THE PREVALENCE OF DYSELECTROLYTEMIA AND ITS EFFECT ON MORTALITY AMONG CRITICALLY ILL CHILDREN

By

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ABSTRACT

Background: *To determine the prevalence and outcome of electrolyte imbalance in critically ill children admitted in Pediatric Intensive Care Unit (PICU) of Fayoum university hospital.*

Methods: *this observational study included 100 children between one month and 14 years admitted in Fayoum university hospital PICU between March and November 2019. Blood samples were drawn to determine sodium, potassium, and magnesium excluding children who received electrolyte solutions within the last 24 hours.*

Results: *A total of 100 children were included in this study. Electrolyte disturbance was present in 65 patients (65%). Hyponatremia was the most common electrolyte abnormality, seen in nearly half of the patients 49 case (49%) while hypernatremia was present only in 4 cases. Percentage of hypomagnesaemia children was 3% and hypermagnesemia was 40%. hypokalemia was present in 18 patients (18%) and hyperkalemia in 10% patients. The majority of patients (88%) were discharged and 12% died. Electrolyte imbalance was seen in 10 out of 12 deaths of the studied patients. According to receiver operating characteristic curve for mortality between serum Magnesium, potassium and sodium show prediction of mortality of sodium is more than that of potassium more than that for magnesium as area under the curve of serum sodium is (0.725) while potassium is (0-.643) and magnesium is (0.598).*

Conclusions: *Dyselectrolytemia is a common problem in pediatric patients admitted to PICU. Mortality was higher in patients with hyponatremia and it is more predictive of mortality than serum magnesium and potassium.*

Keywords: *sodium; potassium; magnesium; mortality; pediatric intensive care unit.*

INTRODUCTION

Electrolyte disturbances are common and important problems in critically ill pediatric patients **(Subba Rao and Thomas, 2000)**. When present; they affect homeostasis of the body which is very important for organ's function and cellular structure **(Balcı et al., 2013)**.

The most common and important electrolyte disturbance is Sodium; sodium has a vital role in the body fluid balance and function of the central nervous system and muscles. The second important electrolyte is Potassium, potassium is vital for electrical impulses, normal function of the brain and also for muscular contractions **(Henry et al., 2005)**. Recently, serum magnesium attracted increasing attention from researchers as a new prognostic indicator. Serum magnesium is related to an increased risk of acute kidney injury, respiratory failure, and shock in critically ill children **(Cheungpasitporn et al., 2015)**. Electrolyte disturbances can adversely affect the outcome; electrolytes should be closely monitored and treated properly **(Kim., 2007)**.

Ethical considerations:

1. This study was approved by the Research Ethical Committee, Faculty of Medicine, Fayoum University, Egypt.
2. Informed consents were obtained from the participants' legal guardians after being informed about the objectives and procedures to be performed.

Conflicts of interests: The authors declare that they have no conflicts of interests.

The confidentiality of their information was respected and their right not to participate in the study was ensured.

The patient has the right to withdraw from the study at any time.

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PATIENTS AND METHODS

Sample size

Our sample size was calculated according to the following equation: n = N / [1 + N x e2] Where n=sample size, N =population size, e =margin of error. A total of 100 patients was estimated to be sufficient sample size.

Inclusion criteria:

Patients between the ages of one month to 14 years admitted for more than two days in Fayoum university hospital PICU.

Exclusion criteria:

Patients on diuretic therapy, received electrolyte solutions within the last 24 hours and patients with known congenital kidney magnesium wasting (e.g., Bartter's syndrome and Gitelaman's syndrome).

Patients and settings:

This prospective observational study was conducted in Pediatric Intensive Care Unit of Fayoum University Hospital including 100 patients between the ages of one month to 14 years admitted for more than two days in Fayoum university hospital PICU between March and November 2019.

All the enrolled patients were subjected to:

I. **Full history taking focusing on** patient's age, sex, admission diagnosis, whether mechanical ventilation support was needed, time of mechanical ventilation, if the patient received diuretics or aminoglycoside on admission or not and length of stay in PICU and hospital.

II. **Full Medical assessment** (including vital signs, anthropometric measurements, systematic examination, and measurement of Glasgow coma scale).

III. **Laboratory investigations: Including:** Complete blood count (CBC), C-reactive protein (CRP), electrolytes (sodium, potassium and magnesium), serum lactate, albumin, Blood Glucose Level, prothrombin time and kidney functions.

Blood samples were obtained immediately after admission and done on Dialab autoanalyzer with the following method: Serum lactate sample was collected in fluoride tube and centrifuged at (2000-3000 RPM) for approximately 20 minutes and stored at -20 oC and was analyzed at the same time and Serum Magnesium sample was collected in chemistry tube and was stored at -20 oC and centrifuged at (2000-3000 RPM) for approximately 20 minutes **(Westgard et al., 2000)**.

The following values were considered normal levels:

- Sodium: 135- 145 mg/dl
- Potassium: one month to five month: 3.5-5.6 mg/dl(from the age of 1month to5 months), 3.6-6.1 mg/dl(from 6 months

to 1 year and 3.3-4.6 mg/dl above the age of 1 year.

- Magnesium: 1.6-2.6 mg/dl up to 2 year and 1.5- 2.3 mg/dl above the age of 2 years. Blood lactate level: up to 18 mg/dl

IV. Pediatric risk of mortality (PRISM) III score was calculated for each patient at the time of admission

Statistical analysis:

The collected data were organized, tabulated, and statistically analyzed using SPSS software statistical computer package version 22 (SPSS Inc, USA). For quantitative data, the median, interquartile range (IQR), minimum and maximum were calculated. Mann-Whitney-U test and Kruskal-Wallis test were used as a test of significance to compare between two and three groups, respectively. Qualitative data were presented as number and percentages, chi square ($\chi 2$) was used as a test of significance. The receiver operating characteristic (ROC) curve was used to determine the discrimination value of magnesium, potassium, sodium and PRISM III for mortality and to define optimal cut-points for sensitivity, specificity, and positive and negative predictive values (PPV and NPV). For interpretation of results of tests of significance, significance was adopted at $P \leq 0.05$.

RESULTS

100 patients were included in this study and their demographic data are summarized in **Table (1)**.

Table (1): Demographic data of studied children (N=100)

Variable	Median	IQR
Age (month)	**18**	**5.5-43.8**
	Number	**Percentage**
Sex		
Male	**58**	**58.0%**
Female	**42**	**42.0%**
Residency		
Urban	**49**	**49%**
Rural	**51**	**51%**

Table (2): Clinical assessment and diagnoses of the studied patient (N=100)

Variable	**Median**	**IQR**	
Weight (KG)	10 kg	5.4-15	
Height (cm)	78 cm	64-93.5	
Diagnosis (according to the system affected)	**Number**	**percentage**	
Respiratory disorders.	32	32%	
CNS disorders.	19	19%	
Trauma	11	11%	
CVS disorders.	6	6%	
sepsis	6	6%	
Renal disorders.	3	3%	
Others	23	23%	
	Median	Minimum	Maximum
Hospital stays (in days)	8	2	45
PICU stay (in days)	7	2	32
M.V. (in days)	4	0	8

Regarding the admitting diagnosis, the most common diagnosis was respiratory illness; 32 case (32%), 19(19%) had neurological illness & the least with renal disorders (3%).

Table (3): Laboratory finding of the studied patients (N=100)

Variable	Median	IQR
complete blood count:		
white blood cells (x 10^3/mm^3)	**12.4**	**9.6-17.7**
platelets (x 10^3/mm^3)	**340**	**216-440**
Hb (g/dL)	**10**	**8-12**
kidney function		
blood urea(mg/dL)	**13**	**7.5-20.5**
creatinine (mg/dL)	**0.5**	**0.4-0.7**
CRP (mg/L) (positive >6)	**66**	**6-108**
blood glucose level(mg/dl.)	**121**	**103-152**
serum albumin (g/dL)	**3.8**	**3.3-4.1**
Prothrombin time (PT)/second	**16.6**	**15-19.1**
serum lactate (mg/dL)	**33.8**	**24.6-46.9**

	minimum	**maximum**	**mean**	**IQR**
Magnesium (mEq/L)	0.6	4.6	2.5	2.3-2.7
Potassium (mEq/L)	1.8	5.8	4.3	4.0-4.8
Sodium (mEq/L)	114	164	134.5	130-137.0

IQR: interquartile range

Table (4): Electrolyte disturbances in studied patients

Electrolyte	number	percentage
Hypomagnesaemia: (<1.6-mg/dl up to 2 year and 1.5mg/dl above the age of 2 years.	3	3%
Hypermagnesemia: **(**>2.6 mg/dl up to 2 year and 2.3 mg/dl above the age of 2 years.	40	40%
Hypokalemia: (<3.5 mg/dl) (from the age of 1month to5 months), <3.6 mg/dl(from 6 months to 1 year and <3.3mg/dl above the age of 1 year.	10	10%
Hyperkalemia: (>5.6 mg/dl(from the age of 1month to5 months), >6.1 mg/dl(from 6 months to 1 year and >4.6 mg/dl above the age of 1 year.	18	18%
Hyponatremia(<135mg/dl)	49	49%
Hypernatremia(>150mg/dl)	4	4%

Hyponatremia was the most common electrolyte abnormality, seen in nearly half of the patients 49 case (49%) while

hypernatremia was present only in 4 cases (4%) **(Table 4)**.

We found hypokalemia in 18 patients (18%) and hyperkalemia in 10% patients (n=10).

Table (5): Mortality and its correlation with serum electrolytes (N=100)

electrolytes	Non survived (N=12)	Survived (N=88)	P-value
	Median (IQR)		
Magnesium	2.3 (2.3-2.6)	2.5 (2.3-2.7)	0.274
Potassium	4.7 (4.3-5.4)	4.3 (4.0-4.8)	0.108
Sodium	137.5 (135.5-140.0)	134.0 (130.0-137.0)	0.012*
	Number (%)		P-value
Hypomagnesaemia	0 (0.0)	3 (100.0)	0.377
Hypermagnesemia	3 (7.5)	37 (92.5)	
Hypokalemia	1 (10.0)	9 (90.0)	0.337
Hyperkalemia	4 (22.2)	14 (77.8)	
Hyponatremia	2 (4.1)	47 (95.5)	0.026*
Hypernatremia	0 (0.0)	4 (100.0)	

IQR: interquartile range; *significant

Electrolyte imbalance was seen in 10 out of 12 deaths of the studied patients. Mortality rates were higher in children with hyponatremia (P-value=0.026) **(Table 5)**.

Out of these 100 admissions, total discharges from PICU were 88patients. Twelve patients (12%) died; three patients had sepsis with is statistically significant difference between sepsis and mortality with P-value=0.022. five patients died had central nervous system illness with significant value between mortality and central nervous system illness (P-value=0.048). Also, there is no statistically significant difference with P-value as regards other diagnoses of admission to PICU.

Table (5): Association between electrolytes disturbances and diagnoses

diagnosis	magnesium		sodium		potassium	
	Hypomag-nesaemia (N=3)	Hypermag-nesemia (N=40)	Hypona-tremia (N=49)	Hyperna-tremia (N=4)	Hypoka-lemia (N=10)	Hyperka-lemia (N=18)
CVS	0 (0.0)	1 (16.7)	3(50)	1 (16.6)	1 (16.6)	1 (16.6)
Sepsis	0 (0.0)	3 (50.0)	3 (50)	1 (16.6)	1 (16.6)	3 (50.0)
Renal	0 (0.0)	1 (33.3)	0 (0.0)	1 (33.3)	0 (0.0)	2 (66.7)
CNS	0 (0.0)	6 (31.6)	10 (52.6)	1 (5.2)	3 (15.78)	6 (31.5)
Respiratory	3 (9.4)	13 (40.6)	18 (56.2)	0 (0)	3(9.37)	3 (9.37)
Trauma	0 (0.0)	6 (54.5)	5 (45.4)	0 (0)	2(18.18)	1(9)
Others	0 (0.0)	10 (43.5)	10 (43.47)	0 (0)	0 (0.0)	2(8.3)
p. value	0.399		0.38		0.42	

No significant difference between different diagnoses and electrolyte disturbances.

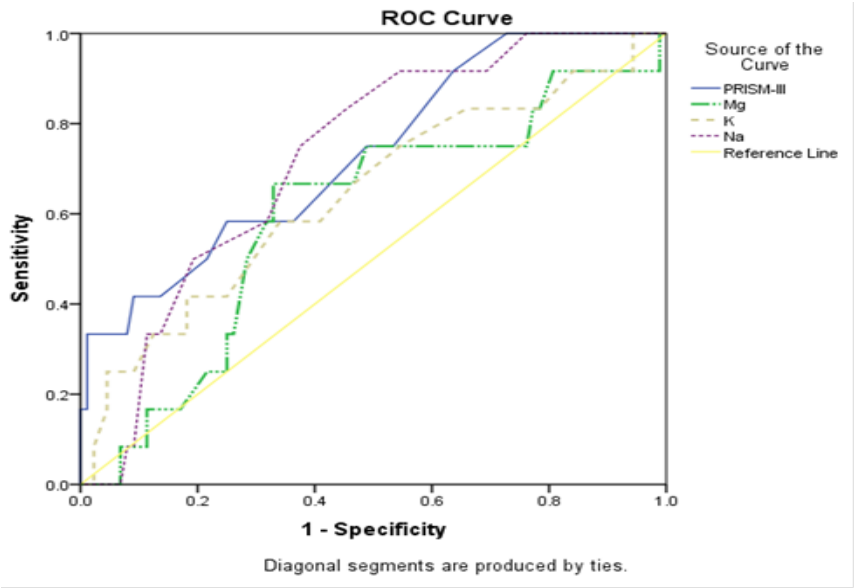

Figure (1): Receiver operating characteristic curve for prediction of mortality

According to receiver operating characteristic (ROC) curve for mortality between serum magnesium, potassium and sodium show prediction of mortality of sodium is more than that of potassium more than that for magnesium as area under the curve (AUC) of serum sodium is (0.725) while potassium is (0-.643) and magnesium is (0.598) **(Figure 1)**.

DISCUSSION

Among 100 enrolled patients in this study, overall electrolyte disturbances were present in 65 cases (65%). We studied incidence of disturbances in sodium, potassium and magnesium. the incidence of electrolyte disturbances varied from a study to another depending on the number of the studied electrolytes and the nature of the disease of the patients. **Subba Rao and Thomas (2000)** found that the incidence to be 32%, but they studied only sodium and potassium. **Naseem et al. (2019)** found high incidence of electrolyte abnormalities in 85% of the cases and this can be related to the high number of electrolytes the studied (five electrolytes).

Dysnatremias (either hyponatremia or hypernatremia) in intensive care pediatric patients has been reported to be about 30% **(Barron et al., 2010)**. Most of the studies had reported hyponatremia to be more common than hypernatremia i.e., 23.2% vs. 16.7%in a study by **Elala and Shimelis (2018)** and 27.43% vs. 3.5% in **Panda and Save (2018)** study. The variation in incidence of hyponatremia may be due to difference in the nature of primary illness included in these studies. In the current study, hyponatremia was the most common electrolyte abnormality seen in 49 out of 100 children (49%). **Jayakumar and Sambasivam (2017)** observed that the risk of mortality is increased by 3-3.5 times in patients with hyponatremia when compared to those with normal serum sodium. In our study the median of Sodium level was higher in dead children than who were survived and there was statistically significant as P-value>0.026, but the risk of mortality is increased in hyponatremia when compared to hypernatremia. Sodium level offers an acceptable discriminative power with AUC=0.725, sensitivity is 75.0% and the specificity is 62.5% and PPV is 26.4% and NPV is 50.7% and is in agreement with the findings of Subba Rao and Thomas study.

The incidence of hypokalemia was 10% in our study. This is similar to a study by **Singhi et al. (1994)** who found that the incidence was 13.9% in contrast to a study by **Agarwal et al. (2018)** who found high incidence of hypokalemia in 34.4% of the patients. This variation in incidence may be related to the incidence of kidney injury in the included cases and malnutrition.

In the current study hyperkalemia was present in 18% of the patients. **Subba Rao and Thomas (2000)** similarly found

hyperkalemia in 14.4% their studied patients.

As far as magnesium is concerned, we found more cases of hypermagnesemia up to 40% than hypomagnesemia in 3% and this in agreement with **Nassem et al. (2019)** who found hypermagnesemia up to 21% than hypomagnesemia in 7%. This is in contrast to most of the published data showing hypomagnesemia to be more common than hypermagnesemia. In **Erdoğan and Seven Menevşe study (2018)**, hypomagnesemia was present in 56.3% of the patients with sepsis, 44.4% of the patients with cancer, and 42.9% of the trauma patients. Limaye et al. reported that of the 100 intensive care patients, 52% were hypomagnesemic, 7% were hypermagnesemic, and 41% were normomagnesemic.

As regard mortality rate among the studied children, it was 12% as delineated. This was comparable or less in **Abdelkader et al. study (2018) and Rady (2014)** study, (mortality rate: 17% and 25% respectively). However, it was higher as compared to many studies from developed countries as **Brady et al. (2006)** and **Pollack et al. (2018)** that showed a mortality rate of 6.2% and 2.7% respectively. When it comes to PRISM III score, The Pediatric Risk of Mortality is a physiologically based score used to quantify physiologic status and can expect mortality risk and expect morbidity risk **(Pollack et al., 2016)**. (In our study its median was 5 (IQR=2-8.5). According to ROC curve for mortality between serum Magnesium, potassium, sodium and PRISM III score, for prediction of mortality, PRISM III and sodium offers an acceptable discriminative power of mortality with significant (AUC=0.732 and 0.725, respectively) while magnesium and potassium weren't significant (AUC=0.598 and 0.643, respectively) and this agree with **Pollack et al. study (2016)**, the area under the ROC for the development and validation sets of PRISM III was 0.88 ± 0.013.

CONCLUSIONS

Dyselectrolytemia is a common problem in pediatric patients admitted to PICU. Mortality was higher in patients with hyponatremia and it is more predictive of mortality than serum magnesium and potassium.

RECOMMENDATION

Measuring level of serum sodium on admission to all children in PICU is more predictive of mortality than magnesium and potassium, in order to prioritize their treatment

plans and to make prompt therapeutic decisions.

LIMITATIONS

This study had several limitations must be mentioned as it was a single center study, did not aim at defining the various factors which may contributed to the higher risk of morbidity and mortality like the nature and degree of severity of the underlying disease.

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