
- Magnesium containing antacids
- Taking aminoglycosides,cisplatin or amphotericinB

Ethical Committee approval

The study was approved by Institutional Human Ethics Committee with the reference number SMIMS/IHEC/No.1/Protocol no: 13/2018.

Procedure

The study was included 78 patients based on inclusion and exclusion criteria. Study

procedure was explained to all the patients and informed consent was obtained. Patients history,clinicalexaminationandlab investigationswere done. For lab investigations blood samples were collected from antecubital vein for Completebloodcount, Ureaandcreatinine, Bilirubin,albumin, Electrolytesincludingsodium,potassium,magnesiumandcalcium. Electrocardiogram (ECG) and Arterial blood gas (ABG) analysis was also done.

Parameterstaken:

- Hypomagnesemia-serummagnesium<1.7mg/dl
- Hypokalemia-serum potassium <3.5mEq/L
- Hypocalcemia–serumcalcium<8mg/dl
- Acute Physiology and Chronic Health Evaluation (APACHE)IIscoring (Table 1, 2)

Statistical analysis

Statistical Analysis was carried out using SPSS 20.0 version. Chi-squaretest,t-testwasappliedinqualitativedata tofindthesignificanceofdifferencebetweentwoproportionsandtofindtheassociationbetweentwovariables. Spearman correlation coefficients were computed to examine the associationamongquantitative variables. A p value less than 0.05 was considered statistically significant.

Results

The presentstudyincludedatotalnumberof78patients. The most common age group of patients included in the present study was 20 to 35 years seen in 39(51%) patients followed by 36 to 55 years in 27(32%) patients. Of the 78 patients 26(33.3%) patients were diagnosed as sepsis and the remaining 52(66.7%) patients had other cases Acute Febrile illness (AFI), coronary artery disease (CAD), Central Nervous system (CNSInfection), Cerebrovascular Accident (CVA), Hematological Disorders, Liver Failure, Poisoning, Renal Failure,RespiratoryFailure, Rheumatic Heart disease (RHD), SeizureDisorder, SnakeBite.Among the study population, 37(47.4%)patientshad hypomagnesemiaand41(52.6%) patients had normal serum magnesium level. Among the 37 patients who had hypomagnesemia, 19(51.35%) were females and 18(48.65%) were males. Comparison of magnesium levels with age, gender showed no statistical significance as the p value was 0.414

and 0.314 respectively which was more the 0.05. Comparison of serum magnesium level with sepsis and Diabetes Mellitus (DM) showed statistical significance (Table-3 and 4). Comparison of serum magnesium level with other lab investigations were described in (Table-5). On comparison with serum potassium and serum calcium, magnesium levels showed statistical significance as the p value was less than 0.05.The mean APACHE score was high in patients with hypomagnesemia. The 'p' value of APACHE II was less than 0.05 showed that there was significant difference between these two groupsinterms ofAPACHEII. APACHE score was described in (Table-6).The need for ventilation and mortality was high in patients with hypomagnesemia compared to normomagnesemia patients (Table-7). Describes the comparison of need for mechanical ventilation and mortalityin patients with low and normal magnesium level.

Discussion

Critically ill individuals frequently have hypomagnesemia. Weakness, cramping of the muscles, cardiac arrhythmia, and raised irritability of the nervous system with tremors, jerks, nystagmus, as well as an extensor plantar reflex are all symptoms of hypomagnesaemia. In addition, there could be tetany, hypertension, tachycardia, hallucinations, disorientation, sadness, and epileptic fits. Hypomagnesaemia is linked to a variety of diseases, including arrhythmias and pre-eclampsia, as well as cerebral ischaemia.[9]In the current study, patients aged 20 to 35 made up the majority of the patient population (representing 51% of patients). Out of the 37 individuals who had hypomagnesemia, 19 (51.35%) were female and 18 (48.65%) were male. According to Gosalia et al.[10], the age group 21–30 years had the highest incidence of patients with critical illnesses in the ICU with 20 (28.99%), followed by the age group 31–40 years with 18 (26.09%). The study conducted by Baloch MF et al.[11] included 120 patients, with a mean age of 42.76±12.77 years and a male-to-female ratio of 1:1. Among the participants in the study, 41 patients (52.6%) had normal serum magnesium levels, compared to 37 patients (47.4%) who had hypomagnesemia. In the study by Gosalia et al.[10] among 69 patients, 39 (56.52%) had hypomagnesemia and 30 (43.48%) had normomagnesemia. Similarly, Baloch MF et al.[11] found that the incidence of hypomagnesemia in their study was 23.33% seen in 28 patients. These findings were comparable to the present study. In the study conducted by Gosalia et al.[10] the comparison of serum magnesium level with DM and sepsis demonstrated statistical significance with a p value of 0.0246. Sepsis is the main cause of death among severely sick patients admitted

to the ICU. Magnesium appears to be crucial in sepsis as well as septic shock. Magnesium influences immune system processes like leukocyte adhesion, lymphocyte proliferation, granulocyte oxidative burst, endotoxin adhesion to monocytes, and increased production of reactive oxygen species (ROS).[12]Other electrolyte abnormalities, such as hypernatremia, hypokalemia, and hypocalcemia, were seen in 6 (100%), 22 (61.11%), and 20 (64.52%) of the hypomagnesemic individuals, respectively. As the p value was less than 0.05, serum calcium and potassium demonstrated statistical significance. Hypokalaemia (58.82%), hyponatremia (47.05%), hypocalcaemia (70.58%), and hypophosphatemia (29.41%) were among the related electrolyte abnormalities identified by Zafar MSH et al.[13] In the study by Sudha R et al.[14] Hypocalcaemia (33% vs 3%), Hyponatremia (40% vs 12.5%), Hypokalaemia (20% vs 6.25%), and Hypoalbuminemia (50% vs 31%) were shown to be statistically significant differences between hypomagnesemia and those with normal magnesium levels. The mean APACHE score for patients with hypomagnesemia in the current research was 20.17. Compared to patients with normal magnesium levels, this was higher. When compared to patients who were hypomagnesemic and those who were normomagnesemic, a statistically significant difference was found. In the study conducted by Baloch MF et al.[11] the mean APACHE II score of the patients was 29.68±2.571.

In the study by Gupta S et al.[15] patients with hypomagnesemia had significantly higher APACHE scores than patients with normomagnesemia. In contrast to the current study, Zeineldin KH et al.[16] observed that the mean APACHE II was 18.19± 8.04 in patients with normomagnesaemia and 17.88± 8.51 in patients with hypomagnesaemia, with a p-value of 0.795.In the current study, the mortality rate in hypomagnesemia patients was higher 21(65.62%) than in normomagnesemia patients 11(34.38%), and this difference was statistically significant. In studies conducted by Zeineldin KH et al.[16] and Pannem RB et al.[17] patients with hypomagnesemia had a higher death rate than those with normomagnesemia (24.6% vs. 30.2% and 49.48% vs. 23.80%, respectively). According to a study by Heidari ZZ et al.[18] hypomagnesemia was linked to increased mortality, the requirement for mechanical ventilation, and the length of stays in intensive care units.Kongara RC et al.[19] found that the incidence of death among hypoglycemic patients was 16.56%, and the relationship between mortality and hypomagnesemia in patients revealed a statistically significant association. In the study conducted by Raju KS et al.[20] the average amount of time patients required invasive breathing was longer (mean = 10±3-17 days) than it was for controls (mean = 3±2-4 days); p-value =

0.001. Death rates were greater in the case group 14(28%) compared to the control group (p-value = 0.02), which had mortality rates of 5(10%).

Conclusion

Hypomagnesemia was significantly correlated with APACHE II score, diabetes mellitus, sepsis, hypocalcemia, hypokalemia, and septic shock. In addition to other indicators, the current study emphasises the significance of measuring serum magnesium levels in all patients admitted to critical care units at the time of admission. In critically ill patients in the ICU, hypomagnesemia was strongly associated with an elevated risk of hospital mortality, sepsis, ICU stay duration, and mechanical ventilation. Future research should assess whether giving critically ill patients a magnesium supplement will enhance their outcomes.

Limitations of study

Only the serum total magnesium level was tested in the study population. The relationship between erythrocyte and ionized magnesium levels was not studied. Further research is required to determine the potential benefits of magnesium correction or supplementation in hypomagnesemic patients.

Conflict of interest: Nil

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Table-1:APACHEIIseverityof diseaseclassificationsystem

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Physiologic Variable	+4	+3	+2	+1	0	+1	+2	+3	+4
Temperature - rectal (°C)	≥41	39-40.9		38.5-38.9	36-38.4	34-35.9	32-33.9	30-31.9	≤29.9
Mean Arterial Pressure (mm Hg)	≥160	130-159	110-129		70-109		50-69		≤49
Heart Rate	≥180	140-179	110-139		70-109		55-69	40-54	≤39
Respiratory Rate (nonventilated or ventilated)	≥50	35-49		25-34	12-24	10-11	6-9		≤5
Oxygenation (mmHg) a. $FiO_2 > 0,5$ use $A\text{-}aDO_2$ b. $FiO_2 < 0,5$ use PaO_2	a ≥500	350-499	200-349		<200				
	b				> 70	61-70		55-60	<55
Arterial pH	≥7.7	7.6-7.69		7.5-7.59	7.33-7.49		7.25-7.32	7.15-7.24	<7.15
Serum Sodium (mmol/l)	≥180	160-179	155-159	150-154	130-149		120-129	111-119	≤110
Serum Potassium (mmol/l)	≥7	6-6.9		5.5-5.9	3.5-5.4	3-3.4	2.5-2.9		<2.5
Serum Creatinine (mg/dl, Double point score for acute renal failure)	≥3.5	2-3.4	1.5-1.9		0.6-1.4		<0.6		
Hematocrit (%)	≥60		50-59.9	46-49.9	30-45.9		20-29.9		<20
White Blood Count (in 1000/mm³)	≥40		20-39.9	15-19.9	3-14.9		1-2.9		<1
Glasgow-Coma-Scale (GCS)	Score = 15 minus actual GCS								
Serum HCO_3 (venous, mmol/l, use if no ABGs)	≥52	41-51.9		32-40.9	22-31.9		18-21.9	15-17.9	<15
A = Total Acute Physiology Score APS	Sum of the 12 individual variable points								
B = Age Points	**C = Chronic Health Points**								
≤44 years 0 points 45-54 years 2 points 55-64 years 3 points 65-74 years 5 points ≥75 years 6 points	If the patient has a history of severe organ system insufficiency or is immunocompromised assign points as follows: a. For nonoperative or emergency postoperative patients – 5 points b. For elective postoperative patients – 2 points								
APACHE II Score = Sum of A (APS points) + B (Age points) + C (Chronic Health points)									

Table-2:Interpretationof Score

Score	Deathrate(%)
0-4	4
4-9	8
10-14	15
15-19	25
20-24	40
25-29	55
30-34	75
>34	85

Table-3: Comparison of serum magnesium level with diabetes mellitus

Hypomagnesemia	Diabetic	Non diabetic	p value
Absent	12 (32.43%)	29 (70.73%)	**0.001556**
Present	25 (67.57%)	12 (29.27%)	
Total	**37**	**41**	

Table-4: Comparison of serum magnesium level with sepsis

Hypomagnesemia	Sepsis	No sepsis	p value
Absent	9 (34.62%)	32(61.53%)	**0.03731**
Present	17(65.38%)	20(38.46%)	
Total	**26**	**52**	

Table-5: Comparison of serum magnesium level with lab investigations

Observation	Normomagnesemia	Hypomagnesemia	p value
Sodium			
Hyponatremia	26(57.78%)	19(42.22%)	**0.440923**
Normal	15(55.56%)	12(44.44%)	
Hypernatremia	0(0%)	6(100%)	
Potassium			
Hypokalemia	14(38.89%)	22(61.11%)	**0. 025137**
Normal	27(64.29%)	15(35.71%)	
Calcium			
Hypocalcemia	11(35.48%)	20(64.52%)	**0.01415**

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Normal	30(63.83%)	17(36.17%)	
Urea			
Normal	22(50%)	22(50%)	**0.605919**
Hyperuricemia	19(55.88%)	15(44.12%)	
Creatinine			
Normal	22(45.83%)	26(54.17%)	**0.132113**
High	19(63.33%)	11(36.67%)	

Table-6: Comparison of serum magnesium level with APACHEII score

Comparison	Hypomagnesemia		Normomagnesemia		Total		't'Value	'p'Value
	Mean	SD	Mean	SD	Mean	SD		
APACHEII score	20.17	7.07	18.02	8.66	19.03	7.98	2.39	**0.0084**

Table-7: Comparison of serum magnesium level with need for ventilation and mortality

Observations	Hypomagnesemia	Normomagnesemia	p value
NeedforMechanicalVentilation			
Yes	26(70.27%)	17(41.46%)	**0.010641**
No	11(29.73%)	24(58.54%)	
Mortality of patients			
Death	21(56.76%)	11(26.83%)	**0.012716**
Discharge	16(43.24%)	30(73.17%)	
Total	37	41	