IMPACT OF HYPONATREMIA ON OUTCOME OF CHILDREN WITH COMMUNITY ACQUIRED PNEUMONIA

By

Refay Refay Hassan Nasser*, Mohsen Taha El Keiy*, Mostafa Mohamed Shaaban and Khalid Ahmed Rashed***

M.B.B.CH,

Departments of Pediatrics* & clinical pathology**, Faculty of Medicine,

Al-Azhar University, Cairo, Egypt

Corresponding author: Refay Refay Hassan Nasser,
Mobile: (+20) 1124199089, **E-mail:** refay1991@gmail.com

ABSTRACT

Background: *Community-acquired (CAP) and nosocomial pneumonias contribute substantially to morbidity and hospital resource utilization. Hyponatremia, occurring in >1/4 of patients with CAP, is associated with greater disease severity and worsened outcomes.*

Aim and objectives: *The aim of this work to identify the incidence of hyponatremia in children with community acquired pneumonia and to study the impact of hyponatremia regarding the severity of symptoms, duration of hospitalization and outcome of community acquired pneumonia.*

Subjects and methods: *This is a case controlled randomized study where the patients will be recruited from the PICU and pediatric department, Al-Azhar university hospitals during the period from September 2022 up to end of February 2023.*

Results: *There is higher assisted ventilation use in hyponatremic group than those with normal sodium however this difference was of no statistically significant value.*

Conclusion: *Hyponatremia is common among hospitalized patients with pneumonia and is associated with worsened clinical and economic outcomes. Studies in this large population are needed to explore whether prompt correction of [Na+] may impact these outcomes.*

Keywords: *Hyponatremia; children; community acquired pneumonia.*

INTRODUCTION

Pneumonia is the single largest infectious cause of death in children worldwide. Pneumonia accounts for 15% of all deaths of children under 5 years old, killing 808 694 children in 2017. The burden Is more common in the developing nations **(WHO 2019)**.

Pneumonia can present in many ways and can also lead to many complications. Hyponatremia (HN) is a common electrolyte disturbance occurring in hospitalized children with pneumonia. **(Lussky et al., 2009)** HN may result from free water retention, sodium losses or a shift of water from the intracellular to the extracellular compartment, or, correspondingly, a shift of sodium from the extracellular to the intracellular compartment **(Moritz ML, Ayus JC, 2002)**.

Serum osmolality mainly depends on serum sodium (and corresponding anions), blood urea nitrogen (BUN) and plasma glucose, and it may be low, normal or high in the case of HN **(Oh MS, 2002)**.

The syndrome of inappropriate secretion of antidiuretic hormone (SIADH) leads to water retention; it is one of the most important causes of HN with hypo-osmolality and it is usually associated with pulmonary, cerebral or malignant diseases, or with drugs **(Adroguè HJ, Madias N, 2000)**.

One study found 531 children with hyponatremia among 3938 children with respiratory infections with incidence of (13.5%) **(Sung Won Park et al., 2018)**.

AIM OF THE STUDY

The aim of this work to identify the incidence of hyponatremia in children with community acquired pneumonia and to study the impact of hyponatremia regarding the severity of symptoms, duration of hospitalization and outcome of community acquired pneumonia.

Our sample size was calculated according to the following equation:

$$\mathbf{n = N / [1 + N \times e^2]}$$

Where n=sample size, N =population size, e =margin of error.

A total of 80 patients was estimated to be sufficient sample size.

Ethical consideration

1. A written informed consent was obtained from parents or the legal guardians before the study.

2. An approved by the local ethical committee was obtained before the study.
3. The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.
4. All the data of the patients and results of the study are confidential &the patients have the right to keep it.
5. The patient has the right to withdraw from the study at any time.

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PATIENTS AND METHODS

This is a case controlled randomized study where the patients will be recruited from the PICU and pediatric department, Al-Azhar university hospitals during the period from September 2022 up to end of February 2023.

The study will include:

The case group:

Inclusions Criteria:

Fifty Children aged 2 months to 5 years' old with signs and/or symptoms compatible with respiratory infection and radiological infiltrations consistent with pneumonia with serum sodium less than 135 mmol/l.

Exclusion Criteria:

- Infants less than 2 months.
- Hospital-acquired pneumonia.
- Patients with chronic underlying illness: renal, thyroidal and adrenal insufficiency.

The control group:

Fifty Children aged 2months to 5 years' old with signs and/or symptoms compatible with respiratory infection and radiological infiltrations consistent with pneumonia with normal serum sodium.

All study children will be subjected to the following:

1. Detailed history, clinical assessment and grading the severity of pneumonia.
2. Laboratory study:
    - CBC using Sysmex XN 350.
    - ABG using SensaCore ST200CC.
    - Serum electrolytes (Na, K, Mg, Ca) using Cornley AFT-C Electrolyte Analyzer.
    - Liver function tests (ALT, AST) and Renal function

tests (urea, creatinine), CRP & Plasma glucose concentration using mindray BS-600M.

3. Radiological study:
   - Chest X.Ray.
   - CT chest if needed.

Statistical analysis design:

Data collected were reviewed and coded. These numerical codes were fed to the computer where statistical analysis was done using the Statistic Package for Social Science Version 22 (SPSS 22).

Descriptive data:

1. Quantitative data: were presented as mean and standard deviation (mean ± SD).
2. Qualitative data: were expressed as numbers and percentage. Comparing groups was done using:
   a. Chi square-test (X^2): for comparison of qualitative data
   b. Student's "t"- test for comparison of quantitative data of 2 independent sample with normal distribution and homogeneity of variance
   c. The coefficient interval was set to 95%. The level of significance was calculated according to the following probability (P) values:

$P<0.05$ was considered statistically significant.

RESULTS

Our results will be demonstrated in the following tables:

Table (1): Demographic data of the studied groups

		Hyponatremia group	Normal sodium group	t/x2	Pvalue
		No. = 50	No. = 50		
Age (month)	Range	4 – 36	6 – 36	0.409	0.684
	Median [IQR]	16 [13.5]	14 [15]		
	Mean ± SD	18.27 ± 9.85	17.47 ± 9.72		
Age distribution	2 m – 1y	18 (36%)	11 (22%)	4.235	0.237
	1y-2y	11 (22%)	8 (16%)		
	2y – 3y	9 (18%)	15 (30%)		
	3y-4y	7 (14%)	9 (18%)		
	4y-5y	5(10%)	7(14%)		
Sex	Male	29 (58%)	28 (56%)	0.041	0.839
	Female	21 (42%)	22 (44%)		

There is no statistically significant difference between the studied groups as regard age, sex.

Table (2): Comparison of vital data of the studied groups

		Hyponatremia group	Normal sodium group	t	Pvalue
		No. = 50	No. = 50		
HR (beat/min)	Range	100 - 128	100 - 125	3.321	0.001*
	Mean ± SD	117.57 ± 7.72	112.57 ± 7.33		
RR (cycle/min)	Range	50 - 65	50 - 63	2.594	0.011*
	Mean ± SD	59.44 ± 4.67	57.25 ± 3.72		
Temperature	Range	37 - 40	36 - 40	2.138	0.035*
	Mean ± SD	38.65 ± 1.27	38.13 ± 1.16		
O2 sat%	Range	90 - 97	90 - 99	0.127	0.829
	Mean ± SD	92.57 ± 1.72	92.48 ± 2.38		

There is statistically significant higher HR, RR, temperature in hyponatremic group than those with normal sodium while no significant difference in O2 saturation between both groups.

Table (3): Laboratory findings of both groups

		Hyponatremia group	Normal sodium group	t	Pvalue
		No. = 50	No. = 50		
HCT		30.44 ± 2.45	31.63 ± 3.65	-1.914	0.058
WBCs $x10^3/mm^3$		9.25 ± 3.15	8.90 ± 2.21	0.643	0.521
Platelets x103/mm3		302.77 ± 19.65	302.32 ± 26.65	-0.096	0.924
AST (IU)		30.00 ± 20.16	24.67 ± 9.79	1.304	0.189
ALT (IU)		37.67 ± 22.03	29.87 ± 6.29	1.865	0.067
Urea (mg/dl)		29.63 ± 18.73	25.41 ± 2.96	1.219	0.228
Creat (mg/dl)		0.77 ± 0.38	0.71 ± 0.11	0.824	0.413
K (mg/dl)		3.36 ± 0.35	3.42 ± 0.33	-0.762	0.449
Ca (mg/dl)		9.47 ± 1.28	9.71 ± 0.11	-1.023	0.311
Mg (mg/dl)		2.09 ± 0.13	2.10 ± 0.13	0.594	0.716
Glucose (mg/dl)		94.47 ± 9.27	93.97 ± 7.84	0.226	0.822
CRP	Positive	40 (80%)	38 (76%)	0.233	0.629
	Negative	10 (20%)	12 (24%)		

There is no statistically significant difference between laboratory findings of both groups.

Table (4): Comparison of arterial blood gases data of the studied groups

	Hyponatremia group	Normal sodium group	t	Pvalue
	No. = 50	No. = 50		
PH	7.35 ± 0.02	7.36 ± 1.03	-2.269	0.027 *
PCO2	36.93 ± 1.95	36.37 ± 1.79	1.174	0.245
PaO2	83.23 ± 3.63	85.40 ± 3.99	-2.202	0.032 *
HCO3	16.43 ± 1.85	18.33 ± 2.14	-3.679	0.001 *

There is statistically significant lower PH, PaO2 and HCO3 in hyponatremic group than those with normal sodium while no significant difference in PCO2 between both groups.

Table (5): Comparison of oxygen administration in the studied groups

		Hyponatremia group	Normal sodium group	X2	P-value
		No. = 50	No. = 50		
O2 administration	Assisted ventilation	11(22%)	5 (10%)	12.148	0.0004
	Nasal prong	39 (88%)	45(90%)		

There is statistically significant higher assisted ventilation use in hyponatremic group than those with normal sodium.

Table (6): Comparison of the duration of ICU stay in the studied groups

		Hyponatremia group	Normal sodium group	X2	P-value
		No. = 50	No. = 50		
ICU hospital stay (days)	Range	6 - 11	5 - 9	3.038	0.003*
	Mean ± SD	8.27 ± 2.83	6.63 ± 2.56		
Ward hospital stay (days)	Range	4 - 6	4 - 5	3.538	<0.0001*
	Mean ± SD	5.42 ± 1.75	4.53 ± 0.32		

There is statistically significant longer duration of hospital stay either in ICU or ward in hyponatremic group than those with normal sodium.

Table (7): Comparison of the outcome in the studied groups

		Hyponatremia group	Normal sodium group	X2	P-value
		No. = 50	No. = 50		
Outcome	Survived	44 (88%)	48 (96%)	6.061	0.014*
	Died	6 (12%)	2 (4%)		

There is statistically significant higher mortality in hyponatremic group than those with normal sodium.

DISCUSSION

Community-acquired pneumonia (CAP) is a common and potentially serious illness with considerable morbidity. It is a major cause of morbidity and mortality in children less than five years old. Pneumonia is a vital reason of morbidity in the developed world, and also important cause of morbidity and mortality inside the growing global **(Nascimento Carvalho, 2020)**.

Hyponatremia (HN, serum sodium < 135 mEq/L) is the most common electrolyte imbalance seen in clinical practice, and also in critically ill children. It is usually present in 3% of hospitalized patients **(Królicka et al., 2020)**.

There is no statistically significant between the studied groups as regard age and sex.

Similarly, in the study of **Haseeb et al., 2019**, the mean age was 2.74±1.23 years with 55 (72%) males and 21 (28%) females. There was no statistically significant difference between those with hyponatremia (n=41) and those with normontremia (n=35) as regard to sex.

The present study showed that there is statistically significant higher HR, RR, temperature in hyponatremic group than those with normal sodium while no significant difference in O2 saturation between both groups. There is no statistically significant difference in anthropometry between both groups. There is no statistically significant difference between both groups.

In accordance with our results, study of **Aly et al., 2021**, as they reported that body temperature was more (38.5vs.37.8 °C, p =0.002) in patients with HN compared to patients with normal serum Na.

Our results were supported by study of **Hamed et al., 2019**, as they reported that vital signs were significantly higher in children with pneumonia when compared to healthy controls (P value 0.001). Furthermore, **Natarajan et al., 2020**, revealed that hyponatremia was more common in children who had high initial temperature (P<0.001), tachycardia (P <0.001) and hemodynamic instability on arrival (P <0.001). Among the children with hemodynamic instability 48.1% (13/27) had mild hyponatremia and 44.4% (12/27) had moderate hyponatremia. In the study in our hands, there is statistically significant lower PH, PaO2 and HCO3 in hyponatremic group than those with normal sodium while no significant difference in PCO2 between both

groups. There is higher assisted ventilation use in hyponatremic group than those with normal sodium however this difference was of no statistically significant value.

Our results were supported by study of **Zilberberg et al., 2008**, as they reported that the proportion of patients requiring mechanical ventilation (MV) (3.9% vs. 2.3%, p = 0.014) was significantly higher in the hyponatremic than the normonatremic group.

Also, **Natarajan et al., 2020**, demonstrated that eleven (9.2%) children required mechanical ventilation and all of them had hyponatremia which was mild in 45.5% (5/11) and moderate in 54.5% (6/11) which is statistically significant.

The present study showed that there is statistically significant longer duration of hospital stay either in ICU or ward in hyponatremic group than those with normal sodium. There is higher mortality in hyponatremic group than those with normal sodium but this difference was of no statistically significant value.

Our results were supported by study of **Zilberberg et al., 2008**, as they reported that hospital mortality, though low in both groups, was greater among patients with hyponatremia (5.4% vs. 4.0%). This difference, however, only approached statistical significance (p = 0.099). The proportion of patients requiring any ICU admission (10.0% vs. 6.3%, p < 0.001) was significantly higher in the hyponatremic than the normonatremic group.

Also, **Aly et al., 2021**, revealed that duration of hospitalization was longer (7vs.6 days, p= 0.002) in patients with HN compared to patients with normal serum Na.

Also, **Natarajan et al., 2020**, demonstrated that hyponatremia was significantly associated with prolonged hospital stay (P <0.001). Of the 120 children enrolled in the study 4 (3.3%) children died and all of them had hyponatremia [mild in 1 and moderate in 3, P = 0.04].

In addition, **Das & Narain, 2019** stated that the duration of hospital stay was significantly higher in the children with hyponatremia (p=0.0005) compared to those children without hyponatremia (p=0.01). Average duration of the hospital stay in the present study in severe pneumonia with normonatremia was 7.3±1.7 days (range of 5-9 days) while that with hyponatremia was 8.2±4.5 days

(range of 1- 14 days) including those cases who died.

This is similar to the study conducted by **Singhi and Dhawan et al, 1992** where they found that in hyponatremic children the duration of hospitalization was prolonged by 60% and the occurrence of complication was about two-fold and the mortality was about 3.5 times higher as compared to normonatremic patients. The mean length of hospital stay was significantly prolonged in children who had coexisting hyponatremia with hypokalemia. **Wrotek. Et al, 2013** concluded in their study that hyponatremia is a frequent finding in CAP which is associated with the disease severity and found that duration of hospitalization was longer in hyponatremic children when compared with non-hyponatremic children.

In addition, **Praneetha et al., 2019**, stated that 48% of patients with hyponatremia compared to 26% of patients without hyponatremia had hospital stay more than 7 days. Children with hyponatremia had prolonged duration of hospital stay compared to children without hyponatremia. The difference was statistically significant. Mortality in patients with community acquired pneumonia was 6.5% (8/122 patients). Mortality was 13 % in patients with hyponatremia compared to 1.5% in patients with normonatremia. The difference was statistically significant (P=0.016).

CONCLUSIONS

Hyponatremia is a common finding in children with CAP. The degree of hyponatremia seems to be related with the severity of pneumonia. Sodium serum level was decreased with increasing the grade of respiratory distress. Serum sodium should be strictly checked at admission and steps needed to be carried out immediately for the better prognosis of the patients.

RECOMMENDATION

- Future research needs to focus not only on how hyponatremia may affect subpopulations of patients with pneumonia, but also how severity of hyponatremia impacts hospital outcomes.
- Most importantly, studies are needed to evaluate the role of currently available therapies aimed at correction of hyponatremia in improving the outcomes of patients with pneumonia.
- Serum electrolytes should be studied at least in children hospitalized for pneumonia; proper fluid management must

be carefully arranged in the case of HN, and both serum and urinary sodium concentrations should be monitored.

- There is much need to continue research on explaining the pathophysiology of electrolyte imbalance in pneumonia.

Limitations of the study: Firstly; relatively small sample size; secondly; cases were taken from a single center and finally; further investigation with serum and urine osmolality and urine sodium could not be done.

REFERENCES

1. **Adroguè HJ, Madias N (2000):** Hyponatremia. N Engl J Med 342:1581–1589
2. **Aly, Y., Mohsen, M., Khalil, M., & Salah, D. (2021):** Prevalence of hyponatremia (HN) in children with community acquired pneumonia (CAP) and its relation to disease severity, outcomes.
3. **Hamed, A. M., Ibrahim, M. F., Fayed, H. K., Abd EL-Meguid, M. M., & Hassen, S. E. (2019):** Serum Sodium Levels in Hospitalized Children with Community-Acquired Pneumonia: A Hospital-Based Case-Control Study. The Egyptian Journal of Hospital Medicine, 75(4), 2706-2711.
4. **Haseeb, M., Engade, M., Valecha, A., Shanbag, N., & Wagh, S. (2019):** Hyponatremia in Children Hospitalised with Community-acquired Pneumonia: A Prospective Observational Study. Journal of Clinical & Diagnostic Research, 13(10).
5. **Królicka, A. L., Kruczkowska, A., Krajewska, M., & Kusztal, M. A. (2020):** Lussky HO, Friedstein H. Water retention in pneumonia. Am J Dis Child.2009;19(5):337-43.
6. **Moritz ML, Ayus JC (2002):** Disorders of water metabolism in children: hyponatremia and hypernatremia. Pediatr Rev 23:371–380.
7. **Nascimento-Carvalho, C. M. (2020):** Community-

acquired pneumonia among children: the latest evidence for an updated management. Jornal de pediatria, 96, 29-38.

8. **Natarajan, T., Sadique, T. N. S., & Shanmugham, K. (2020):** Incidence of hyponatremia and its utility as an indicator of morbidity in children hospitalized with community acquired pneumonia. Int J Contemp Pediatr, 7, 616.

9. **Oh MS (2002):** Pathogenesis and diagnosis of hyponatremia. Nephron 92 [Suppl 1]:2–8.

10. **Praneetha, C. K., Ahirrao, V. S., Srinivasa, K., Premalatha, R., & Ravichander, B. (2019):** Hyponatremia in children of 2 months to 5 years of age with community acquired pneumonia and its correlation with severity of illness and outcome. Pediatric Review: International Journal of Pediatric Research, 6(11), 56.

11. **Singhi S, Dhavan A. (1992):** Frequency and significance of electrolyte abnormalities in pneumonia. Ind Paediatr.;29:735-40.

12. **Zilberberg, M.D., Exuzides, A., Spalding, J. et al. (2008):** Hyponatremia and hospital outcomes among patients with pneumonia: a retrospective cohort study. BMC Pulm Med 8, 16.