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A Study to Correlate Serum Magnesium Levels and Its Outcome in Critically Ill Patients Admitted To Intensive Care Unit at a Tertiary Care Centre

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Abstract:
Backround : *Magnesium is the second most abundant intra cellular cation, potassium being the first and fourth abundant cation in the human body and also serving as cofactor in more than 300 enzymatic reactions. Magnesium deficiency is the most commonly overlooked condition in critically ill patients and associated with other coexisting electrolyte abnormalities. The aim of the present study was to evaluate serum magnesium levels in critically ill patients and to correlate with patient outcome and other parameters like length of stay in ICU, ventilator support, APACHE-II score and duration and mortality.*
Materials and Methods*: A two years cross sectional study after ethical committee approval was conducted at a tertiary care hospital among critically ill patients admitted in ICU. Serum magnesium levels and other relevant investigations were performed within 24 hours of admission . Patients management and progress were followed till the outcome. The data was analysed by using IBM SPSS 20.0 version software.*
Results: *Total of 400 patients with 245 males and 155 females were enrolled. 182 cases (45.5%) of hypomagnesemia were observed and 218 cases (54.5%) with normal serum magnesium levels were observed. Hypomagnesemia cases were compared with normal cases and found that: Hypomagnesemia cases had higher mortality rate, higher APACHE II score, more length of hospital stay and ventilator duration. Significant association was identified with hypertension (p valve <0.05).*
Conclusion: *Monitoring of magnesium levels in critically ill patients has several prognostic and therapeutic implications and should be recommended as a regular parameter as it is commonly out looked condition. Statistically significant association of hypomagnesaemia was found with hyponatremia . Higher APACHE II score is associated with higher mortality and more length of stay in ICU and increased requirement of ventilatory support among the cases of hypomagnesaemia.*
Keyword: *APACHE II score, Critically ill, Hypomagnesemia.*

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I. Introduction

Magnesium is the major intracellular divalent cation. Extracellular magnesium and calcium at normal concentrations crucial for normal neuromuscular activity. Intracellular magnesium is an important cofactor for a wide range of enzymes, transporters, and nucleic acids required for normal cellular function, replication, and energy metabolism after complex with ATP. Normal serum Magnesium concentration in the range of 0.7–1 mmol/L (1.5–2 meq/L; 1.7–2.4 mg/dl) [1]. The normal adult total body Mg content is approximately 25 g (2000 mEq or 1 mol)[2-3]. About 53% of total Mg stores are in bone, 27% in muscle, 19% in soft tissues, 0.5% in erythrocytes, and 0.3% in the serum [2]. However, because serum only contains 0.3% of the total body Mg, so measurements of serum magnesium levels may not accurately reflect the level of total body magnesium store . Magnesium homeostasis involves the kidney, small bowel, and bone [4]. Dietary magnesium content normally ranges from 6 to 15 mmol/d (140–360 mg/d), of which 30–40% is absorbed, mainly in the jejunum and ileum. Intestinal magnesium absorptive efficiency is stimulated by 1,25(OH)2D and can reach 70% during magnesium deprivation[1]. Magnesium reabsorption in the cTAL is increased by PTH but inhibited by hypercalcemia or hypermagnesemia, both of which activate the CaSR in this nephron segment [1]. About 2.4 g of Mg is filtered each day, and 120 mg (5%) is normally excreted in the urine [5].The proximal tubule reabsorbs 15% to 20% of filtered Mg, whereas the thick ascending loop (TAL) of Henle reabsorbs 65% to 75% and the distal tubule is responsible for 5% to 10% of Mg reabsorption[6-7] . Smooth muscle tone is determined by calcium dependent phosphorylation of myosin lightchain . Mg2+ regulates the intracellular calcium levels and there by influences smooth muscle tone [8]. In smooth muscle, low magnesium concentration enhances the vasoconstrictive effects of catecholamine & angiotensin -2. By regulating smooth muscle tone, Mg deficiency has been proposed to cause

Hypertension, Neuromuscular hyper excitability, Bronchial airway constriction, Coronary vasospasm, Acute myocardial infarction, and Seizures. Hypomagnesaemia is commonly associated with other electrolyte abnormalities hypokalemia,hyponatremia,hypophosphatemia,hypocalcemia[9].Hypomagnesemia may cause generalized alteration neuromuscular function, including tetany, tremor, seizures, muscle weakness, ataxia, nystagmus, vertigo, apathy, depression, irritability, delirium, and psychosis. Patients are usually asymptomatic when serum magnesium concentrations are >0.5 mmol/L (1 meq/L; 1.2 mg/dL).Cardiac arrhythmias may occur, including sinus tachycardia, other supraventricular tachycardias, and ventricular arrhythmias. The aim of the present study was to evaluate serum magnesium levels in critically ill patients and to correlate with patient outcome and other parameters like length of stay in ICU, ventilator support, APACHE-II score and duration and mortality.

II. Materials And Methods

This is a prospective study was carried out on patients admitted in Intensive care unit of Basaweshwara Teaching and general Hospital attached to Mahadevappa rampure medical college, Kalaburagi ,Karnataka .
Study period : The Study period from November 2019- April 2021 .

Sample size: 400
Study design: Prospective observational study
Subjects and selection method : All the cases admitted in the ICU (intensive care unit) of the hospital with variable medical and surgical conditions were included in the study. The study details were clearly explained to the cases included in the study. Written informed consent was obtained from all the cases who consented for participation in the study. All the cases admitted in the ICU were scored on the day of admission based on acute physiology and chronic health evaluation (APACHE-II) scoring system which includes acute physiology score, Glasgow coma scale, points assigned to age with chronic disease and chronic health condition score. The socio demographic data, medication history, clinical history, diagnosis and co-morbid conditions were noted in the study designed protocol.

The length of stay in the ICU, development of new complications, mechanical ventilation and its duration and the outcome parameter which are discharge, transfer to the ward, death or discharge against advice were noted for every case enrolled in the study.

INCLUSION CRITERIA :
1 All critically ill patients aged above 18 years admitted to Intensive Care Unit.
2 The Patients with APACHE - 2 score above 18 were included in the study
EXCLUSION CRITERIA :
1 Those Patients whose day 1 sample of serum magnesium not taken in ICU
2 Those patients whose day 1 of ICU stay missed
3 Any patients on magnesium lowering drugs

STATISTICAL ANALYSIS :
Statistical data was analyzed by IBM SPSS 20.0 version software. Collected data were spread on excel sheet and prepared master chart. Through the master chart tables and graphs were constructed. For quantitative data analysis t-test and ANOVA tests were applied. For qualitative data analysis chi-square test and Fisher exact probability tests were applied for statistical significance. If P-value was less than 0.05 considered as significant .

III. Results

In the present prospective observational study, a total of 400 patients were enrolled who fulfilled the inclusion criteria in the study.
In my study observed that, male patients were dominant 245 (61.3%) compared to female patients 155 (38.7%)

Table No.1: Gender wise distribution of patients

Gender	Number of patients	Percentage
Males	245	61.3
Females	155	38.7
Total	400	100.0

Table No.2: Serum magnesium (Mg) level wise distribution of patients

Serum magnesium (mg)	Number of patients	Percentage
< 1.79 (hypomagnesemia)	182	45.5
≥ 1.8 (Normal magnesium)	218	54.5
Total	400	100.0

In the study, out of 400 critically ill patients; 182 (45.5%) of patients serum magnesium level was < 1.79 (hypomagnesemia) and 218 (54.5%) of patients serum magnesium level was ≥ 1.8 (Normal magnesium)

Table No.3: Comparison of serum magnesium level with duration of stay

Duration of stay	**No.**	**Serum magnesium level**	
		< 1.79 (Hypomagnesemia)	**≥ 1.8 (Normal magnesium)**
1—5 days	230	105 (46.1%)	125 (53.9%)
6—10 days	123	46 (37.5%)	77 (62.5%)
11—15 days	36	24 (66.7%)	12 (33.3%)
>15 days	11	7 (63.6%)	4 (36.4%)
Total	**400**	**182**	**218**
χ2-test value and P-value		**χ2 = 7.93 P = 0.027 S**	

NS= not significant, **S=significant**, HS=highly significant, VHS=very highly significant
There was statistical significant association between duration of stay and serum magnesium level (P<0.05). Hypomagnesemia patients were significantly shows more duration of stay as compare to normal magnesium patients.

Table No 4 : Comparison of serum magnesium level with comorbidities of patients

Variables		**Serum magnesium level**		**χ2-test value and P-value**
		< 1.79 (Hypomagnesemia)	**≥ 1.8 (Normal magnesium)**	
DM	**Present**	79 (43.4%)	103 (56.6%)	**χ2 = 0.58 P = 0.893 NS**
	Absent	103 (47.2%)	115 (52.8%)	
HTN	**Present**	73 (52.9%)	65 (47.2%)	**χ2 = 4.65 P = 0.027 S**
	Absent	109 (41.6%)	153 (58.4%)	

NS= not significant, S=significant, HS=highly significant, VHS=very highly significant
There was no statistical significant association between diabetes mellitus and serum magnesium level (P>0.05). There was statistical significant association between hypertension and serum magnesium level (P<0.05). Hypertensive patients had significantly more hypomagnesemia compare to non-hypertensive patients

Table No.5: Comparison of serum electrolytes and creatinine of patients with serum magnesium level

Variables	Serum magnesium level		t-test value and P-value
	< 1.79	≥ 1.8	
	Mean ± SD	Mean ± SD	
Serum sodium	133.43 ± 9.12	136.12 ± 7.36	t = 2.013, P = 0.042 S
Serum potassium	4.33 ± 1.01	4.53 ± 2.74	t = 0.925, P = 0.356 NS
Creatinine	2.94 ± 3.09	1.80 ± 1.78	t = 4.561, P = 0.000 VHS

NS= not significant, S=significant, HS=highly significant, VHS=very highly significant
There was no statistical significant difference of mean serum potassium with serum magnesium level (P>0.05).

There was statistical significant difference of mean serum sodium with serum magnesium level (P<0.05). The mean serum sodium was significantly less in hypomagnesaemia patients as compare to normal magnesium patients .

There was statistically very highly significant difference of mean serum creatinine with serum magnesium level (P<0.001). The mean serum creatinine was significantly high in hypomagnesaemia patients as compare to normal magnesium patients .

Table No.6: Comparison of vital events of patients with serum magnesium level

Vitals	Serum magnesium level		t-test value and P-value
	< 1.79	≥ 1.8	
	Mean ± SD	Mean ± SD	
MBP	86.98 ± 36.10	88.17 ± 32.03	t = 0.345, P = 0.730 NS
Pulse	113.5 ± 29.10	114.08 ± 26.74	t = 0.205, P = 0.838 NS
RR	30.53 ± 8.34	28.78 ± 8.26	t = 2.081, P = 0.038 S
Temp	38.18 ± 1.12	38.35 ± 1.26	t = 1.454, P = 0.147 NS

NS= not significant, S=significant, HS=highly significant, VHS=very highly significant

There was no statistical significant difference of mean MBP, Pulse and Temperature with serum magnesium level (P>0.05).

There was statistical significant difference of mean RR with serum magnesium level (P<0.05). Mean RR was significantly more hypomagnesemia patients as compare to normal maggnesium patients

Table No.7: Comparison of variables with serum magnesium level

Variables	Serum magnesium level		t-test value and P-value
	< 1.79	≥ 1.8	
	Mean ± SD	Mean ± SD	
PH	7.32 ± 012	7.34 ± 0.11	t = 1.99, P = 0.048 S
PaO2	77.16 ± 17.88	76.16 ± 17.75	t = 0.412, P = 0.680 NS
TC	15123.1 ± 8376.83	14484.3 ± 7987.08	t = 0.778, P = 0.437 NS
PCV	32.05 ± 9.24	35.41 ± 7.28	t = 4.053, P = 0.000 VHS
GCS	10.92 ± 4.05	10.31 ± 4.03	t = 1.501, P = 0.133 NS
CHP	5.0 ± 0.0	5.0 ± 0.0	t = 0, P = 1.0
APACHE -II	22.91 ± 4.74	20.78 ± 3.63	t = 5.029, P = 0.000 VHS

NS= not significant, S=significant, HS=highly significant, VHS=very highly significant

There was no statistically significant difference of mean PaO2, TC and GCS with serum magnesium level (P>0.05).

There was statistically significant difference of mean PH with serum magnesium level (P<0.05). The mean PH was significantly less in hypomagnesaemia patients as compare to normal magnesium

There was statistically very highly significant difference of mean PCV and APACHE -II score with serum magnesium level (P<0.001). The mean PCV was significantly low in hypomagnesaemia patients as compare to normal magnesium patients and the mean APACHE -II score was significantly high in hypomagnesaemia patients.

Table No.8: Comparison of serum magnesium level with ventilator dependency

Ventilator	No.	Serum magnesium level	
		< 1.79	≥ 1.8
Patients with ventilators	180	116 (64.4%)	64 (35.6%)
Patients without ventilators	220	66 (30.0%)	154 (70.0%)
Total	400	182	218
$\chi 2$-test value and P-value		$\chi 2$ = 47.36 P = 0.000 VHS	

NS= not significant, S=significant, HS=highly significant, VHS=very highly significant

There was statistically very highly significant difference of Patients with ventilators and serum magnesium level (P<0.001). Patients on ventilators were significantly more in hypomagnesaemia

Table No.9: Comparison of serum magnesium level with study outcome

Study outcome	No.	Serum magnesium level	
		< 1.79	≥ 1.8
Early recovered	110	34 (30.9%)	76 (69.1%)
Delayed recovered	84	43 (51.2%)	41 (48.8%)
Death	206	105 (51.0%)	101 (49.0%)
Total	400	182	218
χ2-test value and P-value		χ2 = 13.03 P = 0.0073 HS	

NS= not significant, S=significant, HS=highly significant, VHS=very highly significant

There was statistically highly significant difference of outcome of patients with serum magnesium level (P<0.01).

Hypomagnesemia patients had delayed recovery and death rate more compare to normal magnesium level patients.

IV. Discussion

Magnesium is second most common intracellular cation which plays a crucial role in homeostasis. It acts as cofactor in most of the adenosine triphosphate (ATP) reactions. Hypomagnesemia is multi factorial in critically ill patients and may be associated with other electrolyte disturbances and is most commonly overlooked condition. Hypermagnesaemia is less common and mostly due to renal failure or iatrogenic.

The prevalence of hypomagnesemia among critically ill patients mentioned in various studies range from 14% to 70% and is variable from place to place and region to region and is mostly dependable upon the clinical condition of the patient.[10] In our study, out of 400 critically ill patients; prevalence of hypomagnesemia was (45.5%) . Limaye et al[11] conducted a study on 100 ICU patients revealed that prevalence was 52% of patients had low serum magnesium levels.

The relationship between mortality and hypomagnesemia is variable from study to study, in our study the mortality was 51.5% among the cases of hypomagnesemia and was found to be statistically highly significant. Findings of our study concurs with the study of Safavi M et al.[12] However reports of Chernow et al, Soliman HM et al, mentioned less rate of mortality in their studies which deviates from the findings of our study.[13,6]

In present study, observed that cases of hypomagnesemia required ventilator support (64.4% vs 35.6%) and duration long and were difficult to wean because of muscle weakness produced by the condition and also few cases of ICU were on respiratory failure . NE Borges et al[14] more frequent need for ventilatory support (73% vs 53%) longer duration of mechanical ventilation (4.27 vs 2.15days).

APACHE II score was higher in cases of hypomagnesemia when compared with normo and hyper magnesaemia patients in our study and higher score was associated with higher mortality in present study. The APACHE II score of hypomagnesemia cases in our study was (22.94±4.7) and was similar to the findings of Sahu et all.[15] however few studies mentioned no significant association between hypomagnesemia and APACHE II score in their study which is against the finding in present study.

Hypomagnesemia is associated with other electrolyte abnormalities which are hypokalemia, hyponatremia and hypophosphatemia [16]. These are considered as predictors of hypomagnesemia.In my study The mean serum sodium was significantly less in hypomagnesaemia patients as compare to normal magnesium patients and it is statistically significant(P<0.05). There was no statistical significant difference of mean serum potassium with serum magnesium level (P>0.05).

In my study there was statistically very highly significant difference of mean serum creatinine with serum magnesium level (P<0.001). The mean serum creatinine was significantly high in hypomagnesaemia patients as compare to normal magnesium patients. Sathish R et all [17] was observed hypomagnesemia in recovery period of acute renal failure.

V. Conclusion

Monitoring of magnesium levels in critically ill patients has several prognostic and therapeutic implications and should be recommended as a regular parameter as it is commonly out looked condition . Higher APACHE II score is associated with higher mortality and more length of stay in ICU and increased requirement of ventilatory support among the cases of hypomagnesaemia.

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