RESEARCH ARTICLE

A PROSPECTIVE STUDY TO IDENTIFY THE ROLE AND TO EVALUATE SERUM HYPONATREMIA WITH THE SEVERITY OF HOSPITALISED COMMUNITY ACQUIRED PNEUMONIA

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ARTICLE INFO	ABSTRACT
	Background: Community-acquired pneumonia (CAP) represents a substantial burden to the Health care system. Pneumonia imposes a staggering clinical and economic burden to our community. Despite being the cause of significant morbidity and mortality, pneumonia is often misdiagnosed, wrongly treated, and underestimated. No perfect bio-marker or scoring system is available to this date to evaluate the severity of CAP patients. The incidence of hyponatremia at hospital admission among CAP patients is found to be 28%and is associated with not only prolongation of hospitalization but also an increase in hospital mortality. ***Aim of the study:*** 1. To evaluate hyponatremia as a possible bio-marker to assess severity of community acquired pneumonia (CAP). 2. To compare hyponatremia with CURB-65 as an initial screening tool for assessment of severity of CAP. ***Materials and methods:*** 100 patients with CAP who were hospitalized were included in study. Serum sodium levels were measured on day 1,3 and 7 after initial assessment of patients and were analyzed with the clinical profile and outcome in these study groups. ***Results:*** CAP was more commonly seen between age group 31-40 years (22%), among males (61%), Type 2 diabetes mellitus was the major co morbidity associated (23%), smoking was an important risk factor (33%). Majority of them belonged to Pneumonia severity index (PSI) risk class 3 and above. Serum sodium levels showed a significant correlation from day 1 to the day of discharge in both resolving and un-resolving pneumonias, and also at the time of admission as compared to CURB-65 score. ***Conclusion:*** In our study patients with severe hyponatremia had high in – hospital morbidity and mortality, whereas those with rising sodium levels showed signs of improvement. This proves that serum sodium levels can be used as a prognostic biomarker in community acquired pneumonia which is cost effective and easily available.

INTRODUCTION

Community Acquired Pneumonia (CAP) is defined as a syndrome caused by acute infection, usually bacterial, characterized by clinical and radiographic signs of consolidation of a part or parts of one lung or both the lungs and often followed by brief viral upper respiratory tract infection (Andews *et al.,* 2003). Pneumonia in adults is estimated to be prevalent in about 4% of the Indian population with significant mortality and morbidity and is one of the most important challenges in clinical medicine, despite advances in diagnosis and treatment (Sowmyal *et al.*). The presentation of pneumonia varies from mild to severe life threating illness and treatment also varies from out patient management to Medical ICU. Hence severity assessment of CAP is required to choose the site of treatment, choice of antibiotic and its route of administration. Hyponatremia is the most common electrolyte imbalance seen in clinical practice (Anderson *et al.,* 1985). The incidence of hyponatremia at hospital admission among CAP patients is found to be 28% and the mechanism behind it has been found to be due to Syndrome of Inappropriate Antidiuretic

Hormone Secretion (SIADH) (Mason *et al.,* 1999). SIADH is the most frequent cause of euvolemic hyponatremia and it is produced when plasma levels of arginine vasopressin are elevated at times during which the physiological secretion of vasopressin from the posterior pituitary would normally be suppressed. Various other pulmonary disorders have been associated with SIADH especially tuberculosis, advanced chronic obstructive lung disease, bronchiectasis (Anthony *et al.,* 2015). The presence of hyponatremia is associated with not only prolongation of hospitalization, but also with an increase in hospital mortality, the incidence of which has been found to be 7% (Mason *et al.,* 1999). SIADH induced euvolemic hyponatremia is the single most common cause of hypo-osmolar hyponatremia of all etiological mechanisms encountered in clinical practice, with prevalence rates from 20% to 40% (Shlomo Mehmed Kenneth Polonsky). Hyponatremia frequently accompanies pulmonary diseases, both infectious and neoplastic (Elliason and Bert, 2007). Hence this study is an effort to explore how hyponatremia is associated with severity and outcomes, in hospitalized patients with pneumonia.

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MATERIALS AND METHODS

The study was a prospective study, conducted on 100 patients admitted to hospitals affiliated to Bangalore Medical College and Research Institute, Bangalore. All clinically diagnosed and radiologically proven pneumonia patients requiring hospitalization based on CURB-65 scores were taken into this study. Routine hematological investigations along with serum electrolytes on day 1, 3 and 7/discharge, ABG, Chest X- ray and other relevant investigations were carried out. Patients were clinically assessed on day 1, 3, 7 and their vital parameters were noted. The lab values of serial serum sodium, total counts and vital signs were analyzed with the clinical profile and outcome. The data was compiled and compared to other global studies. Descriptive and inferential statistical analyses were used and analyses of variance (ANOVA) has been used to find out the significance of study parameters between three or more groups of patients. The statistical software namely SPSS 18.0, and R environment ver. 3.2.2 were used for the analyses of the data.

OBSERVATIONS AND RESULTS

100 patients admitted with community acquired pneumonia were included for this study. Patients were evaluated with detailed history, clinical examination, relevant laboratory and radiological investigations. Majority of the patients in the study were between 31-40 yrs (22%) followed by 61-70 yrs (20%). Majority of the patients were males which constitutes 61% (61 patients). 54% were belonging to rural areas and 46% were belonging to urban areas. Cough, fever and sputum production were seen in most of the patients. Breathlessness was next most common symptom (46%). Most of them had fever of 1-5 days duration, cough of 6-7 days duration and sputum production of 4-5 days duration. Other symptoms were chest pain (15 patients), followed by myalgia, fatigue, generalized body ache, headache. Most of the patients had Type 2 DM, HTN, IHD, COPD, Bronchial asthma, hypothyroidism in decreasing order. Two patients had past history of pulmonary tuberculosis (treated), 3 had COPD, 7 had Type 2 DM and HTN together. About 1/3 rd of patients were smokers, and most of these patients are smoking for the last 10-15 yrs.

Clinical Parameters of patients: Evaluation of vital data at the time of admission showed most patients had pulse rate of 90-110 bpm (82%), respiratory rate of 20-30/ min(82%), SBP of 110-120 mmHg (91%), DBP of <80 mm Hg(86%) and temperature of 100-105 F (78%). Blood investigations showed that majority of them had total count of >11,000. Majority of them belonged to PSI class 4 and had CURB-65 scores of 0 and 1 (44% and 30%).

Sodium analyses: Out of 100 patients evaluated, 40 % of them had sodium levels between 120-130 and 34% of them had sodium levels between 131-134 meq/L at admission. Hyponatremia was associated with increased duration of ICU and in- hospital stay. It was also associated with an increase in the risk of in- hospital deaths. Our study compares hyponatremia with CURB -65 as an initial screening tool for the assessment of severity of CAP. As seen from table 39, the severity of pneumonia increases (indicated by PSI classes 3,4,5 respectively), with decreasing sodium level at admission (Table 1). Analysis of Sodium in pneumonia was done in all 100 patients. Sodium level less than 135meq/l was considered as hyponatremia (Normal being 135-145 meq/L). On the day 1 of admission 40% of patients had serum Sodium levels between 126 to 130, 34 % had levels between 131-134, and 14% of them had levels less than 125 meq/L and 3% had less than 120meq/l. When serum levels were analyzed at the time of discharge, there was significant increase in the sodium levels (p=0.31) in resolving pneumonias. Above table indicates that, there is a decline in serum sodium level with an increase in the severity of pneumonia (indicated by PSI classes 3,4,5 respectively), showing a correlation. But the CURB-65 score was less than 2 in majority of patients whose PSI score belonged to class 4 and 5 (70% and 82% respectively). Hence CURB65 did not correlate well with PSI scoring system. But serum sodium correlated well with the severity and is considered as a better indicator of severity of pneumonia than CURB-65. Whereas in non-resolving pneumonias (n=10) there was either a persistent drop in sodium, with an initial increment followed by a drop or a very slow improvement in serum sodium. Overall sodium levels correlated with severity of pneumonia (all outcomes) in 79 cases. There were 12 deaths noted in this study. 7 of them had serum sodium less than 125 indicating hyponatremia as a contributory factor for initial severity.

Other inferences: Majority of patients (n=68) had serum osmolality on the lower limit of normal, ie less than 280. (Normal value being 275 to 280 mosm/kg) indicating that SIADH contributed to the hyponatremia seen in pneumonia, after ruling out other causes for hyponatremia.21 cases required sodium correction, out of which 16 were resolving pneumonias, 2 were non-resolving (left hospital against advice), 3 were deaths. Chest x ray showed involvement of lower lobe in 44% of patients, followed by multi-lobar pattern and occasionally middle lobe involvement. Most of them were culture negative, showing normal commensals (70.0%). Among the organisms isolated, streptococcus pneumonia species were found in 13 % of the patients, followed by pseudomonas and klebsiella. All patients were treated empirically according to guidelines. Most of them were given a beta lactam and a macrolide (Ceftriaxone + Azithromycin / Cefotaxime + Azithromycin). 30% of all patients admitted required ICU care, and 16% of all required mechanical ventilation. 80% of the patients had their defervescence within 1-3 days. Most of them became afebrile within 48hrs after starting antibiotics. Out of 100 patients, pneumonia resolved in 78 patients with protocol line of treatment and 22 had Non-resolving pneumonia, which included 10 deaths also. The above table indicates that more than 75% of patients had CURB 65 scores of 0 to 1 and scores 2,3 and 5 had more hyponatremia. Table demonstrates that clinical outcomes like ICU requirement and mortality are more common with CAP patients presenting with severe hyponatremia.

DISCUSSION

The main focus of the present study is to evaluate the possibility of hyponatremia as a biomarker in hospitalized CAP patients and to compare both the standard international scoring systems and clinical outcomes including outcomes of hospitalization, requirement of ventilatory support, in-hospital mortality and morbidity. 100 diagnosed CAP patients with hyponatremia were studied for the assessment of Sodium, CURB 65 and treatment outcome. In our study, majority (40%) had moderate hyponatremia (sodium levels between 126-130)

Table 1. Comparision between hyponatremia, PSI, and CURB-65 at the time of admission

PSI Class on admission	Total no. of patients	Average Sodium on admission	Corresponding Pts with CURB 65 scores less than 2 (in %)	Corresponding Pts with CURB 65 score of 3 and more (in %)
3	24	130.54±2.96	75 % (n=18)	25 % (n = 6)
4	32	128.28±4.41	70 % (n=23)	20 % (n=9)
5	23	126.96±4.71	82 % (n=19)	18 % (n=4)

Table 2. Comparison of serial measurements of key clinical parameters in comparison to sodium, on days 1, 3 and 7 in Non-resolving pneumonias

Average of key parameters	Day 1	Day 3	Day 7	P Value
Serum sodium	128	133.4	128.41	0.042
Total Counts	14,891	13,698	10,391	0.080
Pulse rate	101.29	90.31	84.48	0.258
Systolic BP	118.84	110.76	102.44	0.080
Diastolic BP	78.90	80.43	72.66	0.998
Respiratory rate	26.02	20.79	18.23	0.139
Temperature	100.57	99.23	98.65	0.456

Table 3. CURB-65 distribution of patients studied

CURB-65 on admission	No. of patients	%	Day 1 sodium (avg)
0	44	44.0	132.8
1	33	33.0	137.2
2	15	15.0	128.4
3	7	7.0	128.2
4	0	0.0	-
5	1	1.0	127
Total	100	100.0	130.5

Table 4. Correlation between grade of hyponatremia and associated mortality

Grade of hyponatremia	Day 1 sodium (avg)	Mortality (total no. of deaths)	ICU Requirement
Mild	132.8	1	-
Moderate	127.2	2	1
Severe	123.4	7	6

Table 5. Sodium (mEq/l)- Comparison with PSI in patients studied at the time of admission

Sodium (mEq/l)	PSI Classes					Total	P value
	1	2	3	4	5		
Day 1	130.80±3.56	129.75±3.80	130.54±2.96	128.28±4.41	126.96±4.71	128.73±4.19	0.034*

on day 1 of admission, (14% had sodium levels less than 125 and 3% had severe hyponatremia with sodium levels less than 120 meq/L) and justifies with other studies – shlomo melmed reporting hyponatremia as the commonest biochemical abnormality in CAP patients (Shlomo Mehmed Kenneth Polonsky) and Nair *et al* reporting 28% (Nair *et al.,* 2007). A study done by Marya Zilberberg *et al.* (2008) showed, among patients with community acquired pneumonia, hospital mortality was 5.4 % in those who had hyponatremia, as compared to those who didn't have hyponatremia on admission (4 %). The proportion of patients requiring Mechanical Ventilation (3.9% vs. 2.3%, p = 0.014) or any ICU admission (10.0% vs. 6.3%, p < 0.001) was significantly higher in the hyponatremic than the normonatremic group. Our study compares hyponatremia with CURB -65 as an initial screening tool for the assessment of severity of CAP. As seen from table 39, as the severity of pneumonia increases (indicated by PSI classes 3, 4, 5 respectively), the sodium value on admission is also low, showing a correlation. A study done by Bilal Bin Abdulla et al at Bijapur, India in 2012 showed that Hyponatremia was present in 16% of patients among hospitalized CAP patients (Bilal Bin Abdulla *et al.,* 2012). But the CURB-65 score, as seen, is less than 2 in majority of patients with PSI class 4 and 5 (70% and 82% respectively).This indicates that Serum sodium is a better indicator of severity of pneumonia than CURB-65.

A study done by Marya Zilberberg *et al.* (2008) showed mean hospital length of stay to be 6.3 days in CAP patients with hyponatremia v/s 5.3 days in those without hyponatremia. The proportion of patients requiring Mechanical Ventilation (3.9% v/s. 2.3%, p = 0.014) or any ICU admission (10.0% v/s. 6.3%, p < 0.001) was significantly higher in the hyponatremic than the normonatremic group.

Death analysis: There were 12 deaths noted in the present study. 7 of them had serum sodium levels less than 125 indicating hyponatremia as a contributory factor of initial severity of pneumonia. The other 3 had sodium levels between 135-125. Most commonly isolated organism among the deaths was streptococcus pneumoniae. Marya Zilberberg *et al.* (2008) showed that, among patients with community acquired pneumonia, hospital mortality was 5.4 % in those who had hyponatremia, as compared to those who didn't have hyponatremia on admission (4 %). Table 5 shows a definite relationship between the pneumonia severity index class (PSI) and serum sodium levels at admission. Higher PSI scoring was associated with decreased serum sodium levels. The CURB 65 score of 2 was seen in majority of pts with PSI class 4 and 5 (70% and 82% respectively) and did not correlate with severity of CAP. This indicates that Serum sodium is a better indicator of severity of pneumonia than CURB-65. Of 100 hospitalized CAP patients, 88 had clinical resolution at the end of protocol

antibiotic treatment. Out of those Sodium values normalized at discharge (average day-7) in 70 of them (79%), in the rest sodium was on a rising trend and discharge contemplated based on other factors which prompted improvement. In 12 of them (13%), a change in antibiotic regimen facilitated clinical resolution, correlating with a rise in sodium values. Out of 12 patients in whom pneumonia did not resolve, hyponatremia remained in the form of persistently low or worsening sodium values. In 3 of them sodium values improved without correction, although pneumonia did not resolve. Overall mortality being 10%. Day 4 sodium value was thus observed to be a good indicator of clinical outcome from both the above groups.

Conclusion

Community acquired pneumonia is a common and potentially serious illness causing high mortality and morbidity, especially in elderly population. Case fatality with invasive pneumonias in India was reported to be 30% according to IBIS study for a 10 year period.CAP Patients with severe hyponatremia had high morbidity and mortality in the form of non-resolution, complications including deaths. At present there is no single guideline to predict the mortality and morbidity in CAP patients at early stages. There remains some limitations for both CURB 65 and PSI scoring system for out-patient use. Serial serum sodium level estimation is a routine investigation and can be done at all places. It may be used as a prognostic biomarker in community acquired pneumonia which is cost effective and easily available. Biomarkers together with clinical parameters can aid clinicians in assessing the severity of illness and need for the use of antibiotics (Valenti *et al.,* 1978).

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