

## PREVALENCE OF HYPOMAGNESEAEMIA AND ITS PROGNOSTIC VALUE IN CRITICALLY-ILL MEDICAL PATIENTS

Sahul Hameed Peer Mohamed<sup>1</sup>, Gopal Bagialakshmi<sup>2</sup>, Nagarajan Ragavan<sup>3</sup>, Rajendran Kapil<sup>4</sup>, Santhana Krishnan Ramesh Kumar<sup>5</sup>

<sup>1</sup>Assistant Professor, Department of General Medicine, Madurai Medical College, Madurai.

<sup>2</sup>Professor, Department of General Medicine, Madurai Medical College, Madurai.

<sup>3</sup>Assistant Professor, Department of General Medicine, Madurai Medical College, Madurai.

<sup>4</sup>Junior Resident, Department of General Medicine, Madurai Medical College, Madurai.

<sup>5</sup>Scientist (Medical), National Institute for Research in Tuberculosis (ICMR), Madurai.

### ABSTRACT

#### BACKGROUND

Serum magnesium levels in critically-ill ICU patients and its correlation with the prognosis of the patients have been studied. Low serum magnesium levels were seen in critically ill and it was associated increased mortality.

#### MATERIALS AND METHODS

It is a prospective observational study involving 100 critically-ill medical patients admitted in Intensive Medicine Care Unit of Government Rajaji Hospital, Madurai. A detailed medical history, clinical examination, random blood sugar, serum electrolytes (sodium, potassium, magnesium, calcium), ECG, ABG analysis, complete haemogram and APACHE scoring were done. Chi-square test was used to assess the statistical significance of qualitative data.

#### RESULTS

Of the 100 patients, 52 (52%) were males and 48 (48%) were females. Age group from 51-60 years contributed as the major study population. On admission, 50% (50/100) patients had hypomagnesaemia, 39% (39/100) had normal serum magnesium levels and 11% had hypermagnesaemia. The hypomagnesaemia group had increased number of days in ICU, increased incidences of ventilatory support and more duration of ventilation and higher mortality compared with normo or hypermagnesaemia group.

#### CONCLUSION

Hypomagnesaemia in critically-ill medical patients is a poor prognostic indicator in terms of duration of IMCU stay, ventilator dependency and all-cause mortality.

#### KEYWORDS

Hypomagnesaemia, Critically-Ill Medical Patients.

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#### BACKGROUND

Magnesium is the most abundant intracellular cation after potassium. About 50 percent of the total body magnesium (2000 mEq in the human adult) is distributed in bone remaining in soft tissues. Measurements of serum magnesium does not exactly correlate with body stores because the extracellular fluid has 1% of body magnesium.<sup>1</sup> Kidney is major organ maintaining concentration of serum magnesium.<sup>1</sup> The thick ascending limb reabsorbs about 60% of the filtered magnesium, proximal convoluted tubule

absorbs 20% and the distal convoluted tubule absorbs the remaining 5-10%. Magnesium is primarily absorbed by jejunum and ileum, the absorptive capacity of which can be increased to 70% by 1.25-dihydroxycholecalciferol.<sup>1</sup> Serum magnesium although does not exactly correlate with body stores.<sup>1</sup>

Magnesium monitoring is important in critically-ill patients who are more prone for a myriad of electrolyte abnormalities particularly hypokalaemia, hyponatraemia and hypocalcaemia. The total intracellular magnesium content is 8 to 10 mmol/L (10 to 20 mEq/L). Most of the magnesium in cell is bound to ATP, intracellular nucleotides and enzymes.<sup>1</sup> Studies using magnesium-sensitive dyes based on Fura-2 (aminopolycarboxylic acid) indicate that the free cytosolic concentration is 0.6 to 0.8 mmol/L (1.2 to 1.6 mEq/L).<sup>2,3</sup> Intracellular magnesium forms a complex with adenosine triphosphate and is a cofactor for many enzymes and cotransporters.<sup>1</sup> These enzymes and cofactors are necessary for energy metabolism, normal cellular function

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*Corresponding Author:*

*Dr. Sahul Hameed Peer Mohamed,*

*Habiba Speciality Hospital, Vivekanandar Main Road,*

*Thasildar Nagar, Madurai-625020.*

*E-mail: peermdsh@gmail.com*

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and replication. 30% of the normal serum magnesium (1.7-2.4 mg/dL) is bound to albumin and 15% is complexed to phosphate and anions. The bone contains one half of the total magnesium (1000 mmol) and only one half is insoluble in the mineral phase.

Changes in the plasma magnesium levels alter cellular magnesium content slowly. The intracellular free magnesium<sup>3</sup> is significantly below electrochemical equilibrium. A type of energy dependant extrusion mechanism exist. The process of active magnesium transcellular transport is driven by a favourable transmembrane potential. Magnesium enters the distal convoluted tubule through an apical magnesium channel.<sup>1</sup> Since, the intra and extracellular concentrations of magnesium are comparable, the driving force for magnesium is negligible. Magnesium entry into the cells is the rate limiting step. Magnesium diffuses through the cytosol to be extruded against an electrochemical gradient across the basolateral membrane, which increases in hypokalaemic patients to about 61 to 66% in patients in ICU. Low albumin,<sup>4</sup> malnutrition, aminoglycosides play role. The three basic mechanisms that lead to hypomagnesaemia are redistribution, gastrointestinal loss and renal losses.<sup>5</sup>

The incidence of hypomagnesaemia in hospitalised patients was found to be 12 percent.<sup>6</sup> Low magnesium levels were seen in critically ill<sup>7</sup> and it was significantly associated increased mortality among various diseases.<sup>7</sup> We proposed to assess the prevalence of serum magnesium levels in critically-ill patients and also assess the prognostic significance of serum magnesium in critically-ill medical patients.

## MATERIALS AND METHODS

The objectives of the study is to assess the prevalence of serum magnesium levels in critically-ill patients and to assess the prognostic significance of serum magnesium in critically-ill medical patients. It was hypothesised that the hypomagnesaemia in critically-ill medical patients was a poor prognostic indicator in terms of duration of IMCU stay, ventilator dependency and all-cause mortality.

**Study Design-** Prospective, descriptive analytical study.

**Study Setting-** The study was conducted at Government Rajaji Hospital from March 2015 to October 2015.

**Study Population-** This study was conducted among 100 critically-ill medical patients admitted in Intensive Medicine Care Unit of Government Rajaji Hospital, Madurai, from March 2015 to October 2015.

## Inclusion Criteria

Patients suffering from various medical conditions namely pneumonia/interstitial lung disease with respiratory failure, congestive cardiac failure, diabetic ketoacidosis, meningitis, OPC poisoning and snake bite patients requiring ventilator support.

## Exclusion Criteria

Patients who had received intravenous magnesium prior to transfer to IMCU were excluded.

## Study Protocol and Data Collection

Eligible patients as per the criteria said above was enrolled to the study. A detailed medical history, clinical examination and relevant laboratory investigations including random blood sugar, serum electrolytes (sodium, potassium, magnesium and calcium), ECG, arterial blood gas analysis and complete haemogram, radiological investigations were performed as indicated in every patient. It was ensured that a blood sample was collected for estimation of serum total magnesium levels on admission to intensive medical care unit. APACHE score was calculated using the APACHE II scoring system. It was ensured that the study did not interfere with the management of patient in the intensive medical care unit. Blood magnesium levels of the subjects was correlated with their prognosis.

## Data Analysis

The reference range of the normal serum magnesium was fixed between 1.7-2.4 mg/dL. Normal deviate (z) test was applied to find out the significance of difference between two means for quantitative data. Chi-square test was used to assess the statistical significance of qualitative data.

## Ethical Consideration

The study was approved by Government Rajaji Hospital Ethical Committee. Informed consent was obtained before enrolling subjects to the study.

## RESULTS

Of the 100 patients, 52 (52%) were males and 48 (48%) were females. Age group from 51-60 years contributed as the major study population. Organophosphorus poisoning was the common critical illness group contributing to 21% of the total sample size. The various group of critical illness of the study population is shown in Table 1. Table 2 shows the impact of serum magnesium level on various parameters in study population in ICU patients.

On admission, 50% (50/100) patients had hypomagnesaemia, 39% (39/100) had normal serum magnesium levels and 11% had hypermagnesaemia. The lowest serum magnesium value recorded was 0.7 mg/dL while the highest value was 3.7 mg/dL. The range of duration of stay in intensive medical care unit varied from 4 to 20 days.

The mean duration of IMCU stay in the hypomagnesaemic group is 16.5 days while that of the normomagnesaemic group is 10.4 days, which was statistically significant. The mean duration of ventilator requirement in the hypomagnesaemic group is 11.7 days, while that of normomagnesaemic group is 7.4 days, which is statistically significant. The mean APACHE score of the hypomagnesaemic group was 19.52 while that of the normomagnesaemic group is 9.7 days. The incidence of hypokalaemia in the hypomagnesaemic group was 76%

while in the normomagnesaemic group was 24%, which was statistically significant. The incidence of hyponatraemia in the hypomagnesaemic group was 64% while in the normomagnesaemic group was 28%, which was statistically significant. The incidence of hypocalcaemia in the hypomagnesaemic group was 38% while in the normomagnesaemic group was 12%, which was statistically significant.

The incidence of polymorphic ventricular tachycardia in the hypomagnesaemic group was 8% while in the normomagnesaemic group was 2%. Finally, the mortality rate was also higher in the hypomagnesaemic group, which is 84.2% that was statistically significant. The mortality chart showing the details on mortality in the two groups- hypomagnesaemia and normomagnesaemia is presented in Table 3a and 3b. Table 4 shows comparison of serum

magnesium level among patients requiring ventilator support in ICU.

Sl. No.	Type of Critical Illness	Percentage
1.	Organophosphorus poisoning	21
2.	Coronary artery disease	21
3.	Diabetic ketoacidosis	14
4.	Meningitis	8
5.	Snake bite	16
6.	ILD with respiratory failure	13
7.	Others	7

**Table 1. Type of Critical Illness of Enrolled Study Patients**

	Hypomagnesaemia	Normomagnesaemia	Significance
Occurrence	50%	50%	
Duration of hospital stay	16.5 days	10.4 days	P <0.05
Need for ventilation	41/77 (53.2%)	26/77 (33.7%)	P <0.05
Duration of ventilation	11.7 days	7.4 days	P <0.05
APACHE score	19.5±2.5	9.7±2.5	P <0.05
Hypokalaemia	38/50 (76%)	12/50 (24%)	P <0.05
Hyponatraemia	32/50 (64%)	14/50 (28%)	P <0.05
Hypocalcaemia	19/50 (38%)	6/50 (12%)	P <0.05
Arrhythmia	4/50 (8%)	1/50 (2%)	P <0.05
Mortality rate	16/19 (84%)	3/19 (15.79%)	P <0.05

**Table 2. Comparison of Hypomagnesaemia and Normomagnesaemia Group of Patients among the Study Population on Various Parameters**

MORTALITY CHART				
Diagnosis	Total Mortality		Mortality in Hypo-magneseemic Group	Mortality in Normo-magneseemic Group
	Number	Percentage		
CAD	13	68.42	10 (77%)	3
OPC	2	10.52	2 (100%)	Nil
Meningitis	2	10.52	1 (50%)	1 (50%)
ILD / RF	2	10.52	1 (50%)	1 (50%)

**Table 3a. Comparison of Mortality with Serum Magnesium Level among Study Population**

INCIDENCE OF HYPOMAGNESEMIA AND MORTALITY IN SUBGROUPS OF PATIENTS					
Diag-nosis	Total No. of Patients	Low serum Magnesium	Normal serum Magnesium	Incidence of Hypo-magneseemia	Mortality
DKA	14	8	6	57.40%	Nil
CAD	21	15	6	71.40%	13 (61.91%) p<0.05
OPC	21	13	8	61.90%	2 (9.5%) p>0.05
Snake bite	16	10	6	62.50%	Nil
Meningitis	8	5	3	62.50%	2 (25%) p<0.05
ILD / RF	13	8	5	61.50%	2 (15.4%) p<0.05

**Table 3b. Comparison of Mortality with Serum Magnesium Level among the Subgroups**

**of the Study Population**

VENTILATOR REQUIREMENT				
Diagnosis	No. of patient requiring ventilator	VENTILATOR REQUIREMENT		
		Hypo-magneseemic Group	Normo-magneseemic Group	Mean Duration of ventilator stay
DKA	6	4(7%)	2	9
CAD	18	14(23.37%)	4	12
OPC	19	12(24.67%)	7	14
Snake Bite	14	10(18.18%)	4	10
Meningitis	6	3(7.7%)	3	12
ILD	11	6(14.28%)	5	11
Others	3	2(308%)	1	13

**Table 4. Comparison of Serum Magnesium Level among Patients Requiring Ventilator Support in ICU**

**DISCUSSION**

Our study showed that patients with low serum magnesium had longer duration of hospital stay, higher mortality rate and higher incidence of dyselectrolytaemia (hypokalaemia, hyponatraemia, hypocalcaemia). Hypokalaemia is usually refractory to correction in the background of hypomagnesaemia. Magnesium depletion predisposes to hypophosphataemia, which is the underlying cause for

longer ventilator stay. A higher mortality rate was detected in hypomagnesaemic patients as compared to normomagnesaemic patients by Chernow et al<sup>8</sup> (41% vs. 13%) and Rubiez et al<sup>9</sup> (46% vs. 25%), respectively. The mortality rate in our study was similar to these studies.

The cause for high mortality in the hypomagnesaemic group could be multifactorial. The foremost contributing factor is the primary disease itself followed by other electrolyte abnormalities (particularly hypokalaemia, which predisposes to polymorphic ventricular tachycardia), ventilator associated complications, hospital-acquired infections in the order of hierarchy.

In the study carried out by Soliman et al<sup>10</sup> and Limaye et al,<sup>11</sup> there was no difference in the length of ICU stay among the hypo as well as normal magnesium groups whereas in our study hypomagnesaemia had a prolonged stay.

The main implications of the study is that it has been made clear that magnesium monitoring in the intensive care setting can be a diagnostic tool for recalcitrant hypokalaemia, decrease the duration of ventilator stay, decrease in the morbidity and mortality; if suspected and detected, decrease the incidence of ventricular tachycardia.

### Limitations

The mortality rate, duration of hospital stay, need for ventilator stay were all high in the group of patients with coronary artery disease. Most of the patients of coronary artery disease were on long-term diuretics, which could result in hypomagnesaemia. Moreover, the disease process itself is more contributory for the morbidity rather than hypomagnesaemia per se. Next, the major population of the study group is contributed by the age group of 51-60 yrs. Higher age itself is a risk factor for developing multiple dyselectrolytaemias.

### CONCLUSION

Magnesium though is most understudied electrolyte has critical implications in the ICU setting.

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### REFERENCES

- [1] Kasper D, Fauci AS, Hauser S, et al. Harrison's text book of internal medicine. 19<sup>th</sup> edn. McGraw Hill Professional 2015.
- [2] Murphy E, Freudenrich CC, Levy LA, et al. Monitoring cytosolic free magnesium in cultured chicken heart cells by use of the fluorescent indicator Fura2/AM. *Proc Natl Acad Sci USA* 1989;86(8):2981-2984.
- [3] Raju B, Murphy E, Levy LA, et al. A fluorescent indicator for measuring cytosolic free magnesium. *Am J Physiol* 1989;256(3 pt 1):C540-548.
- [4] Pederson KO. Binding of calcium to serum albumin, calcium albumin interaction. IV. Effect of temperature and thermodynamics of calcium-albumin interaction. *Scand J Clin Lab Invest* 1972;30(1):89-94.
- [5] Shareghi GR, Agus Z. Magnesium transport in the cortical thick ascending limb of Henle's loop of the rabbit. *J Clin Invest* 1982;69(4):759-769.
- [6] Wong ET, Rude RK, Singer FR. A high prevalence of hypomagnesemia and hypermagnesemia in hospitalized patients. *Am J Clin Pathol* 1983;79(3):348-352.
- [7] Ryzen E. Magnesium homeostasis in critically ill patients. *Magnesium* 1989;8(3-4):201-212.
- [8] Chernow B, Bamberger S, Stoiko M, et al. Hypomagnesemia in patients in postoperative intensive care unit. *Chest* 1989;95(2):391-397.
- [9] Rubiez GJ, Thill-Baharozian M, Hardie D, et al. Association of hypomagnesemia and mortality in acutely ill medical patients. *Crit Care Med* 1993;21(2):203-209.
- [10] Soliman HM, Mercan D, Lobo SS, et al. Development of ionized hypomagnesemia is associated with higher mortality rates. *Crit Care Med* 2003;31(4):1082-1087.
- [11] Limaye CS, Londhey VA, Nadkarni MY, et al. Hypomagnesemia in critically ill medical patients. *J Assoc Physicians India* 2011;59:19-22.