PREVALENCE OF DYSNATREMIA IN PEDIATRIC ICU AT AL-ZAHRAA UNIVERSITY HOSPITAL AND IT'S RELATION TO OUTCOME

By

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ABSTRACT

Background: *Dysnatremia is relatively common in critically ill patients. The prevalence of sodium disturbances in PICU changes from 20% to 30%. These disorders and their treatment are accompanied by increased mortality and morbidity.*

Aim and objectives: *The aim of this study was to determine the prevalence of dysnatremia in children hospitalized at PICU of Al-Zahraa University Hospital and its relation to outcome.*

Patient and methods: *This was a retrospective observational study that was carried out at the pediatric intensive care unit of Al-Zahraa University Hospital (PICU), Faculty of Medicine for girls Al-Azhar University. The study carried out on 1011 children admitted at PICU from January 2016 to December 2019, both sexes were included with an age range between 1 month to12 years. All data extracted from the hospital database and medical records, exporting demographic data, and diagnosis. Serum sodium was checked on admission and concentrations below 135 and above 145 mEq/L were considered hyponatremia and hypernatremia respectively, outcome data including survival status at PICU, period of hospital stay and respiratory support in the form of CPAP and Mechanical ventilation.*

Results: *The study included 1011 patients where the most common cause of admission at PICU was respiratory tract disorders. The Prevalence of dysnatremia (hyponatremia and hypernatremia was (18.4%) and (2.6%) respectively). The Prevalence of dysnatremia was insignificant between gender, but there was a statistically significant difference in age between isonatremic and hyponatremic patients. Cardiac diseases were statistically significant increase in hyponatremic patients in comparison to Isonatremic patients (p=0.033), Gastroenteritis and CNS infections were statistically significantly increased in hypernatremic patients in comparison to isonatremic patients (p=0.000) (p=0.010) respectively, Dysnatremia was associated with prolonged hospital stay (hyponatremia median was 5(3-8) days, hypernatremia median was 5 (4-8) days with (p=0.007), (p=0.015) respectively).*

There was no statistically significant difference between dysnatremic and isonatremic patients regarding mortality.

Conclusion: *Hyponatremia was more prevalent in critically ill children than hypernatremia. The most common cause of admission in PICU was respiratory tract disorders. Dysnatremia was associated with increased duration of hospital stay.*

Key words: *Dysnatremia, hyponatremia, hypernatremia.*

INTRODUCTION

Dysnatremia is an umbrella to describe hypo or hypernatremia. The changing pattern of serum sodium in hospitalized patients can cause neurological finding and in severe cases, significant morbidity and mortality especially in those with acute or rapid changes in plasma or serum sodium **(Hock et al., 2019)**.

Hyponatremia is often associated with abnormal vasopressin production, loop diuretics, thiazides, osmotic diuretics and tubulo-interstitial damage that reduces sodium and chloride in the diluted part of urine **(Palmer and Clegg, 2018)**.

Signs and symptoms of hyponatremia are observed when sodium level is rapidly reduced to less than 125 mEq/L. It has been demonstrated that seizures and cerebral edema observed in serum sodium less than 110 mEq/L. Hyponatremia symptoms may not be seen in ventilated patients attached to mechanical ventilator and may worsen cerebral edema and create severe effects such as herniation and respiratory tract signs **(Sadeghi-Bojd et al., 2019)**.

Hypernatremia is characterized by deficit of total body water (TBW) relative to total body sodium due to either loss of free water, infrequently administration of sodium solutions, or even more uncommonly administration of plasma like isotonic fluids **(Lehtiranta et al., 2020)**.

In older patients between two weeks and 17 years of age, the most common cause of hypernatremia on admission was excess water loss due to gastroenteritis or systemic infection. However, it was more common for hypernatremia to develop during hospitalization particularly in patients with systemic infection or those who underwent cardiac surgery. In addition, approximately one-third of the patients had an underlying neurologic condition **(Micheal et al., 2020)**.

Aim of the Study

The aim of this study is to determine the prevalence of dysnatremia in children admitted

to the PICU of Al-Zahraa University Hospital and its relation to outcome.

PATIENTS AND METHODS

Ethical consideration:

- Approval was obtained from pediatric department at AL-Zahraa University Hospital before participation, it includes data about aim of the work, study design, site, time, subject, tool and confidentiality
- Approval from Research Ethics Committee in Faculty of Medicine for Girls, Al-Azhar University obtained.
- Confidentially all data was ensured.
- No conflict of interest regarding the study or publication.
- No financial support for the study and publication.

Sample size: The study carried out on 1011 children who were admitted at PICU from January 2016 to December2019.

Study population: All children admitted at PICU from January 2016 to December2019 aged from 1month to 12 years.

Inclusion criteria: Infants aged from 1month to 12 years who were admitted in Al- Zahraa Pediatric Intensive care unit from January 2016 to December 2019.

Exclusion criteria: children with hyperglycemia or hypertriglyceridemia and files with missed data.

Study design: This is a retrospective observational study that carried out at the pediatric intensive care unit of Al- Zahraa University Hospital (PICU), Faculty of Medicine for girls, Al-Azhar University.

Methods: All data collected from the hospital database and medical records from January 2016 to December 2019 included the following:

- Demographic data: age, sex
- Clinical data&- diagnosis
- Laboratory data: serum sodium level (Hyponatremia defined as serum sodium less than 135 meq/L and hypernatremia is defined as serum sodium concentration of more than 145mEq/L)
- Outcome data: including period of stay in hospital,survival status at PICU and hospital discharge.

Statistical Analysis:

a. **Descriptive statistics:** quantitative data: mean and standard deviation were used to measure central tendency

and dispersion and qualitative data: frequency of occurrence was calculated by number and percentage.

b. Analytical statistics: comparing between groups was done using: students T test for Quantitative data of two independent samples. ANOVA test for more than two groups of normally distributed data, mann-Whitney U test between two groups of non-normally distributed data and pearson Chi square test used for qualitative data.

1- The value of significance was taken at (p-value ≤0.05).

2- The results presented in tables and figures.

Finally, writing the thesis, discussion, English and Arabic summaries, conclusion and recommendations.

RESULTS

The results of the present study were illustrated in the following tables and figures:

Table (1): Distribution of studied patients regarding serum sodium level

Groups	Total no. = 1011
Isonatremic	799 (79.0%)
Hyponatremic	186 (18.4%)
Hypernatremic	26 (2.6%)

This table shows that isonatremic patients were 799 patients (79.0%), hyponatremic patients were 186 (18.4%) and hypernatremic patients were 26 (2.6%).

Table (2): Comparison between Isonatremic and hyponatremic patients regarding diagnosis

	Isonatremia No. = 799	Hyponatremia No. = 186	Test value	P-value	Sig.
Respiratory disorders (pneumonia, bronchiolitis, bronchial asthma)	**545(67.1%)**	**134 (72.0%)**	**1.70**	**0.19**	**NS**
Neurological diseases (CNS infection, epilepsy and stroke)	**86 (8.7%)**	**24 (10.8%)**	**0.82**	**0.36**	**NS**
Gastroenteritis and severe dehydration	**30(3.9%)**	**13 (7.0%)**	**3.418**	**0.064**	**NS**
Renal diseases (acute kideny injury, chronic kideny diseases)	**56(7.1%)**	**7 (3.8%)**	**2.821**	**0.093**	**NS**
Cardiac diseases (acute heart failure, arrhythmias, infective endocarditis)	**34(4.4%)**	**2 (1.1%)**	**4.559**	**0.033**	**S**
Metabolic, surgical and multisystem affection disorders	**22 (2.9%)**	**2 (1.1%)**	**1.984**	**0.159**	**NS**
Hematological diseases (acute hemolytic anemia)	**12 (1.6%)**	**4 (2.2%)**	**0.244**	**0.621**	**NS**
Shock	**14(1.9%)**	**0 (0.0%)**	**3.546**	**0.060**	**NS**

This table shows Comparison between Isonatremic and hyponatremic patients regarding diagnosis in which all variables were statistically non-significant except cardiac diseases were statistically significant in hyponatremic patients in comparison to Isonatremic patients.

Table (3): Comparison between Isonatremic and hypernatremic patients regarding diagnosis

	Isonatremia No. = 799	Hypernatremia No. = 26	Test value	P-value	Sig.
Respiratory (pneumonia, bronchiolitis and bronchial asthma)	545(67.1%)	14 (53.8%)	1.986	0.159	NS
Gastroenteritis with dehydration	30(3.9%)	7 (26.9%)	30.430	0.000	HS
Neurological diseases (CNS infection, epilepsy and stroke)	86 (8.6%)	4 (15.4%)	1.422	0.233	NS
Renal diseases (acute kidney injury and chronic renal diseases	56 (7.1%)	1 (3.8%)	0.416	0.519	NS
Shock	14 (1.9%)	0 (0.0%)	0.497	0.481	NS
Cardiac diseases (acute heart failure, arrhythmias and congenital heart diseases)	34 (4.4%)	0 (0.0%)	1.189	0.275	NS
Metabolic, surgical, multisystem system affection an others	22(2.9%)	0 (0.0%)	0.770	0.380	NS
Hematological diseases (acute hemolytic anemia)	12 (1.6%)	0 (0.0%)	0.430	0.512	NS

This table shows Comparison between Isonatremic hyponatremic patients regarding diagnosis which all variables were statistically non-significant except gastroenteritis and CNS infection were statistically significant in hypernatremic patients in comparison to Isonatremic patients.

Table (4): Comparison between Isonatremic and hyponatremic patients regarding duration of stay in PICU

		Isonatremia	Hyponatremia	Test value	P-value	Sig.
		No. = 799	No. = 186			
Duration of stay (days)	Median (IQR)	4 (2 – 7)	5 (3 – 8)			
	Range	1 – 44	1 – 27	-2.678≠	0.007	HS

This table shows that there was statistically highly significantly increase in duration of Hospital stay in hyponatremic patient than in isonatremic patients.

Table (5): Comparison between Isonatremic and hypernatremic patients regarding duration of stay in PICU

		Isonatremia	Hypernatremia	Test value	P-value	Sig.
		No. = 799	No. = 26			
Duration of Hospital stay (days)	Median (IQR)	4 (2 – 7)	5 (4 – 8)	-2.433≠	0.015	S
	Range	1 – 44	2 – 19			

This table shows that there was statistically significant increase in duration of hospital stay in hypernatremic patients than in isonatremic patients.

Table (6): Comparison between hyponatremic and hypernatremic patients regarding outcome

Outcome	Hyponatremia	Hypernatremia	Test value	P-value	Sig.
	No. = 186	No. = 26			
Survivor	161 (86.5%)	23 (88.4%)	0.072	0.788	NS
Non survivors	25 (13.4%)	3 (11.5%)			

This table shows that there was statistically no significant difference between hyponatremic and hypernatremic patients regarding outcome.

DISCUSSION

Dysnatremia is relatively common finding in critically ill patients. The prevalence of sodium disturbances in PICU changes from 20 to 30% These disorders and their treatment are accompanied by increased mortality and morbidity **(Sadeghi-Bojd et al., 2019)**.

Hyponatremia occurs frequently in critically ill children, any condition resulting in increased ADH, syndrome of inappropriate ADH secretion (SIADH), increased right atrial pressure, ineffective extra-cellular fluid, cerebral salt wasting, or increased sensitivity of renal tubes to ADH may cause hyponatremia. In addition, administration of hypotonic intravenous fluids, corticosteroids, mechanical ventilation, diuretics and some other medications, may cause in-hospital hyponatremia **(Jones, 2018)**.

Although pediatric hypernatremia is an uncommon electrolyte abnormality, there can be significant neurologic injury in patients with severe hypernatremia, especially those with acute and rapid changes in serum sodium **(Blohm et al., 2018)**.

In this study we aimed to determine the prevalence of dysnatremia in children hospitalized at PICU of Al-Zahraa university hospital and it's relation to outcome. To our knowledge this is the first local study attempting to examine this relationship in the setting of critical care.

All data extracted from the hospital database and medical records from (January 2016) to (December 2019) exporting the following; Demographic data: age, sex; Clinical data: diagnosis, Laboratory data: serum sodium level and Outcome data: including survival status at PICU, period of stay in hospital and respiratory support in the form CPAP and MV.

This is a retrospective observational study carried out at the PICU of Al-Zahraa University hospital, Al-Azhar Faculty of medicine. The study was carried out on the children admitted at PICU from (January 2016) to (December 2019), both sexes were included, with age range between 1month to 12 years who fulfill the inclusion and exclusion criteria.

Our study included 1011 patients; 799(79.0%) isonatremic patients, 186 (18.4%) hyponatremic patients and 26 (2.6%) hypernatremic patients.

Our study found that (18.4%) of the studied children had hyponatremia. The range of

hyponatremia varies between 11% and 50% in different studies based on the methodology used and definition of hyponatremia **(Bibi et al., 2015)**.

In agreement with our results **Hasegawa et al. (2009)** retrospective study carried out between 2001 and 2005, found that approximately 17% of the hospitalized patients had hyponatremia [serum sodium (Na) < 135 mEq/l].

In disagreement with our results Subba and Thomas (2000) studied 305 children admitted in PICU for electrolyte abnormalities. 99 (32.45%) developed electrolyte abnormalities, Hyponatremia was observed in (9.5%) which was lesser than our results.

The higher incidence of hyponatremia encountered in our study is due to the set cutoff value of serum sodium, i.e., <135 mEq/L. Also, the type of PICU in this study which was a medical one, and defining hyponatremia as serum sodium below 135 mEq/L instead of 130 mEq/L could explain the higher prevalence of hyponatremia in our study.

Unlike hyponatremia, hypernatremia is less common and is less addressed in previous studies in the PICU setting. In our study, the frequency of admission was hypernatremia (serum sodium above 145 mEq/L was (2.6%) in critically ill children.

In agreement with our results **Lindner et al. (2007)** retrospective, single-center study from Austria, which included 981 patients, found that (2%) of patients had hypernatremia on admission in the ICU.

In disagreement with our results **Navaifar et al. (2017)** reported the frequency of admission hypernatremia (serum sodium above 145 mEq/L) was (5.1%).

Hyponatremia in present study was higher in patients with respiratory tract disorders followed by CNS infection, gastroenteritis, renal diseases, cardiac and hematologic diseases.

Admission hyponatremia was present in (72.0%) of the patients with respiratory tract disorders, which is almost higher than the results of previous studies, In agreement with our results **Divecha et al. (2019)** stated that Pneumonia contributed to (66.89%) of respiratory admissions.

In disagreement with our results **Hanna et al. (2003)** found that (33%) of children suffering from bronchiolitis were hyponatremic and **Luu et al.**

(2013) reported hyponatremia in (22%) of the cases with bronchiolitis in the PICU.

The reason for this difference may be due to the difference in the sample size, the difference in the demographic characteristics of patients, the difference in entry and exit criteria, and the reason for the admission of the subjects.

In our study, the rate of hyponatremia was (10.8%) among patients with CNS infections and other neurological diseases such as epilepsy (7.5%), CNS infection (3.2%) and stroke (2.2%).

In agreement with our results **Sorkhi et al. (2013)** reported hyponatremia in (8.8%) the pediatric patients suffering from acute CNS disorders.

In disagreement with our results **Edagotti et al. (2017)** studied sodium disturbances in various diseases and it was observed that incidence of hyponatremia was highest in patients with meningitis (58.82%).

CNS infections and RTI can cause hyponatremia by multiple mechanisms: hypo-volemic state (vomiting, decreased oral intake, high insensible losses secondary to fever) and Syndrome of Inappropriate ADH secretion (SIADH) **(Dineen et al., 2017)**.

In addition, CNS infections can cause hyponatremia by causing a urinary salt wasting state known as Cerebral Salt Wasting syndrome (CSW Syndrome) **(Divecha et al., 2019)**.

In our study, (7.0%) of the patients with Gastroenteritis with severe dehydration had admission hyponatremia, in agreement with our results **Tillman et al. (2013)** reported (3.96%) of hyponatremic patients were diagnosed gastroenteritis.

In disagreement with our results **Youssef et al. (2020)** study of electrolyte disturbance in critically ill children at Sohag university hospital at the emergency department found that (50%) of hyponatremic patients were diagnosed gastroenteritis as most of gastroenteritis managed at the emergency department.

Navaifar et al. (2017) also reported it in (14%) of the patients suffering from gastroenteritis. The reason for this discrepancy could be the type of patients admitted to their center (GIT center and liver diseases).

In our study, hyponatremia was 1 (3.8%) in patients with renal diseases, we found multiple risk factors for hyponatremia including end-stage renal disease complicated with volume

overload, use of diuretics, and renal tubulopathy.

In agreement with our results **Chang et al. (2014)** prospective observational study included a total of 441 incident patients who started Peritoneal dialysis between January 2000 and December 2005 found that (3.3%) of patients with renal diseases were hyponatremic.

In disagreement with our results **Charat et al. (2020)** found (33.3%) with renal diseases were hyponatremic.

Patients suffering from renal diseases have several risk factors for hyponatremia including impaired renal excretion of water, high plasma concentrations of arginine vasopressin, and use of diuretics specially thiazides.

According to our findings, (1.1%) of the cases with cardiovascular diseases had hyponatremia, which was statistically significant (p- =0.033) increased in Isonatremic patients 35 (4.4%) when compared to hyponatremic patients.

In agreement with our results **Hanchinmani et al. (2018)** cross-sectional study was conducted between January 2010 and December 2010 at the Department of Pediatrics of a Tertiary Care Hospital. A total of 100 critically ill children admitted to PICU patients found that hyponatremia in cardiovascular diseases was (3%).

In disagreement with our results **Navaifar et al. (2017)** reported that (16.6%) of the cases with cardiovascular diseases were hyponatremic these explained, that cardiovascular diseases, especially heart failure states, can lead to ineffective extravascular fluid, which can cause hyponatremia together with the use of diuretics and production of atrial natriuretic peptide.

In our study we found the most common diagnosis in hypernatremia was Respiratory tract disorders then gastroenteritis and neurological diseases.

Respiratory tract disorders may sometimes present with dehydration especially in infants and young children 14 (53.8%) with respiratory tract infections who had high serum sodium at presentation.

In disagreement with our results **Omer et al. (2017)** study which was at Pediatric Intensive Care Unit (PICU) Services Hospital Lahore 185 patients were included (11.9%) patients had hypernatremia (1.6%) of patients with RTI had high serum sodium at presentation.

In our study we found that gastroenteritis with dehydration were 7 (26.9%) higher in hypernatremic patients when compared to Isonatremic patients 31(3.9%) and there was statistically highly significant difference (p=0.000) when compared to Isonatremic as well as when compared to hyponatremic patients (p=0.001).

In agreement with our results **Yuca et al. (2017)** found that gastroenteritis was responsible for (25%) of the cases of hypernatremia on admission.

In disagreement with our results **Elise et al. (2007)** study found that, about 10% of infants with dehydration from gastroenteritis have hypernatremia.

We found that 3(11.5%) of hypernatremic were CNS infections Followed by epilepsy (3.8%) and stroke (3.8%).

CNS infections higher in isonatremic patients 22(2.8%) when compared to hypernatremic patients with statistically significant difference (p=0.010) and higher in hypernatremic patients when compared to hyponatremic patients (p=0.049) with statistically significant difference between two groups.

In agreement with our results, **Gupta et al. (2021)** study found that Acute CNS infections constituted (30%) of etiology of hypernatremia followed by intracranial bleeding (11.25%).

In disagreement with our results **Omer et al. (2017)** study at Pediatric Intensive Care Unit (PICU) Services Hospital Lahore stated that (5.4%) CNS infection was hypernatremic and the most common diagnosis in hypernatremia was CNS infections.

The possible causes of hypernatremia in patients with CNS infections can be volume loss due to vomiting or decreased oral intake, increased insensible losses due to high grade fever or development of central diabetes insipidus **Gonda et al. (2013)**.

In our study we found that there were insignificant differences between hyponatremic and hypernatremic patients regarding diagnosis except, gastroenteritis was highly significant increase in hypernatremic patients in comparison to isonatremic as well as CNS infections there were statistically significant increase in hypernatremic patients in comparison to isonatremic patients.

According to the duration of hospitalization in PICU of studied patients the Median (IQR) was 4(2-7) days with range (1-44) (minimum duration of stay was 1 day while maximum duration was 44 days).

In agreement with our results **Ambrosino and Vitacca (2018)** study stated that Mean duration of stay at PICU was 3.89 days (range 1-15 days).

In disagreement with our results **Volakali et al. (2011)** reported 8.85 ± 23.28 days mean duration of PICU stay.

Hyponatremic patients were associated with prolonged hospital stay in relation to Isonatremic with median (interQuartile ratio) (IQR) 5(3-8) days with range 1-27 days which was statistically highly significant (p=0.007).

As well as, hypernatremic patients were associated with prolonged hospital stay in comparison to Isonatremic with median 4.5 (3-6) days with range (1- 19) days which was statistically highly significant (p=0.007).

In agreement with our results **Jayakumar et al. (2017)** also observed that the morbidity (as determined by the PICU stay) was significantly higher in patients with hyponatremia in comparison to Isonatremic.

In a study by **Ontenda et al. (2018)** the study concluded that dysnatremia was associated with increased hospital stay and mortality.

In disagreement with our results **Müller et al. (2018)** retrospective screening of electronic admission data (06/2011-06/2013) of 610 patients were admitted to the ED of Bern University Hospital, Switzerland. Reported that no relationship between sodium levels and hospital stay.

In our study mortality rate in hyponatremic patients was (13.4%) and hypernatremic patients which was (11.5%) in contrast to (10.6%) died in isonatremic patients, The mortality higher in dysnatremia in comparison to isonatremic patients.

In agreement with our results **Sachdev et al. (2017)** study that conducted at tertiary care PICU on hospital acquired hyponatremia in PICU, 123 cases developed hospital acquired hyponatremia in which hyponatremic patients had prolonged PICU stay (P = 0.000) but no difference in the mortality when compared to control Similarly.

Also, **Patel et al. (2021)** prospective observational study was conducted on patients admitted in medical ICU over a period of 1 year who developed dysnatremia during ICU stay. This study concluded that hypernatremia is more common with longer ICU stay. In both hypernatremia and hyponatremia mortality was found similar without any significant difference.

In disagreement **Lindner et al. (2007)**; **Waite et al. (2013)** studies have reported 32%-55% mortality in dysnatremia patients.

CONCLUSIONS

We conclude that: Hyponatremia was more prevalent in critically ill children than hypernatremia, The most common cause of admission in PICU was respiratory tract disorders. Dysnatremia was associated with increased duration of hospital stay.

RECOMMENDATION

- Early detection of dysnatremia and prompt management will improve the prognosis.
- Simplified treatment regimens are proposed for prevention or earier recognition of dysnatremia.
- Further studies for explanation of how dynatremia contributes to adverse outcomes.

LIMITATIONS

This study does have several limitations as lack of electronic health records did not allow authers to have difficulty in getting detailed information and also missing data.

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