Section: Paediatrics

Original Research Article

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

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Abstract

Background: There is a high occurrence of magnesium insufficiency in critical illness, which is linked to an elevated need for mechanical ventilation, higher fatality rates, and longer stays in the intensive care unit (ICU). Understanding hypomagnesemia is crucial due to the limited availability of data and its potential prognostic and therapeutic consequences. The influence of serum magnesium level on the outcome of children admitted to the pediatric intensive care unit. **Materials and Methods:** 200 participants were included in this study. The period of study is from January 2022 to December 2022. The patient's result was assessed based on the duration of their stay in the Paediatric Intensive Care Unit (PICU) and the hospital, as well as the need and duration of mechanical ventilator support. The final outcome at the conclusion of the hospital stay was categorised as either discharge or prolonged ICU stay. The Magnesium was analysed biochemically using the fully automated XL 300 analyzer. **Result:** The gender distribution consisted of 56% men and 44% females. Among the 200 patients, exactly 100 of them, which accounts for 50% of the total, had magnesium levels within the normal range, with an average value of 1.94mg/dl. A total of 80 people were diagnosed with hypomagnesemia, representing 40% of the population. The average magnesium levels were 1.28 milligrammes per deciliter. Out of the total number of patients, 20 individuals, which accounts for 10% of the sample, were diagnosed with hypermagnesemia. The average magnesium level among these patients was measured to be 2.86mg/dL. Of the individuals with normal magnesium levels, 22% experienced mortality, whereas 20% had mortality in the hypermagnesemia group. **Conclusion:** Patients with neurological illnesses had a higher prevalence of hypomagnesemia compared to other disease groups. Hypomagnesemia often co-occurred with hypocalcemia and hypokalemia. The presence of hypomagnesemia was correlated with a considerably extended period of stay in the Paediatric Intensive Care Unit (PICU).

INTRODUCTION

Magnesium is the fourth most abundant mineral in the body and the second most abundant cation inside cells.[1] The distribution of magnesium in the body is as follows: 67% is located in bone, 31% in cells, and 1-2% in extracellular fluids.[2] Magnesium is a crucial electrolyte that helps maintain the potential of cell membranes. It is also an important co-factor for adenylate cyclase and sodium-potassium-adenine triphosphatase. Additionally, magnesium is an essential mineral that plays a role in hundreds of enzymatic reactions and is involved in over 300 biochemical reactions in the body, serving various important physiological functions.[3] Magnesium is crucial for maintaining electrolyte balance, stabilising cell membranes, regulating blood pressure, producing and utilising energy, metabolising proteins, reducing inflammation, facilitating nerve conduction, regulating insulin metabolism, contracting the heart muscle, controlling vascular tone, preventing atherosclerosis and thrombosis, promoting the growth and movement of vascular smooth muscle cells and endothelial cells, and preventing vascular calcification.[4,5]

Magnesium deficiency often occurs in several clinical situations, including protein-energy malnutrition, malabsorption, hypoalbuminemia, sepsis, and others, which are widely seen in children residing in underdeveloped nations. Magnesium imbalances are also probable after extended gastrointestinal suctioning, blood transfusion, excessive catecholamine levels, diuretic and aminoglycoside treatment, and other factors that are relevant in the management of critical care patients. Consequently, magnesium insufficiency is expected to be common among individuals who are severely sick.Research has shown a significant range (20%-70%) in the occurrence of hypomagnesemia in the intensive care unit environment.[6] Observational studies provide robust and persistent clinical evidence that hypomagnesemia is strongly related with a higher need for mechanical ventilation, a longer stay in the intensive care unit, and increased mortality.[7,8] Critically ill patients have a heightened susceptibility to both symptomatic and asymptomatic magnesium insufficiency. This shortfall may result in significant clinical repercussions, including hypokalemia, cardiac arrhythmias, hypocalcemia, neurotoxicity, and psychological disorders. Ultimately, these complications contribute to higher rates of morbidity and death.[9-11] There is a limited amount of evidence about changes in magnesium levels in the paediatric intensive care unit (PICU) setting, particularly from poor countries.

MATERIALS AND METHODS

This research was carried out at the Department of Paediatrics as an observational study. The research included children aged 1 month to 12 years who were hospitalised to the Paediatric Intensive Care Unit (PICU). The study excluded patients who had a documented condition of congenital renal magnesium wasting (such as Bartter syndrome and Gitelman syndrome), patients who had already received magnesium replacement therapy for hypomagnesemia within the past 24 hours, patients with surgical conditions, trauma patients, patients transferred to other paediatric intensive care units (PICUs), and patients with a PICU stay of less than 24 hours.

Following approval from the ethics committee, children who met the inclusion criteria were recruited in the research. The parents or guardians of the children participating in the research provided written informed permission. Every kid who was registered completed a thorough process of gathering information about their medical background and a comprehensive physical examination. The specific information, such as age, gender, anthropometry, and the type of the condition at admission (neurological, respiratory, cardiovascular, gastrointestinal, and others), were documented in a standardised proforma. Upon admission, a 5ml sample of venous blood was obtained using a serum vacutainer. The blood was then centrifuged and the resulting serum was submitted for the purpose of measuring the magnesium levels. Additional standard examinations, such as a complete blood count, renal function test, and measurement of serum electrolytes (sodium, potassium, calcium), were conducted as necessary for the treatment of the patient. Every individual that was registered got care in accordance with the PICU protocol.

The study enrollment had no impact on the standard treatment protocol. The follow-up of all patients continued until their discharge from the hospital. The patient's result was assessed based on the duration of their stay in the Paediatric Intensive Care Unit (PICU) and the hospital, as well as the need and duration of mechanical ventilator support. The final outcome at the conclusion of the hospital stay was categorised as either death or discharge. The Magnesium was analysed biochemically using the fully automated XL 300 analyzer. The estimation of magnesium level was conducted using the XYLIDYL BLUE technique with the assistance of Erba kits. The data were quantified in milligrammes per deciliter (mg/dL). Subjects were divided into three Groups based on their Serum Magnesium concentration defined as below

Normal: 1.5-2.5mg/dL

Hypomagnesemia: <1.5mg/dL

Hypermagnesemia: >2.5mg/dL.

Statistical Analysis: The data was inputted into a Microsoft Excel spreadsheet and subjected to statistical analysis using SPSS version 25.0 software. Categorical data was expressed using frequencies and proportions. The chi-square test was used as a statistical tool to determine the importance of qualitative data. Mean and standard deviation were used to depict continuous data. ANOVA, or analysis of variance, is a statistical test used to determine the significance of the mean difference across many groups for quantitative data. A P value less than 0.05 was deemed statistically significant.

RESULTS

A total of 200 children who satisfied the specified criteria were hospitalised to the Paediatric Intensive Care Unit in the Department of Paediatrics and included in the research. The gender distribution consisted of 56% men and 44% females. The male to female ratio was 1.27:1. The majority of the subjects were under the age of one year (40%), followed by 32% between the ages of one to five years, and 28% were above the age of five years. The majority of the subjects were brought to the Paediatric Intensive Care Unit (PICU) due to neurological symptoms, accounting for 35.5% of the cases. This was followed by respiratory illnesses, which accounted for 25.5% of the cases. Among the 200 patients, exactly 100 of them, which accounts for 50% of the total, had magnesium levels within the normal range, with an average value of 1.94mg/dl. A total of 80 people were diagnosed with hypomagnesemia, representing 40% of the population. The average magnesium levels were 1.28 milligrammes per deciliter. Out of the total number of patients, 20 individuals, which accounts for 10% of the sample, were diagnosed with hypermagnesemia. The average magnesium level among these patients was measured to be 2.86mg/dL, as seen in Table 2. The minimum recorded magnesium concentration was 1mg/dL, while the maximum concentration was 4.21mg/dL. No statistically significant correlation was found

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between hypomagnesemia and gender, age, illness category of admission, and sepsis.

The length of stay in the Paediatric Intensive Care Unit (PICU) ranged from 1 to 20 days, with an average of 3.79±1.14 days. Children diagnosed with hypomagnesemia had a substantially higher average length of stay in the Paediatric Intensive Care Unit (PICU) of 4.55±1.25 days, compared to 3.33±1.01 days for those with normal magnesium levels and 4.25±1.21 days for patients with hypermagnesemia (p- 0.04). The hospitalisation period ranged from 1 to 36 days. The average length of hospital stay for those with hypomagnesemia was 10.05±2.28 days, while those with normal magnesium levels had a stay of 8.78±2.08 days. those with hypermagnesemia had a stay of 9.13±1.69 days. The difference in duration of hospital stay between these groups was not statistically significant (p=0.31).

Among the participants with hypomagnesemia, 35% required mechanical breathing, compared to 25% in the normal magnesium group and 30% in the hypermagnesemia group. No meaningful correlation was found between the length of time mechanical ventilation was used and the levels of magnesium in the blood. Subjects with hypomagnesemia had a higher prevalence of various electrolyte abnormalities compared to the other two groups. The occurrence of hypocalcemia was the most prevalent electrolyte anomaly seen in the group of individuals with hypomagnesemia, accounting for 37.5% of cases. 25% of the participants in the group with normal magnesium levels and 25% of the subjects with hypermagnesemia also had hypocalcemia. The prevalence of hypokalemia was 36.25% among participants with hypomagnesemia, whereas it was 23% among those with normomagnesemia and 30% among those with hypermagnesemia.

Table 1: Socio-demographic data

	Number =200	**Percentage**
Gender		
Female	88	44
Male	112	56
Age		
<1 year	80	40
1 to 5 years	64	32
6 to 10 years	41	20.5
>10 years	15	7.5
Disease category		
Neurological	71	35.5
Respiratory	51	25.5
Others	48	24
Cardiovascular	16	8
Gastrointestinal	14	7

Table 2: Serum Magnesium level of the participants

Serum Magnesium	**Number**	**Percentage**
<1.5 mg/dl	80	40
1.5 to 2.5 mg/dl	100	50
>2.5 mg/dl	20	10

Table 3: correlation of Serum Magnesium level with basic parameter

	Serum Magnesium						**P-value**
	<1.5 mg/dl (n=80)		**1.5 to 2.5 mg/dl (n=100)**		**>2.5 mg/dl (n=20)**		
Gender							
Female	36	45	43	43	9	45	0.22
Male	44	55	57	57	11	55	
Age							
<1 year	36	45	37	37	7	35	0.34
1 to 5 years	23	28.75	31	31	10	50	
6 to 10 years	15	18.75	24	24	2	10	
>10 years	6	7.5	8	8	1	5	
Disease category							
Neurological	33	41.25	34	34	4	20	0.07
Cardiovascular	5	6.25	8	8	3	15	0.27
Respiratory	19	23.75	26	26	6	30	0.31
Gastrointestinal	6	7.5	7	7	1	5	0.21
Others	17	21.25	25	25	6	30	0.14
Sepsis							
Present	17	21.25	15	15	3	15	0.17
Severe acute malnutrition							
Present	21	26.25	25	25	5	25	0.25
Associated electrolyte imbalance (n=200)							
Hypocalcemia (%)	30	37.5	25	25	5	25	0.07
Hypokalemia (%)	29	36.25	23	23	6	30	0.06

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Table 4: Outcome of participants

Outcome (n=200)	<1.5 mg/dl (n=80)		1.5 to 2.5 mg/dl (n=100)		>2.5 mg/dl (n=20)		P value
Duration of PICU stay days	4.55±1.25		3.33±1.01		4.25±1.21		0.04
Duration of hospital stay days	10.05±2.28		8.78±2.08		9.13±1.69		0.31
Duration of mechanical ventilation days	4.11±1.06		3.81±1.34		2.56±0.87		0.36
Requirement of mechanical ventilator (%)	25	35	25	25	6	30	0.41
Discharge (%)	56	70	78	78	16	80%	0.11

DISCUSSION

Hypomagnesemia is often seen in the critical care setting. It is often linked to sepsis, extended stay in the paediatric intensive care unit (PICU), a higher frequency of requiring and longer duration of mechanical ventilation, and an elevated death rate.[12] Understanding the incidence of hypomagnesemia is crucial because detecting and addressing it early may have significant consequences for prognosis and treatment.[13] The majority of the currently available data originates from research conducted in adult critical care units, with less data accessible for the paediatric population.

Among the 200 participants examined in this research, 80 individuals (40%) had hypomagnesemia, whereas 100 individuals (50%) had normal magnesium levels, and 20 individuals (10%) had hypermagnesemia. This aligns with the results reported by Chen et al, who observed hypomagnesemia in 27.27% of their research participants. Specifically, 64.71% of the respondents had normal magnesium levels, whereas 8% had elevated magnesium levels.[14] In a research conducted by Broner et al, which included 98 paediatric patients admitted to the Intensive Care Unit (ICU), it was observed that magnesium (Mg) had the greatest occurrence of aberrant levels compared to all other ions that were examined. The study revealed that 25.6% of the participants had hypomagnesemia, whereas 56.7% had normal magnesium levels and 17.8% had high magnesium levels.[15] The majority of investigations, including the current study, have assessed the overall concentration of magnesium in the bloodstream. The relationship between blood total and ionised magnesium levels during various severe diseases and their management remains incompletely understood. The measurement of serum magnesium does not always indicate the overall amount of magnesium in the body, since magnesium is mostly found within cells and the physiologically active form is ionised magnesium.[16] The large variation in the occurrence of hypomagnesemia in different studies may be attributed to the diverse patient group and the unreliability of blood Mg measurement as an indication of actual magnesium status in the body. Hypermagnesemia is less prevalent than hypomagnesemia, with a reported incidence ranging from 4 to 14% according to the literature. Hypermagnesemia was seen in 10% of patients in this research, a proportion that is similar to what has been reported in earlier studies.[17]

The gender distribution consisted of 56% men and 44% females. The male to female ratio was 1.27 to 1. The majority of the subjects were under the age of one year (40%), followed by 32% between the ages of one and five years, and 28% were above the age of five years. The majority of the subjects were brought to the Paediatric Intensive Care Unit (PICU) due to neurological symptoms, accounting for 35.5% of the cases. This was followed by respiratory illnesses, which accounted for 25.5% of the cases. There was no observed link between age and magnesium levels. Saleem et al. determined that individuals older than one year are at a higher risk for hypomagnesemia.[18] Singhi et al. found that individuals with neurological diseases had a higher incidence of hypomagnesemia compared to other cases ($p < 0.05$).[19] Deshmukh et al. discovered that the occurrence of hypomagnesemia in the paediatric intensive care unit (PICU) was higher in children experiencing convulsions and those with severe levels of altered consciousness.[20] The current research observed that 41.25% of individuals in the hypomagnesemia group had neurological symptoms, whereas only 34% of those in the normal magnesium group experienced such symptoms ($p>0.05$). Singla et al. discovered that children with moderate and severe malnutrition had considerably low serum magnesium levels. In malnourished children, hypomagnesemia may result from insufficient consumption, impaired absorption, diarrhoea, and infection.[21]

No significant disparity was observed in the current investigation. In the hypomagnesemia group, 26.25% of children experienced severe acute malnutrition, compared to 25% in the normal magnesium group and 25% in the hypermagnesemia group ($p>0.05$). The results of this study are comparable to the findings reported by Saleem et al (39.2% versus 38%; $p>0.05$).[18] Magnesium is crucial in the development and progression of sepsis. Hypomagnesemia is linked to heightened secretion of endothelin and proinflammatory cytokines. Several investigations have shown a notably greater occurrence of sepsis in individuals with hypomagnesemia.[12,14] In the current research, the occurrence of sepsis was 21.25% among individuals with hypomagnesemia, whereas it was 15% and 15% among those with normal magnesium levels and hypermagnesemia, respectively. The length of stay in the Paediatric Intensive Care Unit (PICU) ranged from 1 to 20 days, with an average of 3.79±1.14 days. Children diagnosed with hypomagnesemia had a substantially higher average length of stay in the Paediatric Intensive Care Unit (PICU) of 4.55±1.25 days, compared to 3.33±1.01 days for those with normal

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magnesium levels and 4.25±1.21 days for individuals with hypermagnesemia (p-value = 0.04). Desmukh et al, Chen et al, and Kumar et al also reported a similar result, showing that children with hypomagnesemia had a longer length of stay in the paediatric intensive care unit (PICU).[14,20,22] In contrast, Limaye et al identified no disparity in the duration of ICU stay between those with low magnesium levels (8.00±7.92 days) and those with normal magnesium levels (6.17±3.84 days) ($p > 0.05$).[12] Similarly, our investigation did not reveal any noteworthy difference in the length of hospital stay among individuals with hypomagnesemia ($p > 0.05$). Hypomagnesemia is recognised as a cause of muscular weakness and respiratory failure, which may make it challenging to remove the patient from the ventilator. Consequently, this may result in a longer period of mechanical ventilation. In a research conducted by Kumar et al., it was shown that 56.86% of patients with hypomagnesemia required mechanical ventilatory support, but in the normomagnesemic group, only 24.33% required ventilatory support ($p < 0.05$). The study did not find any notable disparity in the average duration of ventilatory support across the groups.[22] The current research found that those with low magnesium levels required mechanical breathing assistance in 35% of cases, whereas those with normal magnesium levels need it in 25% of cases, and those with high magnesium levels required it in 30% of cases. The duration of mechanical ventilation in the low magnesium group was statistically comparable to that of the normal and high magnesium groups ($p > 0.05$). The current investigation revealed that hypomagnesemia was correlated with other electrolyte imbalances in around 33% of the patients. In the present investigation, hypocalcemia was the most often seen electrolyte anomaly in the group of patients with hypomagnesemia. 25% of the participants in the group with normal magnesium levels and 25% of the subjects with hypermagnesemia also had hypocalcemia. In a research conducted by Saleem et al,[18] it was shown that 56% of the individuals in the hypomagnesemic group also had hypocalcemia. Limaye et colleagues discovered that 69% of individuals with hypomagnesemia also had hypocalcemia.[12] Hypocalcemia often occurs due to magnesium insufficiency, which hampers the functioning of the parathyroid glands and may decrease the levels of vitamin D in the blood, resulting in hypocalcemia. Treatment with calcium alone is insufficient to restore hypocalcaemia caused by magnesium insufficiency.[23] Within the scope of this investigation, it was shown that 36.25% of patients diagnosed with hypomagnesemia also exhibited hypokalemia. In their study, Saleem et colleagues discovered that the low magnesium group had a 31% occurrence of hypokalemia.[18] The possible reason of this might be related to underlying conditions that result in the depletion of both magnesium and potassium, such as diuretic treatment, vomiting and diarrhoea, or nasogastric suctioning. Furthermore, hypomagnesemic individuals have heightened renal potassium losses. This kind of hypokalemia is considered to be resistant to potassium supplementation alone until magnesium deficit has been addressed and resolved.[23]

CONCLUSION

Patients with neurological illnesses had a higher prevalence of hypomagnesemia compared to other disease groups. Hypomagnesemia often co-occurred with hypocalcemia and hypokalemia. The presence of hypomagnesemia was correlated with a considerably extended period of stay in the Paediatric Intensive Care Unit (PICU).

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