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To study the association and significance of hyponatremia in pneumonia in paediatric patients in Rims, Raichur

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***Abstract*---**Introduction: Hyponatraemia is reported to be the most frequently occurring electrolyte imbalance which is most commonly seen in critically ill children. The aim and objective of this study was to find out the frequency of hyponatremia in pneumonia and to find the association and significance of hyponatremia in patients affected with Pneumonia. Materials and Methodology: This study has been designed as an in-patient hospital based prospective study will be conducted to evaluate the association and significance of hyponatremia in Paediatric patients affected Pneumonia being treated in RIMS, Raichur. 120 patients will be selected as the study participants for the study after obtaining informed consent from the parents as well. Statistical analysis should be carried out by using appropriate statistical tests. Both the groups have to be compared by the student t – test for continuous variables and Chi-square/ Fischer's exact test for all the categorical variables. The p value of less than 0.05 will be taken as significant. The data will be analysed by statistical software SPSS latest version. Results: . The patient's serum sodium level ranged from 124 - 145 mEq/L (both found at 0 hour) and none were observed to have hypernatraemia. Mean serum sodium levels were seen at 0, 24 and 48 hours and the values are tabulated in Table 2. Community Acquired Hyponatremia (CAH) was present in 25 cases (21%) –the hyponatraemic group (HN) and rest 95 cases (79%) were normo-natraemic (NN). Among the HN group mild, moderate, and

severe hyponatremia was present in 20,4 and 1 cases respectively which were shown in Table 3. Conclusion: Hyponatraemic patients should undergo further examination of urine sodium and osmolality evaluate the fluid status before posing fluid restriction. Hospital acquired and Hospital aggravated HN are also well-documented events in paediatric practice due to regular use of hypotonic fluid where one should be cautious about fluid management of those diseases which are prone to cause SIADH including pneumonia.

***Keywords*---**pneumonia, hospital acquired, hyponatraemia.

Introduction

One of the most frequent electrolyte imbalance conditions being faced in day to day clinical practice is hyponatraemia (HN, serum sodium < 135 mEq/L and it also proved to be common in critically ill children.[1] It contributes almost approximately 3% in all the hospitalized patients.[2] Mild to moderate HN and severe hyponatraemia are observed in 15-30% and 1-4% of hospitalized patientsrespectively.[3] Patho-physiologically, HNs are basically divided into two groups: HN due to non-osmotic hyper-secretion of vasopressin (hypovolaemic, hypervolaemic, euvolaemic) and HN of non-hyper-vasopressinaemic origin (pseudo-hyponatraemia, water intoxication, cerebral salt wasting syndrome).[3]In the year 1920, it was observedin many children with pneumonia mostly retain water,[4] which has been found to be associated with an increased blood volume and a reportedly low plasma chloride value.[5] These findings are better elaborated by the syndrome of inappropriate secretion of anti-diuretic hormone (SIADH), which has been detailed in children with pneumonia[6] and meningitis.[7] It was inferred that HN frequently accompanies pulmonary, infectious and certain neoplastic diseases.[8]

Hyponatraemia mostly considered as a common laboratory finding in children who were affected with communityacquired pneumonia (CAP) which could be defined clinically as the presence of signs and symptoms of pneumonia in an otherwise healthy child due to an infection which has been found to be acquired outside hospital.[9] Few studies, though, explore the correlation of HN and pneumonia in children.[10] Based on the published studies, the severity of CAP and HN due to CAP are associated with the need of hospitalization, the presence of prolonged and high fever, and elevated serum non-specific inflammatory markers, such as serum C-reactive protein (CRP) and serum procalcitonin.[9] Moreover, lower respiratory infections (LRIs), including acute lower respiratory tract infections, pneumonia, atypical pneumonia, bronchitis, bronchiolitis, and severe acute respiratory syndrome (SARS), continue to threaten the health of children worldwide and especially in developing countries, where poor nutrition prevails and access to health care is scarce.[11] Therefore, the aim and objective of this study was to find out the frequency of hyponatremia in pneumonia and to find the association and significance of hyponatremia in patients affected with Pneumonia.

Materials and Methodology

This study has been designed as an in-patient hospitalbased prospective study will be conducted to evaluate the association and significance of hyponatremia in Paediatric patients affected Pneumonia being treated in RIMS, Raichur. 120 patients will be selected as the study participants for the study period between feb 2022 to may 2022 after obtaining informed consent from the parents as well. The various inclusion criteria that had been proposed in this particular study were those patients with the age range between 1month and 5 years of both sexes hospitalized with pneumonia will be chosen for the study, those paediatric patients with informed consent from their parents/guardiansand those patients who acquired hospital pneumonia, patients of asthma, patients with chronic renal and liver diseases, patients taking medication which are prone to cause SIADH, those patients having diarrhoea and dehydration, congestive heart failure, meningitis and endocrine diseases.

Patients who will be diagnosed to have pneumonia based on clinical signs and symptoms and being confirmed with chest radiograph showing lobar/segmental or patchy consolidation. The clinical details of all the study participants who were enrolled for the study will be recorded in the proforma. Other investigations that had undergone on the day of admission before starting intravenous fluids or antibiotics were hemogram, blood urea nitrogen, serum creatinine, erythrocyte sedimentation rate, C-reactive protein, serum sodium ion selective electrode method, random blood sugar, blood culture, urine routine examination. Serum sodium level will be measured at the time of admission, at 24 and 48 hours. Hyponatremia is considered when the serum sodium level falls below 135 mEq/L whereas the normal value as 135-150 mEq/L. Hyponatremia when observed will be graded as mild, moderate and severe as proposed, e.g: mild: 131-134 mEq/L, moderate: 126-130 mEq/L, severe: ≤125 mEq/L. Those paediatric patients having serum sodium level <135 mEq/L [called as community acquired hyponatremia (CAH)] will be taken into hyponatraemic group (HN) and patients with a normal serum sodium level will be consideredas normo-natraemic group (NN). Hospital acquired hyponatremia (HAQ) will be taken when hyponatremia is absent at the time of admission which were developed later on. Hospital aggravated hyponatremia will be taken when, serum sodium is lower by > 5 mEq/ L within 48 hours of admission and CAH is observed. Statistical analysis should be carried out by using appropriate statistical tests. Both the groups have to be compared by the student t – test for continuous variables and Chi-square/ Fischer's exact test for all the categorical variables. The p value of less than 0.05 will be taken as significant. The data will be analysed by statistical software SPSS latest version.

Results

The baseline characteristics of the study population have been tabulated in Table 1. The patient's serum sodium level ranged from 124 - 145 mEq/L (both found at 0 hour) and none were observed to have hypernatraemia. Mean serum sodium levels were seen at 0, 24 and 48 hours and the values are tabulated in Table 2. Community Acquired Hyponatremia (CAH) was present in 25 cases (21%) –the hyponatraemic group (HN) and rest 95 cases (79%) were normo-natraemic (NN). Among the HN group mild, moderate, and severe hyponatremia was present in

20,4 and 1 cases respectively which were shown in Table 3. The HN and NN groups were compared statistically to evaluate the clinical and lab parameters and results are briefed 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 - hyponatraemic patients showed higher CRP values, WBC Count and higher neutrophil proportion (%). p value was observed to be statistically significant. Death was seen in 8 cases (33.3%) among HN group andonly 3 cases (2.5%) among NN group, p value is 0.000 (significant) and Odd's Ratio was 19.27. All the moderate (4 cases) and severe HN (1) cases were expired and therefore it suggests that severity of HN was relatively associated with increased mortality. Hospital acquired HN was seen in 11(9%) of cases but was not found to have significant correlation with increased morbidity and mortality. Hospital aggravated hyponatraemia was seen in 6 (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 tachypnoea but not found to have correlation with increased mortality.

Table-1: Baseline characteristics and laboratory data of 120 children with community-acquired pneumonia. Data are presented as mean ± SD or numbers (percentage)

Characteristic	Data
Age (months)	18.63 ± 18.21
Male	74 (62%)
Body temperature (^oC)	37.89
WBC count (x 10^3/L)	12077.00 ± 5549.31
Neutrophils (% of WBC)	66.31 ± 8.42
ESR (mm/Hg)	13.03 ± 4.32
CRP (>10mg/L)	56 (47%)
Duration of tachypnoea (hours)	39.12 ± 19.45
Time for defervescence (hours)	36.41 ± 18.33
Duration of oxygen requirement (hours)	37.47 ± 46.81
Length of hospital stay (hours)	99.71 ± 53.23

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

0 – hour	137.41 ± 3.45
24 hours	136.32 ± 3.78
48 hours	136.07 ± 3.42

Table-3: Details of hyponatremic cases (n = 25)

Mild	20 (81%)
Moderate	4 (14%)
Severe	1 (5%)

Table-4: Characteristics of 120 children with hyponatremia vs children with normal levels of serum sodium on admission. Data are presented as mean ± SD or number (percentage)

Variables	HN (n = 25)	NN (n = 95)	P
Body temperature (°C)	101.88 ± 1.92	99.98 ± 1.43	0.02
WBC count (x 10^3/L)	16115.32± 5448.71	11002.56±5089.61	0.00
Neutrophils (% of WBC)	72.29 ± 7.41	64.69 ± 7.99	0.00
ESR (mm/Hg)	19.41 ± 4.39	12.05 ± 3.71	0.00
CRP (>10mg/L)	23 (90.5%)	34 (35.4%)	0.00
Duration of tachypnoea (hours)	88.87 ± 80.33	23.44 ± 12.96	0.00
Time for defervescence (hours)	63.53 ± 18.89	34.65 ± 16.03	0.00
Duration of oxygen requirement (hours)	51.81 ± 13.75	34.69 ± 16.04	0.00
Length of hospital stay (hours)	163.41 ± 84.58	82.78 ± 19.37	0.007

Discussion

In our study, Hyponatremia was observed to be present in 21% of the cases admitted with pneumonia and was eventually comparable in few studies being conducted in India where the frequency was reported to be 27- 31%.[11,12] The result is equally in line with 23% in 71 adults with pneumococcal bacteremia[15] and 27.9% in 342 adults with CAP.[16]Moreover it was observed that up to 45% in children in some studies which were conducted outside our country.[12,13] The average serum level of sodium was 132.11 ± 2.58mEq/L in HN group vs 138.79 ± 1.93mEq/L in NN group and it was almost identical with the results obtained by *Liao Hua* et al.[14] 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 4(3%) had moderate HN (< 130 mEq/L) and the observed values werealmost similar with the findings obtained by*Nair* etal[15] who reported that serum sodium level less than 130 mEq/L in only 4.1% of patients. *Don* M also had observed mostly mild hyponatremia- in 92% cases of HN[11] but few indian studies reported to be having moderate to severe HN in 27-31% cases.[10,11]

The results obtained from hyponatraemic (HN) and the normo-natraemic (NN) group were eventually compared by statistical analysis. Age and sex had no correlation with hyponatremia in the present study. This was almost comparable to theresults observed by *Don* M in age, gender or body weight.[12] Patients of HN group had higher initial body temperature similar to another study.[12] In our study all the clinical parameters taken into account which were to assess the severity of pneumonia and were reported to be significantly longer in the hyponatraemic group. On the day of admission,the HN group had higher- body temperature, mean duration of tachypnoea, time for defervescence, greater length of hospital stays, longer duration of oxygen requirement. These findings were equally consistent with the findings of earlier studies obtained in paediatric population. *Singhi* and *Dhawan* reported hyponatremia to be associated with 60% paediatric patients who had longer hospital stay, two-fold increase in complications when

compared to that of normo-natraemia. The above variables were affected further, if hypokalaemia relatively present along with hyponatremia.[10,11]

In study conducted by *Dhawan*, *Narang* and *Singhi*,the clinical symptoms and signs were indicative of severe pneumonia which were two to three times more frequent and the mean duration of tachypnoea, chest-wall retraction and hospital stay were reported to be almost one and a half times longer in children with hyponatraemia.[11]*Don* M could not able to find the difference in time for defervescence between two groups.[12]*Nair* et al observed thathyponatremia to be associated with more severe illness and extended hospital stays. The length of hospital stay was almost increased by 2.3 days in the hyponatraemic group when compared to normo-natraemic group.[16] Among the laboratory parameters examined, mean ESR, CRP value, WBC Count, neutrophil proportion were taken as surrogate markers of severity of illness which were significantly higher in HN group. *Don* M also observed that higher white blood cell count, neutrophil percentage, serum C-reactive proteinin hyponatraemic patients on the day of admission.[9]*Nair* et al reported higher white blood cell count in the hyponatraemic group.[16] In the present study,the mortality rate was reported higher in HN group [8 out of 25 cases (33%) as compared to 4 out of 95 cases in NN group] signifying 19.25 times higher risk of mortality (Odds ratio). It was observed to be 3.5 times higher in the study by *Singhi* and *Dhawan*,[10,11] seven times higher when compared with the study by *Tierney* WM[19] and tripling of in-hospital mortality in another study.[17] In a study conducted by *RonWald*who had performed in adults Community-acquired hyponatremia, Hospital-acquired hyponatremia and hospitalaggravated hyponatremia was relatively associated with in-hospital mortality rate 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 severity.[18] In the present study,hospital acquired HN was not found to be associated with the severity of the disease. 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 appreciated,[15] 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.[12] 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 centre and further investigation with serum and urine osmolality and urine sodium could not be done as facility was not available in this hospital andoutsourcing was not allowed by ethical committee.

Conclusion

Hyponatremia is quite frequently observed in the community acquired pneumonia cases which needed hospitalization. Initial measurement of serum sodium is usually recommended in all hospitalized pneumonia patients and patients who were showing hyponatraemia on admission should get special attention as it is a strong independent indicator of higher morbidity and mortality rate. Hyponatraemic patients should undergo further examination of urine sodium and osmolality evaluatethe fluid status before posing fluid restriction. Hospital acquired and Hospital aggravated HN are also well-documented events in paediatric practice due to regular use of hypotonic fluid where one should be cautious about fluid management of those diseases which are 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.

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