

To Study the Association and Significance of Hyponatremia in Pneumonia in Paediatric Patients Treated in Hospital Setting

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ABSTRACT

Introduction: Hyponatremia commonly occur in pneumonia patients on admission and they are known to have worse outcome. Current study was done to see the association and significance of hyponatremia in relation to severity and final outcome in pneumonia cases.

Material and methods: Current prospective observational study was conducted in patients admitted in paediatric wards of a tertiary care hospital. Study was done in 100 children of 1 month-5 years of age of both sexes having pneumonia. Serum sodium concentration was measured on admission and at 24 and 48 hours in children hospitalised for pneumonia, diagnosed clinically and radiologically. Some other blood investigations were done and clinical outcome e.g- complications, recovery and death were noted. Hyponatremic and normonatremic groups were to be compared for all outcomes by- student-t test or Fischer-exact test as applicable.

Results: Community Acquired Hyponatremia (CAH) [serum sodium < 135 mEq/L at 0 hour] was present in 21 cases (21%) e.g- hyponatremic group (HN) and rest 79 cases (79%) were in normonatremic group (NN). Hyponatremia was mostly mild. On admission, patients in HN group had higher - body temperature, longer tachypnoea, time for defervescence, hospital stay and longer oxygen requirement. Hyponatremic patients also showed higher CRP level, WBC Count and Neutrophil proportion. Death was 19.25 times likely in HN group. All the moderate and severe hyponatremia cases were expired and showed a statistically significant correlation between hyponatremia and worse outcome in pneumonia. Hospital- aggravated hyponatremia had a correlation with increased morbidity but not with mortality and hospital-acquired hyponatremia showed no such correlations.

Conclusion: Hyponatremia is common in pneumonia and it is a strong indicator of higher morbidity in children hospitalized for pneumonia.

Keywords: Community Acquired Pneumonia, Hyponatremia, Sodium, Hospitalized Children

Though the concept of water retention and hyponatremia in pneumonia came in 1920s⁴⁻⁵, only few case reports were published till the 80s⁶⁻⁸ and till date only 5 published studies are there in children⁹⁻¹³ and few more in adults¹⁴⁻¹⁷.

Though danger of fluid overload and importance of fluid restriction has been emphasized in meningitis, precise data about necessary fluid restriction in pneumonia is still lacking. The Aim of our study was to see the frequency of hyponatremia in pneumonia and to study the significance of hyponatremia in relation to disease severity and final outcome in pneumonia cases needed hospitalization.

MATERIAL AND METHODS

This hospital in-patient based prospective study was conducted in the department of Paediatrics in VMMC and Safdarjung Hospital, New Delhi over 1 Year from January 2010 to December 2010.

Assuming mean incidence of hyponatremia to be 35% (varies between 25-45%) in community acquired pneumonia, with alpha = 5% and power = 80%, we needed 87 cases to be included.

100 patients of age between 1month and 5 years of both sexes hospitalized with pneumonia were taken for the study. Ethical clearance for the study was taken from the institution ethical committee.

Patients were diagnosed to have pneumonia based on clinical signs and symptoms, and confirmed with chest radiograph showing lobar/segmental or patchy consolidation. Patients having the following features were excluded from the study e.g. - hospital acquired pneumonia, patients of asthma, patients with chronic renal and liver diseases, patients taking medication known to cause SIADH, patients having diarrhoea and dehydration, congestive heart failure, meningitis and endocrine diseases.

The clinical details of all patients, enrolled for the study, were recorded in proforma after taking informed consent from parents or local guardian.

Other investigations undergone on the day of admission

INTRODUCTION

Pneumonia is the single largest infectious cause of death in pediatric age group worldwide. About 0.92 million under-5 children die from pneumonia in a year¹.

On the other hand, Hyponatremia is the most common electrolyte disorder in hospitalized patients². Water retention in extravascular compartment and increase in plasma volume leads to this hyponatremia and inappropriate secretion of Antidiuretic hormone (SIADH) has been proposed to be one of the most important mechanisms for this change, that occurs in various pulmonary diseases including pneumonia, cerebral and malignant diseases and with some drugs also³.

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before starting intravenous fluids or antibiotics were:- Hemogram, blood urea nitrogen, serum creatinine (analysed by automated chemistry analyser HITACHI 912), erythrocyte sedimentation rate, C-reactive protein, serum sodium ion selective electrode method, automated chemistry analyzer 902), random blood sugar, blood culture, urine routine examination and mantoux test.

Serum sodium level was measured on admission, at 24 and 48 hours. Hyponatremia was taken as serum sodium < 135 mEq/L and normal value as 135-150 mEq/L. Hyponatremia when found was graded as mild, moderate and severe as stated, e.g:- mild: 131-134 mEq/L, moderate: 126-130 mEq/L, severe: \leq 125 mEq/L.

Two groups were considered on the basis of serum sodium level at 0 hour. Those having serum sodium level < 135 mEq/L [called as community acquired hyponatremia (CAH)] were taken into hyponatremic group (HN) and patients with a normal serum sodium level were taken into normonatremic group (NN). Hospital acquired hyponatremia (HAQ) was taken when Hyponatremia was absent on admission and developed later on. Hospital aggravated hyponatremia was taken when, serum sodium was lower by > 5 mEq/L within 48 hour of admission and CAH was present.

Patients who needed at least 48 hours of hospital stay were taken for analysis (except those who died earlier).

Hydration status, details of clinical outcome, any need of life saving measures e.g. mechanical ventilation and final outcome (discharge on recovery/death /others) was recorded in details on a preset proforma and results were tabulated

accordingly.

STATISTICAL ANALYSIS

Both groups were compared by the Student t – test for continuous variables and Chi-square/ Fischer's exact test for categorical variables. Log of the values were taken where needed to make the data normally distributed. The p value < 0.05 were taken as significant. The data was analysed by statistical software SPSS latest version.

RESULTS

The baseline characteristics of the study population have been shown in Table 1. The patients' serum sodium ranged from 124 to 145 mEq/L (both found at 0 hour) and none had hypernatremia. Mean serum sodium levels at 0, 24 and 48 hours are shown in Table 2.

Community Acquired Hyponatremia (CAH) was present in 21 cases (21%) –the hyponatremic group (HN) and rest 79 cases (79%) were normonatremic (NN).

Among the HN group mild, moderate, and severe hyponatremia was present in 17,3 and 1 cases respectively (Table 3).

The HN and NN groups were compared statistically to evaluate the clinical and lab parameters and results are shown in Table 4.

On admission HN group had higher body temperature, higher mean duration of tachypnoea and time for defervescence, greater length of hospital stay (by more than 3 days) and longer oxygen requirement. p value of log was statistically significant in all the parameters.

In lab investigation - hyponatremic patients showed higher CRP values, WBC Count and higher neutrophil proportion (%). p value of log was statistically significant.

Death was seen in 7 cases (33.3%) among HN group and

Characteristic	Data
Age (months)	18.52 \pm 18.16
Male	62 (62%)
Body temperature ($^{\circ}$ C)	37.85
WBC count ($\times 10^3$ /L)	12076.00 \pm 5548.28
Neutrophils (% of WBC)	66.26 \pm 8.40
ESR (mm/h)	13.01 \pm 4.30
CRP (> 10mg/l)	47 (47%)
Duration of tachypnoea (hours)	39.08 \pm 19.43
Time for defervescence (hours)	36.39 \pm 18.30
Duration of oxygen requirement (hours)	37.43 \pm 46.78
Length of hospital stay (hours)	99.68 \pm 53.19

Table-1: Baseline characteristics and laboratory data of 100 children with community-acquired pneumonia. Data are presented as mean \pm SD or numbers (percentage)

0 hour	137.37 \pm 3.41
24 hours	136.27 \pm 3.75
48 hours	136.04 \pm 3.41

Table-2: Serum sodium levels on 3 different occasions in mEq/L (mean \pm SD)

Mild	17 (81%)
Moderate	3 (14%)
Severe	1 (5%)

Table-3: Details of hyponatremic cases (n = 21)

Characteristic	HN (n=21)	NN (n=79)	P
Body temperature ($^{\circ}$ C)	101.82 \pm 1.86	99.95 \pm 1.41	0.02
WBC count ($\times 10^3$ /L)	16114.29 \pm 5447.69	11002.53 \pm 5089.59	0.00
Neutrophils (% of WBC)	72.24 \pm 7.36	64.67 \pm 7.97	0.00
CRP \geq 10 mg/l	19 (90.5%)	28 (35.4%)	0.00
ESR (mm/h)	19.38 \pm 4.37	12.03 \pm 3.69	0.00
Time for defervescence (hours)	63.50 \pm 18.87	34.64 \pm 16.01	0.00
Duration of oxygen requirement (hours)	51.79 \pm 13.70	30.29 \pm 16.26	0.00
Duration of tachypnoea (hours)	88.81 \pm 80.31	23.42 \pm 12.93	0.00
Length of hospital stay (hours)	163.38 \pm 84.56	82.74 \pm 19.34	0.007

Table-4: Characteristics of 100 children with hyponatremia vs children with normal levels of serum sodium on admission. Data are presented as mean \pm SD or number (percentage).

only 2 cases (2.5%) among NN group, p value is 0.000 (significant) and Odd's Ratio was 19.25. Results signify the risk of death is 19.25 times likely when hyponatremia is present in pneumonia cases.

Rest of the cases were cured and discharged. All the moderate (3 cases) and severe HN (1) cases were expired. It suggests that severity of HN was associated with increased mortality. Hospital acquired HN was seen in 9(9%) of cases but was not found to have significant correlation with increased morbidity and mortality.

Hospital aggravated hyponatremia was seen in 5 (5%) of the total cases. It was found to have correlation with high ESR and CRP values, higher neutrophil proportion, blood culture positivity, longer Duration of tachypnea but not found to have correlation with increased mortality.

DISCUSSION

In our study, Hyponatremia was seen in 21% of the pneumonia cases and was comparable with some studies done in India where the frequency was 27- 31%^{9,10}.

The result is in line with 23% in 71 adults with pneumococcal bacteremia¹⁴ and 27.9% in 342 adults with CAP¹⁵. It was upto 45% in children in some studies done abroad^{11,12}

The average serum level of sodium was 132.09 ± 2.56 mEq/L in HN group vs 138.77 ± 1.91 mEq/L in NN group and it was consistent with results shown by Liao Hua et al¹³.

In our study, Hyponatremia seen was mostly mild; only 1 (1%) case having severe HN having a serum sodium value of 124 mEq/L, and 3(3%) had moderate HN (< 130 mEq/L), consistent with the findings of Nair et.al.¹⁵ who showed serum sodium <130 mEq/L in only 4.1% of patients. Don M also had mostly mild hyponatremia- in 92% cases of HN¹¹ but the Indian studies shown rather moderate to severe HN in 27-31% cases⁹⁻¹⁰.

The Hyponatremic (HN) and the normonatremic (NN) group were compared by statistical analysis.

Age and sex had no correlation with hyponatremia in our study. This was comparable to study by Don M in age, gender or body weight¹¹.

Patients of HN group had higher initial body temperature similar to another study¹¹. In our study all the clinical parameters taken to assess the severity of pneumonia, were significantly longer in the Hyponatremic group. On admission HN group had higher- body temperature, mean duration of tachypnoea, time for defervescence, greater length of hospital stay, longer duration of oxygen requirement.

These findings were consistent with the findings of previous studies in pediatric population.

Singhi and Dhawan reported hyponatremia to be associated with 60% longer hospital stay, two fold increase in complications compared to that of normonatremia. The above variables were affected further, if hypokalemia coexisted with hyponatremia⁹.

In study by Dhawan and Narang and Singhi, symptoms and signs indicative of severe pneumonia were two to three times more frequent and the mean duration of tachypnoea, chest-wall retraction and hospital stay about one and a half times

longer in children with hyponatremia¹⁰.

Don M didn't find difference in time for defervescence between two groups¹¹. Nair et al found Hyponatremia to be associated with more severe illness and extended hospital stays. Crude length of hospital stay was increased by 2.3 days in the hyponatremic group.¹⁵

Among the laboratory parameters studied by us e.g.- Mean ESR, CRP value, WBC Count, Neutrophil proportion, taken as surrogate marker of severity of illness, were significantly higher in HN group.

Don M also found higher white blood cell count, neutrophil percentage, serum C-reactive protein, and serum procalcitonin in hyponatremic patients on admission¹¹.

Nair et al showed higher white blood cell count in the hyponatremic group¹⁵.

In our study mortality was also higher in HN group [7 out of 21 cases (33%) as compared to 2 out of 79 cases in NN group] signifying 19.25 times higher risk of mortality (Odds ratio). It was 3.5 times higher in the study by Singhi and Dhawan⁹, seven times higher in study by Tierney WM¹⁶ and tripling of in-hospital mortality in another study¹⁵.

In a study by RonWald done in adults Community-acquired hyponatremia, Hospital-acquired hyponatremia and hospital-aggravated hyponatremia was associated with in-hospital mortality with an adjusted odds ratios (ORs) of 1.52, 1.66 and 2.30 respectively and the strength of these associations tended to increase with hyponatremia severity¹⁷.

In our study Hospital acquired HN was not found to be associated with disease severity. Hospital aggravated hyponatremia was found to have correlation with some morbidities but not with increased mortality.

Now, the key question is whether hyponatremia in most patients is simply a powerful marker of severity of the underlying disease or a direct contributor to the adverse outcomes observed. But whatever it may be, hyponatremia is a compelling independent marker of adverse outcome.

The danger of fluid overload in children with bacterial meningitis is widely appreciated¹², but it has not been appreciated how commonly fluid restriction is indicated in pneumonia in childhood. Also, most of the Standard English textbooks of paediatrics suggest that an increased fluid intake is needed in bacterial pneumonia, and none of them warn of the danger of fluid overload.

An Indian study concluded that fluid therapy in pneumonia should be individualized and could not be generalized. Those having hyponatremia with hyperosmolality need liberal fluids while those with hypoosmolality need fluid restriction and hypotonic fluids including isolyte-P are not the ideal fluid for severe pneumonia patients.⁹

Strength of the study lies in the fact that this is the only study in paediatric age group where correlation of hospital-acquired and hospital-aggravated hyponatremia with morbidity and mortality in hospitalised pneumonia patients is sought for.

Limitation of the study was small sample size, cases were taken from a single center and further investigation with serum and urine osmolality and urine sodium could not be done as facility was not available in this hospital and

outsourcing was not allowed by ethical committee.

CONCLUSION

Hyponatremia is quite common in community acquired pneumonia cases needed hospitalization. Initial measurement of serum sodium is recommended in all hospitalized pneumonia patients and patients showing hyponatremia on admission should get special attention as it is a strong independent indicator of higher morbidity and mortality. Hyponatremic patients should undergo further study of urine sodium and osmolality to assess fluid status before imposing fluid restriction. Hospital acquired and Hospital aggravated HN are also well-known events in paediatric practice due to routine use of hypotonic fluid are maintenance and one should be cautious about fluid management of those diseases prone to cause SIADH including pneumonia. Regular follow up of serum sodium level during the period of hospital stay should be considered to pick up the high risk cases at an early stage. Whether early treatment of hyponatremia improves outcome is not clear and needs further study that can throw light upon the amount of fluid restriction necessary to improve outcome without causing complications.

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