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Magnesium levels among critically ill elderly patients; mortality and morbidity correlation

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ABSTRACT

Objectives: **To evaluate the association between magnesium levels, morbidity and mortality in critically ill elderly patients admitted in ICU. *Methods*: A cross-sectional study was done on patients admitted to the intensive care unit (ICU) of the Geriatrics department at a University Hospital over 1.5 years period. Data collected included patients demographics and medical history, length of stay in the ICU. Lab tests included serum Magnesium on admission, serum sodium and potassium. In addition, the Acute Physiology and Chronic Health Evaluation (APACHE) II score and the Sequential Organ Failure Assessment (SOFA) score were determined at the day of admission. *Results*: A single center, cross sectional study was done on 100 patients who were admitted to the Geriatrics medical ICU at Ain Shams university Hospital in Cairo. At admission 23% of patients had low magnesium (Mg) level and 59% had normal magnesium level and 18% had high Mg level. The mean age of patients with hypomagnesaemia was 71.69 years old while those with normal magnesium level were 69.5 years old and that with hypermagnesaemia were 69.7 years old. The length of ICU stay was longer among patients with high Mg level (11.7 ± 14.4 days) and among those with normal magnesium level (7.6 ± 5.8 days) versus (7.5 ± 3.8 days) those with low Mg level, among the studied groups (55.6%) of patients with Hypermagnesaemia died versus (44.1%) of patients with normal Mg level. Among the studied groups, those with high Mg level were found to have higher APACHE II score (20.7 ± 7.4) and SOFA score (5.5 ± 3.6) than the other subjects. Significant positive correlation was found between mean Mg level and SOFA score. *Conclusion*: Development of hypermagnesaemia during an ICU stay is associated with bad prognosis. Monitoring of serum magnesium levels may have prognostic, and perhaps therapeutic, implications.**

KEYWORDS

Magnesium; Critical Care; Sequential Organ Failure Assessment Score; Mortality

1. INTRODUCTION

Magnesium is the fourth most abundant cation in the human body and the second most abundant intracellular cation after potassium. Magnesium (Mg) is pivotal in the transfer, storage, and utilization of energy as it regulates and catalyzes more than 300 enzyme systems [1,2].

Magnesium deficiency has been associated with a number of clinical manifestations such as atrial and ventricular arrhythmias, cardiac insufficiency, coronary spasm, sudden death, skeletal and respiratory muscle weakness, bronchospasm, tetany, seizures, and other neuromuscular abnormalities and a number of electrolyte abnormalities, including hypokalemia, hypocalcaemia, hyponatremia, and hypophosphatemia [1,3-6].

Hypomagnesaemia is one of the most common electrolyte disturbances in hospitalized patients, especially in the critically ill. The Prevalence of hypomagnesaemia (measuring total serum magnesium) has a wide range (11% to 61%), and considerable controversy exists regarding its effects on morbidity and mortality [7-9].

The severity of hypomagnesaemia can be assessed using subjective clinical evaluation and biochemical markers of organ dysfunction. Objective scoring systems such as, the Acute Physiology and Chronic Health Evaluation

(APACHE) II and Sequential Organ Failure Assessment (SOFA) scores are also commonly used to assess severity of illness and to predict outcome in other groups of critically ill patients [10,11].

The scoring systems may identify high-risk groups among the critically ill, to whom therapeutic interventions may be directed in order to reduce morbidity and mortality, and comparisons may be made of the benefit of such interventions [11].

The development of the Sepsis-related Organ Failure Assessment (SOFA) score was an attempt to objectively and quantitatively describe the degree of organ dysfunction over time and to evaluate morbidity in intensive care unit (ICU) septic patients [12]. Later, when it was realized that it could be applied equally well in non-septic patients, the acronym "SOFA" was taken to refer to Sequential Organ Failure Assessment [13]. The SOFA scoring scheme daily assigns 1 to 4 points to each of the following six organ systems depending on the level of dysfunction: respiratory, circulatory, renal, hematology, hepatic and central nervous system. Since its introduction, the SOFA score has also been used for predicting mortality, although it was not developed for this purpose.

The SOFA score was developed through a consensus process [14] and afterwards validated in a larger population of 1449 critically ill patients [15].

Prevalence of Hypermagnesaemia varies from 5.7% to 9.3% [16]. The highest serum magnesium concentrations reported so far is 13.4 mmol/L in a 78 years old woman who swallowed water from the Dead Sea [16,17] severe hypermagnesaemia in fact that seems to be a feature in patients who drown in the Dead Sea [17].

Hypermagnesaemia commonly occurs due to the excessive administration of magnesium salts or magnesium-containing drugs, especially in patients with reduced renal function. Hypermagnesaemia may rarely be due to redistribution from cells [18].

Disorders of magnesium metabolism are common in hospital patients and are frequently unrecognized. Low magnesium intake may be a contributor to many diseases including diabetes, cardiovascular disease and osteoporosis. Common complications of hypomagnesaemia include cardiac arrhythmias, and hypocalcaemia. Hypermagnesaemia, though less frequent, can also lead to cardiovascular and neuromuscular manifestations. Early recognition of disordered magnesium metabolism and correction of the electrolyte imbalance is necessary to avoid these complications. [18].

The aim of this study was to evaluate the relationship between levels of magnesium and length of ICU stay, electrolyte disturbance and mortality rate. Also, this study was undertaken to establish the value of the APACHE II and SOFA scores in determining the patient's morbidity and mortality in the critically ill patients admitted to an intensive care unit (ICU).

2. MATERIALS AND METHODS

A single center, cross sectional study was carried out in the ICU of the Geriatrics department at Ain Shams University Hospital in Cairo, Egypt from May1/2011 through December 31/2012.

During this period of one and half year, all patients admitted in the ICU were recruited for the study.

Those with burn injury, Mg administration, and addiction were excluded from data collection.

The study was approved by the University and Hospital Ethics Committees.

Tools of Assessment

1) Data collection was done for all participants including patients' demographics and medical history, length of stay in the ICU.

2) The Acute Physiology and Chronic Health Evaluation (APACHE) II score incorporates 12 physiologic variables, age, and an assessment of chronic diseases in individual patient [19].

Renal dysfunction was defined by a serum creatinine of >1.2 mg/dL.

3) The Sequential Organ Failure Assessment (SOFA) score was determined at the day of admission SOFA is composed of scores from six organ systems (respiratory, cardiovascular, hepatic, coagulation, renal, and neurological) graded from 0 to 4 according to the degree of dysfunction/failure [20].

4) Blood collection:

Total serum magnesium (Mg) concentrations were recorded at the day of admission to the ICU.

The variety of lab tests related to magnesium, included (normal values): sodium (136 - 142 mEq/L), potassium (3.8 - 5 mEq/L), and total bilirubin (<1.2 mg/dL), creatinine (0.4 - 1.2 mg/dL).

ICU lengths of stay, and general patient demographics were recorded.

Patients were classified into three groups according to their initial Mg level: hypomagnesaemia (≤1.9 mg/dl) and normomagnesaemia (1.9 - 2.5 mg/dl) and hypermagnesaemia (≥2.5 mg/dl).

3. STATISTICAL ANALYSIS

Data was analyzed using the statistical program SPSS for window, Release 16. All values are reported as mean ± SD. Chi-square and Fisher's exact tests were used for categorical variables. Pearson's correlation coefficient and linear regression were used to evaluate the relationship between Mg and other variables. A P value of <0.05 was considered as statistically significant.

4. RESULTS

A cross sectional study was conducted on 100 patients ≥ 52 years old. Of the total 100 patients, 32 patients were presented with cerebrovascular diseases, 20 patients were represented with cardiovascular diseases, and 13 patients were presented with chest problems, 14 patients with disturbed conscious level (Table 1). 51 patients (50% of the patients) had≥3 co morbid conditions, while 23.8% had only one disease.

Mean age of the studied group, was 69.95 ± 9.9 years in males and 70.19 ± 9.08 years in females 0.33% were males while 67% were females. Whereas, the mean Mg level in males was 2.2 mg/dl while in females it was 2.1 mg/dl with no statistical significance difference (Table 2).

According to serum Mg, patients were divided into 3 groups. 23 (23%) of patients had low magnesium (Mg) level and 59 (59%) had normal magnesium level and 18 (18%) had high Mg level (Table 3).

The mean age of patients with hypomagnesaemia was 71.69 years while those with normal magnesium level were 69.5 years and that with hypermagnesaemia was 69.7 years (Table 3).

The length of ICU stay was longer among patients with high Mg level (11.7 ± 14.4 days) and among those with normal magnesium level (7.6 ± 5.8 days) versus (7.5 ± 3.8 days) for those with low Mg level (Table 3).

Death rate was high among those with high Mg level (55.6%) and those with normal Magnesium level (44.1%) versus (34.8%) among those with Low Magnesium level (Table 3).

Among the studied groups those with high Mg level were found to have higher APACHE II score (20.7 ± 7.4) and SOFA score (5.5 ± 3.6) than the other subjects (Table 3).

Significant positive correlation was found between mean Mg level and SOFA score ($P < 0.05$) (Figure 1) but there was a non significant positive correlation between mean Mg level and APACHE II score ($P > 0.05$) (Table 4).

Table 1. Causes of ICU admission of patients.

Cause of admission	Number of patients	%
Diabetes mellitus	2	1.98
Cerebrovascular diseases	32	31.68
liver diseases	8	7.92
Chest diseases	13	12.87
Dementia	1	0.99
Chronic kidney diseases	2	1.98
Cardiovascular diseases	20	19.8
Shock	13	12.87
Disturbed conscious level	14	13.86
Post operative	2	1.98
Others	5	4.95

Table 2. Demographic data of the studied groups.

		Age	
Sex	Males (n = 33)	Mean ± SD 69.95 ± 9.9	$x^2 = 0.263$ t = 0.366
	Females (n = 67)	Mean ± SD 70.19 ± 9.08	

Table 3. Demographic data, length of ICU stay and Patients outcome, SOFA score, APACHE II score according to Mg level at admission.

		Serum Mg level			Statistical difference
		Low	Normal	High	
Number of patients		23 (23%)	59 (59%)	18 (18%)	
Age (years)		Mean ± SD 71.69 ± 9.13	Mean ± SD 69.5 ± 9.5	Mean ± SD 69.7 ± 8.9	F = 0.446 P = 0.641
Sex	males	3 (13.1%)	22 (37.3%)	8 (44.4%)	t = 5.700 P = 0.58
	females	20 (87%)	37 (62.7%)	10 (55.6%)	
Hospital stay (days)		Mean ± SD 7.5 ± 3.8	Mean ± SD 7.6 ± 5.8	Mean ± SD 11.7 ± 14.4	F = 2.063 P = 0.133
Patients outcome	improvement	15 (65.2%)	33 (55.9%)	8 (44.4%)	t = 1.76 P = 0.413
	death	8 (34.8%)	26 (44.1%)	10 (55.6%)	
SOFA score		Mean ± SD 3.2 ± 2.4	Mean ± SD 3.5 ± 2.6	Mean ± SD 5.5 ± 3.6	F = 4.183 P = 0.018
APACHE II score		Mean ± SD 18.8 ± 7.6	Mean ± SD 18.6 ± 5.7	Mean ± SD 20.7 ± 7.4	F = 0.72 P = 0.489

Table 4. Correlations between Magnesium levels (Mg), SOFA and APACHE II scores.

	Mg
SOFA	r = 0.247* P = 0.013*
APACHE	r = 0.85 P = 0.403

*Means that it is statistically significant.

5. DISCUSSION

In mammals, the magnesium ion plays an important role at the intracellular level as free magnesium regulates intermediary metabolism, DNA and RNA synthesis and structure, cell growth, reproduction and membrane structure, transport of potassium and calcium ions, signal transduction modulation, and fat and protein synthesis. Magnesium is a cofactor for most adenosine triphosphates because it is the adenosine triphosphate-magnesium complex that is bound and hydrolyzed by enzymes [21-23].

The prevalence of hypomagnesaemia in critically ill adult patients varies between 14% - 66% [24-27].

The relation between hypomagnesaemia and mortality has varied among studies. Chernow *et al*. [25] reported no difference in mortality between hypomagnesaemia and normomagnesaemic patients (13% vs 11%).

Guerin *et al*. [26] found no difference in ICU mortality

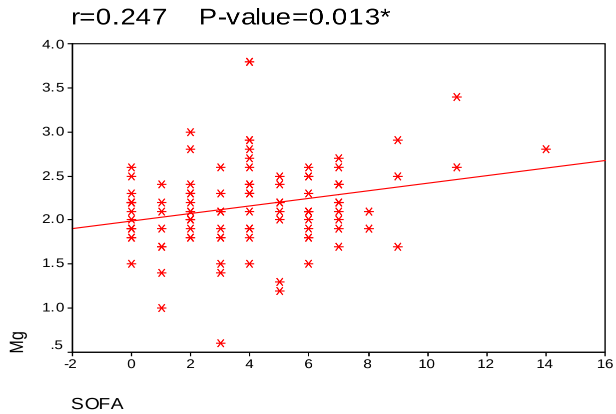

Figure 1. Correlations between Magnesium levels (Mg) and SOFA score.

between hypomagnesaemia and normomagnesaemic patients (18% vs 17%). Rubeiz *et al.* [28] reported nearly double the mortality rates (46% vs 25%) in hypomagnesaemia patients compared with those with normomagnesaemia.

In the current study at admission 23(23%) of patients had low magnesium (Mg) level and 59 (59%) had normal magnesium level and 18 (18%) had high Mg level.

Death rate was high among those with high Mg level (55.6%) than those with normal Magnesium level (44.1%) and Low Magnesium level (34.8%).

(*Guerin et al.*; 1996) in a prospective study to evaluate the prevalence of serum magnesium (Mg) abnormalities in patients on admission to the intensive care unit (ICU) and to test the hypothesis that low levels of Mg are associated with a higher mortality. They confirm the high prevalence of Mgs abnormalities as well as Mg deficiency on admission to a medical ICU. Low levels of Mgs are not associated with higher fatality. HyperMgs was associated with patient death [29].

The admission SOFA reflects the degree of failure already presented when the patient enters the ICU. This measurement, the only admission mortality prediction model, is able to achieve, can be used to stratify patients according to severity of illness, for example, inclusion in clinical trials based on the admission SOFA score [30].

In the current study, the length of ICU stay was longer among patients with high Mg level (11.7 ± 14.4 days) and among those with normal magnesium level (7.6 ± 5.8 days) versus (7.5 ± 3.8 days) for those with low Mg level.

Comparison of the APACHE II and SOFA score reveals that the accuracy of the APACHE II is not significantly better than that of the SOFA for abnormal magnesium level [31]. The APACHE II is not much better than SOFA score in the prediction of hypomagnesaemia, because many biases are found in the use of the APACHE system: First, treatment error is not predictable, especially in surgical patients [31]. Second, the data collected on the day of admission may not reflect completely the unpredicted events which restore them to their previous health and quality of life. The latter is more meaningful, because the functional results are as important as the mortality prediction [32]. In the current study the Acute Physiology and Chronic Health Evaluation II (APACHE II) was higher among those with high Mg level (20.7 ± 7.4) and the Sequential Organ Failure Assessment (SOFA) score was higher among those with high Mg level (5.5 ± 3.6) and significant positive correlation was found between mean Mg level and SOFA score.

In conclusion, the development of hypermagnesaemia during the ICU stay is associated with higher morbidity and mortality rates that may be the result of prolonged disease, or sepsis.

A prospective study is indicated to verify observations regarding outcome prediction, to identify appropriate interventions in the high-risk patient, to confirm the potential benefit of magnesium level measurement to prevent or correct magnesium disorder in critically ill patients, and to determine the impact, if any, of other organ system dysfunction.

AUTHOR CONTRIBUTIONS

Study concept and design: Salma M. S. El Said, Analysis and Interpretation of data: Salma M. S. El Said, Walaa W. Aly.

Drafting of the Manuscript: Salma M. S. El Said, Walaa W. Aly.

Critical revision of the manuscript for important intellectual content: Salma M. S. El Said, Walaa W. Aly.

Statistical Analysis: Salma M. S. El Said, Walaa W. Aly.

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Implications for health policy: the aim of the study was to evaluate the association between magnesium levels, morbidity and mortality in critically ill elderly patients admitted in ICU.

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