

# Outcome and Incidence of Hypomagnesemia in Children Admitted in Pediatric Intensive Care Unit of a Tertiary Care Hospital

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## ABSTRACT

**Background:** Magnesium deficiency is common in serious diseases and is often associated with mechanical ventilation, mortality, and long-term intensive care. Awareness of hypomagnesaemia is essential because little data is available and may have prognostic and therapeutic implications.

**Aim:** This study was conducted to calculate the incidence of hypomagnesaemia at PICU admission and to relate it to length of PICU stay, duration of mechanical ventilation, and outcome of hospital stay or discharge.

**Place and Duration:** In the Pediatric Intensive Care Unit (PICU), Abbasi Shaheed Hospital, Karachi for one-year duration from April 2020 to April 2021.

**Methods:** This is a prospective observational study involving 200 children aged 1 month to 12 years admitted to the PICU. All qualified children underwent an interview and clinical examination. Blood was collected during admission to calculate serum magnesium level. The patients were grouped into three groups: normomagnesemia, hypomagnesaemia and hypermagnesemia, and the data were analyzed.

**Results:** 200 children were included in the inclusion study. Males constituted 57.0% and females 43.0%. The ratio of men to women was 1.2: 1. Most of the respondents were 5 years old. Most of the respondents were in the ICU with neurological symptoms (36.5%), followed by respiratory diseases (27%). Of the 200 patients, 138 (69%) had a mean magnesium level of 1.9 mg / dL. 51 (25.5%) patients had hypomagnesaemia. The average magnesium level was 1.3 mg / dL. 11 (5.5%) patients had hypermagnesemia with a mean magnesium content of 2.7 mg / dl. The lowest measured magnesium level was 1 mg / dl and the highest was 4.2 mg / dl. There was no statistically significant association between hypomagnesaemia and gender, age, disease acceptance category, and sepsis. ≤ 27.4% of children under 5 years of age had severe acute malnutrition in the hypomagnesaemia group. Among those with normal magnesium levels, 24% had severe acute malnutrition and 27.3% had severe acute malnutrition among those with hypermagnesemia. In the study, overall mortality was 25% (50 out of 200). Mortality among people with hypomagnesaemia was 29.40%. Among those with normal magnesium levels, 21.2% died and 18.2% in the hypermagnesemia group.

**Conclusion:** Patients with hypomagnesaemia have prolonged PICU stay, other related electrolyte disturbances and increased mortality. Therefore, in severe ill patients, magnesium levels are monitored.

**Keywords:** Children, Hypomagnesaemia, Intensive Care Unit, Mortality, Outcome, ICU

## INTRODUCTION

Magnesium (mg) is the second most abundant cation in the cell and the fourth most abundant cation in the body<sup>1-2</sup>. It activates about 300 enzymes and is involved in most of the reactions of carbohydrate, lipid, nucleic acid and protein metabolism, regulation of cell permeability and neuromuscular stimulation<sup>3-4</sup>. Magnesium deficiency is common in developing countries with protein energy malnutrition, malabsorption, hypoalbuminemia, sepsis, etc. Magnesium disorders can also persist with prolonged gastric absorption, blood transfusion, over-therapy with catecholamines, diuretics, and aminoglycosides, etc., in intensive care setting<sup>5-6</sup>. Therefore, it is possible that magnesium deficiency is common in severe ill patients. studies showed a large variation in the incidence of hypomagnesaemia (20–70%) in the intensive care unit. There is strong and consistent clinical evidence, mainly from observational studies, that hypomagnesaemia is significantly associated with the need for increased mechanical ventilation, prolonged ICU duration, and

increased mortality<sup>7-8</sup>. Severe patients are confronted with symptomatic and symptomatic magnesium deficiency which can lead to some important clinical consequences such as hypokalemia, arrhythmias, hypocalcemia, neurotoxicity and psychiatric problems, increased mortality and mortality<sup>9</sup>. Data on changes in Mg levels determined in the Pediatric Intensive Care Unit (PICU) are sparse, especially in developing countries. The present study was conducted to calculate the prevalence of hypomagnesaemia in PICU patients admitted to the PICU at a tertiary hospital and from the patient's outcomes for length and duration of PICU stay, the need and duration of mechanical support and results at the end of discharge or death.

## METHODS

This prospective observational study was conducted at Pediatric ICU of Abbasi Shaheed Hospital Karachi for one-year duration from April 2020 to April 2021.

**Admission Criteria:** Children aged 1 to 12 months a month were examined in the PICU.

**Exclusion criteria:** Patients with inherited renal magnesium wasting (e.g, Bartter syndrome, Gitelman syndrome), patients receiving hypomagnesaemia substitution in the last 24 hours, patients with surgical conditions, patients after trauma, patients transferred to other ICUs, ICUs remain less than 24 hours were not included in the study. Children who met the inclusion criteria were enrolled in the study with the consent of the ethical committee. Parents or guardians of the children included in the study received written consent. All qualified children underwent an interview and clinical examination. Details such as age, gender, anthropometry, category of admission like diseases (neurological, respiratory, cardiovascular, gastrointestinal, etc.) have been included in a structured proforma. After hospitalization, 5 ml of blood was collected from the vein in the serum Vacutainer, centrifuged and the serum was sent to calculate the magnesium. For the treatment of these cases, blood counts, Liver function tests, serum electrolytes : sodium, potassium, calcium and other important necessary tests are needed. All enrolled patients received treatment according to the PICU protocol. Joining the research did not change the normal treatment procedure. All patients were followed until death or discharge from hospital. The patient's outcome depends on the length of stay in the ICU and the length of stay in the hospital, the need and duration of mechanical ventilator support after the end of the hospital stay, i.e., death or discharge was recorded. The biochemical analysis of magnesium was carried out completely independently using an XL 300 apparatus. Magnesium levels were calculated by the hospital laboratory. The results are stated in mg / dl. The subjects were divided into three groups according to the serum magnesium concentration specified below.

Normal: 1.5-2.3 mg / dL

Hypomagnesaemia: 2.3 mg / dL and

Hypermagnesemia: >2.3mg/dL.

**Statistical analysis:** The data was entered into the Microsoft Excel tab and statistical analysis was performed with the SPSS 22 versioning software. Categorical data were presented in terms of frequency and proportion. The chi-square test was used as a test for the validity of qualitative data. Continuous data are presented as mean and standard deviation (SD). ANOVA (analysis of variance) was a significance test used to identify the mean difference between more than two groups for quantitative data. p-value (probability of the truthfulness of the result) was considered statistically significant.

## RESULTS

200 children were included in the inclusion study. Males constituted 57.0% and females 43.0%. The ratio of men to women was 1.2: 1. Most of the respondents were 5 years old. Most of the respondents were in the ICU with neurological symptoms (36.5%), followed by respiratory diseases (27%) (Table 1). Of the 200 patients, 138 (69%) had a mean magnesium level of 1.9 mg / dL. 51(25.5%) patients had hypomagnesaemia. The average magnesium level was 1.3 mg / dL. 11 (5.5%) patients had

hypermagnesemia with a mean magnesium content of 2.7 mg / dl. The lowest measured magnesium level was 1 mg / dl and the highest was 4.2 mg / dl. There was no statistically significant association between hypomagnesaemia and gender, age, disease acceptance category, and sepsis.  $\leq 27.4\%$  of children under 5 years of age had severe acute malnutrition in the hypomagnesaemia group. Among those with normal magnesium levels, 24% had severe acute malnutrition and 27.3% had severe acute malnutrition among those with hypermagnesemia.

Table 1:

	Number (n= 200)	Percentage
Gender		
Female	86	43.0%
Male	114	57.0%
Age		
<1 year	78	39.0%
1 to 5 years	64	32.0%
6 to 10 years	42	21.0%
>10 years	16	8.0%
Disease category		
Neurological	125	36.5%
Respiratory	92	27.0%
Others	80	23.0%
Cardiovascular	27	8.0%
Gastrointestinal	19	5.5%

There was no significant association between serum magnesium levels and severe acute malnutrition. The length of ICU stay ranged from 1 to 18 days, mean  $3.88 \pm 3.30$  days. Children with hypomagnesaemia had an average long duration of stay in ICU  $3.89 \pm 2.92$  days compared with  $2.67 \pm 2.71$  days for those with normal magnesium levels and  $3.00 \pm 1.92$  days for hypermagnesemia (p. 0.021). The length of stay in the hospital was from 1 to 34 days. The mean hospital stay for people with hypomagnesaemia was  $8.25 \pm 4.43$  days, with  $7.49 \pm 4.42$  days for those with normal magnesium levels and those with hypermagnesemia; It was  $7.76 \pm 3.82$  days (p-0.174). In the group with hypomagnesaemia, mechanical ventilation was required by 35.50% of the respondents, while in the group with normal magnesium, 26.09% and hypermagnesemia – 27.3% - mechanical ventilation was needed. There was no significant relationship between the duration of mechanical ventilation and serum magnesium concentration. Other electrolyte disturbances were more common in people with hypomagnesaemia compared to the other two groups. Hypocalcemia was the most common electrolyte abnormality in the hypomagnesaemia group (37.25%). 25.4% of those with normal magnesium groups and 27.3% of those with hypermagnesemia also had hypocalcemia. 41.2% of people with hypomagnesaemia had hypokalemia, 23.2% in the group with normomagnesemia and 27.3% in the group with hypermagnesemia. In the study, overall mortality was 25% (50 out of 200). Mortality among people with hypomagnesaemia was 29.40%. Among those with normal magnesium levels, 21.2% died and 18.2% in the hypermagnesemia group (Table 2).

Table 2:

	Serum Magnesium						P value
	<1.5 mg/dl (n=51)		1.5 to 2.3 mg/dl (n=138)		>2.3 mg/dl (n=11)		
Gender (%) (n=200)							
Female	22	43.10%	60	43.48%	5	45.45%	0.878
Male	29	56.90%	78	56.52%	6	54.55%	
Age (%) (n=200)							
<1 year	23	45.10%	51	36.96%	3	27.27%	0.214
1 to 5 years	15	29.40%	43	31.16%	6	54.55%	
6 to 10 years	10	19.60%	32	23%	1	9.09%	
>10 years	3	5.90%	12	9%	1	9.09%	
Disease category (%) (n=200)							
Neurological	23	45.10%	47	34.06%	3	27.27%	0.091
Cardiovascular	3	5.90%	11	7.97%	2	18.18%	0.188
Respiratory	13	26%	37	27%	3	27.27%	0.964
Gastrointestinal	2	3.90%	9	6.52%	0	0.00%	0.691
Others	10	19.60%	34	24.64%	3	27.27%	0.567
Sepsis (%) (n=200)							
Present	11	21.57%	22	15.94%	4	18.18%	0.401
Severe acute malnutrition (%) (n=343)							
Present	14	27.45%	33	24%	6	27.27%	0.869
Associated electrolyte imbalance (n=343)							
Hypocalcemia (%)	19	37.25%	35	25.36%	6	27.27%	0.077
Hypokalemia (%)	21	41.18%	32	23.19%	7	27.27%	0.06
Outcome (n=200)							
Duration of PICU stay days (mean±SD)	3.89	2.92	2.67	2.71	3	1.92	0.021*
Duration of hospital stay days (mean±SD)	8.25	4.43	7.19	4.42	7.76	3.82	0.174
Requirement of mechanical ventilator (%)	18	35.30%	36	26.09%	7	27.27%	0.316
Duration of mechanical ventilation days (mean±SD)	2.8	2.02	2.99	2.96	1.82	0.47	0.533
Discharge (%)	36	70.50%	108	78.26%	20	81.82%	0.252
Death (%)	15	29.40%	30	21.74%	5	18.18%	

## DISCUSSION

Hypomagnesaemia is believed to be a common occurrence in intensive care settings. It is often associated with sepsis, longer PICU stay, longer duration of mechanical ventilation, and longer duration and mortality. Knowledge of the prevalence of hypomagnesaemia is essential because early identification and correction may have prognostic and therapeutic implications<sup>10-11</sup>.

In this study of 200 subjects, 51 (25.4%) had hypomagnesaemia, 138 (69%) had normal magnesium levels, and 11 (5.5%) had hypermagnesaemia. This was compared with the results of Chen et al, where 27.27% of those studying hypomagnesaemia were seen in 64.71% in the normomagnesaemia group and 8% in the hypermagnesaemia group. A study by Broner et al on 98 pediatric patients admitted to the ICU showed that Mg has the highest frequency of abnormal values compared to ions. 25.6% reported hypomagnesaemia, 56.7% normal, and 17.8% had high levels of magnesium. Most of the studies, including these, have looked at serum magnesium<sup>12-13</sup>. The relationship between serum and ionized mg and certain critical diseases is not fully known. Serum magnesium does not necessarily reflect the total level of magnesium in the body as Mg is predominantly intracellular and ionized Mg is a biologically active form<sup>14</sup>. The heterogeneous patient population in all studies and the lack of a reliable indicator of the current state of magnesium in the body as measured by serum Mg levels may have resulted in a high incidence of hypomagnesaemia in several studies<sup>15</sup>. Hypermagnesaemia

is less common than hypomagnesaemia, ranging from 4-14% as mentioned in the literature.

In this study, hypermagnesaemia was observed in 7.3% of patients compared with reports from other studies. The study involved 114 (57%) men and 86 (43%) women, with a ratio of men to women of 1.2: 1. Hypomagnesaemia was more common in infants compared to other age groups. There was no correlation between age and magnesium levels.<sup>16-17</sup> Saleem et al. Identified age over one year as a risk factor for hypomagnesaemia<sup>17</sup>. Hypomagnesaemia was more often described in patients with neurological disorders compared to other cases (p <0.05) by Singhi and Deshmukh et al<sup>18</sup>.

This study found that 45.10% of the patients in the hypomagnesaemia group had neurological complaints compared to those in the normal magnesium group (34.06%) (p > 0.05). Serum magnesium in children have moderate to severe malnutrition stated by Singla et al. Hypomagnesaemia in malnourished children may include inadequate consumption, malabsorption, diarrhea and infection<sup>19-20</sup>.

No such differences were found in this study. 27.45% of the children had severe acute malnutrition in the hypomagnesaemia group, 24% in the normal magnesium group and 27.3% in the hypermagnesaemia group (p > 0.05). These results are similar to those of Saleem et al. (39.2% vs 38%; p > 0.05). Magnesium plays an important role in sepsis. Hypomagnesaemia is associated with the release of endothelin and anti-inflammatory cytokines<sup>21</sup>. Many studies have found a significantly higher incidence of sepsis in patients with hypomagnesaemia. It was found that

patients with hypomagnesaemia had significantly longer PICU duration. A finding similar to the extension of ICU stay in patients with hypomagnesaemia was also found in Deshmukh et al., Chen et al., And Kumar et al study<sup>22</sup>. A relationship between hypomagnesaemia and other electrolyte disturbances was found in one third of the cases in this study. Hypocalcemia is the most frequent accompanying electrolyte abnormality in the hypomagnesaemia group in the present study. The relationship between hypomagnesaemia and mortality varies from study to study. Most studies have observed that mortality in patients with hypomagnesaemia was significantly higher compared to patients with normomagnesemia<sup>23</sup>. Soliman et al found that there is no association between ionized Mg levels and consumption and mortality, but patients who developed ionized hypomagnesaemia while in the ICU had a higher mortality rate<sup>24</sup>. The high mortality rates in hypomagnesaemia patients may be due to the higher incidence of electrolyte disturbances such as hypokalemia, hypocalcemia and arrhythmias, and the strong association between hypomagnesaemia and sepsis and septic shock, which is a common cause of death in ICU patients<sup>25</sup>. However, several results were reported by Safavi et al., Broner et al., And Escuela et al found no association between entry hypomagnesaemia and conviction. Huijjen et al. Found no correlation between extracellular or intracellular dosing and clinical outcome and suggested that the lack of correlation with clinical outcomes is merely a related finding that is not directly related to the state of hypomagnesaemia<sup>26</sup>. In some studies, magnesium and clinical outcomes may be heterogeneous in the patient population across all studies, and that measuring serum Mg is not a reliable indicator of the current level of magnesium in the body. A limitation of the study was that serum magnesium levels were only recorded on admission to the intensive care unit<sup>27</sup>. Magnesium levels were not monitored. Total serum magnesium was measured in place of the ionized magnesium.

## CONCLUSION

One third of patients admitted to the ICU changed their magnesium levels. Hypomagnesaemia was more common in patients with neurological diseases compared with other disease categories. Hypomagnesaemia has usually been associated with hypocalcemia and hypokalemia. Hypomagnesaemia was associated with a much longer ICU stay. People with hypomagnesaemia require more frequent support of mechanical ventilation than normal and hypermagnesemia groups. Mortality is higher in those with hypomagnesaemia than in those with normomagnesemia and hypermagnesemia.

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