THE INFLUENCE OF SERUM MAGNESIUM LEVEL ON THE OUTCOME OF CHILDREN ADMITTED TO THE PEDIATRIC INTENSIVE CARE UNIT

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Abstract:

Background: Magnesium (Mg) deficiency is prevalent in the critically sick and may result in life-threatening consequences. A lack of magnesium is strongly linked to a higher likelihood of mortality.

Objectives: In this research, We aim to evaluate whether or not serum magnesium levels were correlated with prognosis and outcome in child patients hospitalized to the pediatric intensive care unit (PICU).

Methods: A prospective observational research in a single-center tertiary institution included 80 pediatric patients among the ages of one month and twelve years admitted to the PICU during the period from October 2019 to May 2020. The serum Mg level was assessed in all patients.

Findings: 45 (56.25%) patients had hypomagnesemia with Mean ± SD of1.1±0.1. The majority of admitted children had respiratory diseases. In 56.25% of the patients with hypomagnesemia, there was a statistically significant lower Mg level in relation to a higher PRISM score and a lower age group. Hypomagnesemia is significantly present in patients with sepsis and gastroenteritis. There was a positive association among K, Ca, albumin & Mg. Lower levels of Mg were present in children who needed inotropic drugs and a longer duration of mechanical ventilation. The outcome of the 80 children revealed the deaths of 27 patients in the hypomagnesemia group.

Conclusions: Low serum levels of Mg in critically ill children were more commonly seen in cases with sepsis and gastroenteritis and were related to a bad prognosis and a high mortality rate. Serum Mg levels need to be closely monitored and corrected, as they could have prognostic and therapeutic implications.

Key words: Children, Magnesium, outcome, PICU

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Introduction

Magnesium (Mg) is the 2nd most common intracellular cation. [(1)] It functions as a cofactor in above 300 enzymes containing adenosine triphosphate. It also plays a crucial function in regulating the tone of peripheral blood vessels and the contractility of the heart by controlling calcium ion transport in smooth muscle cells. [(2, 3)] In critically ill individuals admitted to ICU, metabolic disorders, including hypomagnesemia, are very common. [(4)] Tremor, tetany, hyperreflexia, tonic-clonic convulsions, nystagmus, ventricular arrhythmia, hypertension, coronary vasospasm, hemiparesis, and bronchospasm are some symptoms that may accompany hypomagnesemia; however, the condition is often asymptomatic. [(5)] Hypomagnesemia under critical conditions can have a wide variety of reasons, involving but not limited to insufficient oral intake, renal & gastrointestinal losses, and changes in intracellular & extracellular distribution. [(6)] Magnesium (Mg) absorption from the gut is reduced with extended usage of proton pump inhibitors. [(7)] Individuals utilizing diuretics & aminoglycosides are also at a greater risk for developing hypomagnesemia. [(8)] Macrophage activation, adhesion, lymphocyte proliferation & endotoxin binding to monocytes are just few of the immunological processes that magnesium aids. Therefore, people with sepsis are more likely to experience hypomagnesemia. [(9, 10)] Hypomagnesemia is strongly linked to an increased requirement for mechanical ventilation, longer ICU stays, and higher mortality, as shown by both randomized controlled trials and observational research. [(4, 9)]

Objectives:

Our study's goals were to (1) measure blood Mg levels in critically sick children admitted to the PICU & (2) determine whether or not these levels were associated with individual's prognosis & outcome.

Patients and Methods

This prospective observational trial was performed out among October 2019 & May 2020 in the PICU

at Minia Maternity and Children's University Hospital. Eighty PICU admissions were included in the research. These kids ranged in age from one month to twelve years. Individuals who had received treatment for low Mg throughout the previous 24 hours, those with substantial trauma or surgical conditions, and those with documented congenital renal magnesium deficiency were excluded from participating in the research. Children who met the inclusion criteria were recruited in the research once clearance from the ethics committee was obtained. All participating minors had their legal guardians sign an informed consent form. All of the enrolled children had their medical histories taken and were physically examined. Patients' demographic data was recorded in a standard format, including their ages, sexes, heights, weights, and admission diagnoses (such as respiratory, gastrointestinal, cardiovascular, neurological, and others). On admission, we checked Mg levels in addition to a CBC, CRP, ESR, renal & liver function tests, serum glucose, electrolytes (Na+, Ca+, K+), albumin & arterial blood gases. Blood cultures, cerebrospinal fluid analyses, computed tomography (CT) or magnetic resonance imaging (MRI) of the brain, electrocardiograms (ECGs) & echocardiograms (Echos) were also necessary in certain situations. At the time of an individual's admission to the PICU, the PRISM score was determined. Every child was cared for in accordance with the PICU's standard operating procedure. Study participation did not alter routine medical care in any way. Both life and death were tracked for every patient. Indicators of the patient's prognosis included the length of their stay in the PICU, the presence of mechanical ventilation, and the the individual's final fate. Magnesium levels were analyzed biochemically using a fully automated clinical chemistry system (Konilab 60i; Thermo Electron Corporation, Finland). XYLIDYL BLUE was employed to determine magnesium concentrations with the use of Erba kits. The numbers came back in milligrams per deciliter. Subjects were separated into 2 Groups dependent upon their serum Mg concentration, referred to as follows:

• Normal: 1.5-2.3mg/dL • Hypomagnesemia: less than1.5mg/dL

Statistical analysis:

IBM SPSS 20.0 was utilized to do the statistical analysis on the data. Shapiro-Wilk & Kolmogorov-Smirnov tests were employed to examine whether or not the data followed a normal distribution. Categorical data were demonstrated as both a number and a percentage, as well as the mean SD, minimum maximum range, median range & range median for quantitative measurements. Parametric data were compared employing the Student t-test, whereas non-parametric data were analyzed utilizing the Mann-Whitney U test. Analysis of variance (ANOVA) was utilized for parametric data to facilitate comparisons among more than two distinct groups. Categorical variables were compared utilizing the chi-square test or the Fisher's exact test. Pearson's correlation analysis was employed to examine the inter-parameter relationships. In this case, significance was defined as a P value below 0.05.

Results

Our research involved 80 critically ill children, 43 males and 37 females, amongst the ages of one month and twelve years, admitted to the PICU. Patients' demographics and diagnostic data are shown in **Table 1**. The majority of them were admitted to the PICU with respiratory diseases (31.25%), followed by cardiovascular diseases (18.75%). Two patients were admitted due to complicated sickle cell anemia with vasoocclusive crisis and acute chest syndrome, and one patient had accidental drug toxicity (3.75%). Laboratory data and serum levels of magnesium for all patients are presented in Table 2. Out of the 80 patients, 45 (56.25%) had hypomagnesemia with a mean± SD of 1.1±0.1. **Table 3** demonstrates that there was no significant distinction in Mg levels by sex, but that there was a significant decrease in Mg levels by both PRISM score ($p = 0.031$) and age group ($p = 0.012$). Hypomagnesaemia was detected in 25 (55.6%) children aged less than 2 years, and regarding diagnosis and disease category, we found that hypomagnesaemia is significantly present in patients with sepsis and gastroenteritis, with p values: 0.009 & 0.037, respectively. There was no significant variation in serum Mg level in relation to the laboratory data except with K, Ca, and albumin serum levels, as there was a positive correlation between them and Mg; the lower K, Ca, and albumin, the less Mg (p values: 0.021, 0.031, and 0.006, respectively), as seen in **figure 1**. Regarding the prognosis of the patients, there were significantly lower levels of Mg in children who needed inotropic drugs and had a longer duration of mechanical ventilation compared to children with normal Mg levels, with p values of 0.001 & 0.033, respectively. The final outcome of the 80 children included in this study revealed the deaths of 29 (36.25%) children, 27 of them in the hypomagnesaemia group, with a mortality rate of 60% and a p value <0.001 **(table 4).**

Table (1) Demographic and Diagnostic data for the examined 80 cases at presentation

Demographic data		
Age	Range (Mean± SD)	1m –12 years (5.6±4.8)
Sex	Male/ Female	43 (53.8%) / 37(46.2%)
Weight (kg)	Range (Mean± SD)	3.5-53 (19.1±5.3)
Length/Height (cm)	Range (Mean± SD)	55-150 (95.8±19.5)
Diagnosis		**No (%)**
Respiratory diseases:		**25 (31.25%)**
Pneumonia		12 (15%)
Bronchiolitis		8 (10 %)
Severe asthmatic attack		5 (6.25%)
Cardiovascular diseases:		**15 (18.75%)**
Heart failure.		8 (10%)
Arrythemia.		3 (3.75%)
Cardiogenic shock.		4(5%)
Neurological diseases:		**9 (11.25%)**
Viral encephalitis		4(5%)
Meningitis		1(1.25%)
Status epilepticus		4 (5 %)
Gastro intestinal diseases:		**12 (15%)**
Complicated gastro-enteritis		9 (11.25%)
Hepatocellular failure		3 (3.75%)
Endocrinal diseases:		**8 (10%)**
DKA		5 (6.25%)
Adrenal insufficiency		3 (3.75%)
Septicaemia		**8 (10%)**
Others*		**3 (3.75%)**

Table (2) Laboratory data for examined cases at presentation

Laboratory tests	***Range***	***Median***	***Mean± SD***
Hemoglobin (g/dl)	8-13	10	9±1.5
Total leucocyte count (x10^9/L)	9.5-23.5	10.5	16.8±9.3
Platelets (x10^9/L)	82.5-310	194.5	222.6±174.9
C-reactive Protein (mg/dl)	3-104	48	61.6±40.4
Alanine transaminase (ALT)	10-485	46	86.8±96.8
Aspartate transaminase (AST)	11-354	44.5	60.2±64.3
Albumin (g/dl)	2.5-5.5	3.6	3.6±0.6
Prothrombin time (seconds)	11-25	16.5	16.8±3.7
Urea (mg/dl)	11-120	36	42.4±26.8
Creatinine (mg/dl)	0.3-2	0.7	0.7±0.4
sodium (mmol/L)	125-168	141	142.7±10.9
potassium (mmol/L)	2.5-6.5	3.5	4.1±0.9
Calcium (mg/dl)	5-10	8	8±1.8
Magnesium (mg/dl)	0.8- 2.3	1.25	1.46±0.45

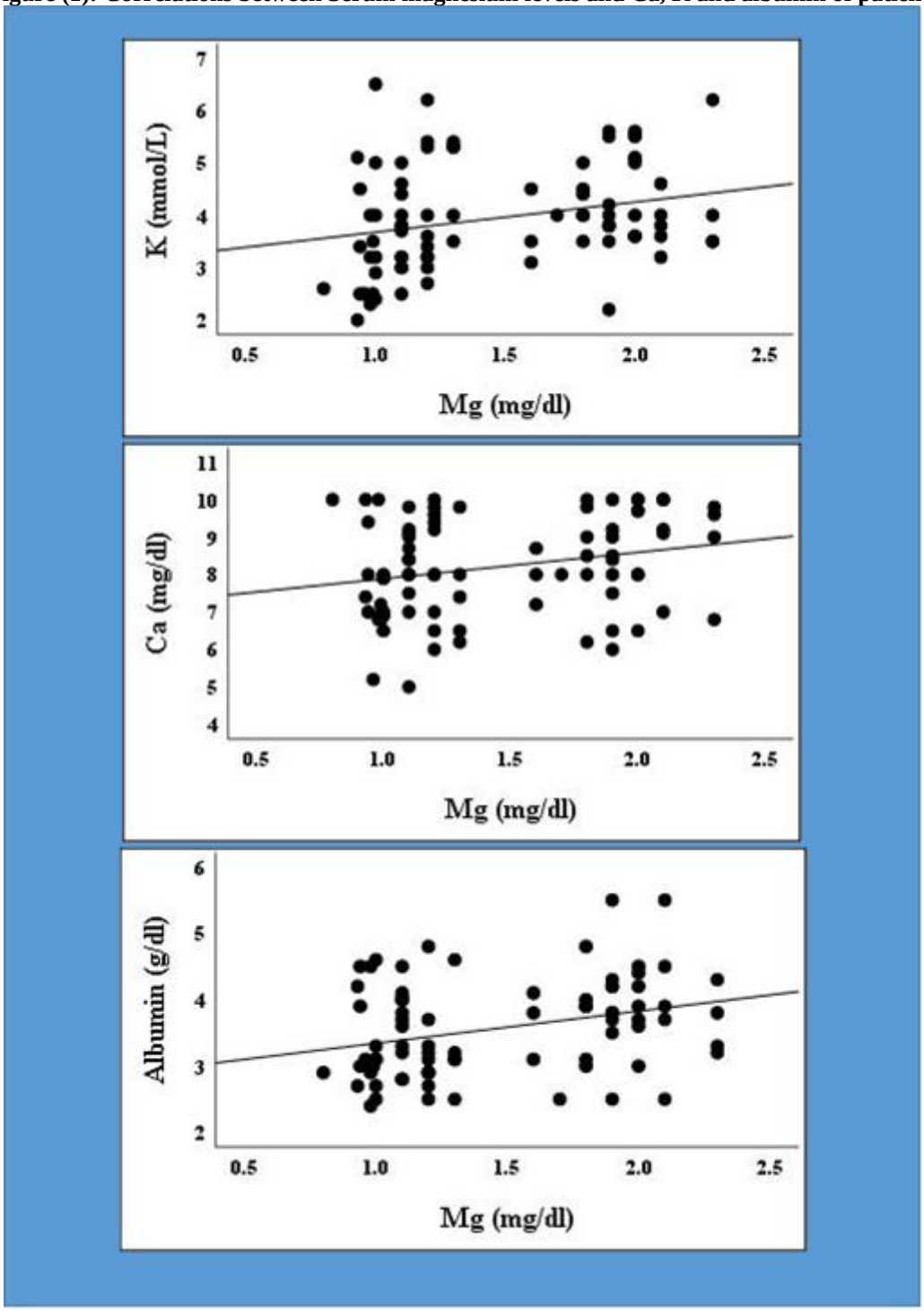
Table (3) Serum magnesium levels in respect to Demographic and Diagnostic data

		Hypomagnesemia N=45 (56.25%)	Normal Mg N=35 (43.75 %)	P value
Age	Range Mean ± SD Median/(IQR)	(0.4-15) 4.6±5.1 2/(0.9-8)	(0.1-16) 6.6±4.9 4.5/(2.5-11)	**0.027***
Age group	1m-2Y >2Y-6Y >6Y-12Y	25(55.6%) 9(20%) 11(24.4%)	8(22.9%) 11(31.4%) 16(45.7%)	**0.012***
Sex	Male/ Female	21(46.7%)/ 24(53.3%)	11(31.4%)/ 24(68.6%)	0.168
PRISM score	Mean ± SD	13.35±6.9	9.1±4.2	0.031
Diagnosis	Pneumonia	6(13.3%)	6(17.1%)	0.638
	Bronchiolitis	5(11.1%)	3(8.6%)	0.709
	Bronchial Asthma	1(2.2%)	4(11.4%)	0.094
	Heart failure	6(13.3%)	2(5.7%)	0.263
	Arrhythmias	0(0%)	3(8.6%)	**0.047***
	Cardiogenic shock	4(8.9%)	0(0%)	0.072
	Sepsis	8(17.8%)	0(0%)	**0.009***
	Gastroenteritis	8(17.8%)	1(2.9%)	**0.037***
	Hepatocellular failure	0(0%)	3(8.6%)	**0.047***
	encephalitis	2(4.4%)	2(5.7%)	0.797
	Meningitis	1(2.2%)	0(0%)	0.378
	status epilepticus	1(2.2%)	3(8.6%)	0.199
	DKA	2(4.4%)	4(11.4%)	0.242
	Adrenal insufficiency	1(2.2%)	1(2.9%)	0.858
	Others	0(0%)	3(8.6%)	**0.047***

Table (4) Serum magnesium levels in relation to prognosis and outcome of patients

			Hypomagnesaemia N=45	Normal Mg N=35	P value
clinical course and Prognosis	**Need of inotropic drugs**	**No** **Yes**	17(37.8%) 28(62.2%)	27(77.1%) 8(22.9%)	**0.001***
	Need of MV	**No** **Yes**	21(46.7%) 24(53.3%)	16(45.7%) 19(54.3%)	**0.932**
	Duration of MV (Hours)	**Range** **Mean ± SD** **Median/(IQR)**	(24-175) 98.4±43.4 101/(72.8-135)	(6-145) 68.5±43.6 72/(24-110)	**0.033***
	Duration of PICU (Days)	**Range** **Mean ± SD** **Median/(IQR)**	(2-15) 7.1±3.7 6/(4-11.5)	(2-15) 6.9±4.2 5/(3-10)	**0.572**
outcome at the end of hospital stay	**Survivors (N=51)**	**Discharge**	18(40%)	33(94.3%)	**<0.001***
	Non-survivors (N=29)	**Death**	27(60%)	2(5.7%)	

Figure (1): Correlations between Serum magnesium levels and Ca, K and albumin of patients



Discussion

Mg deficiency is prevalent among critically ill individuals and may result in potentially fatal complications. [(11)] Magnesium insufficiency (both symptomatic & asymptomatic) is prevalent in critically ill individuals and can have serious clinical repercussions such hypokalemia, cardiac arrhythmias, hypocalcemia, neurotoxicity & psychological disorders, all of which contribute to an already high risk of death. [(12)]

Our study revealed that out of the 80 critically ill children, 45 (56.25%) patients had hypomagnesaemia with serum Mg level Mean ± SD of 1.1±0.1. This comes in accordance with **Haque and Saleem, 2009,** [(4)] who indicated that 44 percent of PICU cases were hypomagnesemic. Also **Safavi and Honarmand, 2007,** [(13)] **Limaye et al.2011,** [(14)] found that 51% and 52% of critically ill patients admitted to ICU had hypomagnesemia. On the other hand, **Seher Erdogan and Tuba Seven Menevse, 2018** [(15)] detected hypomagnesemia in only 43

(29.1%) out of 148 critically ill cases enrolled in their study. Different population and disease category may explain the difference. We found that there was a statistically significant lower Mg levels in relation to higher PRISM score and lower age group with p value: 0.031& 0.012 respectively. Hypomagnesaemia was detected in 25(55.6%) children aged less than 2 years. Regarding diagnosis and disease category we found that hypomagnesemia is significantly presented in patients with sepsis and gastroenteritis with p value: 0.009& 0.037 respectively. This comes in harmony with **Cojocaru et al. 2009, [16]** who found that individuals with sepsis from acute bacterial infection had significantly lower blood magnesium levels and also with the results of **Seher Erdogan and Tuba Seven Menevse, 2018**, **[15]** who observed hypomagnesaemia at a higher rate in cases with sepsis and with **Soliman et al. 2003, [17]** who also found a strong association of hypomagnesaemia with sepsis and septic shock. Regarding gastroenteritis our results are in accordance with **Hansen et al. 2018**, **[18]** who noted that situations involving diarrhea, vomiting & loss of gastrointestinal fluids might lead to Mg shortage and so contribute to the development of hypomagnesaemia.

Hypocalcaemia is a common sign of magnesium insufficiency. Individuals with low levels of parathyroid hormone and low blood calcium and magnesium levels are said to have combined hypocalcaemia and hypomagnesaemia. **[18]** Additionally, we found a positive correlation among Ca, K, and albumin & Mg, where lower levels of Ca, K, and albumin were related with lower levels of Mg (p value: 0.021, 0.031 and0.006 respectively) which are in harmony with **Seher Erdogan and Tuba Seven Menevse, 2018**, **[15]** who detected Hypomagnesemia individuals had a higher incidence of hypokalemia, hypocalcemia & hypoalbuminemia contrasted with normomagnesemia individuals (P< 0.05). This is because of the elevated renal potassium loss and the poor membrane ATPase activity that underlies hypomagnesemia. Our results are also in line with those of **Safavi and Honarmand 2007 [13]** as they reported that Hypomagnesemic intensive care unit individuals had a higher occurrence of hypocalcemia & hypokalemia. **Gupta et al. 2009, [19]** showed that Individuals in critical care should have their hypomagnesemia treated and their serum magnesium levels regularly monitored, since it was shown that administration of Ca and K alone was insufficient to address hypocalcemia & hypokalemia.

Regarding the prognosis of the patients, there were significantly lower levels of Mg in children who needed inotropic drugs and had a longer duration of mechanical ventilation compared to children with normal Mg levels, with p values of 0.001& 0.033, respectively. This comes in agreement with **Safavi and Honarmand 2007[13]** who reported longer duration of mechanical ventilation (7.2 vs 4.7 day) in hypomagnesimic cases. Also, our results come in line with **Limaye et al.2011, [14]** who reported that the patients with hypomagnesemia had more frequent need for ventilatory support (73% vs 53%) and longer duration of mechanical ventilation (4.27 vs 2.15 days). The final outcome of the 80 children included in this study revealed death of 29 (36.25%) children, 27 of them in the hypomagnesemia group (45 patients) with a mortality rate of 60%. Our results come in harmony with **Limaye et al.2011, [14] who** reported that the cases with hypomagnesemia had higher mortality rate (57.7%) and with **Zhonghua et al, 2015, [20]** who concluded that serum There is a strong correlation among Mg levels & ICU mortality, thus doctors are being urged to pay more attention to cases of hypomagnesemia among the critically ill individuals. **Soliman et al. 2003, [17]** also detected People who had hypomagnesemia had a greater incidence of death. It is important to pay more attention to the prevalence of hypomagnesemia in critically ill people since serum magnesium levels are directly associated to death rates in ICU patients also **Lee 2010, [21] advised** that Hypomagnesemia may have a reduced death rate if diagnosed and treated early with magnesium sulfate at a dosage of 25 mg/kg.

The limitation of the present study is the small number of patients involved in it at a single center.

Conclusion

We conclude that there is a low level of serum Mg in critically ill children admitted to the PICU, more commonly presented in individuals with sepsis and gastroenteritis, and related to a bad prognosis and a high mortality rate. Therefore, serum Mg levels need to be closely monitored and corrected, as they could have prognostic and therapeutic implications.

No Conflict of interest

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