

# Hyponatremia in Children Hospitalized with Pneumonia

## Pnömoni Nedeniyle Hastaneye Yatırılan Çocuklarda Hiponatremi

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### Abstract

**Objective:** Hyponatremia is the most common electrolyte disorder in children hospitalized for various reasons. In this study, we aimed to determine the frequency of hyponatremia in children hospitalized due to pneumonia and to analyze the factors associated with its occurrence.

**Material and Methods:** The medical records were retrospectively reviewed for 92 children (57% boys) with pneumonia aged 2 to 17 years. Information on variables including the child's age and gender, clinical features of pneumonia, duration of hospitalization, nonspecific markers of inflammation, and biochemical examinations (urea, creatinine, sodium) were also recorded. Patients were grouped according to serum sodium levels; normonatremia (135-145 mmol/L), mild hyponatremia (131-134 mmol/L), moderate hyponatremia (126-130 mmol/L), severe hyponatremia ( $\leq 125$  mmol/L), and hypernatremia ( $>145$  mmol/L).

**Results:** Twenty five (27%) patients had mild hyponatremia, four (4%) patients had moderate hyponatremia, and no patient with severe hyponatremia or hypernatremia. Although the mean age was similar in children with hyponatremia and normal serum sodium levels, hyponatremia is more common in boys. The serum sodium levels were negatively correlated with acute phase reactants including leucocyte count ( $r=-0.373$ ,  $p=0.001$ ), the percentage of neutrophils ( $r=-0.251$ ,  $p=0.025$ ) and C-reactive protein level ( $r=-0.261$ ,  $p=0.019$ ). However, it was not associated with clinical findings and the duration of hospitalization. The degree of hyponatremia seems to be associated with acute phase reactants including leucocytes count, the percentage of neutrophils and CRP levels.

**Conclusion:** Hyponatremia is very common among children hospitalized with pneumonia but is usually mild. We suggest that serum and urine sodium levels be monitored closely in patients hospitalized with pneumonia. (*J Pediatr Inf 2013; 7: 102-5*)

**Key words:** Hyponatremia, pneumonia, inappropriate ADH syndrome

### Özet

**Amaç:** Hiponatremi hastaneye yatırılarak tedavi edilen olgularda sık görülen bir elektrolit anormalliktir. Bu çalışmanın amacı pnömoni tanısı ile hastaneye yatırılmış çocuklarda hiponatremi sıklığını belirlemek ve oluşumuna eşlik eden faktörleri incelemektir.

**Gereç ve Yöntemler:** Çalışmada pnömoni tanılı 2-17 yaş arasındaki 92 (%57 erkek) hastanın tıbbi kayıtları geriye dönük olarak incelenmiştir. Çocuğun yaşı, cinsi, pnömoninin klinik özellikleri, hastanede yatış süresi, nonspesifik enflamasyon belirteçleri ve biyokimyasal değerleri (üre, kreatinin ve sodyum) kaydedildi. Hastalar serum sodyum düzeylerine göre; normonatremi (135-145 mmol/L), hafif hiponatremi (131-134 mmol/L), orta hiponatremi (126-130 mmol/L), ağır hiponatremi ( $\leq 125$  mmol/L) ve hipernatremi ( $>145$  mmol/L) olarak gruplandırıldı.

**Bulgular:** Yirmi beş (%27) hastada hafif, 4 (%4) hastada orta düzeyde hiponatremi mevcuttu. Ağır hiponatremi ya da hipernatremi hiçbir hastada gözlenmedi. Hiponatremili ve normonatremili olgular arasında yaş açısından bir farklılık yoktu; ancak hiponatremi erkek çocuklarda daha sıklıkla sodyum düzeyleri ile lökosit sayısı ( $r=-0,373$ ,  $p=0,001$ ), mutlak nötrofil sayısı ( $r=-0,251$ ,  $p=0,025$ ) ve C-reaktif protein ( $r=-0,261$ ,  $p=0,019$ ) arasında negatif korelasyon mevcuttu. Hiponatreminin hastanede yatış süresi üzerine herhangi bir etkisi saptanmamıştır. Hiponatreminin derecesi ile lökosit sayısı, mutlak nötrofil sayısı ve CRP arasında anlamlı ilişki görülmektedir.

**Sonuç:** Pnömoni çocuklarda, hafif düzeyde hiponatremi sık görülen bir laboratuvar anormallığıdır. Pnömoni nedeni ile hastaneye yatırılan çocuklarda parenteral sıvı başlanırken bu durum göz önüne alınmalı ve serum sodyum düzeyi yakından izlenmelidir. (*J Pediatr Inf 2013; 7: 102-5*)

**Anahtar kelimeler:** Hiponatremi, pnömoni, uygunsuz ADH sendromu

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## Introduction

Pneumonia is the leading cause of serious illness and death in children worldwide and it can be generally defined as inflammation of the lung parenchyma. Because pneumonia is associated with serious morbidity and mortality, properly diagnosing pneumonia and correctly recognizing any complication are important. There is no single definition of pneumonia in childhood that is sensitive, specific, and can be widely implemented (1). The laboratory tests may not be useful for diagnostic purposes but are useful for classifying severity of illness, associated and admission decisions.

Hyponatremia is one of the most common electrolyte disturbances in patients hospitalized with pneumonia, and is associated with higher disease severity. The precise mechanism is unknown, but primary illness, impaired water excretion, "inappropriate" release of vasopressin, use of hypotonic fluids, redistribution of sodium and water, sickle cell syndrome, and several drugs may contribute to hyponatraemia (2).

The aim of this study was to identify the incidence of hyponatremia in children with pneumonia and to investigate whether there is a link between hyponatremia and the severity and outcome of pneumonia.

## Material and Methods

The records of children hospitalized due to pneumonia in Department of Pediatrics, Istanbul Haseki Educational and Research Hospital, were retrospectively analyzed. The patients were chosen randomly from those who were hospitalized from January 2009 to June 2012. Exclusion criteria were as follows: significant heart disease, malignancy, hemoglobinopathy, immune deficiency, underlying pulmonary pathology (e.g. cystic fibrosis, bronchiectasis or bronchopulmonary dysplasia), upper airway mechanical problems, or genetic syndrome. Information on sociodemographic variables including the child's age and gender, and duration of hospitalization were also recorded. Moreover, laboratory data included complete blood cell count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), serum concentrations of sodium (Na), urea, creatinine. The study group was subdivided into two groups based on hyponatremia: groups with or without hyponatremia. Hyponatraemia was defined as a sodium concentration of <135 mmol/L in serum. Serum sodium concentrations of 131-134 mmol/L represents mild hyponatremia, 126-130 mmol/L moderate hyponatremia, and ≤125 mmol/L severe hyponatremia (3). Hypernatremia was defined as a serum sodium concentration >145 mmol/L.

## Statistical analyses

All the analyses were performed using the SPSS 17.0 (SPSS Inc., Chicago, Illinois, USA). The results were expressed as means±standard deviations or median(min-max). Fisher's exact test was used for categorical variables in order to calculate p values. Mann-Whitney test was used for continuous variables. Spearman's correlation (nonparametric) test was used for bivariate correlation calculations. Values of  $p < 0.05$  were considered as significant.

## Results

The baseline characteristics of the study population are shown in Table 1. The study population consisted of 92 children. The mean age of patients was  $8.2 \pm 4.2$  years, their age ranged from 2 to 17 years, and 52 of them (57%) were boys. On admission, the patients' serum sodium concentrations ranged from 126 mmol/L to 141 mmol/L, while none of our patients had hypernatremia. There was hyponatremia (serum sodium < 135 mmol/L) in 29/92 (31%) patients, only four had moderate hyponatremia, and none had severe hyponatremia. The mean serum sodium concentration was  $131.7 \pm 2.2$  mmol/L in hyponatremic patients and  $137.2 \pm 1.7$  mmol/L in normonatremic patients.

As seen in Table 2, the mean age was similar in the patients with and without hyponatremia, however male gender was more dominant in patients with hyponatremia. No significant differences were found in serum urea, hemoglobin, thrombocyte count, ESR, and duration of hospitalization between the two groups.

The leucocyte count, percentage of neutrophils CRP and creatinine levels were significantly higher in hyponatremic patients compared with those of normonatremic patients.

**Table 1.** Demographic features and laboratory data of all children with pneumonia

Characteristics	All patients (n=92)
Age (year)	8.2±4.2
Male/female	52/40
Sodium (mEq/L)	135.5±3.1
Urea (mg/dL)	24.1±8.5
Creatinine (mg/dL)	0.5±0.2
Leucocytes count (/mm <sup>3</sup> )	17024±9269
Percentage of neutrophils (%)	67.9±18.6
Thrombocytes count (/mm <sup>3</sup> )	365758±152312
C-reactive protein (mg/dL)	21.5±46.7
Erythrocyte sedimentation rate (mm/h)	57.5±30.1
Hemoglobin (g/dL)	11.8±1.4
Duration of hospitalization (day)	10.3±5.4

**Table 2.** Characteristics of children with hyponatremia vs children with normal levels of serum sodium on admission

Characteristics	Hyponatremia (n=29)	No hyponatremia (n=63)	p
Age (year)	9 (2-17)	6.5 (2-16)	0.255
Male/female	21/8	31/32	0.032
Sodium (mmol/L)	132 (126-134)	137 (135-141)	<0.001
Urea (mg/dL)	23.5 (12-70)	21.9 (12.2-43.2)	0.131
Creatinine (mg/dL)	0.59 (0.22-1.08)	0.45 (0.16-0.74)	0.010
Leucocytes count (/mm <sup>3</sup> )	20900 (4100-37400)	12100 (4800-44200)	<0.001
Percentage of neutrophils (%)	86 (41.6-96)	65.5 (26.9-93.8)	<0.001
Thrombocytes count (10 <sup>3</sup> /mm <sup>3</sup> )	317 (204-653)	320 (146-840)	0.861
C-reactive protein (mg/dL)	14.6 (2.15-148.3)	3.89 (0-300)	<0.001
Erythrocytes sedimentation rate (mm/h)	66 (11-124)	51.5 (2-125)	0.078
Hemoglobin (g/dL)	11.7 (7.9-14.6)	11.9 (8.6-15.2)	0.756
Duration of hospitalization (day)	9 (5-21)	9 (2-32)	1.000

**Table 3.** Factors correlated with serum sodium levels in children with pneumonia (only significant correlations shown)\*

	r	p
Leucocyte count (/mm <sup>3</sup> )	-0.373	0.001
Percentage of neutrophils	-0.251	0.025
C-reactive protein (mg/dL)	-0.261	0.019
*Spearman's correlation analysis		

In other words, the serum sodium levels were negatively correlated with acute phase reactants including leucocyte count, the percentage of neutrophils and CRP (Table 3). Also, according to the results of linear regression analysis, the mean leucocyte count was the only significant independent predictor of serum sodium levels. However, the serum sodium levels of our patients were not correlated with the duration of hospitalization, or clinical markers such as fever, heart rate and respiratory rate.

## Discussion

Hyponatremia is the most common electrolyte abnormality. Pathophysiologically, hyponatremias are classified into two groups: hyponatremia due to non-osmotic hypersecretion of vasopressin (hypovolemic, hypervolemic, euvoletic) and hyponatremia of non-hypervasopressinemic origin (pseudohyponatremia, water intoxication, cerebral salt wasting syndrome) (4).

The present study showed that hyponatremia was a frequent finding in children with pneumonia (32%). Fortunately, in the majority of cases, hyponatremia was mild. Only four patients (4%) had moderate hyponatremia, and none of our patients had severe hyponatremia. Patients with mild hyponatremia are almost always asymptomatic. Severe hyponatremia is usually associated with central nervous system symptoms and can be life-threatening. Diagnostic evaluation of patients with

hyponatremia is directed toward identifying the extracellular fluid volume status, neurological symptoms and signs, severity and duration of hyponatremia, and the rate at which hyponatremia developed (4).

Hyponatremia occurring in children with pneumonia comprises part of the syndrome of inappropriate antidiuretic hormone secretion (SIADH) (5-7). Secretion of anti-diuretic hormone typically results in water retention with minimal weight gain, usually with no oedema formation, and normal blood pressure (6). Also, some authors reported that high atrial natriuretic peptide levels (ANP) may play a role in the development of hyponatremia in these patients (6, 8, 9). Atrial natriuretic peptide is a member of the family of natriuretic peptides, and regulates diuresis and natriuresis. Increased levels of ANP is correlated with hypoxia in lung diseases (6). Some studies postulated an interaction between ANP and ADH (6, 8, 9). They measured ANP levels 6 times higher than the normal range in SIADH patients. Haviv et al. (6) demonstrated that high ANP levels may play a role in maintaining water and electrolyte equilibrium during a state of inappropriate ADH secretion accompanying pneumonia.

The rarity of moderate and severe hyponatremia in our children with pneumonia can be explained by observations in recent studies. Haviv et al. (6) demonstrated that pneumonia in children was frequently accompanied by SIADH and that ANP levels were significantly increased in these patients. It is clearly known that ANP may play a role in maintaining water and electrolyte balance in children with pneumonia and SIADH, through its natriuretic, diuretic and vasodilatory effects. Gerigk et al. (10) found that antidiuretic hormone release induced hyponatremia may originate in a nonosmotic, cardiovascular mechanism in acutely ill children, including children with pneumonia.

The analysis of two studies in children with pneumonia has shown a significant association between the

presence of hyponatremia and elevated levels of nonspecific inflammatory markers (2, 4). In our study, the leucocyte count, percentage of neutrophils and CRP levels were significantly higher in hyponatremic patients with pneumonia. Also, the serum sodium levels were negatively correlated with these acute phase reactants. All these parameters reflect the severity of pneumonia. Although in the previous two studies it was reported that hyponatremia seemed to be associated with the longer hospitalization period and a prolonged duration of fever, there was no such relationship in our study.

In some diseases other than pneumonia, hyponatremia has been identified as a predictor of hospital outcomes. When evaluated with complications such as pleural effusion and empyema, no differences were seen between normonatremic and hyponatremic groups. Pleural complications occurred in seven patients, including four in the hyponatremic group and three in the normonatremic groups.

Our study has some limitations. The major limitation of the study was that we did not measure urinary sodium or urinary osmolality, which is an easy way to separate dehydration from SIADH. Another limitation was the relatively small size of our study group, because only four children with pneumonia had moderate hyponatremia, and none of patients had severe hyponatremia. Thus, studies in larger population groups are needed to better clarify these inter-relationships.

## Conclusion

Our findings confirm that mild hyponatremia is common among children hospitalized with pneumonia and that the degree of hyponatremia seems to be associated with the concentrations of acute phase reactants. Thus, serum electrolytes should be measured in children hospitalized for pneumonia; the appropriate fluid therapy must be carefully arranged in children with hyponatremia, and both serum and urine sodium levels should be closely monitored.

## Conflict of Interest

No conflict of interest was declared by the authors.

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## Author Contributions

Concept - N.S.D.; Design - N.S.D., M.Ç.; Supervision - N.S.D., M.Ç.; Funding - N.S.D., S.B.; Materials - N.S.D.,

S.B.; Data Collection and/or Processing - N.S.D., S.B.; Analysis and/or Interpretation - N.S.D., M.Ç.; Literature Review - N.S.D.; Writing - N.S.D.; Critical Review - N.S.D., M.Ç.; Other - M.E.

## Çıkar Çatışması

Yazarlar herhangi bir çıkar çatışması bildirmemişlerdir.

**Hakem değerlendirmesi:** Dış bağımsız.

## Yazar Katkıları

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